ASRM 2019
Scientific Abstracts to be presented at the 75th Scientific Congress of the American Society for Reproductive Medicine, October 12-16, 2019, Philadelphia, Pennsylvania.

(e2) PRIZE PAPER SESSION 1
(e2) ORAL SESSION
(e38) PRIZE PAPER SESSION 2
(e38) ORAL SESSION
(e109) POSTER SESSION
(e429) VIDEO SESSION 1
(e430) VIDEO SESSION 2
(e432) VIDEO SESSION 3
(e434) LATE-BREAKING ABSTRACTS
(e440) AUTHOR INDEX: ORAL, POSTER, AND VIDEO SESSIONS
(e456) TOPIC INDEX: ORAL, POSTER, AND VIDEO SESSIONS
(e459) AUTHOR AND SPOUSE/PARTNER DISCLOSURES INDEX: ORAL, POSTER, AND VIDEO SESSIONS

October 12-16, 2019
Philadelphia, Pennsylvania

These abstracts of research studies, published as submitted by the authors, are presented in the ASRM 2019 Congress sessions and are published in the order of their presentation. Abstracts of plenary lectures, symposia and interactive sessions are not included.
The first six papers are candidates for the ASRM Scientific Congress Prize Paper Awards. Six additional candidates will be presented during the Prize Paper Candidates’ session on Tuesday.

SCIENTIFIC CONGRESS PRIZE PAPER SESSION 1

O-1 Monday, October 14, 2019 10:45 AM

ANTIDEPRESSANT MEDICATION EXPOSURE: TIME TO PREGNANCY AND RISK OF PREGNANCY LOSS. Lindsay A. Sjaarda, PhD, a Jeannie G. Radoc, BS, a Kerry S. Flannagan, PhD, a Sunni L. Mumford, PhD, a Neil J. Perkins, PhD, a Robert M. Silver, MD, b Enrique F. Schisterman, PhD, a Epidemiology Branch, DPHR, NICHD, NIH, Bethesda, MD; b University of Utah, Salt Lake City, UT.

OBJECTIVE: Depressant and antidepressant medication use is prevalent in women of reproductive age. Evidence is conflicting regarding antidepressant exposure and miscarriage risk. Therefore, using prospective data on pregnancy and loss from a cohort of women in the Effects of Aspirin in Gestation and Reproduction Trial, we assessed the association between pre-conception measured antidepressant exposure and time to pregnancy, pregnancy loss, and live birth. DESIGN: Prospective cohort study of 1228 women with proven fecundity and 1-2 prior pregnancy losses, attempting natural conception while participating in a randomized controlled trial of pre-conception-initiated low-dose aspirin. MATERIALS AND METHODS: Fluoxetine, sertraline, escitalopram, citalopram, trazadone, nefazodone, etoperidone, and tricyclic antidepressants and related compounds were measured in urine from enrollment and at each conception cycle and pregnancy visit (weeks 4 and 8) via a biochip competitive chemiluminescent immunoassay (Randox Toxicology). Any antidepressant medication use was also assessed via self-report. Cox proportional hazard regression models estimated fecundability odds ratios; log-binomial models estimated pregnancy loss and live birth incidence. Models adjusted for age, body mass index, education level, employment, smoking, alcohol use, marijuana use, and opioid use.

RESULTS: Of 1218 women, 183 (15%) had positive detection of antidepressant compounds prior to conception (at enrollment or at the last cycle prior to conception). Antidepressant exposure prior to conception was associated with lower fecundability (FOR: 0.77, 95% CI: 0.61, 0.99) though overall all live birth incidence was similar (48% in exposed vs. 56% in non-exposed women; RR: 0.91, 95% CI: 0.77, 1.08). Among 785 hCG pregnancies, there was no association between preconception exposure and pregnancy loss (25% loss in exposed, 24% in non-exposed; RR: 1.04; 95% CI: 0.73, 1.50), and antidepressant exposure at 4 and 8 weeks’ gestation also yielded a null finding. Sensitivity analyses including additional women in the positive exposure category based on self-reported antidepressant use yielded similar findings for all outcomes.

CONCLUSIONS: Antidepressant medications may lengthen time to pregnancy without impacting live birth rates, and importantly, did not increase risk of pregnancy loss. Given the close prospective follow-up of early pregnancy and loss incidence, including antidepressant exposure assessment both prior to and during early pregnancy, these data help alleviate concerns for miscarriage with use of this important class of medications.

SUPPORT: Intramural Research Program, DPHR, NICHD, NIH.

O-2 Monday, October 14, 2019 11:00 AM

EFFECTS OF FOLIC ACID AND ZINC SUPPLEMENTATION IN MEN ON SEMEN QUALITY AND LIVE BIRTH AMONG COUPLES UNDERGOING INFERTILITY TREATMENT: FINDINGS FROM THE FASZT RAN-DOMIZED TRIAL. Enrique F. Schisterman, PhD, a Lindsey A. Sjaarda, PhD, a Traci Clemons, PhD, a Douglas T. Carrell, PhD, a Neil J. Perkins, PhD, a Erica Johnstone, MD, b Denise Lamb, BSN, c Kayla Chaney, BA, c Lake City, UT; f University of Iowa Carver College of Medicine, Iowa City, IA; g National Institutes of Child Health and Human Development, Bethesda, MD; h National Institute of Child Health and Human Development, Bethesda, MD.

OBJECTIVE: Folic acid and zinc are thought to improve semen quality parameters. We conducted a randomized trial to determine the effect of daily folic acid and zinc supplementation on semen quality and live birth. DESIGN: The Folic Acid and Zinc Supplementation Trial (FASZT) was a multi-center, double-blind, block-randomized, placebo-controlled trial. MATERIALS AND METHODS: Men ≥18 years old who with partners were planning infertility treatment were block randomized by site and planned infertility treatment strata (IVF, non-IVF at a study site, and non-IVF at an outside clinic) to receive either 5 mg folic acid and 30 mg elemental zinc or placebo for 6 months during infertility treatment. The primary outcomes were live birth and semen quality parameters, analyzed by intention to treat. RESULTS: Between June 3, 2013, and December 30, 2017, 2370 men were recruited and randomized (1185 active, 1185 placebo). Daily supplementation was not associated with live birth (active 399 [34%], placebo 408 [34%], risk difference -0.76, 95% CI: -4.58, 3.06) or with sperm concentration, motility, morphology, or total motile sperm count. Supplementation was associated with increased DNA fragmentation (risk difference 2.5, 95% CI 0.6, 4.4). No effects on pregnancy rate, pregnancy loss, gestational age at delivery, embryo parameters, or other adverse neonatal outcomes were observed, except that preterm birth was higher with supplementation (risk difference 1.94, 95% CI: 0.24, 3.64). Gastrointestinal symptoms were also more common with supplementation.

CONCLUSIONS: Use of folic acid and zinc supplementation by men did not improve semen quality and increased DNA fragmentation and gastrointestinal problems. The increase in preterm birth warrants further investigation. The widespread impression that supplements will at least ‘do no harm’ may be unfounded. The lack of efficacy and potential risks of folic acid and zinc supplementation can now be communicated to couples seeking infertility treatment.

SUPPORT: Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health.

O-3 Monday, October 14, 2019 11:15 AM

CAN HYSEROSALPINGO FOAM SONOGRAPHY (HYFOSY) REPLACE HYSEROSALPINGOGRAPHY (HSG) AS FIRST CHOICE TUBAL PATENCY TEST: A RANDOMIZED COMPARISON (FOAM STUDY)? Nienke van Welie, M.D., a Jouke van Rijswijk, M.D., c Kim Dreyer, M.D., Ph.D., b Marcel H. A. van Hoeff, M.D., Ph.D., b Harold Verhoeve, M.D., Ph.D., b J. P. de Bruin, M.D., Ph.D., b Femke Mol, M.D., Ph.D., b Marchien van Baal, M.D., Ph.D., b Bob van de Laar, M.D., a Nils B. Lambalk, M.D., Ph.D., a Madelon van Wely, Ph.D., b Jaap Stoker, M.D., Ph.D., b Ben W. Mol, M.D., Ph.D., Prof., a Velja Mijatovic, M.D., Ph.D., a and FOAM study group a Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; b Department of Reproductive Medicine, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; b Franciscau Hospital, Department of Obstetrics and Gynaecology, Rotterdam, Netherlands; b ULVQ Oost Hospital, Department of Obstetrics and Gynaecology, Amsterdam, Netherlands; c Jeroen Bosch Hospital, Department of Obstetrics and Gynaecology, Den Bosch, Netherlands; a Amsterdam UMC, University of Amsterdam, Center for Reproductive Medicine, Amsterdam, Netherlands; b Flevo Hospital, Department of Obstetrics and Gynaecology, Almere, Netherlands; b ULVQ West, Department of Obstetrics and Gynaecology, Amsterdam, Netherlands; a Amsterdam UMC, University of Amsterdam, Department of Epidemiology, Biostatistics and Bioinformatics, Amsterdam, Netherlands; a Amsterdam UMC, University of Amsterdam, Department of Radiology and Nuclear Medicine, Amsterdam, Netherlands; b Monash University, Monash Medical Centre, Department of Obstetrics and Gynaecology, Melbourne, VIC, Australia.

OBJECTIVE: Traditionally, tubal patency testing during fertility work-up is performed by hysterosalpingography (HSG). Hysterosalpingo-foam-sonography (HyFoSy) is an alternative technique without radiation exposure and is less expensive than HSG. Globally, there is a shift towards the use of office-based diagnostic methods, such as HyFoSy. Here, we assess whether HyFoSy is as accurate as HSG in evaluating tubal patency and if it leads to comparable pregnancy outcomes.

DESIGN: Multicenter prospective comparative study with a randomized non-inferiority design.
MATERIALS AND METHODS: Participating women underwent both HyFoSy and HSG, in randomized order, by a physician unaware of the result of the first test (NTR 47446). In case of discordant results for HyFoSy/HSG, women were randomly allocated to either a management strategy based on HSG and women underwent HSG only. Among discordant results, women were invited to participate in the ExEm FOAM number 837001504). ZonMw funded the whole project. IQ Medical Ventures (HSG) in assessing tubal patency in subfertile women? Study protocol for hysterosalpingography (HyFoSy) a cost-effective alternative for hysterosalpingography diation exposure. In case of a discordant result, management based on the re-
PHASE 3 TRIAL RESULTS: EFFICACY AND SAFETY OF ELAGOLIX IN A SUBSET OF WOMEN WITH UTERINE FIBROIDS AND ADENOMYOSIS. Ozgul Muneyyirci-Delele, MD, David F. Archer, MD, Jin Hee Jeannie Kim, MD, Ran Liu, PhD, Charlotte D. Owens, MD, Elizabeth E. Puschek, MD, MS, MBA State University of New York, Brooklyn, NY; Eastern Virginia Medical School, Norfolk, VA; Columbia University, New York, NY; AbbVie, Inc., North Chicago, IL; Wayne State University, Detroit, MI.

OBJECTIVE: Adenomyosis is a benign lesion within the myometrium associated with heavy menstrual bleeding (HMB) and dysmenorrhea, and commonly co-exists with uterine fibroids (UF). Adenomyosis is also present in 15-57% of hysterectomy specimens with leiomyoma (Genc M, et al, 2015; Taran FA, et al, 2010). This analysis evaluated the efficacy and safety of elagolix, an oral, gonadotropin-releasing hormone receptor antagonist, with add-back therapy in a subset of women with UF, HMB and co-existing adenomyosis.

DESIGN: Data were pooled from two 6-month, randomized, double-blind, placebo-controlled phase 3 studies, Elaris UF-1 and UF-2. Premenopausal women (18-51 years) with ultrasound-confirmed diagnosis of UF and HMB (>/=80mL menstrual blood loss [MBL]/cycle) were randomized 1:1:2 to placebo, elagolix 300mg twice daily (BID), or elagolix 300mg BID with 1mg estradiol/0.5mg norethindrone acetate (E2/NETA) once daily.

MATERIALS AND METHODS: This subset analysis was conducted in women with HMB associated with UF and co-existing adenomyosis diagnosed by ultrasound and/or MRI at baseline (BL). The primary endpoint was the proportion of women with <80mL MBL during the final month and ≥50% reduction in MBL from BL to the final month. MBL and the diagnosis of HMB was assessed with the alkaline hematin method. Adverse events (AEs) were monitored.

RESULTS: Of 790 women treated, 16% had ultrasound and/or MRI diagnosed adenomyosis at BL. Pooled data demonstrated that the proportion of responders for the primary endpoint was significantly greater (P<0.001) for elagolix+E2/NETA [76.8% vs 65.84, 87.82%] compared to placebo [12.2% vs 95% CI, 0.97, 23.150]. AEs reported in the adenomyosis subset included hot flushes, night sweats, headache, and nausea.

CONCLUSIONS: In women with HMB associated with UF and co-existing adenomyosis at BL, elagolix+E2/NETA significantly reduced MBL versus placebo similar to the all-subject group. AEs reported in this group were similar to the all subject group. These data suggest that further studies investigating the effect of elagolix in women with HMB associated with UF and adenomyosis may be warranted.


O-7 Monday, October 14, 2019 10:45 AM

IMPLEMENTATION OF AN ELECTRONIC WHITEBOARD FOR QUALITY MANAGEMENT IN THE IN VITRO FERTILIZATION LABORATORY. Phillip A. Romanski, MD, Ann M. Thomas, PhD, Jay Patel, MS, Dan Zhang, MD, PhD, Catherine Racowsky, PhD, Brigham & Women’s Hospital and Harvard Medical School, Boston, MA; Brigham & Women’s Hospital, Boston, MA.

OBJECTIVE: In 2014, we implemented an electronic whiteboard as a quality management tool to assist our embryologists to ensure their adherence to established standards for performing time-sensitive procedures (1). We aimed to test the hypothesis that use of an electronic whiteboard in the IVF laboratory increases the likelihood that critical evaluation procedures are performed within optimum pre-set time ranges.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Retrievals in our IVF clinic between 6/12 and 5/31/18 were included. The pre-electronic whiteboard time-period was 6/1/12 to 4/5/14, during which embryologists strived to adhere to the set optimum evaluation times but without a formal guide. The post-electronic whiteboard time-period was 3/1/15 to 5/31/18. The 13 months after the electronic whiteboard was introduced (4/6/14-2/28/15) were defined as a transition period and were excluded. Optimum pre-set time ranges were 16-18 hours post-insemination or ICSI (HPI) for the pronuclei (PN) check, 65-67 HPI for day 3 evaluations and 114-117 HPI for day 5 evaluations. Log binomial models estimated the risk ratio (RR, 95% confidence interval [CI]) of evaluations occurring within the optimum time ranges. Models were adjusted for parity.

RESULTS: A total of 44,957 oocytes from 6,302 retrievals met inclusion criteria, of which 44.4% underwent ICSI. There were 16,434 oocytes from 2,703 retrievals pre-electronic whiteboard and 28,523 oocytes from 3,599 retrievals post-electronic whiteboard. The proportion of oocytes evaluated at the PN check within the optimum time range was statistically significantly increased after implementation of the electronic whiteboard (89.2% vs 80.8%, RR 1.11 [95% CI 1.10 – 1.12]). The proportion of day 3 and day 5 checks that occurred within the optimum time ranges were also statistically significantly increased after implementation of the electronic whiteboard (day 3: 73.3% vs 57.2%, RR 1.75 [95% CI 1.54 – 1.99]) and (day 5: 74.1% vs 58.8%, RR 1.26 [95% CI 1.24 – 1.29]).

CONCLUSIONS: Our findings indicate that use of an electronic whiteboard that posts optimum time ranges for performing critical IVF laboratory procedures tightens the actual evaluation times towards these ranges. Such improved standardization may lead to positive downstream effects on quality assurance, analysis and embryo transfer and embryo cryopreservation management decisions. Future studies will investigate whether use of an electronic whiteboard in the IVF laboratory improves overall clinical care.


O-8 Monday, October 14, 2019 11:00 AM

THE CLINICAL RESULTS OF PIEZO-ICSI COMPARED TO CONVENTIONAL-ICSI: A SIBLING-OOCYTE STUDY. Noriyuki Okuyama, M.Sc, Ryuichiro Obata, Ph.D., Nao Oka, M.Sc., Nobuya Aono, Ph.D., Masahiro Hashimoto, M.D., Ph.D., Koichi Kyono, M.D., Ph.D., Kyono ART Clinic Takanawa, Tokyo, Japan; Minato-ku, Tokyo, Japan.

OBJECTIVE: Clinically, conventional ICSI (CI) is a common, widely-used method, while there are few reports with respect to Piezo ICSI (PI). PI is effective in degeneration rate and fertilization rate (Kimura, Y & Yana, K, 1995). It is known that the survival rates of mice oocytes are low after CI; however, degeneration rate improved markedly using PI. PI is an effective technique for cases with fragile oocytes. It has been reported that the survival rate is similarly improved in human oocytes (Hiraoka, K & Kimamura, S, 2015). However, most of the studies reporting on PI are retrospective studies. Here, we prospectively compared the degeneration rates, fertilization rates and embryo development of PI and CI in a sibling study.

METHODS: This is a prospective randomized controlled single-center study, using sibling oocytes, conducted from August 2018 to March 2019. Written informed consent was obtained from all patients involved in this study.

MATERIALS AND METHODS: This sibling oocyte study comprised 26 cycles in 26 cases. CI was performed in 149 mature oocytes. CI consists of mechanical penetration of the zona pellucida, breaking the oocyte membrane by aspiration of cytoplasm. PI was performed in 162 mature oocytes. PI consists of piercing the oocyte’s zona pellucida and zona ovum by using a miniature oocyte pulse. PI value of 0.5 or less was considered to be statistically significant. Limitation: The clinical results using vitrified oocytes, artificial oocyte activation, cryopreservation, frozen oocytes, and females aged over 40 years old were not included in this study. The pregnancy outcome has not been confirmed in our study.

RESULTS: There were no statistically significant differences in the fertilization rates, degeneration rates, cleavage rates, blastocyst formation rates or good quality blastocyst rates (according to the Gardner criteria) between CI and PI (75.8% vs 78.4% [P=0.592], 7.4% vs. 3.7% [P=0.146], 100% vs. 96.8% [P=0.160], 61.9% vs. 64.0% [P=0.743] and 41.6% vs. 36.8% [P=0.450], respectively).

CONCLUSIONS: In conclusion, the present study has demonstrated there was no significant difference in the clinical results of piezo-ICSI and conventional-ICSI. However, this may be attributable to the limited number of cases with fragile oocytes, etc. In our experience, PI is safer and easier to learn and
Biomedicina de Valencia, Valencia, Spain; dIVIRMA Global, Valencia.

Assess by a busy embryologist team in the routine clinical practice using Geriocyte origin (fresh or frozen) or patient age (range: 27-44 years). were included regardless of their treatment (egg donation or autologous), mated data from 1,370 embryos (284 patients) at IVIRMA Valencia clinic.

The automated group, as Geri Assess was statistically analyzed with chi-squared and binomial proportion tests. Data were graded and the accuracy in the prediction was assessed between both groups in terms of embryo outcome, bHCG test, and fetal heartbeat. Data were categorized into groups: conventional ICSI (PIEZO), conventional ICSI, Piezo ICSI, and P. Patients were categorized into groups: conventional ICSI (PIEZO), conventional ICSI, Piezo ICSI, and P.

OBJECTIVE: The objective of this study is to compare embryo grading and clinical result prediction obtained with a morphokinetic algorithm using an automated system for embryo developmental events annotations vs. manual annotations performed by an embryologist team.

DESIGN: Retrospective study including morphokinetic manual and automated data from 1,370 embryos (284 patients) at IVIRMA Valencia clinic. All embryos were normally fertilized embryos cultured up to day 5/6. All were included regardless of their treatment (egg donation or autologous), oocyte origin (fresh or frozen) or patient age (range: 27-44 years).

MATERIALS AND METHODS: All embryos were annotated manually by a busy embryologist team in the routine clinical practice using Geri Assess® 1.3 software (IVI). The same videos were retrospectively assessed by the stand-alone Geri Assess® 2.0 software (GA2), including filtration of events falling outside the pre-defined time-ranges, as is done in the full Geri system. The automated annotations were sent through an embryo selection algorithm developed by Basile et al. (2015) considering the morphokinetic parameters. Embryos were graded and the accuracy in the prediction was assessed between both groups in terms of embryo outcome, bHCG test, and fetal heartbeat. Data was statistically analyzed with chi-squared and binomial proportion tests.

RESULTS: High accordance was found between IVI and GA2 embryo grading through Basile’s algorithm. Out of the 1,370 embryos, 1,045 were utilized as transferred or vitrified, showing no statistically significant differences between both groups in all grades: A+, A, B+, B, C+, C, D+ and D; except for No Grade (p < 0.05). More ungraded embryos were found in the automated group, as Geri Assess® 2.0 is designed to eliminate events falling outside of pre-defined time-ranges, as is done in the full Geri system. The automated system is able to define risks of misdiagnosis of subclinical hypothyroidism due to potential underlying changes in TSH levels in a diverse population of patients seeking ART treatment. This study highlights how TSH fluctuations that may occur throughout the day are clinically relevant. Whether there is a misdiagnosis of subclinical hypothyroidism in infertile patients. However, for patients with a thyroid stimulating hormone (TSH) serum level > 2.5mIU/L it is recommended to continue monitoring or administer levothyroxine to reduce TSH serum levels < 2.5mIU/L (ASRM guideline document 2015). TSH levels in adults, have a predictable circadian rhythm, with the highest levels produced between 2am and 4am; while the lowest levels occur between 4pm and 8pm. Whether there is a misdiagnosis of subclinical hypothyroidism and underlying normal circadian rhythm due to testing afternoon blood draw is a current clinical concern. Only one study has shown the potential for this misdiagnosis, albeit the study included a small sample size. [1] The alternative of this study was to identify any differences in the mean TSH levels obtained from morning compared to noon blood draws in patients seeking infertility treatment.

DESIGN: Retrospective cohort analysis

MATERIALS AND METHODS: This study examined patients having routine TSH levels tested for either cycle day 3 evaluations or as part of a new patient consultation from January 2018 and March 2019. Serum TSH concentrations were obtained via electrochemiluminescence immunoassay Elecsys for use on Cobas e601(Roche) Detection range of 0.005 – 100 mIU/L. Chi Square analysis was used to determine statistical significance with p<0.05 considered significant.

RESULTS: Of the 8345 patients who had routine TSH testing performed, 5028 were drawn in the morning and 3281 were drawn in the afternoon. There was no significant difference in the mean (± SD) TSH levels, 2.10408 (4.30) for am blood draws and 2.10408 (4.31) for pm blood draws. There was also no differences in the in the percentage of TSH results showing >2.5mIU/L in morning 25% compared to afternoon blood draw groups 26%.

CONCLUSIONS: This study showed no shift in the mean or in percentage of patients with elevated TSH levels in the morning compared to afternoon blood draw group. This data shows that afternoon blood draws are just as likely to detect elevated TSH levels as blood samples drawn in the morning. The importance of this study is its ability to define risks of misdiagnosis of subclinical hypothyroidism due to potential underlying changes in TSH levels for the different times of blood draw using binomial sorting of patient data in a diverse population of patients seeking ART treatment. This study highlights how TSH fluctuation may occur throughout the day are clinically insignificant. No significant differences were found between the two groups. However, the study included a small sample size. [1] The alternative of this study was to identify any differences in the mean TSH levels obtained from morning compared to noon blood draws in patients seeking infertility treatment.

DESIGN: Retrospective cohort analysis

MATERIALS AND METHODS: This study examined patients having routine TSH levels tested for either cycle day 3 evaluations or as part of a new patient consultation from January 2018 and March 2019. Serum TSH concentrations were obtained via electrochemiluminescence immunoassay Elecsys for use on Cobas e601(Roche) Detection range of 0.005 – 100 mIU/L. Chi Square analysis was used to determine statistical significance with p<0.05 considered significant.

RESULTS: Of the 8345 patients who had routine TSH testing performed, 5028 were drawn in the morning and 3281 were drawn in the afternoon. There was no significant difference in the mean (± SD) TSH levels, 2.10408 (4.30) for am blood draws and 2.10408 (4.31) for pm blood draws. There was also no differences in the in the percentage of TSH results showing >2.5mIU/L in morning 25% compared to afternoon blood draw groups 26%.

CONCLUSIONS: This study showed no shift in the mean or in percentage of patients with elevated TSH levels in the morning compared to afternoon blood draw group. This data shows that afternoon blood draws are just as likely to detect elevated TSH levels as blood samples drawn in the morning. The importance of this study is its ability to define risks of misdiagnosis of subclinical hypothyroidism due to potential underlying changes in TSH levels for the different times of blood draw using binomial sorting of patient data in a diverse population of patients seeking ART treatment. This study highlights how TSH fluctuations that may occur throughout the day are clinically insignificant and even with ultra-sensitive immunoassays not, detectable in a population of patients undergoing reproductive treatment.

OBJECTIVE: Oocyte cytoplasmic dysfunction is a major contributor to impaired embryo development. Since maternal spindle transfer (MST) allows replacement of the entire cytoplasm of a poor quality oocyte, it holds a great promise to enhance oocyte quality. Our previous studies using mice and human oocytes showed that MST may rescue blastocysts of low quality. However, this effect was not detected when we analyzed the number of euploid blastocysts in each group. Similar data was obtained in outcome reproductive results. All these results suggest that MACS technology does not have any effect on PGT-A outcome when performed. Our results are supported by a consistent sample size.

SUPPORT: None.

ART OFFSPRING

O-13 Monday, October 14, 2019 10:45 AM

THIRD GRADE ACADEMIC ACHIEVEMENT AMONG CHILDREN CONCEIVED WITH IVF: A POPULATION-BASED STUDY IN TEXAS. Stephanie Watkins, PhD,a Morton B. Brown, PhD,b Barbara Luke, ScD, MPH,c Mary K. Ethen, MPH,d Mark A. Canfield, PhD,e Ethan Wantman, MBA,e Nina E. Forestieri, MPH,f Mahsa M. Yazdy, PhD,g Sarah C. Fisher, MPH,h Marilyn L. Browne, PhD,i Hazel B. Nichols, PhD,i Valerie L. Baker, MD,j Michael L. Eisenberg, M.D.,k Sergio C. Oehninger, MD,Ph Kevin J. Doody, M.D.;b TARGET PharmaSolutions, Durham, NC;e University of Michigan, Ann Arbor, MI;f Michigan State University, East Lansing, MI;g Texas Department of State Health Services, Austin, TX;h Redshift Technologies, Inc.;i New York, NY;k N.C. Birth Defects Monitoring Program, Raleigh, NC;l Affiliation not provided;m Johns Hopkins University School of Medicine, Division of Reproductive Endocrinology and Infertility, Lutherville, MD; n Stanford University, Stanford, CA;o 300 E. 55th street, New York, NY;1 CARE Fertility, Bedford, TX.

OBJECTIVE: To evaluate public school standardized testing results at the end of third grade among IVF versus non-IVF children.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The Texas Education Agency provided a stand-alone de-identified dataset of children ages 8-9 years who took the 3rd grade tests between 2014-18, indexed by IVF (Y/N), maternal race (White, Black, Hispanic, Asian), maternal age (18-29, 30-34, 35-39, ≥ 40+ years), plurality (singleton, twin), gestation for singletons (preterm, term), sex (M, F), and for IVF infants, embryo state (fresh, thawed). IVF children were matched by first and last names, and birthdate. Analyses were done using generalized linear modeling. Children who were economically disadvantaged or received special education were excluded since they were disproportionally greater in the non-IVF group. We limited the analysis to the standardized scores of the State of Texas Assessments of Academic Readiness (STAAR) test taken in English (99%) since the IVF group used only the English test. Test scores are reported as means ± SE.

RESULTS: After exclusions, there were 5,645 IVF and 10,246 non-IVF children with Reading scores and 5,649 IVF and 10,272 non-IVF children with Mathematics scores. IVF children scored higher in Reading (singletonts (IVF, N=2,663), 1,554 ± 2 vs 1,531 ± 1 (non-IVF, N=9,664), 24 point difference, p<0.0001; twins (IVF, N=2,982), 1,544 ± 2 vs 1,507 ± 5 (non-IVF, N=582), 36 point difference, p<0.0001), as well as in Mathematics (singletonts (IVF, N=2,659), 1,578 ± 3 vs 1,556 ± 1 (non-IVF, N=9,692), 22 point difference, p<0.0001; twins (IVF, N=2,990), 1,565 ± 2 vs 1,527 ± 5 (non-IVF, N=580), 38 point difference, p<0.0001). Children of mothers ages 30 and older scored higher than children of mothers ages 18-29 among non-IVF children, but were similar for IVF. Preterm and term singletonts scored comparably among IVF children. Overall, the IVF group, there were no differences by fresh vs thawed embryo state.

CONCLUSIONS: These results indicate that IVF-conceived children have an academic achievement in third grade that is at least as good as or better than those conceived spontaneously. We were not able to adjust further for socioeconomic status, which may explain some of the observed differences. In the IVF group there was no difference in test results in children born from fresh vs. thawed embryos.

SUPPORT: NIH Grant R01 HD84377. Assisted Reproductive Technology and Child Health: Risk of Birth Defects, Mortality, and Effect on Grade School Performance.
O-14 Monday, October 14, 2019 11:00 AM

SEX DIFFERENCES IN BIRTH OUTCOMES FOR MASSACHUSETTS INFANTS FOLLOWING ART

ART. Sunah S. Hwang, MD MPH,a* Dmitry Dukhovny, MD MPH,b Daksha Gopal, MPH,c Howard Cabral, PhD, MPH,c Hafsatou Diop, MD, MPH,c Judy E. Stern, PhD* University of Colorado School of Medicine, Aurora, CO;†Affiliation not provided; bBoston University, Boston, MA; cMDPH, Boston, MA; Dartment-Hitchcock, Lebanon, OR.

OBJECTIVE: Sex differences in child and adult health outcomes have been demonstrated. While prior studies have shown adverse birth outcomes for infants conceived by assisted reproductive technology (ART), data on whether outcomes differ by infant sex are lacking. Our objective in this study was to determine the presence and magnitude of sex differences in neonatal health outcomes among infants conceived by ART.

DESIGN: Retrospective observational cohort analysis of singletons born in Massachusetts between July 1, 2004 and December 31, 2013 who were conceived by ART.

MATERIALS AND METHODS: We linked the Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS), a clinical database of treatment information on all ART cycles and the Pregnancy to Early Life Longitudinal (PELL) data system, which links birth certificates to hospital discharge records for mothers and infants in Massachusetts. The analysis was limited to singleton, live births to women ≥ 18 years, conceived by ART. Birth outcomes for ART deliveries were compared between male and female infants using chi-square tests. Health outcomes were obtained from PELL. Multivariable logistic regression was used to model the associations between 837,933 CpGs and any infertility treatment have different DNA methylation patterns from newborns not conceived by infertility treatment. Several genes were identified, with biological evidence linking them to infertility. For instance, SYCE1 encodes for a synaptonemal complex protein, which is necessary for meiosis, and whose mutations were previously found in association with male and female infertility. Ongoing child follow-up will validate whether methylation differences persist.

RESULTS: Newborns conceived with infertility treatment (n=335, 39%) had higher methylation at one CpG in CH400186B (cg21616682, p=4.74x10^-10) compared to newborns not conceived with treatment (n=514). When the specific techniques were examined, no genome-wide associations were found for conception by OI/IUI (n=177, 20%). However, ART conceived newborns (n=158, 19%) had hypomethylation (ranging from 1.5 to 5.3%) at four CpGs in several gene regions (Table 1). Additional adjustment for plurality, infant sex, gestational age and birthweight did not meaningfully alter the findings.

CONCLUSIONS: In one of the largest studies examining differences in newborn DNA methylation by conception with infertility treatment, several genes were identified, with biological evidence linking them to infertility. For instance, SYCE1 encodes for a synaptonemal complex protein, which is necessary for meiosis, and whose mutations were previously found in association with male and female infertility. Ongoing child follow-up will validate whether methylation differences persist.

Table 1. newborn DNA methylation differences by conception by ART versus no treatment

<table>
<thead>
<tr>
<th>CpG</th>
<th>Beta</th>
<th>SE</th>
<th>p-value</th>
<th>Chromosome</th>
<th>Position</th>
<th>Gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>cg17676129</td>
<td>-0.01747</td>
<td>0.002484</td>
<td>2.02E-12</td>
<td>10</td>
<td>135382545</td>
<td>SYCE1</td>
</tr>
<tr>
<td>cg24413339</td>
<td>-0.01587</td>
<td>0.002703</td>
<td>4.35E-09</td>
<td>10</td>
<td>135237754</td>
<td>SPRN</td>
</tr>
<tr>
<td>cg01050010</td>
<td>-0.04998</td>
<td>0.008442</td>
<td>3.12E-11</td>
<td>17</td>
<td>31149877</td>
<td>MYO1D</td>
</tr>
<tr>
<td>cg27193138</td>
<td>-0.05358</td>
<td>0.009847</td>
<td>5.28E-08</td>
<td>21</td>
<td>40759754</td>
<td>WRR</td>
</tr>
</tbody>
</table>

O-15 Monday, October 14, 2019 11:15 AM

CONCEPTION BY INFERTILITY TREATMENT AND NEWBORN DNA METHYLATION

Edwina Yenum, PhD,a Pauline Legrand, PhD,a Rajeshram, PhD,a Xuehuo Zeng, PhD,b Welhua Guan, PhD,b Michael Y. Tsai, PhD,b Sonia L. Robinson, PhD,b Judy E. Stern, PhD,b Erin M. Bell, PhD,b "National Institutes of Child Health and Human Development, Bethesda, MD; bGotech Inc, Rockville, MD; cUniversity of Minnesota, Minneapolis, MN; Dartment-Hitchcock, Lebanon, OR; URiver University at Albany, Albany, NY.

OBJECTIVE: To determine whether newborns conceived by infertility treatment have different DNA methylation patterns from newborns not conceived by treatment.

DESIGN: The Upstate KIDS Study recruited women and their newborns (2008-2010), oversampling on infertility treatment exposure.

MATERIALS AND METHODS: Mothers reported on use of infertility treatment and the specific type (assisted reproductive technologies (ART) or ovulation induction (OI) / intrauterine insemination (IUI)) at 4 months postpartum. Maternal report of ART use was previously verified by linkage to SART-CORS. Mothers provided permission to use archived newborn dried blood spots collected by Newborn Screening. DNA methylation was measured using the Infinium EPIC microarray. Samples from 855 newborns were used in analysis. Singletons (n=688) and unrelated twins (n=167) were included to maintain independent samples. Quantile normalization was applied for probe type normalization and robust linear regression used to model the associations between 837,933 CpGs and any infertility treatment as well as by type (i.e., ART, OI/IUI, none). Bonferroni significance of p<6x10^-8 was used to account for multiple testing. Analyses were adjusted for maternal age, race, education, pregnancy smoking, private insurance, estimated cell type and batch effects.

RESULTS: Newborns conceived with infertility treatment (n=335, 39%) had higher methylation at one CpG in CH400186B (cg21616682, p=4.74x10^-10) compared to newborns not conceived with treatment (n=514). When the specific techniques were examined, no genome-wide associations were found for conception by OI/IUI (n=177, 20%). However, ART conceived newborns (n=158, 19%) had hypomethylation (ranging from 1.5 to 5.3%) at four CpGs in several gene regions (Table 1). Additional adjustment for plurality, infant sex, gestational age and birthweight did not meaningfully alter the findings.

CONCLUSIONS: In one of the largest studies examining differences in newborn DNA methylation by conception with infertility treatment, several genes were identified, with biological evidence linking them to infertility. For instance, SYCE1 encodes for a synaptonemal complex protein, which is necessary for meiosis, and whose mutations were previously found in association with male and female infertility. Ongoing child follow-up will validate whether methylation differences persist.

Table 1. newborn DNA methylation differences by conception by ART versus no treatment

<table>
<thead>
<tr>
<th>CpG</th>
<th>Beta</th>
<th>SE</th>
<th>p-value</th>
<th>Chromosome</th>
<th>Position</th>
<th>Gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>cg17676129</td>
<td>-0.01747</td>
<td>0.002484</td>
<td>2.02E-12</td>
<td>10</td>
<td>135382545</td>
<td>SYCE1</td>
</tr>
<tr>
<td>cg24413339</td>
<td>-0.01587</td>
<td>0.002703</td>
<td>4.35E-09</td>
<td>10</td>
<td>135237754</td>
<td>SPRN</td>
</tr>
<tr>
<td>cg01050010</td>
<td>-0.04998</td>
<td>0.008442</td>
<td>3.12E-11</td>
<td>17</td>
<td>31149877</td>
<td>MYO1D</td>
</tr>
<tr>
<td>cg27193138</td>
<td>-0.05358</td>
<td>0.009847</td>
<td>5.28E-08</td>
<td>21</td>
<td>40759754</td>
<td>WRR</td>
</tr>
</tbody>
</table>
O-17 Monday, October 14, 2019 11:45 AM

SIMILAR SUCCESS RATES WITH FROZEN OOCYTES BUT INCREASED RATE OF LARGE FOR GESTATIONAL AGE (LGA) INFANTS COMPARED TO FRESH OOCYTES. Channing Burks, MD, Kristin Van Heurten, MD, Amanda C. Purdue-Smith, PhD, Sumi L. Mumford, PhD, James Goldfarb, MBA, Rachel S. Weinerman, MD *University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH; NICHD, Bethesda, MD; National Institute of Child Health and Human Development, Bethesda, MD; OH.

OBJECTIVE: Evaluate pregnancy and perinatal outcomes of embryos derived from fresh and frozen oocytes in autologous cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The SART database was used to identify autologous oocyte cycles that resulted in an embryo transfer during 2014 and 2015. Generalized linear regression models were used to compare pregnancy and perinatal outcomes of fresh versus frozen oocytes. Models were adjusted for the following factors: maternal age, BMI, current smoking status, parity, infertility diagnosis, prior IVF attempt, ICSI assisted hatching, number of embryos transferred, multiple gestation and fetal heart reduction. Live birth rate was the primary outcome. Secondary outcomes include miscarriage rate and birth weight.

RESULTS: The mean maternal age in autologous oocyte cycles (N=139,734) was 35 years (SD ±3.6). There was no significant difference in the live birth rates when comparing embryos derived from fresh and frozen oocytes in autologous cycles (25.7% versus 23.9%, aRR 0.94, 95% CI 0.8-1.1). No significant differences were noted in biochemical pregnancy losses (5.8% versus 6.9%, aRR 1.3, 95% CI 0.94-1.79) or clinical miscarriages (10.9% versus 11.2%, aRR 1.04, 95%CI 0.82-1.33) in embryos derived from fresh and frozen autologous oocytes. Increased risk for large for gestational age infants (4.5% versus 12.5%, aRR 2.69, 95% CI 1.66-4.33) was seen in embryos derived from frozen oocytes. No significant difference was noted in low birth weight infants between the two groups.

CONCLUSIONS: Frozen oocytes have similar success rates as fresh oocytes in autologous cycles that resulted in embryo transfer. However, an increased rate of large for gestational age infants was seen in embryos derived from frozen oocyte. This finding warrants further study.

O-18 Monday, October 14, 2019 12:00 PM

PREVALENCE OF CLINICALLY SIGNIFICANT CONGENITAL HEART DEFECTS IN LOW- RISK IVF PREGNANCIES. Sarah H. Bjorkman, MD, a Kurt R. Bjorkman, MD, a Anna K. Skakianakis, MD, MPH, a Joshua A. Copel, MD, a Mert Ozan Bahtiyar, MD, a Yale School of Medicine, New Haven, CT, b Department of Pediatrics, Yale School of Medicine, New Haven, CT; c Yale Maternal Fetal Medicine, Fetal Care Center, New Haven, CT.

OBJECTIVE: Current research has shown increased prevalence of congenital heart defects (CHD) among in vitro fertilization (IVF) pregnancies compared to spontaneous pregnancies. We describe the prevalence and characteristics of CHD in IVF pregnancies at a high-volume fetal echocardiography center and outline a low-risk subset of patients for whom echo may not be clinically indicated.

DESIGN: Historical Prospective Observational Study.

MATERIALS AND METHODS: All fetal echocardiograms for singleton and dichorionic twin pregnancies performed January 1, 2004 to December 31, 2018 at a large tertiary care center utilizing gray scale, color Doppler, and spectral Doppler were reviewed and categorized by gestational age (GA), indications for fetal echo, and presence of structural CHD. All initial diagnoses were made by experienced sonographers and a maternal-fetal medicine specialist, recorded on videotape, and confirmed by a pediatric cardiologist. Neonatal echocardiographic examinations were performed to confirm diagnoses in cases with prenatal diagnoses of CHD. Prevalence and 95% confidence intervals (CI) calculated utilizing standard statistical methods. Clinical outcomes were available for cases of CHD after 2011.

RESULTS: 18,879 fetal echocardiograms were completed during the study period. Of those, 3,893 echocardiograms were performed with only indication being IVF gestation. Patients with previous child with CHD, family history of CHD, mediational exposure, diabetes, non-cardiac anomaly, anomaly in previous pregnancy, other abnormality noted on ultrasound, or monochorionic twins were excluded. Mean GA at time of echo for IVF only group was 22.2 ± 1.4 weeks. Prevalence of CHD summarized in Table 1. 25 cases were diagnosed with CHD after 2011. 22 were isolated ventricular septal defects (VSD), 10 CHD were not resolved at time of pediatric cardiology follow-up by 16 months, and 3 were clinically significant requiring intervention or cardiology follow-up after 2 years of age. Prevalence of clinically significant CHD in IVF only pregnancies was 0.15% (95%CI [0 – 0.40%]).

CONCLUSIONS: (1) In this low risk IVF cohort, the prevalence of clinically significant CHD is similar to population risk previously reported. (2) A large proportion of CHD in this population are VSD and most spontaneously resolve.

SUPPORT: None.

TABLE 1. Prevalence of CHD in IVF Pregnancies

<table>
<thead>
<tr>
<th>Group</th>
<th>#</th>
<th>% with CHD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All IVF Pregnancies</td>
<td>4242</td>
<td>76</td>
<td>1.79</td>
</tr>
<tr>
<td>IVF Only Ind.</td>
<td>3893</td>
<td>33</td>
<td>0.85</td>
</tr>
<tr>
<td>IVF Only (2012-18)</td>
<td>2040</td>
<td>25</td>
<td>1.23</td>
</tr>
<tr>
<td>IVF Only (2012-18)</td>
<td>2040</td>
<td>10</td>
<td>0.49</td>
</tr>
<tr>
<td>CHD Not Resolved</td>
<td>2040</td>
<td>3</td>
<td>0.15</td>
</tr>
</tbody>
</table>

* Cases were Coarct/VSD, Pulmonary Stenosis, and asymptomatic vascular ring.

O-19 Monday, October 14, 2019 10:45 AM

TOPICAL LIDOCAINE-PRILOCAINE CREAM Versus LIDOCAINE 1% SUBCUTANEOUS INFILTRATION DURING NEXPLANON INSERTION: A RANDOMIZED CONTROLLED STUDY. Ahmed M. Abbas, MD,a Mohamed Khalaf, MD,a Eman El-said, MB,BCh,b Ahmed Nasr, MD, Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; cDepartment of Obstetrics and Gynecology, Luxor General Hospital, Luxor, Egypt.

OBJECTIVE: Adequate anesthesia is an important procedural step when inserting contraceptive implants. Subcutaneous injection of lidocaine 1% is a widely used anesthetic method in implant insertion. However, lidocaine injection may be painful due to the penetration of the skin by the needle, and there is a theoretical risk of needle stick injury. This may also cause bleeding or edema which may mislead the intact subdermal insertion of the implant. Lidocaine-prilocaine (LP) cream is an oil/water emulsion in which the oil phase is a eutectic mixture of two anesthetics: lidocaine 2.5% and prilocaine 2.5% in a ratio of 1:1 by weight. Our objective is to compare the anesthetic effect of LP cream versus lidocaine subcutaneous infiltration during insertion of Nexplanon.

DESIGN: Randomized, open-label controlled study (Clinicaltrials.gov: NCT03187392).

MATERIALS AND METHODS: Reproductive-aged parous women requesting Nexplanon insertion for contraception were counseled to participate. Eligible women based on WHO guidelines were recruited and randomized (1:1) to LP cream vs. lidocaine 1% subcutaneous infiltration. In the cream group, 5 mg was applied on the insertion site, and Nexplanon rod was inserted after 5 minutes later. In the injection group, 2 ml of 1% lidocaine was slowly injected through a 24 G needle at the Nexplanon insertion.
site of skin with the depth of 2-3 mm, until at least 5 mm of wheel was observed, then the needle was further advanced under the skin in the direction of Nexplanon insertion and the remaining lidocaine was injected subcutaneously. Nexplanon rod was inserted within 3 minutes afterward. The main study outcomes were the participant’s self-rated pain perception utilizing a 10-cm Visual Analogue Scale (VAS) during Nexplanon insertion and 15 minutes post-procedure. A 2-cm difference in VAS score between both arms was considered a clinically significant difference. The secondary outcomes included ease of insertion score, complications of the procedure and patient’s satisfaction using a five-point Likert scale. Student’s t-test and Chi-square test were used for the analysis of the outcomes.

CONCLUSIONS: Topical application of lidocaine-prilocaine cream before Nexplanon insertion significantly reduces the induced pain with subsequent easier insertions and less rate of procedure-related complications.

SUPPORT: None.

O-20 Monday, October 14, 2019 11:00 AM

A RANDOMIZED CLINICAL TRIAL BETWEEN ULTRASOUND-GUIDED AND UTERINE SOUNDS-SPARING APPROACH FOR COPPER INTRAUTERINE DEVICE INSERTION. Mohammed Khairy Ali, MD, a
Ahmed M. Abbas, MD, a
Asmaa Ramadan, MBCh.
Ahmed M. Abdelmagied, MD, a
Mostafa Nasr Ibrahim, MD, a
Abou-Elhassan, MD, bDepartment of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; bDepartment of Obstetrics and Gynecology, Qous Central Hospital, Qena, Egypt.

OBJECTIVE: The intrauterine device (IUD) is a safe, reliable and long-acting reversible contraceptive method. Pain during insertion may be a barrier to choose IUD use. The trans-abdominal ultrasound guided IUD insertion (TAS-guided IUD insertion) effectively decreases the insertion pain; however, the full bladder during insertion and the need of two investigators may decrease acceptability. In “Uterine Sounding Sparing Approach” (USSA); the sonographer performs a transvaginal ultrasound before IUD insertion to evaluate the uterine position and length without using uterine sounding; this method may increase patient’s satisfaction and acceptance toward IUD use. Our objective was to compare the satisfaction score between both approaches during copper IUD insertion.

DESIGN: Randomized Open-label controlled Trial (Clinical Trials. Gov: NCT03135288).

MATERIALS AND METHODS: Reproductive-aged women requesting Copper IUD insertion for birth control were counseled to participate. The eligible women were randomized into two groups; group I (TAS-guided IUD insertion) and group II: USSA. The primary outcome was to measure the satisfaction score of both methods. Other outcomes included the easiness score (ES), the difference in pain scores during IUD insertion (measured by Visual analog scale), the duration of insertion in minutes and the successful device placement after one week, evaluated by transvaginal ultrasound (TVS). The outcome variables were analyzed using independent sample T-test.

RESULTS: Sixty women were analyzed in both groups (30 women in the arm). The baseline demographic data was homogeneous in both groups without statistically significant differences. The mean satisfaction score was significantly higher in the USSA group than TAS-guided IUD insertion group (6.7±0.90 Vs. 5.0±0.74, p=0.0001; respectively). The IUD inserted easier in USSA group than TAS-guided IUD insertion group (p=0.001). Also; the pain during IUD insertion was significantly lower in the USSA group (5.3±0.98 Vs. 6.9±0.75, p=0.0001; respectively). Moreover; significant shorter duration of insertion (3.67±0.71 Vs. 4.87±0.77 minutes; p=0.001) was reported in USSA group. At the one week follow-up; TVS showed that all IUDs were in place in all women without statistically significant difference (p=0.591).

CONCLUSIONS: USSA is associated with higher satisfaction and less pain during insertion than TAS-guided IUD insertion approach. Also, this approach is effective, easy and needs less time for IUD insertion.


SUPPORT: None.

O-21 Monday, October 14, 2019 11:15 AM

EFFECT OF CELL-PHONE ASSISTED POSTPARTUM COUNSELING ON THE USE OF LONG-ACTING REVERSIBLE CONTRACEPTIVES: A RANDOMIZED CONTROLLED TRIAL. Omar M. Shaaban, MD, a
Ahmed M. Abbas, MD, a
Treza Saber, MSc, a
Entisar Youness, MD, b
Manal Farouk, MD, a
Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; bDepartment of Obstetrics & Gynecological Nursing, Faculty of Nursing, Assiut University, Assiut, Egypt.

OBJECTIVE: The use of long-acting reversible contraceptive (LARC) methods remains substantially lower than less effective methods such as pills or condoms. Our objective is to assess the effect of adding cell-phone to the postpartum family planning counseling and service on the intake of postpartum women to LARC and the overall contraceptive performance.

DESIGN: Randomized Open-label controlled Trial (Clinical Trials. Gov: NCT03135288).

MATERIALS AND METHODS: All women delivered a live birth greater than 28 weeks' gestation and requested birth spacing for more than one year were counseled for participation. Eligible women were recruited and randomized (1:1) to Cell-phone assisted (study group) who received a reminder of their postpartum family planning visit five weeks after delivery and a phone call 48 hours before the scheduled visit. They were received two follow-up phone calls to answer any queries and to remind them of the follow-up visits after LARC use. They also provided with a cell phone number working seven days a week from 6 AM to 8 PM to answer any query or questions regarding her family planning program. The control group received the standard postpartum family planning counseling without any phone assistance. A follow-up visit was scheduled at six months to assess the study outcomes. The primary outcome was the rate of initiation of LARC method in the first six months after delivery. The secondary outcomes included the rate of continuation of the LARC method, initiation of another method, and rate of an unplanned pregnancy. Unpaired t and Chi-square tests were used for the analysis of the outcomes.

RESULTS: Eight hundred and sixty-four women were enrolled and randomized (432 women in each group). Both groups were similar regarding age, parity, BMI, educational level, residence and marriage period. The rate of initiation of LARC method was significantly higher in the cell-phone group (30.3% versus 8.4%; p < 0.001). Similarly, the rate of continuation was significantly higher in the cell-phone group (95.1% versus 82.9%; p < 0.001). Three hundred thirty-one (76.6%) of cell-phone group had started any contraceptive method during the first six months as compared 188 (43.5%) women in the control group (p<0.001). There were no cases of unplanned pregnancy in the cell-phone group compared with ten cases in the control group (p=0.009).

CONCLUSIONS: Adding cell-phone to the postpartum family planning counseling and service can improve the intake of postpartum women to LARC methods and the overall contraceptive performance with a subsequent decrease in the rate of an unplanned pregnancy.

SUPPORT: A fund No. (2016-23) received from The Institutional Grants’ office.

O-22 Monday, October 14, 2019 11:30 AM

INFLUENCE OF GENETIC VARIANTS ON WEIGHT GAIN AMONG ETONOGESTREL CONTRACEPTIVE IMPLANT USERS. Aaron Lazarowitz, MD, MSc, a
Eva Dindinger, MPH, a Margaret A. Harrison, BA, b
Christina L. Aquilante, PharmD, b Jeannelle Sheeder, PhD, b Stephanie Teal, MD, MPH cUniversity of Colorado Anschutz Medical Campus, Aurora, CO; dUniversity of Colorado Anschutz Medical Campus, Skaggs School of Pharmacy and Pharmaceutical Sciences, Aurora, CO.

OBJECTIVE: To identify genetic variants that are associated with weight gain related to etonogestrel (ENG) contraceptive implant use.
O-23 Monday, October 14, 2019 11:45 AM

EFFICACY AND SAFETY OF A MULTIPURPOSE VAGINAL PH-REGULATOR: RESULTS FROM THE PHASE 3, AMPPOWER CONTRACEPTION CLINICAL TRIAL. Michael A. Thomas, MD; Kelly R. Culwell, MD, MPH; Clint Dart, MS; Brandi Howard, PhD; University of Cincinnati, Cincinnati, OH; Evofem, Inc., San Diego, CA; Health Decisions, Durham, NC.

OBJECTIVE: Amphora® (formerly known as Acidform), a multipurpose vaginal pH-regulator (MVP-R), is a novel, non-hormonal, woman-controlled, on-demand, water-based, petroleum-free vaginal gel being investigated for prevention of pregnancy and sexually transmitted infections. Here we present primary results from the confirmatory phase 3 contraception trial, AMPPOWER.

DESIGN: This was a single-arm, open-label study conducted at 112 sites within the US (ClinicalTrials.gov number NCT03234305).

MATERIALS AND METHODS: All sites obtained IRB approval and all women provided informed consent. Eligibility criteria included healthy, monogamous, sexually active women aged 18-35 years who had normal cyclic menses of length 21-35 days, reported having intercourse ≥3 times per cycle, and were willing to use the study drug as the only method of contraception over the course of the study. Women were instructed to administer a single prefilled applicator of study drug intravaginally immediately before or up to 1 hour before each episode of vaginal intercourse. Women used ED-aries to record timing of product administration, coital information, and side effects. The primary efficacy analysis was the cumulative pregnancy percentage over 7 cycles with typical-use calculated by the Kaplan-Meier method.

RESULTS: A total of 1384 women were included in the Intent-to-Treat (ITT) population, 1182 were included in the primary efficacy analysis (modified ITT [mITT]), and 1330 used at least 1 application of study product and were included in the Safety population. In the ITT population, the demographic and characteristics were as follows: mean age, 27.7 years (standard deviation [SD], 4.5); mean body mass index, 28.7 kg/m² (SD, 8.1); Caucasian, 69.0% (955/1384); and non-Hispanic or non-Latino origin, 58.2% (805/1384). The mean number of prior pregnancies was 2.5 (SD, 1.8) and the most common contraceptive methods used immediately prior to enrollment were male condom (56.9% [787/1384]), withdrawal method (14.2% [196/1384]), and rhythm method (5.1%, 103/1384). Fewer than 2% of study participants discontinued due to adverse events (AEs) (1.7% [23/1384]). For the primary efficacy analysis in the mITT population, the 7-cycle cumulative pregnancy percentage with typical-use was 13.9% (95% confidence interval [CI]; 10.0%, 17.8%), which met the prespecified primary endpoint of having the upper bound 95% CI ≤21%. The most common AEs (>2.0%) were vulvovaginal burning sensation (20.0%, 266/1330), vulvovaginal pruritus (11.2%, 149/1330), urinary tract infection (5.7%, 76/1330), vulvovaginal mycotic infection (2.9%, 38/1330), and dyspareunia (2.6% [35/1330]). Fourteen women (1.1%) experienced a serious AE with only 1 event (cystitis, 0.1%) considered treatment related.

CONCLUSIONS: In this large phase 3 study, the MVP-R, Amphora, was found to be safe and effective in preventing pregnancy. Amphora provides women with an important new non-hormonal, woman-controlled contraceptive option.

SUPPORT: Evofem Inc.
Of the 156 women in the endometrial safety sub-study, 83 had follow-up biopsies. Pathologists reported no cases of endometrial hyperplasia or carcinoma at cycle 6 (n=24), cycles 12/13 (n=30) or other end of therapy times (n=29). The most frequent histologic diagnoses were atrophic/inactive or secretory, atrophic/secretive (cycle 6: 29%, cycles 12/13: 27%, and other end times: 28%, respectively), secretory (29%, 37%, and 45%, respectively), proliferative (17%, 7%, and 21%, respectively), mixed (17%, 10% and 3%, respectively), menstrual (4%, 7%, and 0%, respectively), or insufficient/no tissue (0%, 10%, and 3%, respectively).

CONCLUSIONS: Women using the SA/EE CVS (FDA approved in August 2016) for up to 13 cycles experienced good cycle control with few bleeding discontinuations, and did not have any unexpected endometrial histology safety findings.

SUPPORT: The Eunice Kennedy Shriver National Institute of Child Health and Human Development of the National Institutes of Health (NICHD; Contract Number HHSN27500403372) funded and conducted the US study; the US Agency for International Development (USAID; Grant Number GPO-A-00-04-00019-00) funded the international study, which was conducted by the Population Council; the World Health Organization (WHO) Reproductive Health Research Department funded two international study sites.

CRYOPRESERVATION AND FROZEN EMBRYO TRANSFER

O-25 Monday, October 14, 2019 10:45 AM

UNIVERSAL WARMING PROTOCOL* FOR A TRANSNATIONAL EGG DONATION PROGRAM WITH VITRIFIED OOCYTES: A RETROSPECTIVE MULTI-CENTRE STUDY. Lodovico Lodovico Parmegiani, PhD, Maria Giulia Minasi, M Sc, Alessandra Arnone, M Sc, Valentina Casciani, PhD, Graciela Estela Cognigni, MD, Rita Viola, MD, Maria Teresa Varricchio, MD, Luis Alberto Quintero, MD, Ermanno Greco, MD, Marco Filicori, MD, GynEPro Medical Centers-NextClinics International, Bologna, Italy.

OBJECTIVE: We have previously demonstrated that it is possible to warm vitrified human oocytes using a “universal warming protocol” based on subsequent steps with 1M and 0.5 M of ECCP regardless of the warming kit; this study investigated the clinical efficiency of this protocol on shipped oocytes in a transnational donor program.

DESIGN: Retrospective multi-center observational study on a cohort of 238 patients enrolled in egg donation programs from 02 March 2017 to 19 September 2018. Primary endpoint was the survival rate (n/oocytes surviving/n/oocytes warmed). Secondary endpoints were fertilization rate (n/oocytes fertilized/n/oocytes injected oocytes), blastulation rate (n/blastocysts obtained/n/fertilized oocytes), implantation rate (n/implanted embryos/n/ transferred embryos) and live birth rate (n/pregnancies giving births/n/oocytes transferred).

MATERIALS AND METHODS: Donated oocytes vitrified in Spain, warmed in 2 centers in Italy where ICSI and embryo transfer (ET) were performed. Number of oocytes 1898, ET 238. Vitrification with Vitrification Kit (Kitazato); embryo culture with EmbryoScope (Vitrolife, Sweden). ET at blastocyst stage.

RESULTS: Mean age of donors and recipients was comparable. Survival, fertilization, blastulation and implantation rates were all statistically comparable between the study groups. Survival rate was 84.6% (795/939) in group KK vs 82.1% (787/959) in group KI. Fertilization rate was 75.7% (602/795) vs 80.4% (633/787), and blastulation rate 58.5% (352/602) vs 57.8% (356/ 633). Implantation rate was 38.3% (80/209) in group KK vs 45.9% (84/ 183) in group KI. Live birth rate was 52.5% (62/118) in KK and 45.0% (54/120) in KI.

CONCLUSIONS: The proven clinical efficiency of this “universal warming protocol” with ready-to-use warming kits with 1 and 0.5 M of ECCP simplifies vitrified oocyte exchange between AR centers in different countries, overcoming potential regulatory/commercial/availability differences affecting clinical practice.


SUPPORT: None.

O-26 Monday, October 14, 2019 11:00 AM

MORPHOLOGY STILL MATTERS WHEN SELECTING EUPLOID EMBRYOS: INNER CELL MASS (ICM) AND TROPHECTODERM (TE) ARE PREDICTIVE OF PREGNANCY OUTCOMES. Sarah Druckenmiller, MD, Nicole Noyes, MD, Megan E. Sutter, PhD, David H. McCulloh, PhD, James A. Grifo, MD, PhD* NYU Langone Health, New York, NY; bNorthwell Health, New York, NY; cNYU Langone Prelupe Fertility Center, New York, NY.

OBJECTIVE: Morphologic grading of embryos has been an ART standard for nearly 4 decades. More recently, PGT-A has improved embryo selection. Data conflicts regarding whether morphological evaluation improves outcomes of euploid embryo transfers [1, 2, 3]. Our objective was to determine whether morphology is predictive of pregnancy outcomes among single thawed euploid embryo transfers (STEETs).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We reviewed all STEETs at a university-based ART center from 2014-2018. STEETs were excluded if oocytes were cryopreserved, embryos were created at another facility, embryos were frozen or biopsied twice, PGT-M or -SR was used, or an oocyte donor or gestational carrier was used. Only the first STEET during the study period that did not meet any exclusion criterion from each patient was included. Embryo morphology was graded according to Gardner [4]. Outcomes included implantation rate of all transfers and live birth (LB) rate, excluding 154 ongoing pregnancies and 28 pregnancies with unknown birth outcomes. Statistical analysis included chi-square, one-way ANOVA, and 2 multivariable log-binomial regression models to determine the association of predictors (age, expansion, ICM, TE) with implantation and LB.

RESULTS: We reviewed 1323 STEETs (mean age 37y; range 24-46y).
Overall, implantation was 69% and LB (n=1141) was 55%. ICM and TE were bivariately associated with both implantation and LB (p<0.01), but age and expansion were not. ICM significantly predicted implantation, but TE did not. Both ICM and TE independently predicted LB (see Table for adjusted predicted probabilities of implantation and LB based on ICM and TE grades at mean levels of all covariates in the models).

CONCLUSIONS: Ploidy status is not the sole determinant of embryo competence. ICM and TE are strong predictors of LB and can improve selection among euploid embryos. Poor ICM is the greatest negative morphologic predictor of implantation and LB. Our model can serve as a counseling tool for patients banking embryos.

MORPHOLOGICAL GRADING OF EMBRYOS

<table>
<thead>
<tr>
<th>ICM</th>
<th>TE</th>
<th>Probability of Implantation (95% CI)</th>
<th>Probability of LB (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>a</td>
<td>75% (61 – 89%)</td>
<td>71% (55 – 87%)</td>
</tr>
<tr>
<td>B</td>
<td>a</td>
<td>73% (58 – 87%)</td>
<td>68% (52 – 86%)</td>
</tr>
<tr>
<td>C</td>
<td>a</td>
<td>73% (66 – 80%)</td>
<td>59% (51 – 67%)</td>
</tr>
<tr>
<td>C</td>
<td>b</td>
<td>71% (68 – 74%)</td>
<td>57% (53 – 60%)</td>
</tr>
<tr>
<td>C</td>
<td>e</td>
<td>38% (24 – 52%)</td>
<td>32% (18 – 45%)</td>
</tr>
<tr>
<td>C</td>
<td>c</td>
<td>60% (51 – 69%)</td>
<td>44% (35 – 53%)</td>
</tr>
<tr>
<td>C</td>
<td>e</td>
<td>32% (20 – 44%)</td>
<td>25% (13 – 36%)</td>
</tr>
</tbody>
</table>

No combinations of ICM-A + TE-c or ICM-C + TE-a were present in the sample so these probabilities are not shown.
O-27 Monday, October 14, 2019 11:15 AM

CLINICAL FACTORS ASSOCIATED WITH THAW SURVIVAL IN A COHORT OF 6167 VITRIFIED-WARMED, EUPLOID BLASTOCYSTS. Margareta Oliva, MD, Christine Briton-Jones, PhD, HCLD, Dmitry Gounko, MD, Joseph A. Lee, BA, Alan B. Cockerman, MD, Lucky Sekhon, MD “Icahn School of Medicine at Mount Sinai, New York, NY; Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Embryo cryopreservation has become integral to IVF treatment. While an embryo failing to survive vitrification-warming is rare, understanding of factors that predict embryo thaw survival could allow for individualized patient counseling. Prior studies on the predictors of thaw survival have been limited by the use of slow-freeze protocols and unscreened embryos. This study analyzed embryo-related factors associated with euploid embryo thaw survival.

DESIGN: Retrospective, case-control.

MATERIALS AND METHODS: This single center study included vitrified-warmed euploid embryos from autologous IVF-PGT-A cycles from 2010-2019. Blastocysts that did not survive warming were compared to those that survived. Independent variables: patient age, basal antral follicle count (BAFC), body mass index (BMI), stimulation protocol, cumulative gonadotropin (GND) dose, estradiol (E2) and progesterone (P4) level at surge, embryo development day, oocytes retrieved, fertilization method, cleavage stage embryo cell number/fragmentation, number of trophectoderm biopsies and vitrification-warming, embryo sex, Gardner morphology. Student’s t-test, chi-square, and linear regression (generalized estimating equation models) were used.

RESULTS: Of the euploid blastocysts thawed (n=6167), 2.8% (n=175) warmed embryos did not survive. Embryos that did not survive came from women with higher BAFC (OR 0.97, 95% CI 0.95-0.99), E2 levels at surge (p=0.03), and number of oocytes retrieved (p=0.005). Embryos cryopreserved on day 5/6 were more likely to survive than day 7 (4.5, 95% CI 2.5-8.1). Blastocysts that underwent two trophectoderm biopsies had lower odds of thaw survival (OR 0.21, 95% CI 1.7-5.9) than those that had a single biopsy. Repeat vitrification-warming was not associated with thaw survival (OR 0.26, 95% CI 0.04-1.9). While cleavage stage cell count was similar between groups, increased fragmentation was associated with reduced survival (OR 0.97, 95% CI 0.94-0.99). Embryos with expansion grade 4 (OR 4.5, 95% CI 2.5-8.1) and 5 (OR 2.1, 95% CI 1.2-3.7) had higher odds of surviving than fully hatched blastocysts. ICM grade was positive correlated with thaw survival (OR 2.2, 95% CI 1.4-3.4), whereas trophectoderm grade was not. Controlling for relevant confounders, increased BAFC, double trophectoderm biopsy, and fully hatched blastocysts remained associated with reduced thaw survival.

CONCLUSIONS: Blastocysts that undergo a second trophectoderm biopsy, and/or are fully hatched prior to vitrification are less likely to survive warming. Embryos from ‘high responders’ also have reduced odds of thaw survival. These findings may be related to the link between polycystic ovarian syndrome and poor oocyte quality. Repeat trophectoderm biopsy and increased exposure of fully hatched embryos may reduce vitrification-warming tolerance. Providers can use this data to better counsel patients regarding the risk of their embryo(s) not surviving the thaw. At the molecular level, studies comparing the transcriptome of fresh and vitrified-warmed embryos may provide insights to optimize vitrification protocols.


O-28 Monday, October 14, 2019 11:30 AM

ANTIOXIDANTS INCREASE BLASTOCYST CRYOSURVIVAL AND VIABILITY POST VITRIFICATION. Thi T. Truong, Bachelor of Sciences, David Gardner, Ph.D., School of BioSciences, University of Melbourne, Melbourne, VIC, Australia.

OBJECTIVE: Cryopreservation is important for the preservation of gametes and embryos and consequently is used extensively in human ART. However, cryopreservation can induce oxidative stress resulting in an increase in reactive oxygen species. A combination of antioxidants has been shown to confer significant benefit to mouse IVF and culture, resulting significant improvements in embryo and fetal development. Here, we have examined the effects of the combined antioxidants as a strategy to reduce cellular stress during cryopreservation and hence improve ART outcomes.

MATERIALS AND METHODS: Pronucleate mouse oocytes were collected and cultured in groups under 20% or 5% oxygen to day 4 blastocysts. Expanded blastocysts were vitrified and warmed in medium with and without antioxidants (10 μM Acetyl-L-Carnitine/10 μM N-Acetyl-L-Cysteine/5 μM α-Lipoic Acid), cultured for a further 24 h, and cell numbers and apoptotic cells analysed. Histones H3K9ac and H3K27ac acetylation levels (as a mark of epigenetic impact) were quantified in blastocysts, and outgrowths and synchronous embryo transfers were performed on vitrified blastocysts.

RESULTS: Combined antioxidants supplemented to vitrification and warming media significantly increased ICM (28.34 ± 1.48 vs. 17.92 ± 1.13; P < 0.001) and total cell number (91.86 ± 3.71 vs. 77.61 ± 4.44; P < 0.01) compared to controls vitrified with no antioxidants. Furthermore, blastocysts vitrified with antioxidants resulted in similar total cell number and apoptotic rates to non-vitrified controls. Blastocysts vitrified with antioxidants also showed a significant increase in in vitro outgrowth area and perimeter (P < 0.05). Subsequent synchronous blastocyst transfer, following culture in 20% oxygen, resulted in increased fetal weight (190.19 ± 4.61 mg vs. 174.29 ± 5.52 mg; P<0.05), crown rump length (11.09 ± 0.10 vs. 10.76 ± 0.11; P<0.05) and limb development (14.89 ± 0.07 vs. 14.56 ± 0.11; P<0.05) when blastocysts were vitrified and warmed with antioxidants. Embryos cultured at 5% oxygen to the blastocyst stage and vitrified with antioxidants also showed increased crown rump length (11.29 ± 0.08 vs. 10.74 ± 0.12; P<0.001) and ear development (14.90 ± 0.05 vs. 14.64 ± 0.11; P<0.05). Importantly, while vitrification reduced acetylation of histones H3K27ac and H3K9ac in vitrified blastocysts, the inclusion of antioxidants significantly ameliorated this (P<0.05).

CONCLUSIONS: Vitrification and warming of blastocysts have detrimental effects on embryo development irrespective of oxygen culture conditions. Combined antioxidants in vitrification media significantly reduced the negative effects, resulting in blastocysts with higher developmental potential in vitro and increased viability. Thus, viability of vitrified human embryos may be improved by the inclusion of antioxidants during cryopreservation.

O-29 Monday, October 14, 2019 11:45 AM

DIFFERENCES IN OOCYTE SURVIVAL BETWEEN DONOR EGG BANKS AND SATELLITE CLINICS WITHIN THE SAME COMPANY. Whitney Hewitt, BS, Jennifer L. Patrick, MD, Lauren Johnson, MD, MSCE, Matrika Johnson, MD, Seth Katz, MD, Joe Whelan, III, MD, Tyl Taylor, PhD “Reproductive Endocrinology Associates of Charlotte, Charlotte, NC; REACH, Charlotte, NC.

OBJECTIVE: Vitrification of donor oocytes has become a staple in the IVF community. In fact, there are multiple vendors in multiple locations stimulating donors, freezing oocytes, and offering a limited number of oocytes to recipients across the globe. Although oocytes can come from the same company and follow the same protocols, they can come from different satellite locations, thus exposing receiving clinics to different variables that may impact clinical outcomes. This study has two objectives: to compare clinical outcomes of three different egg bank vendors and compare if there are differences between oocytes originating from the same company’s different satellite locations.
O-31 Monday, October 14, 2019 10:45 AM

EFFECT OF WILDFIRE SMOKE ON PREGNANCY OUTCOMES IN THE NON-HUMAN PRIMATE. Bryn Erin Willson, MD,1 Kent E. Pinkerton, PhD,1 Bill Lasley, PhD,1 Nancy Gee, PhD2 UC Davis Health, Sacramento, CA;2 UC Davis Center for Health and the Environment, Davis, CA;2 Center for Health & Environment, Davis, CA;2 UC Davis - Center for Health & Environment, Davis, CA.

OBJECTIVE: In November 2018, the “Camp Fire” wildfire was deemed the most destructive and deadliest wildfire in California history. The resulting poor air quality and ambient particulate matter in the Northern California region offered a rare opportunity to study the effect of wildfire smoke on conception and live birth rates in the non-human primates (M. mulatta) that reside outdoors at the California National Primate Research Center (CNPRC) in nearby Davis, CA.

DESIGN: We conducted a pilot prospective cohort study investigating pregnancy outcomes after exposure to ambient smoke from the Camp Fire that burned from 11/8-18/1122/18 about 160 kilometers away. This cohort was exposed to elevated fine particulate matter as recorded by California Air Resource Board (CARB). The fine particulate matter (PM2.5 – particles less than 2.5 μm in diameter) measured by CARB indicated a rise above national and state ambient air quality standards (15μg/m³) for 12 days and nights during the 2018-2019 breeding season reaching levels as high as 185μg/m³. The primary outcome of these data is conception and live birth rates.

MATERIALS AND METHODS: Through CNPRC, 66 blood (serum) samples were collected from female macaques in the outdoor colony following exposure to ambient smoke during the 2018-2019 breeding season. The primates have since undergone routine surveillance for conception and birth outcomes. For comparison, data was collected from the 2016 and 2017 breeding seasons.

RESULTS: Preliminary results show that out of 66 primates sampled, a total of 44 primates have confirmed pregnancies by physical exam (palpation) and/or positive serum macaque chorionic gonadotropin (mCG) samples were collected from female macaques in the outdoor colony prior to conception/early in pregnancy may have an effect on both conception rate and pregnancy outcomes in the non-human primate. This study joins the overall small body of literature that has shown deleterious effects of wildfire smoke exposure in pregnancy. Further research is needed to evaluate the mechanism in which wildfire smoke affects placentation and early pregnancy growth and development.

Breeding Season Conception Rate Live Birth Rate
2016-2017 92% 86%
2017-2018 84% 76%
2018-2019 66% x
OBJECTIVE: Women who experienced early life stress (ELS) have aberrant hypothalamic-pituitary-adrenal and autonomic responses as well as an increased inflammatory response to induced stress when compared to ELS naïve women. The impact of ELS on infertile women is largely unknown. We sought to determine the prevalence of ELS in the infertile population and the impact of this dysregulated stress reactivity on IVF cycle characteristics and outcomes.

METHODS: Prospective cohort study.

MATERIALS AND METHODS: Women aged 18-42 were recruited for enrollment in an autologous IVF cycle. Patients pursuing third party reproduction or fertility preservation were excluded. Consenting participants provided demographic information and completed the CDC-Kaiser Adverse Childhood Experience Questionnaire. Those who indicated 24+10 positive responses were considered to be ELS positive. A power analysis indicated that a sample size of 277 subjects would provide at least 80% power to detect a 40% relative difference in live birth rates between groups. Continuous variables were compared using Student’s t-test or Mann–Whitney U test based on normality, while χ² or Fisher’s exact tests were used to compare categorical variables by ELS status. Logistic regression was used to assess for predictors of live birth and early pregnancy failure adjusting for confounders as appropriate.

RESULTS: The prevalence of ELS positivity in this infertile cohort was 29.2% (n=83/284). ELS positive women and controls were similar in age, race/ethnicity, and history of anxiety/depression, however higher BMIs were observed in the ELS positive group (mean BMI 27.4 vs 25.6 kg/m², p=.02). There were no differences in infertility diagnosis, pregnancy history, number of prior IVF cycles or ovarian reserve parameters. While live birth rates were similar in the two groups (37% vs 35%; aOR 1.13, 95% CI 0.65–1.95, p=0.658), ELS positive women had significantly higher rates of early pregnancy loss (EPL) per transfer (28% vs 17%, p=0.04). This association persisted when the analysis was restricted to patients undergoing their first IVF cycle and excluding cycles in which preimplantation genetic testing was performed. After controlling for BMI and parity, ELS positivity remained significantly associated with EPL (aOR 1.95, 95% CI 1.05-3.62, p=0.03). However, when EPL rates were considered only among those who achieved a pregnancy (positive pregnancy test), no difference was observed between groups.

CONCLUSIONS: Early life stress has a longstanding impact on adult health. Differences in IVF cycle rates do not seem to be impacted, infertile women who experienced ELS have significantly higher rates of early pregnancy loss per transfer. Further studies are needed to elucidate the precise mechanisms of these findings to identify risk reduction strategies in this unique, potentially vulnerable, subpopulation of patients pursuing fertility services.

with a robust error variance. Models adjusted for age, percent body fat, race, and smoking. Models were also adjusted for dietary factors that are potentially related to cadmium exposure and PCOS, such as intakes of rice, total grains, and green leafy vegetables.

RESULTS: Mean (standard deviation) age and percent body fat were 27.3 (8.2) years and 29.7% (6.0), respectively. Median (interquartile range) cadmium levels were 0.30 (0.19–0.43) μg/L. Cadmium was associated with higher total testosterone (26% difference; 95% confidence interval [CI] 0.7, 4.5; P = 0.01), SHBG (30% difference; 95% CI 0.4, 5.7; P = 0.03), and AMH (7.0% difference; 95% CI 0.2, 14.2; P = 0.04), per 0.1 μg/L increase. Our data also suggests that higher cadmium concentrations were associated with a 25% higher probability of having a mild PCOS-phenotype with a borderline significance (relative risk 1.12; 95% CI 0.98, 1.29; per 0.1 μg/L increase; P = 0.09). No associations were found for free androgen index, insulin, and glucagon levels. Further adjustment for intakes of rice, total grains, and leafy vegetables did not change these associations.

CONCLUSIONS: Among healthy women, cadmium was associated with endocrine features central to PCOS, including total testosterone and AMH. However, we observed no associations with metabolic markers, such as fasting glucose and insulin. Among women without a PCOS diagnosis, these results suggest a potential role of cadmium in the hormonal milieu associated with PCOS.

O-35 Monday, October 14, 2019 11:45 AM
THE ASSOCIATION OF URINARY CONCENTRATIONS OF BISPHENOL-A, AND DI-ETHYLHEXYL PHthalate METABOLITES WITH THYROID FUNCTION & AUTOIMMUNITY IN WOMEN FROM A FERTILITY CENTER: RESULTS FROM THE ENVIRONMENT AND REPRODUCTIVE HEALTH STUDY. Irene Souter, MD,a Lidia Mínguez-Alarcón, PhD,b Tim Korevaar, MD, PhD,b Jennifer B. Ford, RN, c Jorge E. Chavarro, MD, Sc.D.,c Russ Hauser, MD, MPH, Sc.D.c 1MGH Fertility Center and Harvard Medical School, Boston, MA; 2Harvard T.H. Chan School of Public Health, Boston, MA; 3Harvard School of Public Health, Boston, MA.

OBJECTIVE: To evaluate the association of urinary concentrations of bisphenol-A (BPA) and di-ethylhexyl phthalate (DEHP) metabolites with markers of thyroid function and autoimmunity among women seeking fertility treatments.

DESIGN: Prospective Cohort Study.

MATERIALS AND METHODS: Urine and serum samples were collected from 558 women seeking infertility treatment at an academic institution and participating at the environment and reproductive health (EARTH) study. Urinary BPA and phthalate metabolite concentrations were quantified by isotope dilution tandem mass spectrometry, and the molar sum of four DEHP metabolites was calculated. Biomarkers of thyroid function [thyroid stimulating hormone (TSH), free and total thyroxine (FT4, T T4), and triiodothyronine (FT3, TT3)], and thyroid autoimmunity [thyroid peroxidase (TPO) antibodies] were quantified in serum using electrochemiluminescence assays.

Linear regression models adjusted for covariates (age, body mass index, diagnosis, specific gravity, BPA for DEHP metabolites and DEHP metabolites for BPA analyses) were used to estimate the relations between urinary BPA and DEHP concentrations, in tertiles, and serum thyroid function and autoimmunity biomarkers.

RESULTS: Higher urinary concentrations of DEHP metabolites were associated with lower serum levels of FT3, TT3, FT4, and FTI in both adjusted and unadjusted models. The multivariable adjusted means (95% CI) of thyroid function biomarkers for women in the lowest, middle, and highest tertile of urinary DEHP were: 15.6 (15.2, 15.9), 15.3 (14.9, 15.6), and 15.1 (14.7, 15.4) pmol/L for FTI (p-trend 0.06); 101 (97.8, 104), 98.6 (95.9, 101), and 94.8 (91.7, 97.8)* pmol/L for TT3 (p-trend 0.01); 4.9 (4.8, 5.0), 4.8 (4.7, 4.9), and 4.7 (4.6, 4.8)* pmol/L for FT3 (p-trend 0.01); and 1.9 (1.9, 2.0), 1.8 (1.8, 1.9),* and 1.8 (1.7, 1.8)* pmol/L for TT3 (p-trend 0.005); * p-value <0.05 when comparing that tertile to the lowest tertile of exposure.

DEHP was not related to either TSH [2.0 (0.8, 2.2), 2.2 (2.0, 2.3), and 1.9 (1.8, 2.1)] mU/L, for lowest, middle, and highest tertile respectively; p-trend 0.5], or thyroid autoantibody biomarkers [12.9, 17.0, 14.7 (13.1, 16.5), 14.1 (12.4, 16.1) μU/mL for TPO Ab (p-trend 0.6); 22.6 (18.8, 27.1), 22.7 (19.5, 26.4), and 19.0 (16.0, 22.6) μU/mL for TgAb (p-trend 0.02), for lowest, middle, and highest tertile, respectively.

Urinary BPA concentrations were unrelated to thyroid function or thyroid autoimmunity biomarkers.

CONCLUSIONS: Urinary DEHP, but not BPA, was inversely related to markers of thyroid function but not of thyroid autoimmunity. Our data suggest that current levels of exposure to certain phthalates negatively impacts thyroid function of reproductive age women through mechanisms that do not involve autoimmunity.

SUPPORT: National Institute of Environmental Health Sciences (NIEHS): R01ES022955, R01ES009718, and P30ES000002.

O-36 Monday, October 14, 2019 12:00 PM
NON-CHRONIC PRECONCEPTION OPIOID USE AND REPRODUCTIVE OUTCOMES. Kerry S. Flannagan, PhD,a Jeannie G. Radoc, BS,b Sunny L. Mumford, PhD,c Victoria C. Andriessen, BS,b Lindsey A. Sjaarda, PhD,b Jessica R. Zolton, DO,c Neil J. Perkins, PhD,c Keeswan Kim, Phdc Robert M. Silver, MD,d Enrique F. Schusterman, PhD,c 1Epidemiology Branch, DIPHR, NICHLD, NIH, Bethesda, MD; 2NICHLD, Bethesda, MD; 3National Institute of Child Health and Human Development, NIH, Bethesda, MD; 4University of Utah, Salt Lake City, UT.

OBJECTIVE: In recent decades, prescription opioid use has increased dramatically among reproductive age women. While much is known about the adverse outcomes of opioid abuse during pregnancy, the risk of limited opioid use during the periconception period is unclear. Thus, we examined associations of preconception and early-pregnancy opioid use with fecundability, live birth, and pregnancy loss in a cohort of women from the EAGeR trial.

DESIGN: Prospective cohort of 1228 women with 1–2 prior pregnancy losses enrolled in a randomized trial of preconception low-dose aspirin and followed for up to 6 cycles while attempting conception or through pregnancy resolution.

MATERIALS AND METHODS: We measured urinary concentrations of opioids by chemiluminescent immunoassay during preconception and, among women who became pregnant, at weeks 4 and 8 of pregnancy. We defined a positive screen as any opioid detected above manufacturer-defined cut points. Women self-reported use of opioid medications during or in the year prior to their last pregnancy and during preconception follow-up cycles. We estimated fecundability odds ratios (FOR) and confidence intervals (CI) with discrete Cox proportional hazard models. We estimated risk ratios (RR) of live birth and pregnancy loss with log binomial models. We adjusted for age, race, BMI, education, smoking, use of alcohol, marijuana, and antidepresants, time since last pregnancy, and gynecological indications for opioid use (e.g. fibroids, cramping).

RESULTS: 110 (9%) women screened positive for opioids during the preconception period and 33 (4.8% of 8-week pregnancies) screened positive during week 4 or 8 of pregnancy. 166 (13.6%) women self-reported opioid use during or before their previous pregnancy or during preconception follow-up. Most women screened positive or self-reported use only once. Positive preconception opioid use by screening or self-report was associated with longer time to pregnancy (FOR: 0.75; 95% CI 0.61, 0.93) and marginally associated with probability of live birth (RR: 0.81; 95% CI 0.64, 1.01). Positive opioid screening during pregnancy was associated with 2.90 times higher risk of pregnancy loss (95% CI: 1.51, 5.55).

CONCLUSIONS: Preconception opioid use was associated with lower fecundability and live birth rate. Use in pregnancy was associated with risk of loss. Opioid use may have adverse reproductive consequences even in non-addicted populations. Further studies are needed to determine the duration of use and specific types of opioids that may be harmful.

SUPPORT: This work was supported by the A Intramural Research Program, Division of Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development.

GENETIC COUNSELING

O-37 Monday, October 14, 2019 10:45 AM
LESSONS LEARNED FROM EVALUATING DECISIONAL REGRET SURROUNDING PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY. Amy Wijekoon, MD,a Mitchell P. Rosen, MD, HCLD,a Molly M. Quinn, MD,a 1University of California, San Francisco, San Francisco, CA; 2UCSF, San Francisco, CA; 3University of California, Los Angeles, Los Angeles, CA.
TABLE 1. Aneuploidy rates by PA

<table>
<thead>
<tr>
<th>Paternal age (years)</th>
<th>Cases (n)</th>
<th>Embryos (n)</th>
<th>Average number of embryos per case (n)</th>
<th>Euploid Rate ± SD (%)</th>
<th>Aneuploid Rate ± SD (%)</th>
<th>Aneuploid Rate of Maternal Origin ± SD (%)</th>
<th>Aneuploid Rate of Paternal Origin ± SD (%)</th>
<th>Aneuploid Rate of Mixed Origin ± SD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>173</td>
<td>1156</td>
<td>6.7</td>
<td>66.3 ± 1.4</td>
<td>33.7 ± 1.4</td>
<td>50.6 ± 3.1</td>
<td>31.1 ± 2.9</td>
<td>18.3 ± 2.4</td>
</tr>
<tr>
<td>35-37</td>
<td>233</td>
<td>1452</td>
<td>6.2</td>
<td>67.7 ± 1.2</td>
<td>32.3 ± 1.2</td>
<td>54.3 ± 2.8</td>
<td>31.8 ± 2.6</td>
<td>13.9 ± 1.9</td>
</tr>
<tr>
<td>38-40</td>
<td>287</td>
<td>1972</td>
<td>6.9</td>
<td>66.5 ± 1.1</td>
<td>33.5 ± 1.1</td>
<td>57.4 ± 2.3</td>
<td>24.4 ± 2.0</td>
<td>18.2 ± 1.8</td>
</tr>
<tr>
<td>41-42</td>
<td>201</td>
<td>1493</td>
<td>7.4</td>
<td>67.6 ± 1.2</td>
<td>32.4 ± 1.2</td>
<td>59.2 ± 2.7</td>
<td>25.0 ± 2.4</td>
<td>15.8 ± 2.0</td>
</tr>
<tr>
<td>&gt;42</td>
<td>964</td>
<td>7321</td>
<td>7.6</td>
<td>66.4 ± 0.6</td>
<td>33.6 ± 0.6</td>
<td>54.1 ± 1.2</td>
<td>28.7 ± 1.1</td>
<td>17.2 ± 0.9</td>
</tr>
<tr>
<td>Overall</td>
<td>1858</td>
<td>13394</td>
<td>7.2</td>
<td>66.7 ± 0.4</td>
<td>33.3 ± 0.4</td>
<td>54.9 ± 0.9</td>
<td>28.2 ± 1.2</td>
<td>16.9 ± 0.7</td>
</tr>
</tbody>
</table>

OBJECTIVE: Patients are often expected to make informed decisions about the use of preimplantation genetic testing for aneuploidy (PGT-A) based upon limited knowledge of its risks and benefits. This study aims to assess whether there are differences in degree of decisional regret between patients who decide to undergo/not undergo PGT-A, and to elucidate whether there are personal beliefs or clinical outcomes that correlate with level of decisional regret.

DESIGN: Retrospective cohort survey.

MATERIALS AND METHODS: An online survey was distributed to patients who underwent in vitro fertilization (IVF) with or without PGT-A between January 1st of 2016 to 2018. The survey consisted of 4 sections: 1) Demographic and Clinical Outcomes, 2) Decision-making factors, 3) Beliefs about PGT-A, and 4) Decision regret scale (DRS). Strength of belief in purported risks and benefits of PGT-A were assessed on a 0-100 scale (0: not true, 100: absolutely true). DRS scores ranged from 0-100, with a validated threshold of >25 indicating moderate to severe regret (MSR). Student’s t-test, Wilcoxon Rank-Sum, or Chi square test was applied, as appropriate, to compare baseline characteristics, DRS scores, and MSR rate between those who did or did not complete PGT-A. Multivariate linear regression was used to assess the impact of surveyed factors on DRS scores. Multinomial logistic regression was used to evaluate risk factors for MSR. All patients received evidence-based counseling regarding risks and benefits of PGT-A during a mandatory pre-treatment IVF orientation.

RESULTS: At this time, three hundred and thirty-five women completed the eligibility survey. Of the 261 women deemed eligible, 123 women completed the study survey (47%); 66 underwent PGT-A and 57 did not. There were no differences in demographic characteristics between the two groups. In raw analysis, DRS scores were significantly higher in those who did not complete PGT-A, compared to those who did (Median 20 vs 0, IQR 0-30 vs 0-20, p = 0.02); however, that difference diminished after controlling for live birth outcomes. In the group of patients with no live birth after index IVF cycle, there was no statistically significant difference in DRS scores between those who did and did not complete PGT-A (22 vs 34, p = 0.15). Participants who completed PGT-A were significantly more likely to believe PGT-A improved the chance of having a healthy baby (88 vs 76, p < 0.001) and that belief correlated with lower DRS scores regardless of live birth outcomes. MSR was noted in 14 women (21%) who had PGT-A vs those who did not (p = 0.13). Lack of live birth (RRR=0.18, p=0.02) and low overall patient satisfaction (RRR=0.98, p=0.03) significantly increased risk of MSR.

CONCLUSIONS: Decisional regret surrounding PGT-A is largely driven by overall patient satisfaction and live birth outcomes. However, our findings suggest that in the setting of a poor clinical outcome, there is no difference in level of decisional regret between those who do or do not elect for PGT-A. Physicians should feel comfortable counseling patients regarding the risks and benefits of PGT-A, and then allow them to choose.


SUPPORT: None.

O-38 Monday, October 14, 2019 11:00 AM

FOCUSING ON PARENTAL ORIGIN OF ANEUPLOIDY: DOES PATERNAL AGE IMPACT ANEUPLOIDY RATES IN EMBRYOS? Katrina Merrion, MS;† Diane Ahern, MS;† Jessica Adsit, MS;† Katherine L. Howard, MS;† Dusan Kijacic, MS;† Michelle Kiehl, MS;‡ Natera, Inc., San Carlos, CA;§ Affiliation not provided.

OBJECTIVE: While it is known that aneuploidy rates increase with advancing maternal age (MA) due to deterioration of the oocyte’s meiotic spindle, there has been no proven paternal age (PA) association. Some authors have postulated that advancing PA may be associated with increased risks for aneuploidy, while other studies have shown no association.

In this study, we report the 24-chromosome preimplantation genetic testing for aneuploidy (PGT-A) results for trophectoderm (TE) samples from a series of men who underwent in vitro fertilization (IVF) cycles using oocyte donors, broken down by PA.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: All PGT-A cases with TE biopsy and an oocyte donor between July 2010 and April 2019 were included in the analysis. TE and biological parental samples were run on Illumina Cyto12 array and matched microarrays with informatics to determine parental origin of each chromosome and establish chromosome copy number. Statistical analysis was performed using a two-tailed t-test.

RESULTS: Results were obtained on 13,018/13,394 (97.2%) of submitted TE samples. The average PA for this patient cohort was 43.5 ± 6.9 years (range 23–73). Aneuploidy rates are broken down by PA using SART age groups (Table 1). Additional analysis performed for men >50 years showed an aneuploidy rate of 704/2031 (34.7%) which was not statistically different from the other PA groups. Moreover, there was no statistical difference in the paternal aneuploidy rates or aneuploidy of mixed origin between PA groups (p > 0.05).

CONCLUSIONS: In this study, we did not observe an increase in aneuploidy rates with advanced PA, adding to existing literature showing a lack of PA effect. SNP microarrays with informatics uniquely allows determination of parental origin of aneuploidy in embryo samples. The difference in overall aneuploidy rates and paternally inherited aneuploidy rates among the PA groups was not statistically significant (p > 0.05). This information can be used to aid in patient counseling by providing reassurance that estimates for aneuploidy rates should be based primarily on the age of the oocyte contributor.


SUPPORT: Natera, Inc.

O-39 Monday, October 14, 2019 11:15 AM

DO BRCA MUTATIONS IMPACT ANEUPLOIDY RATES IN EMBRYOS? Carrie Chou, MS;*, Ellen Thomas, MS;*, Katrina Merrion, MS;† Nina Wemmer, MS;‖ Natera, Inc., San Carlos, CA;§ Affiliation not provided.

OBJECTIVE: Analyze chromosome ploidy results in a patient cohort who pursued preimplantation genetic testing for monogenic/single gene defects (PGT-M) for familial BRCA1 or BRCA2 mutations with concurrent 24-chromosome preimplantation genetic testing for aneuploidy (PGT-A).

Prior studies suggest BRCA mutations may be associated with diminished ovarian reserve and infertility, and that the effects of BRCA1 mutations may differ from BRCA2. Furthermore, mouse models have shown
Values within rows with the same superscript letter were significantly different.
CONCLUSIONS: TP53 (rs1625895) C>T polymorphism was associated with ovarian reserve and apparently affected ovarian response to rFSH and the clinical outcomes of IVF/ICSI cycles. Homozygosity of the T allele was associated with significantly poorer results. The identified SNP might provide an additional tool to test patients for ovarian reserve/response and thus help in the individualization of ovarian stimulation protocols. To the best of our knowledge, this was the first study to associate this SNP and ovarian response to gonadotropins.

SUPPORT: Merck Grant for Fertility Innovation (GFI-2014).

O-41 Monday, October 14, 2019 11:45 AM
NON-INVASIVE PREGNATAL TESTING HAS ALTERED POSITIVE PREDICTIVE VALUE FOLLOWING TRANSFER OF A EUPLOID BLASTOCYST. Amber M. Klimczak, MD, Christine V. Whitehead, BSN, RN, Shelby A. Neal, MD, Ashley W. Tieg, MD, Emily K. Osman, MD, Brent M. Hanson, MD, Julia G. Kim, MD, MPH, Marie D. Werner, MD, Jason M. Fransasiak, MD, Richard Thomas Scott, Jr., MD. IVI-RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: The positive predictive value (PPV) of non-invasive prenatal testing (NIPT) has been reported to range from 91.3-97.2% in the general population (1,2). However, PPV is dependent upon the prevalence of the disease in the population being tested. Patients who undergo in vitro fertilization (IVF) with preimplantation genetic testing for aneuploidy (PGT-A) and transfer a euploid embryo are presumably a lower risk population when compared to the general population. The objective of this study is to explore the PPV for NIPT following transfer of a euploid blastocyst.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All patients at a single IVF center between 2014 and 2018 who pursued pre-implantation genetic testing for aneuploidy (PGT-A) and underwent transfer of a euploid blastocyst between 2014 and 2018 were contacted to request completion of a medical record release form authorizing release of antenatal records. Records were reviewed, and patients who had documentation of an abnormal NIPT were included in this study. Results of any subsequent prenatal or postnatal diagnostic testing were used to classify each positive NIPT as a “true positive” or a “false positive”. The PPV of NIPT was calculated.

RESULTS: A total of 1,202 patients eligible for inclusion were contacted for completion of the medical record release form. Five patients with abnormal NIPT following transfer of a euploid blastocyst were identified. Four of these patients (80%) had subsequent definitive prenatal diagnostic testing which revealed a euploid karyotype concordant with their PGT-A results. One patient, who had a PGT-A result indicating 46,XX but a NIPT positive for Turner syndrome, underwent amniocentesis which confirmed Turner mosaicism (45,X karyotype in 80% of cells). Therefore, the PPV of NIPT in this patient cohort was 20%.

CONCLUSIONS: The PPV of NIPT for patients undergoing transfer of a euploid blastocyst is lower than that for the general population. PGT-A may be more likely to yield inaccurate results in the presence of embryonic mosaicism, as illustrated by the true positive NIPT case in this study cohort. PGT-A is an imperfect screening tool and follow-up antenatal screening is advisable; however, clinicians and patients should recognize that patients undergoing transfer of a euploid blastocyst are at a relatively lower risk for fetal aneuploidy when compared to the general population and, as a result, the PPV of NIPT is altered in this setting.


O-42 Monday, October 14, 2019 12:00 PM
SONOGRAPHIC ABNORMALITIES IN PREGNANCIES CONCEIVED FOLLOWING IVF WITH AND WITHOUT PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY. Carrie Rietseneberg, MD,a Kimberly Myole, MD, Neil Silverman, MD,b Lawrence D. Platt, MD, Christina Stih-chi Han, MD,b Molly M. Quinn, MD,c University of California, Los Angeles, Los Angeles, CA; Cedars-Sinai Medical Center, Los Angeles, CA; Center for Fetal Medicine and Women’s Ultrasound, Los Angeles, CA.

OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) has been increasingly adopted in IVF clinics across the US. While PGT-A may improve pregnancy rates on a per transfer basis, data demonstrate that patients often hold misconceptions that use of PGT-A will result in a healthy baby. In an effort to improve patient counseling on the benefits and limitations of PGT-A we report the rates and specific types of anomalies detected on anatomy ultrasounds in women who underwent IVF with PGT-A compared to women who conceived following IVF with unscreened embryos.

DESIGN: Retrospective cohort at a maternal-fetal medicine referral practice.

MATERIALS AND METHODS: All patients with singleton pregnancies who had a mid-trimester anatomy ultrasound between January 1-December 31, 2018 at a single clinic were assessed for inclusion. The charts of patients who conceived with IVF with or without PGT-A were systematically examined. The primary outcome was the rate of anomalies detected on anatomy ultrasound. Nuchal translucency (NT), first trimester and/or serum integrated screening, non-invasive prenatal testing (NIPT), and invasive diagnostic testing results were also extracted as available. Statistical analysis was performed using the student t-test, chi-square, or fisher’s exact test where applicable.

RESULTS: Of 4,095 singleton pregnancies during the study period, 433 conceived with IVF, including 278 who had PGT-A and 155 who did not. Rate of low risk nuchal translucency or noninvasive prenatal testing did not differ between patients who did or did not undergo PGT-A. There was a low overall rate of abnormal first trimester and/or serum integrated screen, yet it occurred more commonly in those who had undergone PGT-A (7.6 vs 1.8% p=0.006). Abnormalities of fetal anatomy or placenta were found at similar rates between the two groups.

CONCLUSIONS: The rate of abnormal ultrasound findings did not differ in patients who conceived after IVF with PGT-A compared to those who underwent IVF without PGT-A, but there was an increased risk of abnormal analytes on serum screening. Patients should be counseled that standard prenatal screening and ultrasounds are recommended following IVF with PGT-A.

SUPPORT: None.

<table>
<thead>
<tr>
<th>Age (mean±SD)</th>
<th>PGT-A (n=278)</th>
<th>IVF/no PGT-A (n=155)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk nuchal translucency (n, %)</td>
<td>187 (of 189), 98.9%</td>
<td>107 (of 107), 100%</td>
<td>0.54</td>
</tr>
<tr>
<td>First trimester screen normal (n, %)</td>
<td>181 (of 196), 92.4%</td>
<td>105 (of 107), 98.1%</td>
<td>0.006</td>
</tr>
<tr>
<td>Low risk noninvasive prenatal testing (n, %)</td>
<td>243 (of 244), 99.6%</td>
<td>126 (of 128), 98.4%</td>
<td>0.27</td>
</tr>
<tr>
<td>Invasive diagnostic testing normal (n, %)</td>
<td>22 (of 22), 100%</td>
<td>11 (of 12), 81.7%</td>
<td>0.35</td>
</tr>
<tr>
<td>Anatomy ultrasound normal (n, %)</td>
<td>230, 86.8%</td>
<td>128, 85.9%</td>
<td>0.8</td>
</tr>
<tr>
<td>Placenta normal by ultrasound (n, %)</td>
<td>191, 72.4%</td>
<td>107, 71.8%</td>
<td>0.91</td>
</tr>
</tbody>
</table>

*a-test. 
*Chi-square. 
*fisher’s exact.
HEALTH DISPARITIES

O-43 Monday, October 14, 2019 10:45 AM

COMPARISON OF EUPLOID RATES VIA PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) AND SUBSEQUENT PREGNANCY OUTCOMES BETWEEN ASIAN AND WHITE PATIENTS. David Huang, MD, a Eleni A. Greenwood, MD, MSc, a Phil Marsh, BS, a Andrew Runge, BS, b Marcella L. Cedars, MD, b Mitchell P. Rosen, MD, HCLD a University of California San Francisco, San Francisco, CA; b University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: Prior observational studies have suggested Asian ethnicity as a risk factor for poor IVF outcomes. We sought to compare euploid rates by PGT-A between Asian and White patients and their pregnancy outcomes after euploid single embryo transfer (SET).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We analyzed all day 5 and 6 blastocyst trophectoderm biopsy results via PGT-A from 2010-2019 at a single academic center, with the primary outcome being euploid rate. Euploid rate was determined by dividing the number of euploid blastocysts generated from a single egg retrieval cycle by the total number of blastocysts biopsied in the same cycle. Euploid rates were then compared based on self-reported race of the female partner, focusing on White versus Asian ethnicity. Generalized linear models were employed given clustered nature of the data and to control for oocyte age (STATA v14.2). We further compared pregnancy outcomes by race of the female partner after euploid SET in a subsequent frozen embryo transfer cycle, focusing on live birth or ongoing pregnancy as the outcome.

RESULTS: A total of 5,776 blastocyst PGT-A biopsies over 1,291 IVF cycles from 820 White and Asian female patients were identified. Of the blastocyst biopsies analyzed, 3,658 blastocysts were from White female patients and 2,118 blastocysts were from Asian female patients. Overall euploid rates did not vary significantly by female partner race: 43.9% in couples with a White female partner and 43.1% in those with an Asian female partner. After controlling for age of the oocyte, the odds of euploidy in couples with an Asian female partner compared to those with a White female partner were similar (OR 1.02, 95% CI 0.89,1.17, p = 0.75). We also observed no statistically significant differences in ongoing pregnancy or live birth rates between couples with an Asian female partner and those with a White female partner (57.8% vs 54.3%, respectively; p = 0.42) following subsequent euploid SET.

CONCLUSIONS: We observed no significant differences in euploid rates via PGT-A by female partner race (Asian versus White). We also did not note significant differences in pregnancy outcomes between Asian and White female patients in the setting of frozen euploid SET. These findings suggest that the less successful IVF outcomes among Asians in prior observational studies may be attributed to mechanisms other than poor oocyte/embryo quality or inferior inherent endometrial receptivity.

O-44 Monday, October 14, 2019 11:00 AM

INTERSECTION OF SEXUALLY TRANSMITTED INFECTIONS AND SUBSTANCE USE AMONG LOW-INCOME MINORITY WOMEN: ROUTINE CARE AS A CRITICAL POINT FOR REDUCING REPRODUCTIVE HEALTH DISPARITIES. Tyler McClung, BS, MS, a Morgan Snow, BA, a Chrystal G. Thomas, BS, MSc, a Phil Marsh, BS, a Andrew Runge, BS, b Marcella L. Cedars, MD, b Mitchell P. Rosen, MD, HCLD a University of California San Francisco, San Francisco, CA; b University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: To determine the relationship between clinically reported substance use on the prevalence of STIs among AYA women seeking routine well-adolescent and gynecological services in a STI prevalent community.

BACKGROUND: Previous data suggest that adolescent and young adult (AYA) women with sexually transmitted infections (STIs) report only one sexual partner and low condom use. While concurrency may be a key factor, the impact of substance use on effective sexual decision making around condom use may be critically important.

MATERIALS AND METHODS: This analysis utilizes AYA data from the Women’s BioHealth Study (WBS), a large human subjects approved cohort study prospectively enrolling mostly African American low-income female patients 13-29 years during routine well AYA and gynecologic visits in which specimens were also collected for Neisseria gonorrhoeae (NG), Chlamydia trachomatis (CT) to assess for sexual risk and infection of Mycoplasma genitalium (MG) and Trichomonas vaginalis (TV). Participants provided demographic, clinical, sexual risk behavior, and biological specimens for Trichomonas vaginalis (TV) and Mycoplasma genitalium (MG) testing. Additionally, for this analysis, serial electronic medical records (EMR) from visits were reviewed to explore STI outcomes associated with reported substance use behaviors during clinical visits for women ≤25 years, a defining point for AYA STI risk.

RESULTS: 443 patients with a mean age of 20.8 years (SD 2.7) were reviewed. Thirty-nine percent had a history of marijuana use, 43% had a history of alcohol use, and 3% had a history of substance use other than alcohol or marijuana. AYA < 21 were 1.5 times more likely AYA ≥ 21 years to use marijuana (OR: 1.53, 95% CI 1.02 to 2.29, P = 0.032). Marijuana was a predictor of increased behavioral risk scores (0.53 average difference, 95% CI 0.26 to 0.80, P < 0.001) and of not always using a condom (OR: 0.54, 95% CI 0.32 to 0.92, P = 0.024). Participants with a history of marijuana use (OR: 1.68 95% CI 1.11 to 2.56, P = 0.015) or other substance use (OR: 3.81, 95% CI 1.33 to 10.95, P = 0.013) were more likely to test positive for an STI.

CONCLUSIONS: A history of marijuana or substance use other than alcohol put AYA patients at a greater risk of not using a condom and contracting an STI, which could negatively affect reproductive health. Strategic approaches to addressing substance use disorders alongside STI prevention efforts among AYA served by practices in low income minority, STI-prevalent communities are warranted.

FERTILITY & STERILITY®

e19
smoking status and current hormonal contraception use at baseline, the overall estimated AMH trajectory showed minimal decrease until age 25 years after which the levels followed a relative linear decline, with accelerated rate after age 30. The correlation between random slopes and random intercepts was -0.93. The rates of AMH decline were similar among women (variance of random slopes: 0.0055) and AMH levels exhibited very little within-individual correlation (intraclass correlation coefficient: 0.17).

CONCLUSIONS: This is the first longitudinal study of AMH trajectories over a substantial period of time in reproductive aged AAW, a group that is largely underrepresented in the ovarian reserve literature. In this population, AMH decline with age seems to follow a common pattern with women with higher AMH levels at baseline exhibiting slightly slower rate of decline than women with lower than average initial levels. As reproductive lifespan and outcomes seem to be influenced by race, a better understanding of AMH trajectories and the role of potential modifiable factors on AMH decline in women of different backgrounds will improve physician counseling and empower women to make well-informed reproductive choices.

O-46 Monday, October 14, 2019 11:30 AM
PERSISTENT WIDENING IN RACIAL DISPARITIES BETWEEN BLACK AND WHITE WOMEN UNDERGOING ART OVER THE LAST 10 YEARS. Alexander Kolarov, MD, David B. Seifer, MD, Burcin Simsek, Ph.D., Ethan Wantman, MBA, Yale Fertility Center/ Yale University, New Haven, CT; Yale University, New Haven, CT; University of Pittsburgh, Pittsburgh, PA; Redshift Technologies, Inc., New York, NY.

OBJECTIVE: To determine if the trends in disparities of outcomes between black, non-Hispanic (BNH) and white women undergoing ART over the last 10 years have changed and to identify possible contributing factors that may have influenced such change.

DESIGN: Retrospective, cohort study and comparison of reported outcomes in the SARTCORS database for 2014-2016 with those previously reported in 2004-2006.

MATERIALS AND METHODS: Analysis of 2014-2016 SARTCORS for member clinics that performed at least 50 cycles of ART and reported race in greater than 95% of cycles. 165,551 cycles were analyzed of which 16,551 cycles were from BNH women and 109,004 cycles were from white women. Findings from this analysis were compared with previously analyzed cycles reported for 2004-2006 (Fertil Steril 93:626-35, 2010).

RESULTS: Reporting of race of 60% of cycles was essentially unchanged over the 10 year period. The proportion of cycles from BNH women increased nominally over the same period. When comparing 2014-16 to 2004-06, a greater proportion of BNH cycles were from older ages (≥38) and cycles with diminished ovarian reserve (DOR) compared to cycles from white women (p<0.001). The number of cycles with BMI ≥50 kg/m² was greater in cycles from black versus white women (p<0.001). Similar to 2004-06 data, cycles from BNH women were 3 times more likely to be associated with tubal factor and/or uterine factor and SAB rates continued to be greater (p<0.001) compared to cycles from white women. The proportion of live birth (LB) per cycle started remained less for cycles from BNH women compared to white women (p<0.001), as was observed from 2004-06. Race was an independent predictor of LB. Multivariate logistic regression demonstrated that cycles from black women were less likely to have a LB than white women for their initial cycle (OR 0.69; p<0.001). These findings were independent of age, parity, BMI, etiology of infertility, use of ICSI or number of embryos transferred. While similar proportions of black and white cycles were noted in mandated states there was a significant percentage of black cycles less represented among non-mandated states compared to cycles from white women (p<0.001).

CONCLUSIONS: While the proportion of cycles from BNH women using ART has incrementally increased, significant disparities have increased compared to white women over the last 10 years. This may be in part due to the increasing proportion of older age BNH women accompanied by DOR, increased BMI and greater SAB rates concomitant with a persistence of tubal and uterine factor. Access to state non-mandated insurance may have a significant impact upon relevant clinical differences between cycles from BNH and white women. Race has continued to be an independent prognostic factor for LB from ART over time. Further analysis of these persistent trends over time is necessary to address racial disparities in access and outcomes to ART treatment for infertility. Such insight could lead to strategic approaches that could potentially narrow the racial disparity gap and eventually be evaluated for their effectiveness.

O-47 Monday, October 14, 2019 11:45 AM
SOUTH ASIAN WOMEN HAVE POORER IVF OUTCOMES DESPITE BEING YOUNGER AND HAVING BETTER OVARIAN RESERVE COMPARED TO CAUCASIANS. Fady I. Sharara, M.D., Kaci D. Rogers, MS, Megan Goodwin, MS. Virginia Center for Reproductive Medicine, Reston, VA.

OBJECTIVE: IVF outcomes in ethnic minorities have been reported previously to be worse compared to Caucasians (C), including those of South Asian (SA) descent (India, Pakistan, Bangladesh, Nepal). Little has been published on ovarian stimulation parameters in SA as compared to C.

DESIGN: Retrospective.

MATERIALS AND METHODS: A total of 557 cycles were reviewed (176 in SA and 401 in C). Markers of ovarian reserve (AMH, AFC, FSH, E2) and cycle outcomes were compared between the two groups. The clinical outcome of those who had a fresh embryo transfer were also compared.

RESULTS: SA women were significantly younger (34.3 vs 35.7 yrs, P<0.001), had lower basal E2 (37.8 vs 42.1 pg/ml, P=0.042), higher AMH (3.54 vs 2.84 ng/ml, P=0.018), lower basal Vit D (31.9 vs 36.6 ng/ml, P=0.001), required less gonadotropins (3374.6 vs 3567 IU, P=0.045), had lower peak Vit D (40.8 vs 45.4, P=0.008), and had lower total blastocyst number (2.64 vs 3.1, P=0.036). For those who had a fresh ET (43 SA and 75 C), the live birth rate was lower in SA (52.7% vs 67.4%, P=0.014). For those undergoing PGT-A, there was a lower incidence of euploid embryos in C (150 cycles in C and 87 in SA) (45.6% in SA vs 35.6% in C, P=0.042).

RESULTS: Age: 34.3 ± 4.2 vs 35.7 ± 4.1, P<0.0001. AMH: 3.5 ± 6.50 vs 2.84 ± 2.91, P=0.018. AFC: 15.1 ± 9.7 vs 14.2 ± 8.8, P=0.29. Basal E2: 37.8 ± 21.5 vs 42.1 ± 23.9, P=0.042. Basal Vit D: 31.9 ± 14.03 vs 36.6 ± 13.13, P<0.0001. Gonadotropins (IU): 3375 ± 1068 vs 3567 ± 1054, P=0.045. Peak Vit D: 40.8 ± 14.3 vs 45.4 ± 13.5, P=0.008. Blastocysts: 2.64 ± 2.2 vs 3.1 ± 2.5, P=0.036.

CONCLUSIONS: Despite being significantly younger and having better ovarian reserve, SA women had significant differences in stimulation parameters. For those who had a fresh ET, SA women had a significantly lower live birth rate compared to Caucasians.


O-48 Monday, October 14, 2019 12:00 PM
REGIONAL DISPARITIES IN ASSISTED REPRODUCTIVE TECHNOLOGY ACCESS TO CARE: EMPLOYING MODERN TECHNOLOGY TO CLOSE THE GAP. Sasha Mikhail, MD/MS, Anna Gaidis, MD, Hannah N. Smith, BS, Larisa Gavrilova-Jordan, MD, Medical College of Georgia at Augusta University, Augusta, GA; Medical College of Georgia at Augusta University, Augusta, GA; Augusta University, Augusta, GA.

OBJECTIVE: Today, significant disparities still exist for access to assisted reproductive technology (ART) treatments in the United States. Only 60% of women who require ART are able to proceed with treatment. One of the major obstacles for access is the scarcity of fertility specialists in some regions of the US. Furthermore, the physical and financial burden associated with
time off from work and travel within or out of state, creates additional barriers. Telehealth is a well-established tool that alleviates these burdens. While other areas of medicine have welcomed this technology, reproductive medicine has yet to utilize it to its full potential. We implemented a regional telehealth program to close the gap in ART access in the rural Southeastern US. Our aim is to evaluate our telehealth program’s ART outcomes and patient satisfaction of those living remotely.

DESIGN: Retrospective cohort and cross-sectional survey study.

MATERIALS AND METHODS: Patients who utilized the telehealth application for ART services at Augusta University (AU) between September 2015 to November 2018 were identified. The study was approved by AU IRB.

Demographic variables were collected using the electronic medical record including age, type of ART cycles, travel distance, number of visits, and treatment outcomes. Patients were electronically mailed a validated questionnaire created via the qualtrics application. The survey included a patient satisfaction questionnaire as well as travel distance, number of visits, and ART treatment outcome. Data analysis was performed with descriptive statistics methods.

RESULTS: A total of 58 patients were identified of which 53% were < 35 years old (y/o), 16% were 35-37 y/o and 31% >38 y/o. 78% of patients had autologous fresh oocytes, 3%, donor oocytes, 1.4% embryo adoption, and 1.4% gestational carrier. The overall clinical pregnancy rate was 60.3% (77/35 y/o and 37/35 y/o) with an overall live birth rate of 38% (48/35 y/o and 22/35 y/o). The cohort’s mean number of visits was 2.93 (+/- 0.82). The survey response rate was 27/58 (46%), 56% of responders were <35 y/o and 44% >35 y/o. The mean number of visits for responders was 3 (+/- 0.99) and mean travel distance 171.4 miles (+/- 0.67). All responders underwent transvaginal oocyte retrieval and embryo transfer. For surveys, the clinical pregnancy rate was 19/27 (70.3%) with a live birth rate of 16/27 (59.3%). 93% of patients reported being highly satisfied with the telehealth service to enhance access to ART. All responders stated they would recommend telehealth use for ART to others.

CONCLUSIONS: Our study demonstrates that employing modern telehealth applications improves access to ART care in underserved areas. Fewer office visits maintains high patient satisfaction due to accessibility and cost reduction associated with travel and time off work. Reproductive health providers may consider utilizing telehealth in delivering ART treatment.

SUPPORT: None.

INFERTILITY AND CANCER

O-49 Monday, October 14, 2019 10:45 AM

PREGNANCIES IN CANCER SURVIVORS: OVARIAN RESERVE IS A POOR PROGNOSTICATOR.

Julie A. Suyama, MD, PhD,a Katherine E. Cameron, MD,a OVARIAN RESERVE IS A POOR PROGNOSTICATOR.

Monday, October 14, 2019 10:45 AM

O-49

and cost reduction associated with travel and time off work. Reproductive health applications improves access to ART care in underserved areas. All responders stated they would recommend telehealth use for ART to enhance access to ART. For surveyors, the clinical pregnancy rate was lower than in controls who conceived (47/96 [49.0%] survivors; 47/79 [59.5%] controls). There was no difference in the survival distributions for the two groups (p = 0.27).

Four survivors conceived with SOI/UI and seven with IVF. Survivors who conceived were older, more likely to be married or cohabitating, but received similar cyclophosphamide equivalent doses of chemotherapy compared to survivors who did not conceive. Anti-Müllerian hormone measured prior to pregnancy in survivors who conceived was lower than in controls who conceived (1561 vs. 2486 pg/mL, p = 0.02), but similar to survivors who did not conceive (p = 0.26).

Importantly, half of the captured pregnancies in both groups were unplanned (52% in survivors vs. 48% in controls, p = 0.9). Among planned pregnancies, survivors reported an average of 16 months (median 9 months) to conceive compared to 11 months (median 1 month) for controls (p = 0.16).

CONCLUSIONS: Pregnancy rate and time to pregnancy was similar in cancer survivors compared to controls despite diminished measures of ovarian reserve. These findings suggest that predictions about the fertility potential of cancer survivors cannot be made on the basis of measures of ovarian reserve alone.

O-50 Monday, October 14, 2019 11:00 AM

THE POTENTIAL IMPACT OF NEWER CHEMOTHERAPY REGIMENS ON FUTURE FERTILITY IN MEN AND WOMEN TREATED FOR LYMPHOMA.

Deepika Garg, MD,a Taylor P. Kohn, MD, MPhil,a Alexander W. Fasatuszak, MD, PhD,a Joseph M. Letourneau, MD,a James Hotaling, MDa aUniversity of Utah, Salt Lake City, UT; bJohns Hopkins University School of Medicine, Baltimore, MD; cUniversity of Utah School of Medicine, Salt Lake City, UT.

OBJECTIVE: The treatment of lymphoma is rapidly advancing to include more non-ABVD-based chemotherapy regimens. The fertility risks for men and women who receive non-ABVD regimens like BEACOPP are poorly understood.

DESIGN: Systematic review and meta-analysis.

MATERIALS AND METHODS: We searched the MEDLINE, PUBMED, and COCHRANE databases, online trial registries and conference proceedings for published manuscripts and abstracts from 1980 to April 2019. Studies were deemed eligible for meta-analysis if they included reproductive-age women or men with lymphomas (Hodgkin’s and non-Hodgkin’s) and the following were reported: chemotherapy regimen, patient age, duration from chemotherapy to ovarian reserve assessment (Anti-Müllerian Hormone (AMH)) or semen analysis, and rate of either severe oligo- or azoospermia (men). Estimates were pooled using random-effects meta-analysis comparing AMH levels in women, and rates of nornospermia in men, with ABVD versus non-ABVD treatment. For the purpose of meta-analysis, nornospermia was defined by a lack of either severe oligo- or azoospermia.

RESULTS: Data were extracted from 4 studies involving 440 women and from an additional 7 studies involving 400 men. The range of numbers of women and men included in each of the studies was between 30 to 263 and 19 to 141, respectively. The majority of the cancer diagnoses in all 11 studies were Hodgkin’s lymphomas. Three studies had follow-up AMH levels 36 months after completion of cancer treatment; one study measured AMH levels 18 months after treatment. Post-treatment AMH levels (pmol/L) were higher when comparing women who underwent ABVD versus non-ABVD, however this difference did not reach statistical significance (13.3 [95% CI: 1.3 – 30] versus 3.5 95% CI: [1.8-8.8], p = 0.22). Duration of follow-up for post-treatment semen analyses ranged from one to seven years after completion of treatment. There was a significant difference in the rate of post-treatment nornospermia among men who underwent ABVD regimen 89% 95% CI 70 - 96%) versus non-ABVD regimen 28.4% [95% CI 15 - 47.0], p < 0.001).
CONCLUSIONS: As lymphoma treatment evolves, fertility preservation physicians need to be aware that lymphomas may increasingly be treated with chemotherapy regimens that appear to have a more negative impact on future fertility in men and may likely impact it in women as well, though more data are needed.

O-51 Monday, October 14, 2019 11:15 AM
CANCER TREATMENT IS ASSOCIATED WITH A MEASURABLE DECREASE IN LIVE BIRTHS IN A LARGE, POPULATION-BASED STUDY. Deepika Garg, MD,a Huong Dieu Meeks, PhD,a Erica Johnstone, MD,a Alexander W. Ptaszuk, MD, PhD,b Sarah L. Berga, MD,c Ken R. Smith, PhD,c James Hotaling, MD, Joseph M. Letourneau, MD,b* University of Utah, Salt Lake City, UT; University of Utah School of Medicine, Salt Lake City, UT.

OBJECTIVE: Research on the impact of cancer treatment on fertility has evolved over time. Initially, studies tracked rates of amenorrhea and, more recently, rates of conception after cancer treatment. The aim of the present study is to define rates of live birth in a large, population-based study of the most common reproductive-age cancer in women.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: We performed a retrospective cohort study using the Utah Population Data Base (UPDB) relating first time cancer diagnosed between 1966 and 2014 to subsequent pregnancy in women in Utah aged 18-45 years. UPDB is a comprehensive source of birth, medical and cancer records of the Utah state population. Women from the study group who had live births after cancer diagnosis (n = 17,960) were compared with age matched controls at the time of cancer diagnosis (n = 89,436) and healthy sisters who had never been diagnosed with cancer (n = 15,099). Age-matched controls were the same age as cancer survivors in the year of cancer diagnosis. Both groups were followed from the year of diagnosis until 2014 and pregnancies achieved during this time recorded. We used conditional Poisson regression models, adjusted for birth year, BMI, and ethnicity, to estimate the association between history of cancer and subsequent live birth.

RESULTS: Based on Poisson regression modeling, the total number of live births was 15% lower among cancer survivors compared to healthy sisters (p < 0.001). When compared to age-matched healthy controls from the general population, cancer survivors had 25% fewer live births (p < 0.01). When compared with their healthy sisters, the reduction in live birth rate was 15% for all cancer types, 16% for breast cancer, 17% for central nervous system cancers, and 36% for soft tissue cancers (p < 0.001). 3% of cancer survivors who had a live birth utilized fertility treatment, compared to 2% (p = 0.13) of healthy controls who achieved live births. In addition, there were more stillbirths among cancer survivors when compared with their healthy sisters (14 per 1000 births versus 11 per 1000 births, p < 0.01).

CONCLUSIONS: In this large, population-based study in the Western United States, cancer and its treatment were associated with lower live birth rates when comparing women with cancer versus age-matched controls and healthy siblings. Live birth as a metric may reflect not only decreased fertility, but also an increase in adverse pregnancy outcomes such as stillbirth.

O-52 Monday, October 14, 2019 11:30 AM
PREGNANCY OUTCOMES AMONG CANCER SURVIVORS: A POPULATION-BASED ANALYSIS. Deepika Garg, MD,a Huong Dieu Meeks, PhD,a Erica Johnstone, MD,a Alexander W. Ptaszuk, MD, PhD,b Sarah L. Berga, MD,c Ken R. Smith, PhD,c James Hotaling, MD, Joseph M. Letourneau, MD,b* University of Utah, Salt Lake City, UT; University of Utah School of Medicine, Salt Lake City, UT.

OBJECTIVE: The growing field of onco-fertility has brought necessary attention to improving patients’ ability to achieve a pregnancy after cancer treatment. However, relatively little is known about frequency of healthy births, particularly with regard to preterm birth, pre-eclampsia, and low birth-weight, among survivors of cancers diagnosed during the young adult years.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The Utah Population Data Base (UPDB) was used to identify female cancer survivors (ages 18-45) who were diagnosed from 1966 to February 2014. The UPDB is a comprehensive source of birth, medical, and cancer records of the Utah state population. We identified pregnancy outcomes of female cancer survivors (n = 17,960) and compared these with age matched healthy women without a cancer diagnosis who were randomly included based on birth certificates (n = 89,436). Cases were matched to controls who were the same age during the age of the cases during the 5 year period of their cancer diagnosis. Cases and age-matched controls were then followed from the year of diagnosis until 2014 and pregnancies achieved during this time were recorded. Live birth rates, Apgar scores after delivery, pre-term delivery, low birth weight (defined as birth weight between 1500-2500 grams), prevalence of pre-eclampsia, and children with congenital malformations were determined. Descriptive statistics and chi-square tests were used, were appropriate.

RESULTS: Overall, 3126 births to cancer survivors and 19,405 births to healthy controls were included. In comparison to the control group, cancer survivors had significantly lower live birth rates (18% reduction, p < 0.001), an increased rate of preterm delivery (17% vs 13%, P < 0.001), and a higher risk of a child with low birth weight (11% vs 8%, p < 0.001). The higher prevalence of these outcomes was mostly due to cancer related chemotherapy and radiotherapy. The number of women with pre-eclampsia, children with congenital malformations, and Apgar score (<7) did not differ significantly between groups.

CONCLUSIONS: Currently, a significant focus in onco-fertility is on achieving live birth after cancer treatment. A better understanding of how to achieve a healthy pregnancy after cancer is needed. We find that female cancer survivors have a lower live birth rate and higher risk of pregnancy related complications, including preterm delivery and low birth rate than women without a history of cancer. Whether poorer outcomes reflect gamete, endometrial, and/or uterine mechanisms remain to be determined and may shed light on how to ensure healthier reproductive outcomes.

O-53 Monday, October 14, 2019 11:45 AM
STIMULATION OF THE OVARIES IN WOMEN WITH BREAST CANCER UNDERGOING FERTILITY PRESERVATION: ALTERNATIVE VERSUS STANDARD STIMULATION PROTOCOLS. E. M. E. Balkenende, MD,a T. Dahlhan, M.D., PhD,b C. C. M. Beerendonk, M.D., PhD,b K. Fleischer, MD, PhD,a A. M. E. Bos, M.D., PhD., C. B. Lambalk, MD, PhD,c Roelof Schats, MD, PhD,c L. Louwe, M.D.,a A. E. P. Cantuine, M.D., PhD,a J. M. J. Smeenk, M.D., PhD,c J. P. de Bruin, M.D., PhD,a F. F. van der Veen, MD, PhD., Prof.,a S. C. Linn, M.D., PhD., Prof.,a M. van Wely, PhD, Dr.,a Mariette Goddijn, MD, PhD. Prof. Dr. a*Amsterdam University Medical Center, Amsterdam, Netherlands; bRadboud UMC, Nijmegen, Netherlands; cAmsterdam AMC, Amsterdam, Netherlands; dLeiden University Medical Center, Leiden, Netherlands; eUMCG, Groningen, Netherlands; ETZ, Tilburg, Netherlands; fJeroen Bosch Hospital, Department of Obstetrics and Gynaecology, Den Bosch, Netherlands; gNetherlands Cancer Institute, Amsterdam, Netherlands.

OBJECTIVE: to evaluate the effectiveness of ovarian stimulation with tamoxifen or letrozole compared to standard ovarian stimulation on the number of oocytes retrieved in women with breast cancer in the course of fertility preservation.

DESIGN: Multi-center randomized open-label trial in the Netherlands and Belgium.

MATERIALS AND METHODS: Women between 18 and 43 years with breast cancer who opted for banking of oocytes or embryos in the course of fertility preservation were included. We randomly assigned them to one of the three study groups; group 1 ovarian stimulation plus tamoxifen (60 mg per day), group 2 ovarian stimulation plus letrozole (5 mg per day) or group 3 standard ovarian stimulation without additional medication. Primary outcome was the number of oocytes retrieved at follicle aspiration. Secondary outcomes were number of mature oocytes retrieved, number of oocytes or embryos banked and peak E2 levels during ovarian stimulation.

RESULTS: Between January 2014 and December 2018, we randomised 162 women with breast cancer. We analysed the primary outcome for 148 (91%) women of which 142 women (88%) underwent ovum pick up. Mean age of the women was 32 years.51 women underwent ovarian stimulation plus tamoxifen, 51 plus letrozole and 46 standard ovarian stimulation without additional medication. Primary outcome was the number of oocytes retrieved at follicle aspiration. Secondary outcomes were number of mature oocytes retrieved, number of oocytes or embryos banked and peak E2 levels during ovarian stimulation.

CONCLUSIONS: As lymphoma treatment evolves, fertility preservation physicians need to be aware that lymphomas may increasingly be treated with chemotherapy regimens that appear to have a more negative impact on future fertility in men and may likely impact it in women as well, though more data are needed.
group 3 0.243; 95% CI: -4.2 to 4.7; group 2 vs. group 3 0.297; 95% CI: -4.2 to 4.8). Mean number of embryos banked was 5.9 (group 1) versus 4.9 (group 2) versus 5.0 (group 3) (mean difference in number of embryos banked: group 1 vs. group 2 0.857; 95% CI: -3.0 to 4.7; group 2 vs. group 3 -1.33; 95% CI: -4.0 to 3.7).

CONCLUSIONS: These results show that the addition of tamoxifen or letrozole to standard ovarian stimulation did not affect the number of oocytes or embryos banked in the course of fertility preservation for women with breast cancer. Whether the addition of tamoxifen or letrozole to standard ovarian stimulation affects the long-term follow up in terms of safety in women with breast cancer, remains to be seen.

SUPPORT: The STIM trial was funded by the Pink Ribbon foundation.

O-54 Monday, October 14, 2019 12:00 PM

DESCRIBING LIVE BIRTHS AFTER CANCER TREATMENT: WHEN DO PATIENTS CONCEIVE AND HOW MANY CHILDREN DO THEY HAVE? A POPULATION-BASED STUDY IN THE WESTERN UNITED STATES. Deepika Garg, MD, a Huang Dieu Meeks, PhD, a Erica Johnstone, MD, a Alexander W. Pastuszak, MD, PhD, b Sarah L. Berga, MD, b Ken R. Smith, PhD, c James Hotaling, MD, c Joseph M. Letourneau, MD d University of Utah School of Medicine; a University of Utah, Salt Lake City, UT; b University of Miami Miller School of Medicine, Miami, FL; c Section of Urology, University of Manitoba, Winnipeg, MB, Canada; d Johns Hopkins University School of Medicine.

OBJECTIVE: Oncologists typically advise women to wait for two to five years after cancer treatment before trying to conceive. Age-related fertility concerns can be increased by both this period of waiting and the acceleration of ovarian follicle loss during and after cancer treatment.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The Utah Population Data Base (UPDB) was used to identify female cancer survivors in Utah state with first time cancer diagnosis between 1966 and 2014. We identified first and last live births of cancer survivors (n= 17,960) in various age groups and reported these relative to the timing of their cancer diagnosis. Descriptive statistics and chi-square testing were used where appropriate.

RESULTS: Our population included 17,960 women with first cancer diagnosis at age 18-45 years. These age groups were split into 18-25, 26-30, 31-35, 36-40, > 40 years old with the fraction of patients included in each group as follows: 18-25=14%, 26-30=16%, 31-35=19%, 36-40=23%, >40= 28%. The most common cancer types among the cohort were breast cancer in 23%, gynecologic cancers in 29%, lymphomas in 4%, and leukemia in 2%. A total of 36% of women had no children at the time of their cancer diagnosis. Nulliparity at the time of diagnosis was more common in the 18-25-year-old age group (62%). Approximately 17% of women had children after their diagnosis of cancer and they tended to have children approximately 2-3 years after cancer diagnosis. Women in the 18-25 age group tended to have their first post treatment child further from diagnosis than women who were > 40. Also, women 18-25 years old tend to have their last child 7 years after their cancer diagnosis, whereas women >40 tend to have their last children approximately 2 years after cancer diagnosis. Number of live births after cancer diagnosis was also higher among younger women, as reflected in the table below.

CONCLUSIONS: For both oncologists and infertility specialists, it is important to understand the timeline of when women with a history of cancer tend to build their families, and to incorporate this information into counseling about treatment-related infertility risk. Since the choice of when to build a family is highly personal and may vary across regions, more time-to-pregnancy data from other populations should also be collected.

MALE REPRODUCTION AND UROLOGY: TRAVELING SCHOLARS

O-55 Monday, October 14, 2019 10:45 AM

EVALUATION OF FERTILITY PRESERVATION COUNSELING AND REFERRALS IN US CLINICAL PRACTICES: REVIEW OF ASCO’S QUALITY ONCOLOGY PRACTICE INITIATIVE (QOPI). Taylor P. Kohn, MD, MPH; a Premal Patel, MD, b Benjamin Shiff, MD, c Jaden R. Kohn, MD, d Ranjith Ramasamy, M.D e Johns Hopkins University School of Medicine, Baltimore, MD; b University of Miami Miller School of Medicine, Miami, FL; c Section of Urology, University of Manitoba, Winnipeg, MB, Canada; d Johns Hopkins University School of Medicine, Department of GYN/Ob, Baltimore, MD.

Live birth after first cancer diagnosis 18-25 (N=2537) 26-30 (N=2870) 31-35 (N=3413) 36-40 (N=4162) >40 (N=4162) P value

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-21</td>
<td>1218 (48.0%)</td>
<td>1822 (64%)</td>
</tr>
<tr>
<td>22-25</td>
<td>545 (22%)</td>
<td>595 (21%)</td>
</tr>
<tr>
<td>26-30</td>
<td>420 (17%)</td>
<td>308 (11%)</td>
</tr>
<tr>
<td>≥ 3</td>
<td>354 (14%)</td>
<td>145 (5%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Ratio</th>
<th>Percentage</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>1031/1799</td>
<td>57.3%</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>GI</td>
<td>171/394</td>
<td>43.4%</td>
<td>&lt;0.05**</td>
</tr>
<tr>
<td>GU</td>
<td>69/100</td>
<td>69.0%</td>
<td>&lt;0.05**</td>
</tr>
<tr>
<td>Thoracic</td>
<td>27/70</td>
<td>38.6%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>8/22</td>
<td>36.4%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Gender</th>
<th>Ratio</th>
<th>Percentage</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI</td>
<td>Men</td>
<td>462/1686</td>
<td>27.4%</td>
<td></td>
</tr>
<tr>
<td>Thoracic</td>
<td>Men</td>
<td>124/423</td>
<td>29.3%</td>
<td></td>
</tr>
<tr>
<td>GU</td>
<td>Men</td>
<td>144/263</td>
<td>54.8%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Men</td>
<td>17/63</td>
<td>27.0%</td>
<td></td>
</tr>
<tr>
<td>Bone/Skin</td>
<td>Men</td>
<td>11/43</td>
<td>25.6%</td>
<td></td>
</tr>
</tbody>
</table>

* P-value Chi-Squared for Trend.
** P-value Chi-Squared.

FERTILITY & STERILITY®
OBJECTIVE: Discussions about fertility preservation are essential in reproductive-aged patients with newly diagnosed cancer. Our objective was to identify factors affecting decision making about fertility risks in reproductive-aged patients prior to initiating chemotherapy.

DESIGN: The American Society for Reproductive Medicine (ASRM) Quality Oncology Practice Initiative (QOPI) is an oncologist-led quality assessment program that surveys 994 oncology practices on a yearly basis.

MATERIALS AND METHODS: Each practice in the ASRM QOPI submitted individual patient data from 2015 to 2018. Patients of reproductive age were females 18-40 years and males 18-50 years. Primary outcome was whether fertility risks were discussed prior to chemotherapy. Multivariate logistic regression was performed to identify predictors of fertility preservation counseling, controlling for the below variables.

RESULTS: Of 5,887 reproductive age patients, 42.1% discussed the risk of infertility associated with chemotherapy. Females were more likely to be counseled about the risk of infertility (1540/2831, 54.4%) compared with men (942/3055, 30.8%; p<0.001). Type of cancer and other variables appear in Table 1. In regression to assess whether fertility risks associated with chemotherapy were discussed, male sex (OR 0.73; CI 0.60-0.88) and increasing age (0.93; 0.92-0.94) reduced the likelihood of discussion while breast cancer (1.44; 1.19-1.75), hematopoietic cancers (1.55; 1.17-2.05), and receiving care in an academic clinic (1.45; 1.05-2.01) predicted higher rates. States with legislatively-mandated coverage of fertility preservation had significantly higher rates of fertility risk discussion (48.6% vs 39.6%, p<0.001).

CONCLUSIONS: Providers are more likely to counsel younger patients and female patients. State laws improve frequency of discussing fertility risk; further research is needed to identify factors that optimize fertility counseling prior to chemotherapy.

Reference: None.

SUPPORT: Department of Urology, University of Miami.

O-56 Monday, October 14, 2019 11:00 AM

LOWER TOTAL MOTILE COUNT IS ASSOCIATED WITH SMALLER HISTORIC INTERGENERATIONAL FAMILY SIZE: A PEDIGREE ANALYSIS FROM THE UTAH POPULATION DATABASE (UPDB).

Darshan P. Patel, MD,1,2 Huong Dieu Meeks, PhD,1,2 Alexander W. Pastuszak, MD, PhD,1,2 James Hotaling, MD1,2 1University of Utah Health, Salt Lake City, UT; 2University of Utah, Salt Lake City, UT

OBJECTIVE: Genetic heritability of male factor infertility may contribute to intergenerational variations in family size. We sought to assess the correlation of total motile count and intergeneration family size within the Utah Population Database (UPDB).

DESIGN: This is a retrospective, population-based, cohort analysis of men with at least a single measure of total motile count (TMC) within the UPDB and with complete pedigree data.

MATERIALS AND METHODS: These men must have at least one generation within their pedigree born in and prior to 1935 for inclusion to reduce the effect of contraception on the results. We identified the average number of generations for each individual overall, as well as the average number of generations and offspring within each generation occurring in and prior to 1935. Linear logistic regression models with clustered sample design were used to assess the relationship between TMC within 5th and 25th percentile and intergenerational family size and offspring prior to 1935. Additionally, generalized estimating equations with independence correlation structure and clustered sample design were created to estimate the change in TMC per increase in number of offspring among proband ancestors.

RESULTS: We identified 2,182 men with a measure of TMC within the UPDB and complete pedigree information. 541 men (24.8%) were within the 25th percentile for TMC while 112 men (5.1%) were within the 5th percentile for TMC (including azoospermic men). The average number of generations across each individual’s pedigree was 4.2 (SD: 1.1). The average number of generations and offspring within each generation occurring prior to 1935 were 3.6 (SD: 1.0) and 6.5 (SD: 1.6), respectively. We found no significant association between intergenerational size and TMC within the 5th percentile (including azoospermic men) (RR = 0.97, 95% CI 0.93-1.01, p = 0.18) or the 25th percentile (RR = 1.00, 95% CI 0.97-1.03, p = 0.38). When TMC was analyzed as a continuous variable, generalized estimating equations suggest that lower TMC is related to smaller intergenerational family size. For every additional child in their historical pedigree back to 9 generations, we saw an increase in TMC of 1.88 million (p = 0.031).

CONCLUSIONS: This is one of the first studies examining the relationship between intergenerational family size and TMC as a marker of male factor infertility. We found a significant association between TMC as markers of male factor infertility and family size, suggesting that lower TMC is related to smaller intergeneration family size. This hypothesis generating data questions an effect of genetic heritability and male factor infertility on intergenerational family size.

O-57 Monday, October 14, 2019 11:15 AM

DECISIONAL CONFLICT AND KNOWLEDGE AMONG PATIENTS WITH VARICOCELE SEEKING TREATMENT FOR INFERTILITY: A PRELIMINARY STUDY

Raj N. Chopra, MD,1,2 Arash Amighi, B.S.,3 Ali Al Almuzeni, MD,4 Steven Alexander Mills, MD,1 Justin Nork, D.O.,5 Lorna Kwan, MPH,1 Matthew Pollard, M.D.,6 Sylvia I. Lambrechts, MPH, MA,7 Siriram Eleswarapu, M.D., Ph.D.,8 Jesse Mills, M.D.9 David Geffen School of Medicine at UCLA, Los Angeles, CA; 1University of California, Los Angeles, Los Angeles, CA; 2University of Miami, Coral Gables, MI.

OBJECTIVE: To measure disease-specific knowledge and decisional conflict in men with varicoceles being counseled for infertility, and to gain insight into decision-making in male versus female-centric treatments for infertility.

DESIGN: This was a cross-sectional, observational, survey-based study of patients with clinical varicoceles and infertility.

MATERIALS AND METHODS: 84 patients were identified prior to their initial infertility consultation with a fellowship-trained male reproductive surgeon at the University of California, Los Angeles. Following consultation, patients completed a survey instrument measuring disease-specific knowledge, decisional conflict, satisfaction with care, and impression that shared decision-making occurred at the time of consultation. This instrument also queried patients’ preferred infertility treatment modality both before and after consultation. Treatment-associated decisional conflict was measured with the validated SURE metric. Patient characteristics and survey responses were compared between those without decisional conflict (SURE score of 4) and those with some degree of decisional conflict (SURE score of 1-3) using Chi-squared (Fisher’s exact if needed) and Wilcoxon rank-sum tests.

RESULTS: Mean age (SD) of patients and their partners were 36.3 (6.1) years and 34.4 (5.3) years, respectively. 66% of varicoceles were grade 2 or greater. The mean knowledge score was 57% ± 15% in those with no decisional conflict. Compared to those with decisional conflict, men without decisional conflict scored higher on the infertility knowledge assessment (63% vs 51% correct), were more likely to feel included in the treatment decision (100% vs 83%), and were more likely to feel that they discussed treatment options with their physician in detail (100% vs 82%) (all p<0.01). Prior to consultation, 27% of all patients preferred assisted reproductive technologies (ART) including IUI and 2% preferred varicocelectomy as the primary treatment for infertility. Following consultation, 14% and 17% preferred assisted reproductive technologies and varicocelectomy, respectively. The increase in treatment preference for varicocelectomy was greater in men with no decisional conflict (5% to 29%) than those with decisional conflict (0% to 7%) (p=0.03). There was a concomitant decrease in preference for assisted reproductive technologies following consultation (34% to 18% vs 22% to 9%).

CONCLUSIONS: Patient knowledge on the etiology and treatment of male infertility is insufficient and associated with decisional conflict. Prior to consultation, men with varicoceles showed preference for assisted reproductive technology over varicocelectomy; this trend reversed after consultation. Men with decisional conflict were much less likely to prefer varicocelectomy, even after consultation. An intervention that improves infertility knowledge may reduce decisional conflict and optimize shared decision-making in the treatment of infertility for men with varicoceles.

O-58 Monday, October 14, 2019 11:30 AM

SPERM EXTRACTED FROM MEN WITH OBSTRUCTIVE AZOSPERMIA VIA MINIMALLY-INVASIVE EPIDIDYMAL SPERM ASPIRATION (MESA) RESULTS IN NON-INFERIOR IVF OUTCOMES COMPARED WITH NORMAL EJACULATED SEMEN IN COUPLES WITH UNEXPLAINED INFERTILITY.

Solomon Hayon, MD, ASRM Abstracts Vol. 112, No. 3, Supplement, September 2019

Robert M. Coward, MD,1,2 Sarah M. Moustafa, MD,1,2,3 Caitlin Boylan, BS,1,2 Mary Peavey, MD,1,2 Robert M. Coward, MD,4 University of North Carolina, Chapel Hill, NC; 1UNC School of Medicine, Chapel Hill, NC; 2Affiliation not provided.
OBJECTIVE: Surgically extracted sperm is generally expected to have inferior IVF outcomes compared to ejaculated sperm. We sought to evaluate sperm quality and IVF outcomes of cryopreserved epididymal sperm samples obtained from patients with obstructive azoospermia (OA) via office-based MIESA. We report sample characteristics and compare fertility outcomes of MIESA patients who underwent IVF with intraepididymal sperm injection (ICSI) to a control group of couples who underwent ICSI for unexplained infertility with fresh, normal ejaculated sperm samples.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The MIESA is performed in the office with oral or intravenous sedation using only loupe magnification. Samples are cryopreserved for later IVF/ICSI. Epididymal sperm is extracted in the same manner as an obliterate microsurgical epididymal aspiration (MESA), except without the need for general anesthesia, an operating microscope, or complete epididymal exposure. We analyzed MIESA samples for sperm quality/quantity and compared IVF cycle outcomes to a computer-generated control group of age-matched females who underwent IVF/ICSI for unexplained infertility. All couples with identified female factor infertility were excluded. Chi Square and student t test analysis were used to determine statistical significance.

RESULTS: 43 MIESA procedures were performed between December 2013 and July 2018. Causes of OA included vasectomy (35%), failed vasectomy reversal (55%), congenital bilateral absence of the vas deferens (16%), and other (6%). High quality MIESA samples were obtained with a mean retrieved total motile sperm count of 13.7 million which were cryopreserved in 1.6 vials. Mean semen parameters of the controls were all within normal limits. The mean female partner ages were 34.0 and 33.3 years (p = 0.45) for the MIESA group and controls, respectively. With the primary embryo transfer, 53.5% of MIESA couples achieved a live birth compared to 48.8% of controls (p = 0.67). There was no significant difference in the fertilization rate (70.7% vs 78.1%, p = 0.06) or the blastulation rate (58.9% vs 62.0%, p = 0.59) between the MIESA and control groups, respectively. The cumulative birth rate, defined as the combined fresh and subsequent frozen embryo transfer from the same IVF cycle was 79% in the MIESA group compared to 61% in the control group (p = 0.13) with an average of 1.72 and 1.54 transfers per live birth, respectively.

CONCLUSIONS: MIESA provides high-quality cryopreserved sperm samples for men with OA. IVF/ICSI outcomes, including fertilization rate, blastulation rate, and live birth rate, were noninferior to a comparison group of controls with female partners ages all within normal limits. The mean female partner ages were 34.0 and 33.3 years (p = 0.45) for the MIESA group and controls, respectively. With the primary embryo transfer, 53.5% of MIESA couples achieved a live birth compared to 48.8% of controls (p = 0.67). There was no significant difference in the fertilization rate (70.7% vs 78.1%, p = 0.06) or the blastulation rate (58.9% vs 62.0%, p = 0.59) between the MIESA and control groups, respectively. The cumulative birth rate, defined as the combined fresh and subsequent frozen embryo transfer from the same IVF cycle was 79% in the MIESA group compared to 61% in the control group (p = 0.13) with an average of 1.72 and 1.54 transfers per live birth, respectively.

O-59 Monday, October 14, 2019 11:45 AM

GONADAL END ORGAN EFFECTS IN MALE TO FEMALE TRANSGENDER PATIENTS ON HORMONAL THERAPY. Priyanka Bearelly, MD, Jaromir Slama, MD, Robert D. Oates, M.D. Boston University School of Medicine, Boston, MA.

OBJECTIVE: The objective of this study is to investigate changes in spermatogenesis as a consequence of the quantitative reduction in testosterone production and action and/or possible direct effects of estrogen on seminiferous epithelium. This unique patient population provides this unusual opportunity because of the high volume of individuals undergoing gender confirmation surgery.

DESIGN: An IRB-approved retrospective review of 35 neovaginoplasty patients and 21 patients who underwent bilateral orchietomy as a stand-alone procedure was conducted. Testicular histology of 56 patients (112 testicles) was examined by the investigators, and predominant patterns of spermatogenesis were recorded. The primary objective, retroactively, is to determine if spermatogenesis has been affected by estrogen therapy and testosterone blockers (spironolactone). Present study, a prospective, IRB-approved analysis is being conducted on these same two patient populations comparing IVF outcomes with normal histology. As part of the early prospective cohort, 6 patients underwent bilateral orchietomy, and 2 patients underwent neovaginoplasty. Intraoperative testicular wet prep findings were recorded as number of spermatozoa per high powered field.

RESULTS: Retrospectively, of the 35 neovaginoplasty patients, the following histology was seen: 2 with complete absence of germ cells, 3 with mild hypospermatogenesis, 8 with SMA only, and the remaining with a combination of SMA with mild (4), moderate (5), and severe (11) hypospermatogenesis. Of the 21 orchietomy patients, the following histology was seen: 4 with SMA only, and the remaining with a combination of SMA and mild (4), moderate (6), and severe (7) hypospermatogenesis. In our early prospective data set, 2 out of 8 patients had spermatozoa seen on intraoperative wet prep (T:70, E2:168 : T18, E2:120).

CONCLUSIONS: Estrogen therapy and testosterone blockers (spironolactone) are routinely used in combination in MTF individuals to suppress testosterone and its androgenic effects while promoting estrogenic bodily changes. The consequent reduction in spermatogenesis is quite variable, as clearly demonstrated by the unexpected results of the retrospective review—meiotic progression was uniformly impaired while a decrease in the total number of germ cells per tubule was not uncommon. We envision our nascent prospective study to allow us to formulate some mechanistic models of biological causality.

O-60 Monday, October 14, 2019 12:00 PM

THE UTILITY OF SPERM CRYOPRESERVATION AT THE TIME OF VASECTOMY REVERSAL. Jessica A. Marinaro, MD, a Robert D. Oates, M.D., b Russell P. Hayden, M.D., a Paul Shin, M.D., c Cigdem Tanrikut, M.D., d MedStar Georgetown University Hospital, Washington, DC; Weill Cornell Medicine, New York, NY; e Shady Grove Fertility, Washington DC, DC; f Shady Grove Fertility, Rockville, MD.

OBJECTIVE: To evaluate the utility of cryopreserving sperm at the time of vasectomy reversal.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: From April 2016 through December 2018, 26 men underwent vasectomy reversal. Sperm cryopreservation is routinely offered at the time of vasectomy reversal at our institution. We sought to assess utilization of cryopreserved sperm by those men with early or late failure.

RESULTS: Of 26 patients presenting for vasectomy reversal, 22 elected to cryopreserve sperm (85%); sperm were obtained for freezing from the vasal fluid (N=3), epididymal fluid (N=7), or via testicular biopsy (N=12). Three patients were lost to follow-up post-operatively. Of the 23 who presented for post-procedure follow-up, 19 either had semen analyses (SAs) with motile sperm or a live birth (83% success rate). There were 2 early failures and 4 late failures; all failures had elected to cryopreserve sperm at the time of initial reversal. Two of the six individuals with vasectomy reversal failure elected to use cryopreserved sperm for IVF-ICSI, both resulting in ongoing clinical intrauterine pregnancies.

CONCLUSIONS: Of those patients who experienced vasectomy reversal failure, 1/3 elected to use cryopreserved sperm that had been procured at the time of initial reversal. Cryopreservation of sperm at the time of vasectomy reversal should be routinely offered given potential for early or late failure as a means of avoiding added expense and potential morbidity of future surgical sperm retrieval.

NUTRITION

O-61 Monday, October 14, 2019 10:45 AM

PRECONCEPTION MARIJUANA USE, ANOVULATION, AND PREGNANCY OUTCOMES. Sunni L. Mumford, PhD,a Kerry S. Flannagan, PhD,a Jeannie G. Radoc, BS,b Torie C. Flowed, MD,c Keewon Kim, PhD,d Alexandra C. Purdue-Smith, PhD,e Jessica R. Zolton, DO,e Lindsey A. Sjaarda, PhD,e Neil J. Perkins, PhD,e Jessica R. Zolton, DO,b Lindsey A. Sjaarda, PhD,c Neil J. Perkins, PhD,e Enrique F. Schisterman, PhD,a Jessica A. Marinaro, MD,a Robert M. Silver, MD, d Shady Grove Fertility, Washington, DC; e Weill Cornell Medicine, New York, NY; f University of Utah, Salt Lake City, UT.

OBJECTIVE: To investigate changes in spermatogenesis as a consequence of the quantitative reduction in testosterone production and action and/or possible direct effects of estrogen on seminiferous epithelium. This unique patient population provides this unusual opportunity because of the high volume of individuals undergoing gender confirmation surgery.

DESIGN: An IRB-approved retrospective review of 35 neovaginoplasty patients and 21 patients who underwent bilateral orchietomy as a stand-alone procedure was conducted. Testicular histology of 56 patients (112 testicles) was examined by the investigators, and predominant patterns of spermatogenesis were recorded. Present study, a prospective, IRB-approved analysis is being conducted on these same two patient populations comparing IVF outcomes with normal histology. As part of the early prospective cohort, 6 patients underwent bilateral orchietomy, and 2 patients underwent neovaginoplasty. Intraoperative testicular wet prep findings were recorded as number of spermatozoa per high powered field. 

RESULTS: Retrospectively, of the 35 neovaginoplasty patients, the following histology was seen: 2 with complete absence of germ cells, 3 with mild hypospermatogenesis, 8 with SMA only, and the remaining with a combination of SMA with mild (4), moderate (5), and severe (11) hypospermatogenesis. Of the 21 orchietomy patients, the following histology was seen: 4 with SMA only, and the remaining with a combination of SMA and mild (4), moderate (6), and severe (7) hypospermatogenesis. In our early prospective data set, 2 out of 8 patients had spermatozoa seen on intraoperative wet prep (T:70, E2:168 : T18, E2:120).

CONCLUSIONS: Estrogen therapy and testosterone blockers (spironolactone) are routinely used in combination in MTF individuals to suppress testosterone and its androgenic effects while promoting estrogenic bodily changes. The consequent reduction in spermatogenesis is quite variable, as clearly demonstrated by the unexpected results of the retrospective review—meiotic progression was uniformly impaired while a decrease in the total number of germ cells per tubule was not uncommon. We envision our nascent prospective study to allow us to formulate some mechanistic models of biological causality.

不得使用
OBJECTIVE: Marijuana is the most widely used illicit drug in the US, with legalization further increasing both medical and recreational use. Studies evaluating self-reported use yield mixed results about whether marijuana is harmful in pregnancy. However, there is concern for underreporting due to the stigma of marijuana use as it is not federally legalized. Our aim was to examine associations between preconception marijuana use, via both self-report and urinary tetrahydrocannabinol (THC), and fecundability, live birth, and pregnancy loss. We also evaluated these relationships in the context of ovulatory function and anti-müllerian hormone (AMH).

DESIGN: A prospective cohort of 1212 women enrolled in the EAGeR trial, aged 18-40 years, with regular menstrual cycles and a history of 1-2 prior pregnancy losses.

MATERIALS AND METHODS: Women were screened for urinary THC up to 2 time points prior to conception using a homogenous enzyme immunoassay (Randox Laboratories) and reported past year marijuana use at baseline. Women were followed for up to 6 cycles while attempting pregnancy. Anovulation was assessed using fertility monitors and, where available in the first 2 cycles of follow-up, supplemented with urinary pregnanediol glucuronide measures. Serum AMH was measured at the baseline visit. Cox proportional hazard regression was used to calculate fecundability odds ratios (FOR), and log-binomial regression was used to estimate risk ratios (RR) for live birth, pregnancy loss, anovulation, and low AMH (≤1.0 vs >1.0 ng/ml) adjusting for age, race, BMI, education, smoking, alcohol, and antidepressant use.

RESULTS: Of the 33 (2.7%) women who screened positive for THC, only 14 self-reported marijuana use. A total of 62 women (5.1%) screened positive for THC or self-reported use in the year prior. Women positive for urinary THC or with self-reported marijuana use had reduced fecundability (FOR 0.53, 95% CI 0.33, 0.86). No associations were observed with live birth (RR 0.71; 95% CI 0.41, 1.22) or pregnancy loss (RR 0.78; 95% CI 0.28, 2.18). Further, no associations were observed with anovulation (RR 0.94, 95% CI 0.51, 1.73) or with low AMH (RR 1.25, 95% CI 0.71, 2.20).

CONCLUSIONS: Women who screened positive for THC during preconception, or self-reported use during the past year, had reduced fecundability, though no associations were observed with live birth or pregnancy loss. Associations with reduced fecundability are not likely to be explained by anovulation or AMH levels, suggesting that other mechanisms may be at play. Further investigations are needed to confirm these observations, determine potential mechanisms and what duration and dose of marijuana may negatively impact fecundity.

SUPPORT: Intramural Research Program, Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development.

O-63 Monday, October 14, 2019 11:15 AM

THE ROLE OF MATERNAL PRECONCEPTION VITAMIN D STATUS IN HUMAN OFFSPRING SEX RATIO. Alexandra C. Purdue-Smith, PhD,a Keewin Kim, PhD,Carrie J. Nobles, PhD,b Enrique F. Schisterman, PhD,c Karen C. Schliep, PhD,b Neil J. Perkins, PhD,a Lindsey A. Sjaarda, PhD,d Josh Freeman, MPH,e Sonia L. Robinson, PhD,d Jeannie G. Radoc, BS,a James L. Mills, MD,MS,a Robert M. Silver, MD,f Sunni L. Mumford, PhD,a NICHD, Bethesda, MD;b University of Utah, Salt Lake City, UT;e Epidemiology Branch, DIPHR, NICHD, NIH, Bethesda, MD;f National Institutes of Child Health and Human Development, Bethesda, MD; National Institute of Child Health and Human Development, Bethesda, MD.

OBJECTIVE: Experimental data suggests that maternal inflammation is specifically detrimental to the implantation or survival of male embryos, which may contribute to sex ratio reduction on the population scale. However, it is currently unknown whether other factors associated with both pregnancy and inflammation, such as vitamin D status, are associated with altered offspring sex ratio. Our objective was to therefore evaluate the association of preconception serum 25-hydroxyvitamin D levels (25(OH)D) and male live birth among reproductive-age women attempting pregnancy.

DESIGN: This was a prospective secondary analysis of the Effects of Aspirin in Gestation and Reproduction trial, which included 1,228 reproductive-age women attempting to conceive.

MATERIALS AND METHODS: 25(OH)D and high sensitivity C-reactive protein (hsCRP) levels were measured in serum at baseline. Participants were classified as vitamin D sufficient versus insufficient [25(OH)D ≥ 30 vs. <30 ng/mL]. Fetal sex was ascertained by medical record abstraction among live births and by chromosomal analysis among clinical pregnancy losses. We estimated unadjusted and adjusted relative risks (RRs) and 95% confidence intervals (CIs) for male live birth and pregnancy with a male fetus according to preconception vitamin D status using generalized estimating equations of log-binominal regression with robust standard errors.

RESULTS: Among 1,094 women who completed follow-up, the proportion of male live births was 24% (n=136) and 30% (n=156) in the vitamin D insufficient and sufficient groups, respectively. In multivariable models, women in the vitamin D sufficient group were 25% (RR = 1.25; 95% CI = 1.02, 1.52) more likely to have a live-born male infant compared to the insufficient group. These associations were stronger among women with high versus low levels of preconception hsCRP (>1.95 ng/mL: RR = 1.44;
95% CI = 1.01, 2.05, versus ≤ 1.95 ng/mL RR = 1.08; 95% CI = 0.81, 1.43), a marker of systemic low-grade inflammation. In analyses utilizing available karyotype data from clinical pregnancy losses, sufficient versus insufficient vitamin D was also positively associated with pregnancy with a male fetus (RR = 1.21, 95% CI = 1.01, 1.46). Excess caffeine intake was associated with higher levels of hCG in women with high versus low levels of hCGRR (≥ 1.95 ng/mL: RR = 1.34; 95% CI = 0.96, 1.88 versus ≤ 1.95 ng/mL RR = 1.12; 95% CI = 0.90, 1.39), though not statistically significant.

CONCLUSIONS: Our findings that preconception vitamin D status is positively associated with male live birth and pregnancy with a male fetus, particularly among women with elevated inflammation, suggest that sufficient levels of preconception vitamin D may mitigate maternal inflammation that would otherwise be detrimental to the implantation or survival of male conceptions in utero. These findings highlight the importance of vitamin D in reproduction and implicate a novel factor associated with altered offspring sex ratio in humans. SUPPORT: This research was supported by the Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (National Institutes of Health, Bethesda, MD, USA; contract numbers HHSN276200603423, HHSN267200603424, and HHSN267200603426).

O-64 Monday, October 14, 2019 11:30 AM
CAFFEINATED BEVERAGE INTAKE AND SERUM CAFFEINE METABOLITES AND RISK OF PREGNANCY LOSS. Alexandra C. Purdie-Smith, PhD,a Keewan Kim, PhD,a Enrique F. Schisterman, PhD,a Karen C. Schliep, PhD,a Neil I. Perkins, PhD,a Lindsey A. Sjardal, PhD,a James L. Mills, MD, MS,a Robert M. Silver, MD,b Victoria C. Andriessen, BS,a Zeina Alkalaf, MPH,a Jeannie G. Radoc, BS,a Sunni L. Mumford, PhD,a NICHD, Bethesda, MD; University of Utah, Salt Lake City, UT; Epidemiology Branch, DIPHR, NICHD, NIH, Bethesda, MD; National Institute of Child Health and Human Development, Bethesda, MD.

OBJECTIVE: According to current ACOG recommendations, moderate intake of caffeine (<200 mg/day) during pregnancy does not increase risk of pregnancy loss, though epidemiologic evidence to support this recommendation is controversial. Our objective was to address limitations of prior studies by evaluating associations of both self-reported intake of caffeinated beverages and preconception and early pregnancy serum caffeine biomarkers and risk of pregnancy loss, while accounting for nausea and vomiting, smoking, and alcohol intake in early pregnancy.

DESIGN: This was a secondary analysis of the EAGeR trial, which included 1,228 reproductive-age women attempting pregnancy during 2007-2011.

MATERIALS AND METHODS: Questionnaires administered at baseline assessed self-reported intake of caffeinated beverages and other demographic and lifestyle variables. During pregnancy, daily questionnaires assessed caffeinated beverage intake, nausea and vomiting, alcohol intake, and smoking. Serum caffeine, paraxanthine, and theobromine were measured at preconception and during the 8th week of gestation. HCG-detected losses occurred prior to ultrasound confirmation and clinical pregnancy losses occurred after ultrasound visualization of a gestation sac. We used Cox proportional hazards regression to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for pregnancy loss according to: 1) baseline caffeinated beverage intake and caffeine biomarkers measured at preconception and the 8th week of gestation, adjusted for baseline factors and; 2) time-varying caffeinated beverage intake during pregnancy adjusted for baseline factors and time-varying nausea and vomiting, alcohol intake, and smoking.

RESULTS: 67%, 28%, and 9% of women reported any preconception intake of caffeinated sodas, coffee, and tea, respectively. Preconception total caffeinated beverage intake of ≥ 2 servings/d was marginally associated with increased risk of any loss (HR = 1.51, 95% CI = 0.98, 2.34), and associations were stronger for hCG-detected losses than for clinical losses. Soda intake was more strongly associated with hCG-detected losses, whereas coffee intake was more strongly associated with clinical losses. Any detectable level of serum caffeine (>0.2 vs. ≤ 0.2 ng/mL) at preconception was strongly associated with hCG-detected loss (HR = 4.36; 95% CI = 1.53, 11.91), but biomarkers measured during the 8th week of gestation were not associated with loss. Further adjustment for nausea and vomiting and other factors that change during early pregnancy showed that caffeinated beverage intake at levels lower than those corresponding to current medical recommendation was positively associated with risk of loss (0 vs. ≥ 1 servings/day HR = 1.73; 95% CI = 1.02, 2.94), particularly among hCG-detected losses (HR = 2.83; 95% CI = 1.08, 7.39).

CONCLUSIONS: Our findings suggest that any level of caffeine intake during pregnancy may increase risk of pregnancy loss, particularly in the first 8 weeks of gestation. Women should be encouraged to avoid caffeine to eliminate caffeine intake during preconception and early pregnancy.

SUPPORT: This research was supported by the Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (National Institutes of Health, Bethesda, MD, USA; contract numbers HHSN267200603423, HHSN267200603424, and HHSN267200603426). Jeannie G. Radoc was supported by the NIH Medical Rehabilitation Research and Rehabilitation Training Program, and the NIH and generous contributions to the Foundation for the NIH from the Doris Duke Charitable Foundation (DDCFC Grant # 2014194), Genentech, Elsevier, and other private donors.

O-65 Monday, October 14, 2019 11:45 AM
LEPTIN IS A MEDIATOR IN THE ASSOCIATION BETWEEN PERCENT BODY FAT AND DECREASED AMH AMONG HEALTHY WOMEN. Jasmine Aly, MD,a Elizabeth A. DeVilbiss, PhD,b Sunni L. Mumford, PhD,a Micah J. Hill, DO,a Alan H. DeCherney, MD,a Laura Zalles, MD,a Neil J. Perkins, PhD,a Robert M. Silver, MD,a Enrique F. Schisterman, PhD,a Program in Reproductive Endocrinology and Gynecology, NICHD, NIH, Bethesda, MD; National Institute of Child Health and Human Development, Epidemiology Branch, DIPHR, NICHD, NIH, Bethesda, MD; Cooper University Hospital, Department of Obstetrics and Gynecology, Camden, NJ; University of Utah, Salt Lake City, UT.

OBJECTIVE: While obesity is associated with decreased serum AMH, the mechanism by which this occurs is unknown. Studies have found that increased adipokines produced in the adipose tissue, such as leptin, can directly inhibit ovarian function. A recent study by our group found that increases in leptin were associated with lower serum AMH. Because percent body fat and leptin are closely related there is a need to understand the impact of percent body fat on AMH, and to what extent this relationship is driven by leptin. We hypothesize that increased leptin is associated with decreased AMH and that leptin is a direct mediator of this relationship.

DESIGN: Prospective analysis of 259 women aged 18–44 years from western New York State, followed for up to 2 menstrual cycles.

MATERIALS AND METHODS: Serum AMH and leptin were measured five to eight times per cycle for one (n = 9) or two (n = 250) cycles per woman. Participant characteristics and mean AMH hormone levels were examined by tertile of average leptin over 2 cycles (First leptin tertile: 4.1-1.42 ng/mL; Second tertile: 14.4-29.8 ng/mL; Third tertile: 29.9-563 ng/mL). 248 women participated in a dual energy absorptiometry (DXA) scan to measure fat and lean mass from which total percent body fat and percent truncal fat were derived. Using the product method, a mediation analysis was performed for percent body fat (exposure), leptin (mediator), and serum AMH (outcome) to determine the extent to which leptin mediates the association between body fat and AMH. Marginal structural models with inverse probability of exposure weights were used to relate body fat to leptin (mediator model) and body fat and leptin to serum AMH at the next visit (outcome model). The mediator model was adjusted for FSH, LH, estrogen, and progesterone, and the outcome model was adjusted for age, smoking status, caloric intake, and physical activity.

RESULTS: Overall, we observed an inverse relationship between percent body fat and serum AMH, such that for each 10% increase in body fat there was a 14% decrease in AMH (95% CI -24.5- -2.1). Mediation analysis results showed that the 14% decrease in AMH was mostly explained by leptin (indirect effect -7.7%, 95% CI -11.6, -3.7), though some of the decrease was also due to other non-leptin mediated pathways (direct effect -5.7%, 95% CI -18, 8.3).

CONCLUSIONS: Among healthy women, higher body fat and serum leptin were both associated with lower AMH concentrations. The inverse relationship between percent body fat and AMH is largely mediated by leptin.

SUPPORT: This research was supported by the Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (National Institutes of Health, Bethesda, MD, USA; contract numbers HHSN275200403394C HHSN275201100002I, and Task I HHSN275000001), and the Program in Reproductive and Adult Endocrinology, NICHD, NIH.
OMEGA-3 FATTY ACID SUPPLEMENTATION AND FECUNDABILITY. Jamie Stanbiser, M.D.,* Anne Marie Jukic, Ph.D.,* Anne Z. Steiner, MD, MPH “University of North Carolina, Chapel Hill, NC; *National Institute of Environmental Health Sciences, Durham, NC; ‡Duke University Medical Center, Durham, NC.

OBJECTIVE: Omega-3 fatty acids supplementation in animal models have been shown to alter prostaglandin biosynthetic pathways in the ovary and endometrium, and thereby improve folliculogenesis, oocyte maturation, embryo quality, and implantation. However, little is known about the effects of omega-3 supplementation on human fecundity. We sought to determine the association between omega-3 fatty acid supplementation and fecundability, the probability of natural conception in a given menstrual cycle.

DESIGN: Secondary data analysis of Time to Conceive (TTC), a prospective, time to pregnancy cohort study.

MATERIALS AND METHODS: In TTC, women aged 30 – 44 years, trying to conceive <3 months, with no history of infertility were followed for up to one year of pregnancy attempt using standardized pregnancy testing. While attempting to conceive, women daily recorded intercourse, menstrual cycle events, and vitamin, supplement, and medication intake using the Cerner Multum Drug Database. For this analysis, supplements and vitamins containing omega 3 (for example: docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), prenatal vitamin formulations including omega 3, and fish oil) were identified. The percentage of days in a given menstrual cycle on which a woman took omega-3 supplements was calculated, and, based on the Akaike Information Criterion, a cut-off value of 20% was used to dichotomize omega-3 use in each cycle. A positive urinary pregnancy test was used to define conception. A discrete-time Cox proportional hazards model was used to calculate the fecundability ratio, adjusting for age, obesity, history of prior pregnancy, race, and Vitamin D intake in the cycle.

RESULTS: Of 1036 women enrolled in TTC comprising 4,775 cycles, 136 women and 2,265 cycles were missing daily diary data and were excluded. 900 women comprising 2,510 cycles were analyzed. ≥3.11 years. Women taking omega-3 supplements were younger, thinner, and more likely to be nulligravid and white compared to women not taking omega-3. After adjusting for age, obesity, previous pregnancy, race, and Vitamin D intake, women taking omega-3 supplements had 1.83 (95% CI 1.42, 2.35) times the probability of conceiving in a given menstrual cycle compared to women not taking omega-3 supplements.

CONCLUSIONS: These data suggest omega-3 supplementation significantly increases the probability of a woman conceiving. Randomized controlled trials are needed to further investigate the benefits from omega-3 supplementation for women trying to conceive naturally.

Reference: N/A.

SUPPORT: N/A.

OVARIAN STIMULATION

O-67 Monday, October 14, 2019 10:45 AM

A COMPUTERIZED DECISION SUPPORT SYSTEM FOR DAY TO DAY MANAGEMENT OF OVARIAN STIMULATION CYCLES DURING IN VITRO FERTILIZATION. Gerard S. Letterie, DO, Andrew MacDonald, MS Seattle Reproductive Medicine, Seattle, WA.

OBJECTIVE: The purpose is to describe a computer algorithm designed for IVF management and to assess accuracy in decision making during ovarian stimulation for IVF when compared to evidence based decisions by the clinical team.

DESIGN: Evaluation study of novel software; comparative; quantitative.

MATERIALS AND METHODS: Data was in the form of IVF cycles. Our data set included estradiol concentrations (pg/ml); ultrasound measurements of follicle diameters in 2 dimensions in mm; cycle day and dose of recombinant FSH during ovarian stimulation for IVF. In a pilot study we evaluated 5 predictive analytics including classification and regression trees, random forests, support vector machines, logistic regression and neural networks. We then developed a hybrid algorithm for automated prediction of 4 decisions critical to management during ovarian stimulation: (1) Stop the cycle (trigger or cancel) or (2) continue and return for follow-up. If decision was to stop, the algorithm added a modifier regarding trigger or cancellation. If the decision was to return, the algorithm identified (3) number of days to follow up and (4) dosage adjustment if needed. Database consisted of 2603 total cycles. (1853 autologous and 750 donor) incorporating 7,376 visits. Seventy percent of the cycles were used for training and validation and 30% for challenge. There were 10,760 data points. We compared DSS performance against evidence based decisions by 12 clinicians. Performance was defined as outcome accuracy or agreement between the clinicians’ decisions and the DSS when challenged using 556 cycles to which the algorithm was naïve (no prior exposure). Algorithms were written in “R” language for stat analysis and data manipulation and converted to C++.

RESULTS: Outcome accuracy of the algorithm, sensitivity and positive predictive value (PPV) for automated prediction are listed in Table 1 for the final trained model on held-out challenge data for the four decisions analyzed.

<table>
<thead>
<tr>
<th>DECISIONS</th>
<th>ACCURACY</th>
<th>SENSITIVITY</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Stop cycle: Trigger or cancel</td>
<td>0.92</td>
<td>0.94</td>
<td>0.95</td>
</tr>
<tr>
<td>(2) Return for follow-up</td>
<td>0.96</td>
<td>0.98</td>
<td>0.97</td>
</tr>
<tr>
<td>(3) Number days to follow-up</td>
<td>0.87</td>
<td>0.89</td>
<td>0.86</td>
</tr>
<tr>
<td>(4) Dosage</td>
<td>0.82</td>
<td>0.96</td>
<td>0.67</td>
</tr>
</tbody>
</table>

CONCLUSIONS: We describe a first iteration, predictive analytic algorithm for decision support of 4 key management decisions during ovarian stimulation for IVF. Algorithm performance for the decisions to trigger/cancel, return and days to follow-up was highly accurate and in concordance with clinical decisions. Dose changes (increase or decrease) were relatively infrequent clinical decisions in the database resulting in the lowest outcome accuracy of the algorithm. This algorithm offers the possibility of improved clinical and cost efficiencies for IVF management.

SUPPORT: None.

O-68 Monday, October 14, 2019 11:00 AM

DUAL TRIGGERING OF FINAL OOCYTE MATURATION IN POOR OVARIAN RESPONDERS: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL. Dalia Khalife, M.D., Johnny Awwad, M.D., HCLD, Suleiman Ghunaïm, M.D., Antoine Abu-Musa, M.D., Christine Beyrouthy, MPH, Ghina Said Ghazeeri, M.D. American University of Beirut Medical Center, Beirut, Lebanon.

OBJECTIVE: Women with POR (Bologna criteria) manifest a very low follicular response to controlled ovarian stimulation irrespective of the stimulation protocol utilized. Dual triggering of oocyte maturation was shown to improve follicle collection yield and oocyte maturation in women with predicted normal ovarian response. These benefits have been attributed to the GnRH-induced FSH surge believed to promote oocyte nuclear maturation and cumulus expansion. The aim of the study is to show whether the co-administration of a GnRH agonist and hCG for final oocyte maturation improve oocyte collection and maturation rates in women with poor ovarian response (POR) compared with hCG alone.

DESIGN: This is an ongoing prospective randomized controlled trial seeking to randomize 140 women with POR undergoing IVF/ICSI treatment into receiving a dual trigger for final oocyte maturation compared with conventional hCG, between May 2018 and December 2019.

MATERIALS AND METHODS: Women with POR (Bologna criteria) were randomized to receive either a combination of 0.3 mg Triptorelin subcutaneously (Decapeptyl; Ipsen Beaufour; Denmark) and 10,000 IU hCG subcutaneously (Choriomon; IPSA Pharmaceuticals; Switzerland) or 10,000 IU hCG alone. Primary outcomes were oocyte collection and maturation rates. Secondary outcomes were clinical and ongoing pregnancy rates. Chi Square analysis was utilized for categorical data and student t test for continuous variables. A p <0.05 was considered for statistical significance.

RESULTS: Sixty-eight patients have been recruited to this point with a cycle cancelation of 7.35% (5/68). A total of 63 patients were randomly allocated to the dual trigger (n=28) and hCG alone (n=35) groups. Baseline demographic and stimulation characteristics were comparable between the two groups. The total number of oocytes (4 vs. 4.2; p=0.65), number of mature oocytes (3.1 vs. 3.2; p=0.81), and number of 2PN zygotes (2.6 vs.
OBJECTIVE: Premature luteinization or early elevation in progesterone (P4) levels is often observed in patients who undergo a GnRH-antagonist protocol for controlled ovarian hyper stimulation (COH). High levels of P4 have been shown to impact endometrial receptivity which might decrease pregnancy rates. No difference in P4 levels has been described in per embryo transfer, the clinical pregnancy rates (15.2 vs. 12.6; p=0.90) and ongoing pregnancy rates (13.8 vs 12.6; p=0.63) showed no statistical differences.

CONCLUSIONS: There was no significant increase in oocyte collection or maturation rates following dual triggering of final oocyte maturation compared with hCG alone in women with POR. POR (Bologna criteria) represents a subgroup of women with a very poor pregnancy prognosis and also a very challenging fertility management. Although the preliminary findings of this trial do not seem to hold promises in favor of an improved outcome with dual triggering of oocyte maturation in this subgroup of women, conclusive evidence are expected only following completion of the recruitment period.

SUPPORT: None.

OBJECTIVE: Premature luteinization or early elevation in progesterone (P4) levels is often observed in patients who undergo a GnRH-antagonist protocol for controlled ovarian hyper stimulation (COH). High levels of P4 have been shown to impact endometrial receptivity which might decrease pregnancy rates. No difference in P4 levels has been described in per embryo transfer, the clinical pregnancy rates (15.2 vs. 12.6; p=0.90) and ongoing pregnancy rates (13.8 vs 12.6; p=0.63) showed no statistical differences.

CONCLUSIONS: There was no significant increase in oocyte collection or maturation rates following dual triggering of final oocyte maturation compared with hCG alone in women with POR. POR (Bologna criteria) represents a subgroup of women with a very poor pregnancy prognosis and also a very challenging fertility management. Although the preliminary findings of this trial do not seem to hold promises in favor of an improved outcome with dual triggering of oocyte maturation in this subgroup of women, conclusive evidence are expected only following completion of the recruitment period.

SUPPORT: None.
OBJECTIVE: The use of dual trigger for final oocyte maturation using GnRH agonists in conjunction with human chorionic gonadotropin (hCG) has been shown to reduce the risk of developing ovarian hyperstimulation syndrome (OHSS), largely by allowing a lower dose of hCG to be used. It has been well established that absorption of hCG varies by body mass index (BMI), yet there have been no studies published correlating BMI with minimum hCG dose requirement to achieve a targeted post-trigger serum hCG (post b-hCG) level. In previous studies, optimal oocyte maturity with controlled ovarian hyperstimulation (COH) was shown to occur at a minimum post b-hCG value of 50 mIU/mL. This study aims to establish minimum hCG dose requirements per unit BMI to achieve specific post-b-hCG levels. DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All charts between 1/2009 and 3/2019 were reviewed to identify patients who had undergone COH stimulation at our institution and had received a dual trigger (leuprolide acetate 2mg and 4mg and variable doses of hCG from 1,000 to 10,000 units). The total dose of hCG administered was normalized by BMI, and post b-hCG levels were analyzed. Direct correlation analysis was used to analyze the minimum hCG dose required to achieve a specific post b-hCG level based on BMI.

RESULTS: 129 IVF cycles met inclusion criteria, derived from 3655 women aged 14-49 years old with a BMI range of 15.54 kg/m². The mean BMI of the cohort was 24.4 kg/m². There was a direct correlation between BMI and post b-hCG levels. This is also applicable for those patients who are not candidates for the provider to titrate the desired post b-hCG value in order to achieve the absorption and physiologic response to hCG is independent of GnRH doses, allowing for creation of a dosing scale based on BMI. However, as received a dual trigger, as this cohort encompassed a wide range of hCG dose requirements per unit BMI to achieve specific post b-hCG levels.

CONCLUSIONS: Our findings suggest that a dual trigger with a sliding hCG scale in accordance with BMI can be utilized with accuracy to predict a specific post b-hCG value. Our current study analyzed only patients who received a dual trigger, as this cohort encompassed a wide range of hCG doses, allowing for creation of a dosing scale based on BMI. However, as the absorption and physiologic response to hCG is independent of GnRH agonist administration, these results can be extrapolated for use in hCG only trigger cycles. This dosing protocol for hCG in dual triggers allows the provider to titrate the desired post b-hCG value in order to achieve optimum oocyte maturation while minimizing side effects and risk of OHSS. This is also applicable for those patients who are not candidates for a pure GnRH agonist trigger and are at risk of OHSS with traditional higher-dose hCG trigger.


### Post-trigger serum b-hCG range (mIU/mL) | Required dose of HCG (units) per point BMI
---|---
15-19 | 58.4
20-24 | 59.7
25-29 | 62.8
30-34 | 68.7
35-39 | 71.6
40-44 | 77.7
45-49 | 79.5
50-54 | 84.1
55-59 | 87.1
60-64 | 98.4
65-69 | 105.1
70-74 | 108.5
75-79 | 120.4


O-72 Monday, October 14, 2019 12:00 PM

**EFFECT OF DEHYDROEPIANDROSTERONE (DHEA) SUPPLEMENTATION ON INTRACYTOPLASMIC SPERM INJECTION OUTCOME IN INFERTILE WOMEN WITH ANTICIPATED NORMO-OVARIAN RESPONSE.** Mustafa Khodry, MD, 1 Hazem Ahmed, MD, 1 Abd El-Naser Ali, MD, 1 Sayed Taha, MD, 1 Mohammed Fawzy, MD, 1 Ahmed M. Abbas, MD 1Department of Obstetrics & Gynecology, Faculty of Medicine, South Valley University, Qena, Egypt; 2Inb-Sina and Banon IVF Centers, Sohag, Egypt; 2Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: To study the effect of dehydroepiandrosterone (DHEA) supplementation in infertile women with expected normo-ovarian response before intracytoplasmic sperm injection (ICSI) procedure.

DESIGN: Randomized, double-blind, placebo-controlled study.

MATERIALS AND METHODS: All women attended the ART unit for first planned fresh embryo transfer ICSI cycles with expected normo-ovarian response were invited to participate in the study. Women were randomized in a 1:1 ratio to either group I (DHEA group) received two capsules of DHEA 25 mg (DHEA), MRM Co., USA) or group II (placebo group) received two placebo capsules has the same shape, color and consistency starting eight weeks before the date of controlled ovarian hyperstimulation (COH) and continued throughout the whole stimulation period till the HCG triggering day. The primary outcome of the study was the mean antral follicle count (AFC) after eight weeks of treatment. The secondary outcomes included the duration of gonadotrophins stimulation in days, the dose of gonadotrophins, the number and quality of retrieved oocytes, the endometrial thickness at HCG triggering day, the fertilization rate, implantation rate, clinical pregnancy rate (CBR) and the adverse effects of the medications.

RESULTS: We randomly assigned 108 women into both groups (54 in each arm). No significant difference between both groups regarding the baseline demographic characteristics or serum AMH levels. The mean basal AFC after eight weeks of DHEA supplementation was (10.2 ± 4.4 vs. 13.8 ± 5.3, respectively, p = 0.001), while no significant difference in the placebo group (10.4 ± 4.5 vs. 10.7 ± 4.6, respectively, p = 0.24). No significant difference in the total gonadotrophins doses in both groups (p = 0.64). DHEA group had statistically significantly higher total number of retrieved oocytes (15.3 ± 6.20 vs. 12.9 ± 5.70, p = 0.001), and the percentage of good quality oocytes (70.6% vs. 52.3%, p = 0.007). No difference between both groups regarding the fertilization rate (62.4% vs. 51.7%, p = 0.13), implantation rate (23.1% vs 20.4%, p = 0.52), and the clinical pregnancy rate (37.0% vs. 35.2%, p = 0.41). Regarding adverse effects, no patients reported major adverse effects during the study period. Only two patients from the DHEA group complained of hot flushes after four weeks of the supplement not interfering with their daily activities.

CONCLUSIONS: The use of DHEA in anticipated normal responders eight weeks before ICSI could be valuable in increasing the AFC, the number and quality of the retrieved oocytes relative to placebo, however no improvement in the fertilization, implantation, and clinical pregnancy rates.

**SUPPORT:** None.

### PREIMPLANTATION GENETIC TESTING

O-73 Monday, October 14, 2019 10:45 AM

**PGT FOR ANEUPLOIDY IMPROVES PERINATAL OUTCOMES COMPARED WITH FET ALONE: AN ANALYSIS OF THE 2014 AND 2015 SART DATA.** Kristin Van Heerum, MD, 1 Channing Burks, MD, 1 Kerry S. Flannagan, PhD, 2 Sunni L. Mumford, PhD, 2 Alexandra C. Purdue-Smith, PhD, 2
OBJECTIVE: Clinical studies have shown a difference in the incidence of preterm delivery (PTD) and low birthweight (LBW) following IVF compared with natural conception. In recent years, frozen embryo transfer (FET) and pre-implantation genetic testing (PGT) have become increasingly common. However, few studies have evaluated the effects of embryo biopsy itself on perinatal outcomes. This study aims to assess the differences in perinatal outcomes of autologous FET using embryos that underwent biopsy for PGT versus those that did not.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The Society for Assisted Reproductive Technology (SART) database was used to identify day 5 FET cycles that did and did not undergo PGT from 2014-2015. Log binomial regression models were used to assess associations between embryo biopsy and pregnancy/outcome. A sub-analysis assessed the effects of PGT for aneuploidy (PGT-A) or PGT for monogenic disorders (PGT-M) on perinatal outcomes versus no biopsy. Models were adjusted for covariates including maternal age, race, BMI, smoking, prior IVF cycles, prior preterm/full-term births and cause of infertility. LBW was the primary outcome.

RESULTS: The incidence of LBW among no biopsy patients (N=74970) and biopsy patients (N=103672) was 33.9% and 35.1%, respectively (P<0.01). The mean number of embryos transferred was 1.6 and 1.2 (P<0.01) for non-biopsy and biopsy, respectively. Compared to patients whose embryos were not biopsied, patients whose embryos were biopsied were significantly more likely to have a clinical pregnancy (64.9 vs. 57.7%, adjusted risk ratio (aRR) 1.16, 95% confidence interval (CI) 1.13,1.19) and live birth (56.2 vs. 46.8%, aRR 1.25, 95% CI 1.21,1.3). The incidence of multiple gestation was, unsurprisingly, higher in the non-biopsy group (21.4 vs. 12.6%, aRR 0.68, 95% CI 0.60, 0.77). Of the live births (N=18,457 no biopsy, N=5,815 biopsy), the incidence of LBW was significantly lower following transfer of biopsied embryos versus those that were not biopsied (16.5 vs. 23.8%, aRR 0.74, 95% CI 0.66,0.83). The odds of PTD was also significantly lower in the biopsy group compared to the non-biopsy group (16.0 vs. 21.5%, aRR 0.79, 95% CI 0.71,0.88). These differences persisted when comparing PGT-A only versus no biopsy (LBW aRR 0.73, 95% CI 0.65, 0.83; PTD aRR 0.79, 95% CI 0.71, 0.89), but not PGT-M versus no biopsy (LBW aRR 1.08, 95% CI 0.73, 1.58; PTD aRR 0.93, 95% CI 0.63, 1.38).

CONCLUSIONS: The higher incidence of PTD and LBW in the non-biopsy group compared with the biopsy group can likely be, at least in part, explained by the larger proportion of multiple gestation pregnancies seen in that group. PGT-A, by reducing the number of embryos transferred, also incurs improved perinatal outcomes. Further analysis will assess for the contribution of multiple gestations to the differences in perinatal outcomes. However, it is overall reassuring that embryo biopsy is not associated with any negative effects on perinatal outcomes in FETs, and may potentially be associated with improved outcomes.

SUPPORT: None.

O-74 Monday, October 14, 2019 11:00 AM

DOES PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) HARM EMBRYOS? NO—A MULTICENTER, PROSPECTIVE, BLINDED, NON-SELECTION STUDY EVALUATING THE PREDICTIVE VALUE OF AN ANEUPLOID DIAGNOSIS AND IMPACT OF BIOPSY.

Ashley W. Tieg, MD, a Christina V. Whitehead, BSN, RN, a Shelby A. Neal, MD, a Emily K. Osman, MD, a Julia G. Kim, MD, MPH, a Brent M. Hanson, MD, a Emilie Soli, M.D., a George Patounakis, MD, Ph.D, a Jacqueline Gutmann, MD, a Arthur J. Castelbaum, MD, a Richard Thomas Scott, Jr, MD, b Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA; bThe Foundation for Embryonic Competence, Basking Ridge, NJ; c1V1-RMA New Jersey, Basking Ridge, NJ; dSidney Kimmel College of Medicine, Thomas Jefferson University, Philadelphia, PA; e1V1-RMA Florida, Lake Mary, FL; f1V1-RMA Philadelphia, Philadelphia, PA.

OBJECTIVE: Two common concerns regarding PGT-A are: 1) tropho-derm (TE) biopsy may have an adverse effect on embryo reproductive potential, and 2) embryos labeled aneuploid may have the potential to implant and deliver and thus may be wrongly discarded. This study addresses these concerns by 1) comparing implantation rates of the overall study group to a control group, in which biopsy/PGT-A were not utilized, and 2) directly measuring the predictive value (PV) of a diagnosis of embryonic aneuploidy.

DESIGN: Prospective, blinded, non-selection study.

MATERIALS AND METHODS: All study participants underwent ICSI and blastocyst culture. Usable blastocysts underwent TE biopsy then vitrification. In the next cycle, patients underwent single embryo transfer (SET) of the best embryo selected solely on morphology. PGT-A analysis (targeted amplification-NGS-based) was performed only after the clinical outcome was known. Power analysis yielded a required sample size of 257 to detect a whole chromosome aneuploidy rate of 20% and estimate the PV within 5%. Control group (n=1000) consisted of patients having a cryo-SET not using PGT-A. As relates to the impact of biopsy, the sustained implantation rate (SIR) of the study group was compared to the SIR of the control group using logistic regression. As neither had access to PGT-A results, the groups differed only in that embryos in the study group had undergone TE biopsy. The second goal was to determine PVs of both euploid and aneuploid PGT-A results to correctly prognosticate clinical outcomes.

RESULTS: 285 transfers in the non-selection group and 1000 in the control group have known clinical outcomes. The SIRs in the study group (all independent of PGT-A result) were 53%, which is equivalent to that of the controls (54%), demonstrating no detectable detrimental effect of TE biopsy. The PV of an aneuploid result for failure to deliver was 100% - the SIR was 0/50 (0%). The PV for a euploid result was 68% (134 of 197). SIRs of embryos labeled mosaic (6 of 9) and segmental aneuploid (7 of 25) are reported but inadequately powered.

CONCLUSIONS: These data demonstrate that PGT-A results in no detectable adverse impact on clinical outcomes. The PV of an euploid result is sufficiently high that reproductively competent embryos are not being discarded with any demonstrable frequency. The error rate can never be zero, but it must be quite low. This study provides strong evidence regarding the safety of targeted sequencing NextGen PGT-A that may assist clinicians in counseling patients.

SUPPORT: Foundation for Embryonic Competence.

FERTILITY & STERILITY® e31
4,000g. Multivariable generalized estimating equation models were fit to analyze the effect of PGT vs no PGT. Models were adjusted with a priori covariates: donor age; recipient age; BMI; smoking, parity; prior preterm birth; assisted hatching; single ET; and blast transfer. Interaction effect between transfer type (fresh vs frozen) and PGT was tested. Sensitivity analysis of the first cycle per patient was performed.

RESULTS: Of 25,387 included cycles, 2,372 had PGT performed while 23,015 did not. PGT was associated with increased rates of frozen ET (70% vs 41%, P = 0.001), single ET (67% vs 44%, P < 0.001) and blast transfer (87% vs 65%, P = 0.003). Interaction effect between transfer type and PGT was not significant, so the model was fit without an interaction term. Unadjusted rates of live birth and ongoing pregnancy were similar. After adjustment, cycles using PGT significantly increased the probability of a GBO (26.2% vs 23.7%, 1.08 risk ratio (RR), 95% confidence interval (CI) 1.00-1.14). When only the first cycle was tested (n = 24,007), there was a significant interaction between PGT and transfer type with superior outcomes for PGT in frozen ETs but no effect in fresh ETs (Table).

CONCLUSIONS: PGT, as practiced during the most recently available national data in women using donor oocytes, is associated with improved probability of a healthy live birth.


O-76 Monday, October 14, 2019 11:30 AM
PREGNANCY OUTCOMES FOLLOWING IN VITRO FERTILIZATION FROZEN EMBRYO TRANSFER (IVF-FET) WITH OR WITHOUT PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) IN WOMEN WITH RECURRENT PREGNANCY LOSS (RPL): A SART-CORS STUDY. Shweta Bhatt, MD,a Jason Roy, PhD,b Sara S. Morelli, MD, PhD,a Peter McGovern, MD*a Rutgers New Jersey Medical School, Newark, NJ; *Rutgers - Department of Biostatistics and Epidemiology, Piscataway, NJ; †University Reproductive Associates, NJ.

OBJECTIVE: Euploid embryo transfer is thought to optimize outcomes in some couples with infertility, but there is insufficient evidence supporting this approach to management of recurrent pregnancy loss; thus, the aim of this study was to assess the pregnancy outcomes in couples with RPL after use of IVF-FET with PGT-A compared to IVF-FET without PGT-A.

DESIGN: Retrospective cohort study.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Effect of PGT within Fresh ET RR (95% CI) P value</th>
<th>Effect of PGT within Frozen ET RR (95% CI) P value</th>
<th>Interaction P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good birth outcome</td>
<td>0.99 (0.87, 1.12) 0.892</td>
<td>1.23 (1.11, 1.37) &lt;0.001</td>
<td>0.100</td>
</tr>
<tr>
<td>Live birth</td>
<td>1.04 (0.97, 1.11) 0.310</td>
<td>1.18 (1.10, 1.27) &lt;0.001</td>
<td>0.007</td>
</tr>
<tr>
<td>Term</td>
<td>1.04 (0.93, 1.15) 0.507</td>
<td>1.17 (1.05, 1.29) 0.001</td>
<td>0.093</td>
</tr>
<tr>
<td>Clinical pregnancy</td>
<td>1.04 (0.99, 1.10) 0.143</td>
<td>1.16 (1.09, 1.22) &lt;0.001</td>
<td>0.010</td>
</tr>
<tr>
<td>Singleton</td>
<td>1.03 (0.94, 1.12) 0.563</td>
<td>1.17 (1.09, 1.27) &lt;0.001</td>
<td>0.250</td>
</tr>
</tbody>
</table>

MATERIALS AND METHODS: This study included data collected by the Society of Assisted Reproductive Technologies Clinical Outcomes Reporting System (SART-CORS) for IVF-FET cycles between years 2010 through 2016. The experimental group included couples with RPL (strictly defined as a history of 3 or more pregnancy losses) undergoing IVF-FET with or without PGT-A. The analysis was restricted to autologous frozen embryo transfer cycles to better compare outcomes with and without PGT-A.

The primary outcome was live birth rate. Secondary outcomes included clinical pregnancy rate and spontaneous abortion rate. Differences were analyzed using generalized estimating equations (GEE) logistic regression models. GEE were used to account for multiple cycles per patient. Covariates included in the model were age, geographic region, race/ethnicity, and indication for assisted reproductive technologies. Analyses were stratified for age less than 35 years versus older than 35 years.

RESULTS: Of 24,007 IVF-FET cycles from the PGT-A group and 43,811 cycles from the control group were included in the analysis (Table 1). The adjusted odds ratio (OR) comparing IVF-FET with PGT-A versus without PGT-A for live birth outcome was 1.30 (95% CI: 1.24, 1.37) for age < 35 and 2.01 (95% CI: 1.92, 2.11) for age ≥ 35. For clinical pregnancy, the OR was 1.26 (1.20, 1.33) for age < 35 and 1.82 (1.74, 1.91) for age ≥ 35. Finally, for spontaneous abortion, the OR was 0.90 (0.82, 0.98) for age < 35 and 0.79 (0.73, 0.86) for age ≥ 35.

CONCLUSIONS: This is the largest study to date assessing the utility of PGT-A in women with RPL. PGT-A was associated with improvement in live birth, clinical pregnancy, and spontaneous abortion rates in women with RPL, with a larger difference noted in women with age greater than 35 years. Couples with RPL warrant counseling on all management options to reduce subsequent miscarriage, which may include IVF with PGT-A for euploid embryo selection.

Reference: N/A.

SUPPORT: None.

O-77 Monday, October 14, 2019 11:45 AM
CONCURRENCE PRE-IMPLANTATION GENETIC TESTING FOR SINGLE GENE DISORDERS AND ANEUPLOIDY SCREENING FROM A SINGLE TROPHOBLAST (TE) BIOPSY USING TARGETED NEXT GENERATION SEQUENCING (NGS) WITHOUT WHOLE GENOME AMPLIFICATION (WGA). Heather Garney, BS, MPS,a Chaim Jalas, N/A,a Yiping Zhan, Ph.D,a Cara Vega, BS,a Vaidehi Jobanputra, Ph.D,* Richard Thomas Scott, Jr., MD,* Xin Tao, Ph.D* "Foundation for Embryonic Competence, Basking Ridge, NJ; The Foundation for Embryonic Competence, Basking Ridge, NJ; IVI-RMA New Jersey, Basking Ridge, NJ.

TABLE 1. Pregnancy Outcomes Following IVF-FET Cycles With and Without PGT-A

<table>
<thead>
<tr>
<th>Live Birth Rate (%)</th>
<th>Clinical Pregnancy Rate (%)</th>
<th>Spontaneous Abortion Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35 years</td>
<td>≥35 years</td>
<td>&lt;35 years</td>
</tr>
<tr>
<td>IVF-FET without PGT-A n=43,811</td>
<td>48.6</td>
<td>35.3</td>
</tr>
<tr>
<td>IVF-FET with PGT-A n=24,007</td>
<td>55.3</td>
<td>52.5</td>
</tr>
<tr>
<td>P Value</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>
OBJECTIVE: NGS provides an unprecedented high-throughput, highly parallel, and base pair resolution data for genetic analysis. In this study, we developed a targeted NGS methodology for simultaneous pre-implantation genetic testing for monogenic/single gene disorders (PGT-M) and aneuploidy (PGT-A) from a single TE biopsy in a single procedure without the need of WGA.

DESIGN: Experimental Study

MATERIALS AND METHODS: Patients whose TE biopsies underwent PGT-M with clinical validated Taqman genotyping were included. Sequencing primers were designed for 11 different variants, including single nucleotide alterations, deletions, and insertions, and then validated on parental genomic DNA. Abnormal embryos donated for research were thawed, re-biopsied, and lysed. Two re-biopsies from each embryo were pre-amplified with a multiplex primer pool for PGT-M and PGT-A, using a two-step PCR strategy to incorporate sequencing library adapters and indexes. Sequencing was performed on Illumina NextSeq 550 using single 150bp reads. The average read depth was approximately 700X. Reads were aligned to a human reference genome (GRCh37/hg19) with the Burrows-Wheeler Aligner (BWA). The variants were called using Samtools and were aligned to a human reference genome (GRCh37/hg19) with the Burrows-Wheeler Aligner (BWA). The variants were called using Samtools for the PGT-M. Karyotypes were analyzed using an in-house clinical validated bioinformatics workflow. Taqman genotyping was performed on the amplified re-biopsies to further confirm the SGD results.

RESULTS: Two TE biopsies of 13 embryos from 7 families, including 9 variants (CFTR c.350G>A, CFTR c.1521_1522delCTT, HEXA c.1421+1G>C, HEXA c.1274_1277dupTATC, PAX6 c.76C>G, TBX3 c.342C>G, PHF6 c.1180C>T, HMGCL c.122G>A, HMGCL c.4974A>G), showed 100% concordant PGT-M diagnoses when compared to previous PGT-M based on Taqman qPCR genotyping. The PGT-A from multiple biopsies of the same embryos also demonstrated consistent karyotypes. For one variant, MKS1 c.1411dupG, Taqman genotyping assay design was not possible due to the presence of a string of Gs at the mutation site. The targeted NGS provided accurate genotypes for parental DNA and 5 lymphocyte samples. Another X chromosome-linked nonsense mutation (PCDH19 c.595 G>T) was validated on genomic DNA and 5 fibroblast samples.

CONCLUSIONS: This study provides proof of principle that PGT-M and PGT-A can be reliably and consistently performed simultaneously from the same TE biopsy in only one procedure without additional genotyping assays. Selecting euploid blastocysts that are unaffected by the PGT-M may provide the greatest opportunity for a successful outcome.

---

**O-78 Monday, October 14, 2019 12:00 PM**

**MOsaic EMbryos - A COMPREHENSIVE AND POWERED ANALYSIS OF CLINICAL OUTCOMES.**

Manuel Viotti, PhD,a Andrea Victor, MS,b Alan Brake, MS,c Santiago Munne, PhD,d Frank Barnes, PhD,e Christo Zouves, MD,f Zouves Foundation for Reproductive Medicine, Foster City, CA; Zouves Fertility Center, Foster City, CA; Overture Life, Madrid, Spain.

OBJECTIVE: To perform the largest analysis of mosaic embryo transfers to date, in order to achieve adequate power of analysis when evaluating which characteristics of mosaicism affect clinical outcomes.

DESIGN: Compiled analysis of data from multiple participating clinics.

MATERIALS AND METHODS: We collected clinical outcome data (implantation, ongoing pregnancy, birth) for transferred embryos classified as ‘mosaic’ by Preimplantation Genetic Testing (PGT). The following characteristics of mosaicism were considered: general mosaicism versus control (euploid), type of aneuploidy involved in the mosaicism, level of mosaicism (using 40% or 50% as cutoffs), mosaic monosomies versus trisomies, and age. Chi-squared or Fisher’s test was used to compare groups and evaluate statistical significance.

RESULTS: In the adjoining table we present our results from 372 mosaic embryo transfers, with more data presently being collected. This current analysis (powered to 100%) demonstrates that mosaic embryo transfers can result in pregnancies and births, albeit with decreased success rates compared to euploid embryos. Importantly, complex mosaics involving more than two chromosomes should be deprioritized, and higher levels of mosaicism correlate with poor clinical outcome.

CONCLUSIONS: This is the largest analysis of mosaic embryo transfers to date, and represents a valuable reference to generate guidelines on mosaic embryo selection and prioritization in the clinic.

**SUPPORT: Zouves Foundation for Reproductive Medicine.**

---

**REPRODUCTIVE BIOLOGY: HUMAN STUDIES**

O-79 Monday, October 14, 2019 10:45 AM

**THE RELATIONSHIP BETWEEN CHRONOLOGIC AGE, OVARIAN RESPONSE, AND DNA METHYLATION OF WHITE BLOOD CELLS AND CUMULUS CELLS AMONG INFERTILE WOMEN UNDERGOING IVF.**

Brent M. Hanson, MD,a Xin Tao, Ph.D,b Yiping Zhan, Ph.D,c Timothy G. Jenkins, PhD,c Julia G. Kim, MD, MPH,a Emily K. Osman, MD,a Ashley W. Tieg, MD,b Shelby A. Neal, MD,a Richard Thomas Scott, Jr., MD,b Emre Seli, M.D.d IVI-RMA New Jersey, Basking Ridge, NJ; The Foundation for Embryonic Competence, Basking Ridge, NJ; Foundation for Embryonic Competence, Basking Ridge, NJ; University of Utah Department of Surgery, Salt Lake City, UT.

OBJECTIVE: Aging is associated with predictable changes in DNA methylation in human somatic cells. An epigenetic clock model has been developed that allows for the calculation of chronological age (CA) from cellular age (CA).

**MATERIALS AND METHODS: We collected clinical outcome data (implantation, ongoing pregnancy, birth) for transferred embryos classified as ‘mosaic’ by Preimplantation Genetic Testing (PGT). The following characteristics of mosaicism were considered: general mosaicism versus control (euploid), type of aneuploidy involved in the mosaicism, level of mosaicism (using 40% or 50% as cutoffs), mosaic monosomies versus trisomies, and age. Chi-squared or Fisher’s test was used to compare groups and evaluate statistical significance.**

**RESULTS: In the adjoining table we present our results from 372 mosaic embryo transfers, with more data presently being collected. This current analysis (powered to 100%) demonstrates that mosaic embryo transfers can result in pregnancies and births, albeit with decreased success rates compared to euploid embryos. Importantly, complex mosaics involving more than two chromosomes should be deprioritized, and higher levels of mosaicism correlate with poor clinical outcome.**

**CONCLUSIONS: This is the largest analysis of mosaic embryo transfers to date, and represents a valuable reference to generate guidelines on mosaic embryo selection and prioritization in the clinic.**

**SUPPORT: Zouves Foundation for Reproductive Medicine.**

---

**Table: Mosaic Embryos - A Comprehensive and Powered Analysis of Clinical Outcomes.**

<table>
<thead>
<tr>
<th>General</th>
<th>Mosaic Embryos Transferred (n)</th>
<th>Control Group (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levels 40</td>
<td>256</td>
<td>116</td>
</tr>
<tr>
<td>Levels 50</td>
<td>278</td>
<td>94</td>
</tr>
<tr>
<td>Age</td>
<td>120</td>
<td>251</td>
</tr>
<tr>
<td>Losses vs Gains</td>
<td>89</td>
<td>53</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type</th>
<th>Segemental Implantation (%)</th>
<th>Complex Implantation (%)</th>
<th>P (Complex vs Rest)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 or 2 Whole Chr</td>
<td>61</td>
<td>26.2</td>
<td>&lt;0.0001#</td>
</tr>
<tr>
<td>Complex Chr</td>
<td>35.3%</td>
<td>37.9%</td>
<td>19.7%</td>
</tr>
</tbody>
</table>

*OP/B = Ongoing Pregnancy/Birth.
# These statistically significant findings stem from an analysis that is >80% powered.
described by Horvath based on the methylation status of 353 CpG sites on human DNA (1). This model has been shown to accurately predict the chronologic age of individuals. The current study sought to determine whether the age predicted using the Horvath algorithm in white blood cells (WBC) and cultured cells (CC) is concordant with the true age of patients and their response to ovarian stimulation.

**DESIGN:** Prospective cohort study.

**MATERIALS AND METHODS:** Patients undergoing in vitro fertilization (IVF) between July 2017 and December 2018 were recruited under Institutional Review Board approval. On the day of oocyte retrieval, samples of peripheral blood and CC were collected from enrolled patients, and genomic DNA was isolated and stored at −80°C. DNA from WBC was analyzed using the QIAsymphony kit (Qiagen, Redwood City, CA, USA). DNA from CC was purified using DNeasy blood and tissue kit (Qiagen, Redwood City, CA, USA). Bisulfite conversion was performed using the Zymo EZ DNA methylation kit (Zymo Research, Irvine, CA, USA). The Illumina 850K DNA methylation EPIC array (San Diego, CA, USA) was then utilized to measure DNA methylation levels. Likelihood ratio tests based on nested linear models were utilized to assess the relationship between predicted age and true age.

**RESULTS:** Methylation data was analyzed for a total of 175 women undergoing IVF (mean age 35.26 ± 4.14 years). The Horvath-predicted age calculation for WBC samples was consistent with the true chronologic age of patients (p < 0.0001). However, the predicted age from CC was significantly younger than patients’ chronologic age. The mean predicted age of patients using methylation-based calculations from CC was 8.56 ± 2.07 years. Poor response to ovarian stimulation during IVF, defined as five or fewer oocytes obtained during oocyte retrieval, did not affect the Horvath-predicted age based on calculations from WBC (p = 0.131) or CC (p = 0.502).

**CONCLUSIONS:** In women undergoing IVF, the epigenetic algorithm described previously by Horvath accurately predicts age when applied to WBC but not to CC. The methylation-based predicted age obtained from analysis of CC is substantially younger than the true age of patients, suggesting that CC exhibit unique methylation patterns that are distinct from those demonstrated by WBC. A poor response to ovarian stimulation is not associated with predictable changes in CpG methylation sites consistent with aging within WBC or CC. CC may have their own distinct methylation pattern which changes with age and must be clearly delineated since this may have implications for reproductive lifespan. Further studies are already required to determine whether alternative CpG sites can accurately predict chronologic age or response to stimulation from CC samples.


**SUPPORT:** None.

---

**O-80** Monday, October 14, 2019 11:00 AM

**THE INCLUSION OF BLASTOMERES INTO THE INNER CELL MASS IN EARLY-STAGE HUMAN EMBRYOS DEPENDS ON THE SEQUENCE OF CELL CLEAVAGES DURING THE FOURTH DIVISION.** Junko Otsuki, Ph.D.a Toshiro IWasaki, D.V. M., Ph.D.a Noritoshi Ematsu, M.D. Ph.D.a Yuya Katada, B.S.a Kohyu Furuhashi, B.S.a Masahide Shiotsani, M.D., Ph.D.a Okayama University, Okayama, Japan; bHanabusa Womens clinic, Kobe, Japan.

**OBJECTIVE:** In mouse embryos, the fate of the inner cell mass (ICM) is known to be determined during divisions that occur from 8–16 cells. The outer cells give rise mainly to trophodermid (TE). In contrast, cells positioned inside the embryo give rise to ICM. However, there is no information on the order of incorporation of blastomeres into the ICM in human embryos. Blastomere bodies (RBs) are some of the dysmorphic phenotypes that are frequently observed in human oocytes. RBs remain present, and almost unchanged in size, at least until embryos reach the blastocyst stage. Thus, our aim was to examine such early developmental stages using time-lapse recorded data, taking advantage of the large RBs within blastomeres as cellular markers.

**DESIGN:** Time series study.

**MATERIALS AND METHODS:** A total of 201 large refractile bodies in fertilized oocytes progressing through normal 2-cell to 8-cell stages were traced until they developed into a blastocyst. Cluster analysis was conducted to group the blastomeres according to the timing of cell division. Simple and multiple logistic regression analysis were both used to estimate the order in which the cells divided from the second to the fourth division, with the attainment of ICM defined as the endpoint.

**RESULTS:** Following the second division, from 2 cells to 4 cells, the rates of RBs that were distributed to the ICM of blastomeres which cleaved first and second were 20.0% (20/100) and 18.8% (19/101) respectively. During the third division from 4 cells to 8 cells, the rates of RBs that were distribution to the ICM of blastomeres which cleaved first to fourth were 24.1% (13/54), 28.1% (16/57), 10.3% (4/39) and 11.8% (6/51) respectively. During the fourth division from 8 cells to 16 cells, the rates of RBs that were distributed to the ICM of blastomeres which cleaved first to eighth were 35.1% (13/37), 30.8% (9/29), 26.9% (7/26), 30.4% (7/23), 5.3% (1/19), 4.8% (1/21), 4.0% (1/25) and 0% (0/24) respectively. Cluster analysis showed that blastomeres which cleaved earlier tended to reach the ICM and there was a distinct difference between the rates of the second to the fourth divisions. Furthermore, the first 50% of cleaved blastomeres during the fourth division had significantly higher rates of being incorporated in the ICM (p < 0.001). Simple logistic regression analysis was used to estimate the order in which the cells cleaved during both the third and fourth division before being included in the ICM, whereas multiple logistic regression analysis was only applied to the fourth cleavage. The third division was thereby removed as a confounding factor and the fourth division was found to be a predictor for ICM (OR:16, CI:4.1-63, p < 0.001).

**CONCLUSIONS:** This study found that the cellular composition of the ICM is largely determined at the time of the fourth division. Moreover, it was shown that blastomeres which cleave first to fourth, during the fourth division from 8 cells to 16 cells, gain the ability to be incorporated in the ICM.

**O-81** Monday, October 14, 2019 11:15 AM

**THE EFFECT OF AGE ON BIOENERGETICS OF HUMAN GRANULOSA CELLS.** Gustavo N. Cecchino, MD.a Alberto Pacheco, PhD.b Juan A. Garcia-Velasco, PhD.b Eduardo Rial, PhD.c IVIRMA-Madrid, Madrid, Spain; dCentro de Investigaciones Biológicas - CSIC, Madrid, Spain.

**OBJECTIVE:** Granulosa cells (GCs) support the synchronization of follicle development along with oocyte growth and maturation, being a potential biomarker of oocyte quality and in-vitro fertilization (IVF) outcomes. However, little is known about GC bioenergetics and its impact on female fertility. Our aim was to characterize the bioenergetic profile of human GCs and detect the potential impact of aging on the energy metabolism.

**DESIGN:** Observational prospective cohort.

**MATERIALS AND METHODS:** From December 2017 to December 2018, the bioenergetic properties of GCs from 53 egg donors aged < 35 years and 40 infertile patients ≥ 38 years were determined. Antagonist protocol was used to carry out controlled ovarian stimulation in all cases and women with diseases that could potentially impair mitochondrial function were excluded. Purified GCs from fresh samples of follicular fluid were seeded in Seahorse XF 24-well microplates. Primary culture was performed for 24 h and followed by a real-time assessment of the oxygen consumption rate (OCR) and the extracellular acidification rate (ECAR) as a proxy for lactate formation on a Seahorse XF24 Extracellular Flux Analyzer (Seahorse Bioscience, Agilent Technologies, Santa Clara, CA, USA). The addition of a set of mitochondrial inhibitors/uncouplers allowed the evaluation of the bioenergetic profile of the samples. Results were normalized according to the protein concentration in each well. Furthermore, adenine nucleotides levels (AMP, ADP and ATP) in GCs were determined by reverse-phase high performance liquid chromatography after extraction with perchloric acid. Statistical analysis was performed using SPSS v24 (SPSS Inc., Chicago, IL, USA) and variables were compared using the ANOVA test, as appropriate.

**RESULTS:** GCs from oocyte donors aged < 35 years showed a higher basal mitochondrial OCR compared to infertile women ≥ 38 years (12.8 ± 1.6 pmol O2/min/mg vs. 11.2 ± 1.6; p = 0.046). Such difference is unlikely to be a result of reduced mitochondrial mass, once the maximum respiratory capacity remained unchanged (24.5 ± 3.3 pmol O2/min/mg vs. 22.4 ± 4.3; p = 0.226). Thus, the difference in the basal mitochondrial respiration was due to a combined decrease in OCR and ECAR (R22.4 vs. 35.3; p = 0.01). The OCR and ECAR of GCs in both groups were similar. Granulosa cells displayed a very high rate of glycolysis as estimated by the ECAR measurements. However, GCs from older patients showed a substantially lower rate of lactate formation (12.9 ± 1.3 mpH/min/mg vs. 10.9 ± 0.5; p = 0.009). Moreover, GCs from younger patients presented higher ATP/ADP...
ratio (4.45 ± 0.34 vs. 3.37 ± 0.46; p < 0.001) and increased energy charge (0.87 ± 0.01 vs. 0.83 ± 0.02; p < 0.001).

CONCLUSIONS: The diminished rates of both mitochondrial respiration and glycolytic capacity reflect a marked reduction on the energy metabolism of GCs as women age, which was corroborated by the decreased ATP/ADP ratio and energy charge. Such a detrimental effect of age on GCs bioenergetics are likely to influence overall IVF performance. A new window of opportunity for diagnostic and therapeutic tools may arise from studies focusing on the bioenergetics of granulosa cells, oocytes and embryos.

SUPPORT: IVIRMA Madrid.

O-82 Monday, October 14, 2019 11:30 AM

REPEATED IMPLANTATION FAILURE PATIENTS DIS-PLAY A GREATER DELAY OF THEIR RECEPTIVITY WINDOW DIAGNOSED USING A GENOMIC TEST UN-DER HRT TREATMENT COMPARED TO NATURAL CYCLES. Delphine Haouzi, PhD,a Frida Entezami, MD,b Charlene Innocenti, Engineer,c Alice Ferrieres-Hsa, MD,c Chloe Baron, PhD, student,c Claire Vincens, MD,c Sophie Bringer-Deutsch, MD,c Cecile Brunet, MD,a Antoine Torre, MD, PhD,c Samir Hamamah, MD, PhD,c *Inserm U1203, CHU Montpellier, St-Eloi Hospital, Montpellier, France; aAmerican Hospital of Paris, Neuilly-sur-Seine, France; ART-PGD department, Arnaud de Villeneuve Hospital, CHU Montpellier, Montpellier, France; cDivision of Child Health, Obstetrics & Gynaecology department, University of Nottingham, Nottingham, United Kingdom; bArnaud de Villeneuve Hospital, CHU Montpellier, Montpellier, France.

OBJECTIVE: To identify the receptivity window in patients with repeated implantation failure prepared for frozen embryo transfer under hormone replacement therapy (HRT) treatment or natural cycle.

DESIGN: Endometrial biopsies were performed during the implantation window 7-9 days after the LH surge in natural cycle or 5-9 days after progesterone administration under HRT respectively. According to genomic testing result, the transfer strategy was: blastocysts transferred at the specific day where endometrium is identified as ‘receptive’; D2/D3 cleavage stage embryos transferred 72/48 hours before the specific cycle day where endometrium is identified as receptive.

RESULTS: Analyses of endometrial receptivity status in 141 RIF patients (age 37.9 ± 3.8 years) revealed a strong inter-patient variability in the occurrence of the receptivity window with mostly a delay between 1 to 3 days. More precisely, biopsies were evaluated using natural cycle (n=29), natural cycle with recombinant human chorionic gonadotropin (hCG, Ovitreel) (n=7) HRT (n=68) and HRT with GnRH analogue (n=6) patients respectively. In patients evaluated under natural cycle, the majority were receptive at LH+8 (52%). The remaining 48% displayed receptivity equally at LH+6/7+ (24%) and LH+4+ (24%). Under natural cycle with recombinant hCG, 72 % of RIF patients were receptive at hCG+9 while 14% were at hCG+6/7+ and 14 % at hCG+8. In patients under HRT, 38% and 41% were receptive at P4+7 and P4+8, respectively, whereas the remaining 21% were receptive (P4+7 or P4+8) and 37% were receptive. Under HRT with GnRH analogue, the majority of RIF patients were receptive at P4+8 (67%). Others were receptive at P4+5/6+ (22%), P4+7 (5%) and P4+9 (8%). After personalized embryo transfer using the genomic testing strategy, the clinical pregnancy and live birth rates were 36.2 % and 28.4 % respectively.

CONCLUSIONS: The acquisition of the endometrial receptivity phenotype is more progressive under HRT compared with natural cycle. The majority of RIF patients displayed a delay in occurrence of their receptivity window revealing a potential cause for the implantation failure. Personalized embryo transfer according to the specific cycle day where endometrium is said receptive improves both clinical pregnancy and LBR in RIF patients under both HRT and natural cycle.

SUPPORT: This work was partially supported by a grant from the Ferring Pharmaceutical Company.

O-83 Monday, October 14, 2019 11:45 AM

THE ROLE OF VITAMIN D AS A PIECE OF THE UTERINE FACTOR INFERTILITY PUZZLE. Karine Matevosian, DO,a Laurent Grimm, MA,b Elisabeth Rosen, BS, MA,b Lucas E. Rasnic, BSE, MA,b Jacqueline Sehring, MA,b Jody M. Esquerra, MA,b Anisa Hussain, MA,b Angeline Beltos, MD,a Roohi Jeelani, MD,b *Advocate Lutheran General Hospital, Park Ridge, IL; bVios Fertility Institute, Chicago, IL.

OBJECTIVE: Previous research has proven that there are vitamin D receptors in the endometrial cavity. This study aims to better understand the role of vitamin D on reproductive outcomes and uterine factor infertility. We sought to investigate the impact of vitamin D deficiency on endometrial thickness in patients with an elevated anti-mullerian hormone (AMH) representative of Polycystic Ovary Syndrome (PCOS).

DESIGN: Retrospective chart review at a private multi-location fertility clinic.

MATERIALS AND METHODS: A total of 1065 cycles were identified in patients with an AMH > 5 ng/ml between August 2016 to March 2019. All patients underwent timed intercourse or intrauterine insemination. Patients received Letrozole or Clomid therapy and were triggered for ovulation induction following the maturation of 1-3 follicles greater than 18 mm. Patients were divided into two groups: vitamin D < 30 ng/ml in the deficient group, and those with a vitamin D ≥ 30 ng/ml, in the sufficient group. The endometrial thickness was compared between the groups. Two sample t-tests and chi-square analysis were used to analyze the data using SPSS 21.0 (SPSS Inc., Chicago, IL, USA).

RESULTS: Baseline characteristic differences between the two groups, including age, race, BMI, and parity were not significant (p>0.05). The mean endometrial thickness was not significantly different between groups (p>0.05). The mean endometrial thickness in patients with an elevated AMH with vitamin D deficiency and sufficiency was 6.986 mm versus 6.345 mm, respectively (p=0.023). There was also a slight negative correlation between vitamin D levels and endometrial thickness. When this data was extrapolated and analyzed in the first phase of the study, pregnancy outcome was compared between the two groups and no difference was noted (p>0.05).

CONCLUSIONS: Vitamin D deficiency is extremely prevalent and affects up to 36% of Americans. It has implications for many aspects of physiology and recent research has explored its effects on reproductive biology. It is hypothesized that decreased vitamin D leads to disruption of estrogen signaling and impaired reproductive outcomes. The endometrium has vitamin D receptors and a deficiency is associated with uterine hypoplasia in animal models. In a human model, vitamin D deficiency may be more prevalent in PCOS patients. Women with PCOS have also been shown to have elevated AMH levels >5 ng/ml. Moreover, previous research in a PCOS model has shown a strong correlation between vitamin D deficiency and uterine factors leading to increased miscarriage risk. Therefore, we sought to explore the connection between AMH, vitamin D and endometrial lining.

Interestingly, our study results were statistically significant and showed that higher levels of vitamin D were correlated with a thinner endometrial lining. Thus, we conclude that though vitamin D plays a role in infertility and the endometrium, it is not a factor in determining endometrial thickness. Future studies are needed to determine how vitamin D interacts with the endometrium in PCOS patients leading to poorer reproductive outcomes and can focus on implantation, receptivity and miscarriage.

SUPPORT: None.

O-84 Monday, October 14, 2019 12:00 PM

DYNAMIC DNA METHYLATION DURING TROPHOBLAST DIFFERENTIATION IN HUMAN PERI-IMPLANTATION STAGE EMBRYOS REVEALED BY SINGLE-CELL WHOLE GENOME BISULFITE SEQUENCING. Ye Yuan, PhD,a Jiangwen Sun, Ph.D.,b Hao Ming, M.S.,c Deirdre M. Logsdon, MS,a William B. Schoolcraft, MD,a Rebecca L. Krisher, PhD,c Zhongliang Jiang, Ph.D.c *Colorado Center for Reproductive Medicine, Lone Tree, CO; bOld Dominion University, Norfolk, VA; cLouisiana State University, Baton Rouge, LA.

OBJECTIVE: Trophoblast cells play an essential role in the interactions between the fetus and mother. Multipotent trophoblast cells undergo dynamic morphological migration and differentiation around the time of implantation to generate functional placenta, and their coordinated proliferation and differentiation are dependent upon the dynamic expression of a series of genes which are regulated in large part by epigenetic mechanisms. The aim of the
Training is unsubstantiated since a majority of programs appear to have exposure to microsurgery training from a fellowship-trained faculty.

The northeast and southeast sections had the lowest percentage (67% and 68%). The percentage of fellowship-trained microsurgeons per program did not vary

Gery, 87% for penile implants, and 88% for artificial urinary sphincters. The (78%) of programs had fellowship-trained physicians for training in microsur-

by a fellowship trained academic faculty member, a private practice fellow-

Additionally, we evaluated whether the residents were trained

email. For programs that did not reply, we performed a search of the program

reconstruction, a sub-specialty with surgical minimums.

the availability of microsurgery training among urology residency programs

Currently there is not a requirement for microsurgery, likely from

CONCLUSIONS: Using the human embryo in vitro extended culture sys-

MATERIALS AND METHODS: Vitrified and warmed day 5 (D5) human

OBJECTIVE: To evaluate the results of laparoscopic salpingooovario-

spermatozoa. Precautions for prevention or minimization of postopera-

reproductive adhesion reformation are also important for success of the recon-

CONCLUSIONS: Using the human embryo in vitro extended culture sys-

MATERIALS AND METHODS: Vitrified and warmed day 5 (D5) human

OBJECTIVE: The Accreditation council of graduate medical educations

A SURVEY OF MICRO SURGERY TRAINING AMONG UROLOGY RESIDENCY PROGRAMS.

Thomas A. Masterson, III, MD, Quinn Carroll Rainer, BS, 
Sirpi Nackereran, BA, Ranjith Ramasamy, MD University of Miami Miller School of Medicine, Miami, FL; Medical Student, Miami, FL.

OBJECTIVE: The Accreditation council of graduate medical educations (ACGME) establishes surgical minimum numbers of cases for urologic training. Currently there is not a requirement for microsurgery, likely from a belief that residents do not have enough exposure. In an effort to evaluate the availability of microsurgery training among urology residency programs we conducted a survey of the programs. We compared microsurgery to male reconstruction, a sub-specialty with surgical minimums.

DESIGN: Cross sectional survey.

MATERIALS AND METHODS: We obtained a list of the 138 ACGME-accredited urology residencies and contact information from the American Urology Association. We contacted the residency programs by phone or email. For programs that did not reply, we performed a search of the program website. We administered a 3-question survey to assess resident subspecialty training in microsurgery, penile implant and artificial urinary sphincter. In cooperation with the AUA, we evaluated whether the residents were trained by a fellowship trained academic faulty member, a private practice fellowship trained physician, or a non fellowship trained physician. Data are reported as frequencies.

RESULTS: We obtained data from 134 (97%) programs. A total of 104 (78%) of programs had fellowship-trained physicians for training in microsurgery. 87% for penile implants, and 88% for artificial urinary sphincters. The percentage of fellowship-trained microsurgeons per program did not vary significantly when comparing the different sections of the AUA, however the northeast and southeast sections had the lowest percentage (67% and 68%).

CONCLUSIONS: Approximately 80% of urology residency programs have exposure to microsurgery training from a fellowship-trained faculty member. We believe that the lack of a requirement for urologic microsurgery training is unsubstantiated since a majority of programs appear to have fellowship trained faculty. In order to provide an equal exposure to all graduating urology residents, it is imperative that urology residency programs that lack microsurgery as a specialty identify a faculty member who is fellowship-trained.

Reference: None.

SUPPORT: None.
OBJECTIVE: To evaluate the feasibility and effectiveness of embryo biopsy under direct visualization during operative hysteroscopy to avoid maternal contamination of products of conception (POCs) in cases of early miscarriages. Chromosomal analysis of POCs plays a fundamental role in the evaluation and treatment of recurrent pregnancy loss. With traditional Dilatation and Curettage maternal contamination is around 22%.

DESIGN: A series of 20 consecutive operative hysteroscopies was performed in infertile patients with miscarriage between 6-6+ and 12 weeks from September 2015 through January 2019 in a private infertility clinic.

MATERIALS AND METHODS: Six spontaneous pregnancies plus 14 pregnancies obtained with Assisted Reproductive Technologies (ART): 5 fresh IVF cycles, 3 frozen IVF cycles, 2 fresh egg donation cycles and 4 frozen egg donation cycles. Mean patient age was 39 years. CRL was 2 to 51 mm. In 80% of cases a heartbeat was seen before miscarriage.

RESULTS: Maternal contamination was reported in one case. Of the remaining 19 cases 14 were aneuploidies, 1 was a 45X mosaic, and 4 presented an euploid karyotype. There were no surgical complications. Sixteen of the patients had a sonohysteroscopy performed postoperatively and there was no case of intrauterine adhesions or retained POCs.

CONCLUSIONS: Embryo biopsy under direct visualization during operative hysteroscopy is feasible and could be an effective method to limit maternal contamination and furnish targeted biopsies. By offering the ability to separately sample embryo vs. trophoblast this method could illuminate the implications of mosaicism in trophoblast biopsies. This technique may be less disturbing to the endometrium as shown by absence of intrauterine adhesions in postoperative sonography. A living donor team that included a Nurse Coordinator, a Psychologist, a Living Donor Advocate, Transplant Surgeon, a Gynecologist, and a Fertility Specialist looked after the needs of the donor throughout the evaluation and donation process. The transplant surgeon and gynecologic surgeon decided the best surgical approach and options included abdominal hysterectomy, a robotic hysterectomy, or a laparoscopic hysterectomy. Adverse events related to the surgery were found in a private inpatient setting or with two donors requiring intraoperative blood transfusion. Median hospital stay was 6 days and only one donor required intensive care unit (ICU). Intraoperative complications were uncommon. Five donors had short-term complications (<30 days after surgery) including gluteal claudication with ambulation that resolved 4 weeks post discharge (grade I), UTI (grade I), anemia requiring 1 unit of pRBC (grade II) and CDI (grade II). Three donors experienced long-term (>30 days) postoperative complications. These included vaginal cuff dehiscence (grade Ib) and UTI (grade II). The vaginal cuff dehiscence was surgically repaired, and the UTI resolved with oral antibiotics.

O-89 Monday, October 14, 2019 11:45 AM

PREGNANCY OUTCOMES FOLLOWING HYSTEROSCOPIC CORRECTION OF T-SHAPED UTERI. Shelby A. Neal, MD,* Richard Thomas Scott, Jr., MD, Linnea R. Goodman, MD, †IVI-RMA New Jersey, Basking Ridge, NJ; ‡University of North Carolina, Raleigh, NC.

OBJECTIVE: To evaluate pregnancy outcomes following hysteroscopic correction of T-shaped uteri in patients with poor reproductive histories and T-shaped uterine cavities diagnosed by three-dimensional (3D) ultrasound.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: All patients at a single large IVF center undergoing fertility evaluation between 2016 and 2018 with a T-shaped uterine cavity diagnosed by 3D saline infusion sonohysteroscopy and a poor reproductive history (defined as ≥ 2 of the following events: clinical miscarriage, failed transfer of a euploid blastocyst, ectopic pregnancy, cycle cancellation secondary to endometrial hypoproliferation) were eligible for hysteroscopic correction and inclusion in the study. Surgery was performed in the early proliferative phase under conscious sedation. With saline as a distention medium, a hysteroscopic tissue morcellator was used to shave the lateral walls of the uterine cavity until both tubal ostia could be visualized simultaneously or healthy vascularized tissue was encountered. Post-operative imaging was performed the next month. All patients were followed for up to 6 treatment cycles. The primary outcome was ongoing pregnancy (presence of a fetal heartbeat at 8 weeks gestation). Secondary outcomes included miscarriage (pregnancy loss following documentation of gestational sac), ectopic pregnancy, and mean number of treatment cycles to achieve an
ongoing pregnancy. Patients who achieved an ongoing pregnancy were compared to those who did not using Student’s t-test and Fisher’s exact test.

RESULTS: Sixteen patients (age 37.4 ± 5.4 years, median of 22.5 months attempting conception) with T-shaped uterus were included in this study. Indications for surgery included recurrent pregnancy loss (n=3), recurrent implantation failure (n=2), recurrent ectopic pregnancy (n=1), endometrial hypoproliferation (n=3), or a combination of factors (n=7). There were no surgical complications. Post-operative imaging revealed expansion of the uterine cavity for 14 (87.5%) patients, as assessed by a single independent reviewer.

Following surgery, a total of 34 treatment cycles were attempted by 15 patients, resulting in 6 (17.6%) ongoing pregnancies, 3 (8.8%) miscarriages and 3 (8.8%) ectopic pregnancies. The cumulative ongoing pregnancy rate was 40.0%, with those who achieved an ongoing pregnancy requiring a mean number of 1.5 treatment cycles. There were no differences in age, body mass index, reproductive history or treatment modalities between patients who achieved an ongoing pregnancy and those who did not.

CONCLUSIONS: Patients who underwent hysteroscopic correction of a T-shaped uterus achieved a cumulative ongoing pregnancy rate of 40% over six treatment cycles. Further prospective studies with appropriate control groups are needed in order to ascertain if our findings represent a true improvement in pregnancy outcomes or simply regression to the mean.

O-90 Monday, October 14, 2019 12:00 PM

SINGLE EUPOID FROZEN EMBRYO TRANSFER: EVALUATING IMPACT OF INTERVAL SINCE OPERATIVE HYSTEROSCOPY. Allison C. Petrini, MD, Catherine W. Chan, MD, Kelly McCarter, MD, Micha Thompson, BA, Monica Pasternak, MD, Nigel Pereira, MD, Steven Spandorfer, M.D., Ronald O. Perlman and Claudia Cohen Center for Reproductive Medicine, New York, NY; Weill Cornell Medicine, New York, NY.

OBJECTIVE: There is limited data on the optimal time between operative hysteroscopy and embryo transfer1. Previous studies have demonstrated no difference in pregnancy outcome if the interval between polypectomy or all indications and embryo transfer (ET) is increased, but did not address operative hysteroscopy solely in the ideal group of patients undergoing single euploid embryo transfers. Our aim was to determine whether a difference in pregnancy outcome exists if the time between operative hysteroscopy and single euploid embryo transfer is increased.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients undergoing single euploid ET at our center over 3 years were examined for history of hysteroscopy prior to ET. Patients were grouped by surgical pathologic diagnosis and were further stratified into groups based on time between hysteroscopy and ET. They were designated as group 1, 2, or 3 to indicate an interval to next menstrual cycle, within 2 menstrual cycles, or within 3 menstrual cycles, respectively. Treatment outcomes were examined and classified as pregnant or not pregnant and then grouped into ongoing pregnancy or pregnancy loss. Student’s and nonparametric t-tests, Mann-Whitney U-test, and chi-square tests were used as indicated with p < 0.05.

RESULTS: A total of 1123 patients met inclusion criteria; 375 underwent hysteroscopy prior to ET during the study period. 77.7% of cases were operative, and 22.3% were diagnostic. Of operative cases, polyps represented 40% (n=98), adhesions 34% (n=84), andomyomas 11% (n=28). There were no differences in the baseline demographics between those who were pregnant and not pregnant, or between those with an ongoing pregnancy versus pregnancy loss. The baseline demographics were also comparable between those who underwent hysteroscopy and those who did not. There was no difference in the pregnancy rate between the groups who underwent ET 1, 2, or 3 menstrual cycles from operative hysteroscopy. In addition, there was no difference in the rate of ongoing pregnancy between groups.

<table>
<thead>
<tr>
<th>Group 1 (ET in next menstrual cycle)</th>
<th>Group 2 (ET in 2 menstrual cycles)</th>
<th>Group 3 (ET in 3 menstrual cycles)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pregnancy rate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mean age (years)</strong></td>
<td>36.3 (±4.0)</td>
<td>36.7 (±4.1)</td>
<td>69.6%</td>
</tr>
<tr>
<td><strong>Mean BMI (kg/m²)</strong></td>
<td>24.0 (±5.7)</td>
<td>24.3 (±5.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Ongoing pregnancy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mean age (years)</strong></td>
<td>37.1 (±3.7)</td>
<td>37.1 (±3.6)</td>
<td>58.9%</td>
</tr>
<tr>
<td><strong>Mean BMI (kg/m²)</strong></td>
<td>23.6 (±4.6)</td>
<td>23.5 (±4.6)</td>
<td></td>
</tr>
</tbody>
</table>

CONCLUSIONS: The time between operative hysteroscopy and euploid frozen embryo transfer did not have an effect on the ability to become pregnant or the chance of having an ongoing pregnancy. Thus, clinicians can advise patients that they may proceed with a frozen transfer as soon as the next menstrual cycle after operative hysteroscopy.


SCIENTIFIC CONGRESS PRIZE PAPER SESSION 2

O-91 Tuesday, October 15, 2019 10:45 AM

ARTIFICIAL INTELLIGENCE ASSESSMENT OF TIME-LAPSE IMAGES CAN PREDICT WITH 77% ACCURACY WHETHER A HUMAN EMBRYO CAPABLE OF ACHIEVING A PREGNANCY WILL MISCARRY. Rishabh Harilaharan, BSc, Peter He, Marcos Meseguer, PhD, Marco Toschi, MSc, Jose Celso Rocha, PhD, Nikica Zaninovic, Ph.D., Jonas Malmsten, MSc, Qiansheng Zhan, MSc, Cristina Hickman, PhD "Imperial College London, London, United Kingdom; IVIRMA Global, Valencia, Spain; IVIRMA, Rome, Italy; State University of São Paulo Júlio de Mesquita Filho, Assis, Brazil; Ronald O. Perlman and Claudia Cohen Center for Reproductive Medicine, New York, NY.

OBJECTIVE: To determine whether convolutional neural network (CNN) can be used to predict whether an embryo capable of achieving a pregnancy will ultimately miscarry or lead to live birth based on Artificial Intelligence (AI) analysis of time-lapse (TLM) embryo images.

DESIGN: Diagnostic efficacy assessment of the capability of an Artificial Intelligence system predicting outcome of blind data from two independent clinics, qualitatively assessed using ROC curves with AUC scores and confusion matrices to quantify sensitivity and specificity (True Positive = TP; True Negative = TN; False Positive = FP; False Negative = FN).

MATERIALS AND METHODS: 3412 Time Lapse images of blastocysts with known live birth outcome following a single embryo transfer (“Live Birth”, n = 1756, 51%; “Miscarriage”, n = 1656, 49%), were used to train a CNN model for image classification using Tensor Flow. These images were all derived from the same brand of time-lapse incubator (Embryoscope™) and the same time post insemination (111.5 hours) to optimise input data normalisation. Images were allocated into Training (63%, n=2140), Validation (15.5%, n=536) and Test (21.5%, n=736) with an even distribution for confounding factors (patient age cohort, clinic, oocyte donation and outcome).

“The Positive” data was labelled as embryos with a Live Birth outcome, “negative” data, as embryos with a Miscarriage outcome.

RESULTS: Following training (AUC=0.85; loss=0.3), the AI had a performance that improved on current embryo selection methods within a blind data set (AUC=0.79); True Positive = 358, True Negative = 207, False Positive = 153, False Negative = 18. 565/736 images were correctly predicted with the blind data set (77% accuracy), with a 58% specificity (207/360) and 95% sensitivity (358/376). Amongst embryos classified as High risk of miscarriage, miscarriage rate was 92% (207/225), compared with 30% (153/511, p<0.001) when embryos were classified as reduced risk of miscarriage.

CONCLUSIONS: This is the first time that such a large data of single embryo transfer embryos from multiple clinics is used to assess AI capabilities.
in predicting miscarriage once pregnancy was confirmed. The high accuracy rate achieved suggests that visible embryo characteristics play a predominant role in maintaining pregnancy to live birth, once the biochemical pregnancy is established, compared to other factors, such as, the endometrium, or other non-visible embryo factors. Additional information (i.e. embryo genetic or proteomic information, or endometrial information) may help improve the specificity of miscarriage prediction.

This technology will now be tested prospectively in other clinics to assess whether these results can be generalised and whether this technology can be used to help advance embryo diagnosis and selection, not only in terms of prediction of live birth, but also miscarriage, an outcome associated with considerable emotional distress to patients.

**SUPPORT:** This research was funded by São Paulo Research Foundation (FAPESP), grant number 2017/19323-5.

---

**O-92 Tuesday, October 15, 2019 11:00 AM**

**CONTRIBUTIONS TO PREMATURITY OF MATERNAL HEALTH CONDITIONS, SUBFERTILITY, AND ASSISTED REPRODUCTIVE TECHNOLOGY (ART).** Judy E. Stern, PhD, a Chia-Ling Liu, ScD, b Hafsato Diop, MD, MPH, b Howard Cahral, PhD, MPH a Dartmouth-Hitchcock, Lebanon, OR; a MPH DL, Boston, MA; b Boston University, Boston, MA.

**OBJECTIVE:** Previous studies show subfertility and ART to increase rates of prematurity. Our goal was to evaluate health conditions that underlie prematurity and assess whether subfertility/ART influence these.

**DESIGN:** Retrospective cohort study

**MATERIALS AND METHODS:** Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS) deliveries were linked to Massachusetts birth certificates and hospital stays to identify privately insured singleton first births to women ≥ 18 years of age between 2004-2013. Deliveries were classified as ART when they linked to SART CORS, medically assisted reproduction (MAR) when fertility treatment was indicated on the birth certificate, unassisted subfertility (USF) when they had infertility diagnosis in prior hospital records or treatment for fertility in a prior delivery, and fertile if in none of the above groups. Late preterm birth (LPTB: 34-36 weeks) and early preterm birth (EPTB: <34 weeks) deliveries were compared to term deliveries (≥37 weeks). Covariates that significantly influenced the outcome of prematurity were classified as ART when they linked to SART CORS, medically assisted reproduction (MAR) when fertility treatment was indicated on the birth certificate, unassisted subfertility (USF) when they had infertility diagnosis in prior hospital records or treatment for fertility in a prior delivery, and fertile if in none of the above groups. Late preterm birth (LPTB: 34-36 weeks) and early preterm birth (EPTB: <34 weeks) deliveries were compared to term deliveries (≥37 weeks). Covariates that significantly influenced the outcome of prematurity were compared to term deliveries (≥37 weeks). Covariates that significantly influenced the outcome of prematurity were compared to term deliveries (≥37 weeks). Covariates that significantly influenced the outcome of prematurity were compared to term deliveries (≥37 weeks). Covariates that significantly influenced the outcome of prematurity were compared to term deliveries (≥37 weeks).

**RESULTS:** We identified 42,391 unique women with PCOS and 795,480 women without PCOS. Women with PCOS were more likely to have depression (4% vs 3%), diabetes (5% vs 1%), hypertension (6% vs 3%) and obesity (15% vs 5%) compared to women without PCOS (p<0.001 for all). They had a higher prevalence of gestational diabetes (24% vs 13%), gestational hypertension (14% vs 8%) and antepartum preeclampsia (5% vs 3%) than women without PCOS (p<0.001). In multivariable models, women with PCOS had a significantly higher odds of both perinatal and postpartum depression and postpartum preeclampsia and eclampsia compared to those without PCOS (Table). Postpartum results remained similar in planned sensitivity analyses in women with at least one year of pre-conception data, when including date of delivery in outcome definition and when varying the definition of perinatal and postpartum depression from the DSM-V criteria of 4 weeks postpartum to a commonly utilized literature length of one year postpartum.

**CONCLUSIONS:** This study demonstrates for the first time that women with PCOS are at higher risk for depression, preeclampsia and eclampsia in the fourth trimester of pregnancy. Our results highlight the need for comprehensive screening and targeted interventions during the postpartum period in this high-risk population.

**SUPPORT:** Snigdha Alur-Gupta is supported by the NIH T32 Training Grant: HD007440.

---

**O-93 Tuesday, October 15, 2019 11:15 AM**

**HIGHER INCIDENCE OF POSTPARTUM COMPLICATIONS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME.** Snigdha Alur-Gupta, M.D., a Mary Regina Boland, Ph.D., b Mary D. Sammel, Sc.D. c Kurt T. Barnhart, MD, MSCE, d Anuja Dokras, M.D., Ph.D. e University of Pennsylvania Perelman School of Medicine, Philadelphia, PA; f Affiliation not provided; g Department of Biostatistics, Epidemiology and Informatics, University of Pennsylvania, Philadelphia, PA; h University of Pennsylvania, Philadelphia, PA; i University of Pennsylvania Health System, Philadelphia, PA.

**OBJECTIVE:** To assess the risk of perinatal and postpartum depression and postpartum cardiovascular complications in women with PCOS.

**DESIGN:** Retrospective cohort study using administrative claims from 2000-2016.

**MATERIALS AND METHODS:** We included women aged 18-50 years enrolled continuously in the claims database Optum for a minimum of 6 months prior to conception, their entire pregnancy and at least 6 weeks following delivery. The PCOS cohort and all comorbidities were identified using specific codes from the International Classification of Diseases (ICD). Primary outcomes were incidence of perinatal and postpartum depression (within 3 months after date of delivery). Secondary outcomes included postpartum preeclampsia, postpartum eclampsia (within 6 weeks after the date of delivery), and peripartum cardiomyopathy (within the last month before or first 5 months after date of delivery). We compared outcomes between the PCOS and non-PCOS cohorts using univariate and multivariable logistic regression models adjusting for covariates including age, geographic location, preterm delivery, ART use, multiple births, pre-pregnancy depression, pre-pregnancy diabetes, pre-pregnancy hypertension, gestational diabetes, gestational hypertension, obesity, history of hyperlipidemia, smoking and race.

**RESULTS:** We identified 42,391 unique women with PCOS and 795,480 women without PCOS. Women with PCOS were more likely to have depression (4% vs 3%), diabetes (5% vs 1%), hypertension (6% vs 3%) and obesity (15% vs 5%) compared to women without PCOS (p<0.001 for all). They had a higher prevalence of gestational diabetes (24% vs 13%), gestational hypertension (14% vs 8%) and antepartum preeclampsia (5% vs 3%) than women without PCOS (p<0.001). In multivariable models, women with PCOS had a significantly higher odds of both perinatal and postpartum depression and postpartum preeclampsia and eclampsia compared to those without PCOS (Table). Postpartum results remained similar in planned sensitivity analyses in women with at least one year of pre-conception data, when including date of delivery in outcome definition and when varying the definition of perinatal and postpartum depression from the DSM-V criteria of 4 weeks postpartum to a commonly utilized literature length of one year postpartum.

**CONCLUSIONS:** This study demonstrates for the first time that women with PCOS are at higher risk for depression, preeclampsia and eclampsia in the fourth trimester of pregnancy. Our results highlight the need for comprehensive screening and targeted interventions during the postpartum period in this high-risk population.

**SUPPORT:** Snigdha Alur-Gupta is supported by the NIH T32 Training Grant: HD007440.

---

**O-94 Tuesday, October 15, 2019 11:30 AM**

**DEVELOPMENTAL POTENTIAL OF ANEUPLOID HUMAN EMBRYOS BEYOND IMPLANTATION.** Marta Nasila Shahbazi, Ph.D.a Tiannen Wang, M.D., Ph.D.a Yin Tao, Ph.D.a Li Sun, Ph.D.a Ying Zhan, Ph.D.b Antonio Pellicer, MD, PhD.c Richard Thomas Scott, Jr., MD.d Emre Selı, M.D.d Magdalena Zernicka-Goetz, Ph.D. d Department of Physiology, Development and Neuroscience, Mamalian Embryo and Stem Cell Group, University of Cambridge, Cambridge, United Kingdom; e The Foundation for Embryonic Competence, Basking Ridge, NJ; f IVIRMA ROMA, Roma, Italy; g IVI-RMA New Jersey, Basking Ridge, NJ.
OBJECTIVE: Aneuploidy is one of the major limitations of human reproduction. However, the developmental consequences of specific aneuploidies during the early stages of post-implantation development remain poorly characterized. In this study, we investigated the post-implantation development of human embryos with specific aneuploidies compared to euploid embryos.

DESIGN: Experimental study

MATERIALS AND METHODS: Aneuploid (n=71) and euploid (n=22) human blastocyst stage embryos were cultured up to day 9 of development, using a novel methodology that allows human embryo development in vitro to post-implantation stages. Embryos with specific aneuploidies (trisomy 21 [n=14], trisomy 15 [n=16], trisomy 16 [n=24], monosomy 21 [n=17]), which have a high global incidence and lack strong pre-implantation alterations in development, were assessed. Immunofluorescent techniques were used to detect the expression of molecular makers associated with development of embryonic and extra-embryonic lineages on day 9: OCT4+/ embryonic epiblast (precursor of the fetus and amnion), GATA6+ extra-embryonic hypoblast (precursor of the yolk sac), and OCT4- GATA6- extra-embryonic trophoblast (precursor of the placenta). Chromosome copy number in post-implantation embryos was determined by targeted next generation sequencing (tNGS).

RESULTS: We first analysed the global development of the different aneuploidies, and observed that monosomy 21 embryos had a higher incidence of arrest in culture (p=0.0105), which was specific to the implantation phase of development. The three trisomies analyzed developed similarly up to day 9 in terms of attachment, and preservation of the embryonic and extra-embryonic lineages. However, careful analyses of cell numbers revealed that while trisomy 15 and trisomy 16 embryos developed similarly to euploid embryos, trisomy 15 embryos had a specific hypoproliferation defect of the trophoblast (p<0.004), while the epiblast and primitive endoderm tissues (derived from the inner cell mass) were not affected (p=NS). In addition, analyses of the specific subset of monosomy 21 embryos that did not arrest during culture, unveiled a similar hypoproliferation phenotype of the trophoblast. To test whether this phenotype was due to mosaicism, embryos were dissected into different pieces for tNGS. This revealed 3 non-concordant cases out of a total of 6 embryos analysed. One case was identified as 45,XX,-21 based on trophectoderm biopsy at day 5 and PGT-A by tNGS, but showed 45,XX,-21 and 46,XX on day 9. Remarkably, this embryo developed well up to day 9 in vitro, although it displayed a hypoproliferative trophoblast.

CONCLUSIONS: Our results show that specific aneuploidies lead to specific developmental phenotypes during the first days of post-implantation development. Culturing human embryos beyond day 7 in vitro is a powerful tool to understand how chromosomal alterations influence embryo morphogenesis and to detect cases of mosaicism that cannot be identified by sampling trophectoderm cells on day 5.


O-95 Tuesday, October 15, 2019 11:45 AM

A LIFESTYLE INTERVENTION TARGETING WOMEN WITH OBESITY AND INFERTILITY IMPROVES THEIR FERTILITY OUTCOMES, ESPECIALLY IN WOMEN WITH PCOS: A RANDOMIZED CONTROLLED TRIAL

Maite Beltran, MSc; Belina Carranza-Mane, MD; Youssef Amin-Melk, MD; Marie-Hélène Pesant, MD; Karine Duval, PhD; Farrah Jean-Denis, MSc; Marie-France Langlois, MD; Hélène Lavoie, MD; Guy Waddell, MD; Jean-Patrice Baillargeon, MD*

OBJECTIVE: To evaluate the impacts of a lifestyle intervention on fertility outcomes in women with obesity seeking fertility treatments, with or without the polycystic ovary syndrome (PCOS).

DESIGN: Randomized controlled trial including 127 women with infertility and obesity, with no major infertility factor (female or male).

MATERIALS AND METHODS: Women were randomized either in the control group (CG; usual standard of care) or the lifestyle program group (LPG; lifestyle intervention with individual sessions (kinesiologist and nutritionist) and group sessions). A total of 108 women have completed ≥ 6 months of the study (51 LPG and 57 CG). Since randomization was stratified according to the presence of PCOS (PCOS: CG=35, LPG=33, Non PCOS: CG=22, LPG=18), we present results on fertility outcomes at 18 months of follow-up, and anthropometric and lifestyle changes at 6 months, in all women as well as in women with or without PCOS. Student’s t tests were used to compare means and chi-squared tests for proportions. P-values ≤ 0.05 were considered significant.

RESULTS: As compared to the CG, our lifestyle program increased significantly the pregnancy rates for all women (60.8% vs 36.6%, 1.58 fold, p=0.021) or for women with PCOS (57.6% vs 34.3%, 1.68 fold, p=0.005), but this difference was not significant for women without PCOS (66.7% vs 55.3%, 1.21 fold, p=0.18). Overall, our lifestyle intervention affects the probability of spontaneous pregnancy (All: 33.3% vs 12.3%, 2.7 folds, p=0.009; PCOS: 27.3% vs 5.7%, 4.8 folds, p=0.016; Non PCOS: 44.4% vs 22.7%, 2.0 folds, p=0.145) and live birth (all: 51.0% vs 36.8%, 1.39 fold, p=0.139; PCOS: 54.8% vs 31.4%, 1.75 fold, p=0.05; Non PCOS: 66.7% vs 45.5%, 1.47 fold, p=0.18). Pregnancy rates in women using an assisted reproductive technology (ART, n=63) were increased in the LPG for all women (58.6% vs 47.1%, 1.24 fold, p=0.36) and mildly for women with PCOS (51.3% vs 47.6%, 1.09 fold, p=0.744), although this was not statistically significant. Finally, compared to the CG, the LPG has lost significantly more weight at 6 months (all: 3.43% ± 4.45 vs 0.89 ± 3.67, p=0.003; PCOS: 3.66% ± 4.47 vs 0.93% ± 4.22, p=0.015), except for non-PCOS women who lost less weight (-2.31% ± 4.34 vs -0.48% ± 2.84,p=0.139). Women in the LPG also improved significantly more the quality of their diet (healthy eating index, all: +18.0 ± 13.7 vs +5.3 ± 12.4 on 100, p<0.001; PCOS: +13.6 ± 10.4 vs +46.5 ± 11.3 on 100, p=0.055).

CONCLUSIONS: A lifestyle intervention targeting women with obesity and infertility improves their chances of conceiving, especially spontaneously (with no fertility treatment). Our results suggest that such intervention could benefit women with PCOS even more. It is also possible that lifestyle modifications improve the effectiveness of ART in these women, but to a lower extent. Accordingly, this study supports the need of lifestyle intervention to reduce the costs associated with the fertility care of women with obesity and infertility.

O-96 Tuesday, October 15, 2019 12:00 PM

CONSERVATIVE SURGERY FOR OVARIAN TORSION IN YOUNG WOMEN: PERIOPERATIVE COMPLICATIONS AND NATIONAL TRENDS

Rachel S. Mandelbaum, MD, Meghan B. Smith, MD, Lynda D. Roman, MD, Richard J. Paulson, MD, MS, Koji Matsuow, MD, PhD University of Southern California, Los Angeles, CA.

OBJECTIVE: Ovarian torsion represents a gynecologic emergency for which oophorectomy was traditionally performed due to hypothetic risk of thrombotic events or necrosis following detorsion. Mounting evidence, however, has supported ovarian-preserving surgery in young women. This study compared incidence of perioperative complications and analyzed recent populational trends following conservative surgery vs. oophorectomy in young women.


MATERIALS AND METHODS: Women <50 years of age who underwent inpatient surgery for ovarian torsion were included. Those with ovarian malignancy were excluded. ICD-9 codes were used to compare those who had conservative surgery (detorsion with or without cystectomy) vs. oophorectomy. Perioperative complications were compared between the two groups after fitting a propensity score-based inverse probability of treatment weighting (IPTW) model to adjust for background differences. Multivariable analyses with a binary logistic regression model were performed to determine independent factors associated with conservative surgery, and temporal trends were assessed.

RESULTS: There were 89,801 cases of ovarian torsion during the study period; 20,643 (23.0%, 95% confidence interval (CI) 22.7-23.3) women had conservative surgery, while 69,158 (77.0%) women had oophorectomy. In the IPTW model, conservative surgery was independently associated with a decreased risk of perioperative complications by approximately 30% after controlling for patient demographics, surgical factors, and hospital characteristics (8.3% vs. 11.9%, adjusted-odds ratio 0.70, 95%CI [0.649-0.754], P<0.001). In particular, conservative surgery was not associated with venous thromboembolism (0.3% vs. 0.3%, P=0.615) or sepsis (0.3% vs. 0.3%, P=0.843). Rate of conservative surgery inversely decreasing; at age 14 and then more increasing at age 55 (P<0.001). On multivariable analysis, younger women, those with higher income, residents of the Northeast, those who had laparoscopic surgery, and those who had surgery at large and urban teaching hospitals were more likely to undergo conservative surgery (all, P<0.001). Conversely, those with higher comorbidity and morbidity obese women were less likely to have conservative surgery (all, P<0.001). Performance of conservative surgery significantly increased from 18.8% in 2001 to 25.1% in 2015 (13.3% relative increase, P=0.001).

CONCLUSIONS: Conservative surgical management of ovarian torsion is not associated with increased perioperative complications. While utilization of conservative surgery for ovarian torsion is increasing in the United States overall, significant variation exists based on patient demographic, surgical, hospital, and geographic factors. This supports continued efforts for ovarian preservation after detorsion in young women given long-term hormonal and fertility benefits.
OBJECTIVE: As of April 2019, six U.S. states now mandate private insurers to cover FP for patients facing iatrogenic infertility. In Illinois, this mandate extends to cover Medicaid recipients. We sought to assess how SART clinic representatives address questions relating to insurance coverage for cancer patients seeking FP.

DESIGN: ‘Mystery caller’ telephone survey of SART member clinics in FP coverage-mandated states.

MATERIALS AND METHODS: We developed and piloted two telephone scripts of a caller posing as a 30-year-old breast cancer patient interested in FP; one script specific to private and the other to public insurance. Our primary outcome was whether information provided reflected state FP coverage mandates. We called all SART member clinics in FP coverage-mandated states (as of 1/1/2019) and performed a second call for Illinois clinics to assess responses specific to public insurance. Clinics were categorized by state, practice type (university-affiliated vs private practice), and time since enactment of coverage mandate (pre- vs post-1/1/2019). All responses were recorded and coded for analysis. Responses to “Does insurance [or Medicaid] ever cover FP for cancer patients?” were categorized as positive (yes, usually, sometimes or it depends) versus negative (no, usually not, and I don’t know), and subcategorized as confident (yes, usually, no, and usually not) or not confident (sometimes, it depends, or I don’t know). Data are presented as %, and Fisher’s exact test (p<0.05) was used to compare responses across clinic characteristics and insurer.

RESULTS: We identified 35 SART member clinics in IL, CT, DE, MD, and RI; 3 were excluded due to nonresponse or conflicts. Of 32 clinics, 29 (91%) offered FP for cancer patients. Less than half (39%; n=11) were confident that insurance would cover FP, and 7% reported they did not accept any insurance. Only 21% (n=6, 4 from IL) referenced legislation mandating FP-coverage. Neither practice type nor time since enactment of state mandate influenced clinic responses regarding insurance coverage of FP (p>0.05). In IL, less than half (44%) were confident that private insurance would cover FP. We found that IL clinics were more likely to report any positive confirmation for coverage if the patient reported she had private compared to Medicaid insurance (81% vs. 14%, p<0.005). 87% of IL clinics did not accept Medicaid, and none provided a direct referral. University clinics in IL were more likely than private clinics to accept Medicaid (66.7% vs 0%, p<0.05) and know that Medicaid covered FP (66.7% vs 0%, p<0.05).

CONCLUSIONS: In states where FP coverage is mandated, the SART clinic representatives were often unaware of insurance coverage of FP. In IL, clinic staff are especially uninformed of Medicaid coverage of FP. Our findings identify a critical gap in knowledge among SART clinics, as patients may choose to permanently abandon FP due to misinformation regarding financial coverage. This study highlights the need for educational interventions and improved clinic protocols to reflect state mandates. Future research should examine public awareness of coverage mandates.
coverage for infertility treatment. In fact, the majority do not. Federal pre-
pretensions and other exemptions in state law restrict fertility coverage even
in states with mandates. The goal of this study was to determine the percent-
age of reproductive age women in Massachusetts with coverage for infertility
treatment.

DESIGN: Population based cross-sectional study

MATERIALS AND METHODS: We obtained de-identified population level
data from 3 sources: the State Census Bureau (number of women aged
20-44 living in Massachusetts in 2016); the Center for Health Informa-
tion and Analysis (CHIA) (number of women self-insured or with public
assistance insurance); and the US Department of Defense (number of women
with military health insurance).

RESULTS: In 2016, 1,142,542 women aged 20-44 lived in Massachusetts.
Table 1 shows their health insurance enrollment.

<table>
<thead>
<tr>
<th>Population</th>
<th># of Women</th>
<th>% of Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Census data: age 20-44 residing in MA in 2016</td>
<td>1,142,542</td>
<td>100%</td>
</tr>
<tr>
<td>Exempt from Coverage</td>
<td># of Women</td>
<td>% of Women</td>
</tr>
<tr>
<td>Self-insured employer sponsored Plans</td>
<td>498,931</td>
<td>43.7%</td>
</tr>
<tr>
<td>Public Assistance Insurance</td>
<td>184,179</td>
<td>16.1%</td>
</tr>
<tr>
<td>Military Insurance</td>
<td>5,080</td>
<td>0.4%</td>
</tr>
<tr>
<td>No Insurance</td>
<td>39,746</td>
<td>3.5%</td>
</tr>
<tr>
<td>Subtotal</td>
<td>727,936</td>
<td>65.7%</td>
</tr>
<tr>
<td>Potential Coverage</td>
<td># of Women</td>
<td>% of Women</td>
</tr>
<tr>
<td>Mandate Eligible Insurance</td>
<td>414,606</td>
<td>36.3%</td>
</tr>
</tbody>
</table>

CONCLUSIONS: There are notable exemptions to Massachusetts’
mandated health benefits statutes. Self-insured policies provided by em-
ployers are governed by the Federal Employee Retirement Income Security
Act (ERISA) and are not subject to state mandated benefits. Federally-funded
plans covering Military and Civilian federal employees as well as Mas-
achusetts’ Medicaid, which administers the Massachusetts Medicaid program, are also
exempt.

As a result, only 36.3% of reproductive aged women in Massachusetts
have health insurance subject to the mandate. Moreover, the Massachusetts
Division of Insurance permits insurers latitude in applying the law. Thus,
women who do not meet certain biological criteria, have exceeded a prede-
termined number of treatment cycles, or have surpassed a total dollar cap are
exempt from coverage. Un-partnered women may not have treatment
coverage until they have paid out-of-pocket for 6-12 months of treatment.

Massachusetts is often cited as the model state for health insurance
coverage of infertility treatment. Yet, only 36.3% of reproductive aged
women are subject to the mandate and even fewer have meaningful access to
services when exceptions are considered. Given that Massachusetts’
mandate has fallen short of affording women real access to care, future study
is warranted with the hope of informing legislative action.

O-101 Tuesday, October 15, 2019 11:45 AM

THE PRICE IS RIGHT? ANALYSIS OF
PRICE TRANSPARENCY IN ASSISTED
REPRODUCTION. Katherine Elise McDaniel, MD,
Meghan B. Smith, MD, Brittany L. Klooster, MD,
Rachel Blair Danis, MD, Kristin Bendikson, M.D., Richard J. Paulson,
MD, MS, Jacqueline Ho, MD MS. University of Southern California, Los
Angeles, CA.

O-100 Tuesday, October 15, 2019 11:30 AM

RIGHT TO HEALTH: THE SITUATION OF ASSISTED
REPRODUCTION TECHNIQUES WITH GAMETES
DONATION IN ITALY. Giulia Scaravelli, PhD,
Roberto De Luca, Master degree, Roberta Spolletini, Master de-
gree, Vincenzo Vigiliano, Master degree. Simone Bolli, high school,
Simone Fiacavento, high school, Lucia Speziale, Master degree,
Anna Bertini, Master degree Italian Assisted Reproductive Technology Regis-
ter, Italian National Institute of Health, Rome, Italy.

OBJECTIVE: The postponement of childbearing age in Italy, determine a
large number of older women wanting a baby. In these cases and in many
others gametes donation could represent an important option for infertility
treatments. Only the recent change of the Law 40/2004 in Italy in April
2014 allowed infertile couples to access to gametes donation. The objective
is to analyze the number and type of gametes donation cycles collected by
The Italian Assisted Reproductive Technology Register (IARTR) since 2014.

DESIGN: In this study IARTR analyzed retrospectively data on 16807
gametes donation cycles performed from May 2014 till December 2017 on
14577 patients. 220 Assisted Reproductive Technology (ART) clinics and
179 Intrauterine Insemination (IUI) clinics sent data to the National Italian
Register and participated in the study with 102 out of 220 (46.4%) and 3
out of 179 (1.7%) performing donation cycles.

MATERIALS AND METHODS: All ART and IUI centres which has
performed at least one cycle with gametes donation, that have sent data
during the study period were included in the study. Parameters regarding
number of patients, number of cycles, treatment indications, age classes,
pregnancies and live births rates were statistically analysed using SPSS
statistic 25.0.

RESULTS: The centers participating in the annual data collection and
which performed at least one donation cycle were 105, of which only
12 were public structures. 14577 patients underwent 16807 initiated cy-
cles (4.4% of all ART and IUI cycles performed in the same period)
that included 14800 cycles performed with complex ART techniques
and 2007 cycles performed with IUI-D. Most cycles (44.6%) were carried
out with oocyte donation, 25.8% with sperm donation and 29.6% with
cryopreserved embryos obtained after a donation. The main indication
for treatment for oocyte donation was the maternal advanced reproductive
age (37.9%), while for sperm donation, 94.0% of indications refer to dis-
eases that affect sperm vitality. Almost all the gametes used for the treat-
ments come from abroad (97.8% of the oocytes and 80.7% of semen).

The pregnancy rate per transfer carried out in the study period was
37.7% for fresh egg donation, 34% for cryopreserved oocytes, 33.5%
for cryopreserved embryos and 36.6% for sperm. The percentage of mul-
tiple deliveries was 32.6%, 17.5%, 13.8% and 18.1% respectively. For the
semen used in intrauterine insemination the pregnancy rate per cycle
started was 20% and the multiple delivery rate was 14.4%. In these 4
years 3857 children were born alive, equal to 7.3% of those born from
all ART techniques in the same period.

CONCLUSIONS: The Italian situation regarding gametes donation policy,
dares the question of equity in access to these procedures. The impossibility
of finding donors in our country, dictated by the absence of information cam-
paigns and the lack of possibility of compensation for donors limits the use of
these techniques in public structures. Only a few regions have adopted pol-
ics to improve donation cycles in public centers.

| Price or Discount Information | Clini
| Type | Percentage of Clinics Reporting Mean Cost Reported |
| --- | --- | --- | --- |
| Any Price Listed | 78 (20.8%) | N/A |
| Consultation | 33 (8.8%) | $364.84 (SD $159.64) |
| IUI Cycle | 26 (6.9%) | $1,665.07 (SD $900.10) |
| IVF Cycle | 48 (12.8%) | $10,334 (SD $2,980.00) |
| FET Cycle | 24 (6.4%) | $4,060.00 (SD $1,017.86) |
| OC Cycle | 33 (8.8%) | $7,190.00 (SD $2,694.00) |
| Any Discount/Financing Listed | 249 (66.4%) | N/A |
| Medication Discounts | 69 (18.4%) | N/A |
| Shared Risk Refund | 75 (20.0%) | N/A |
| Lending Programs | 151 (40.2%) | N/A |
| External Financing or Grants | 98 (26.1%) | N/A |
| Internal Financing (e.g.: Multi-Cycle Discounts) | 88 (23.4%) | N/A |
| Military Discounts | 74 (19.7%) | N/A |
| Cancer Discounts | 36 (9.6%) | N/A |
OBJECTIVE: A recent influx of assisted reproductive technology (ART) and services promote price transparency, with detailed costs of services listed on websites. Given current market trends, we sought to determine how existing clinics perform in terms of price transparency and to what extent they provide information on available discounts and financial assistance.

DESIGN: Cross-sectional analysis of Society for Assisted Reproductive Technology (SART) registry clinics.

MATERIALS AND METHODS: Clinics were identified through the SART website clinic search function on 4/14/19. Military clinics and those clinics without a website were excluded. Between 4/15/19 and 4/22/19, each clinic’s website was queried. Practice location (city, state) and type (private vs. academic vs. other [e.g., managed care]) were recorded. Prices for consultation, intrauterine insemination (IUI; including monitoring and sperm preparation), in vitro fertilization (IVF; excluding pre-implantation genetic testing), frozen embryo transfer (FET), and oocyte cryopreservation (OC) were recorded. Mean costs were calculated for each reported price.

RESULTS: 382 clinics were listed on the SART website and 375 met study inclusion criteria. Table 1 illustrates the number and percentage of clinics that provided costs for services, information on discounts, and available financial assistance on their websites. Only 22.8% (67/293) of private practices and 11.7% (9/77) of academic practices reported the price of one or more services.

CONCLUSIONS: Most existing clinics do not report the costs of consultation or of various treatments on their websites. This lack of transparency may actually create barriers to care if costs are lower than anticipated. The majority of clinics provide information on available discounts and/or financing information, the most common being links to lending programs. Full disclosure of cost on clinic websites will not only match new market trends in ART, but also demystify the costs of fertility treatment and potentially democratize fertility care by fostering price competition.

O-102 12:00 PM Tuesday, October 15, 2019

EMERGENCY COS IN ONCOFERTILITY PRESERVATION. Marouen Brahem, Associate professor, a Sarah Amari, Medical Degree, b Khadija Feriel Kacem Berjeb, Associate professor, a Mokla Bouricha, resident, c Wissal Jaafar, Medical Degree, d Manel Hamdoun, Medical Degree, e Linda Debabi, Medical Degree, f Olfa Bahri, Sr., Professor, g Anis Fadhlaoui, Associate Professor, h Fethi Zhioua, Pr i Aziza Othmana University Hospital, Tunis, Tunisia; j Gyneecology, Obstetric and Reproductive Medicine Department. Aziza Othmana University Hospital, Tunis, Tunisia; k Reproductive Medicine Laboratory. Aziza Othmana University Hospital, Tunis, Tunisia; l Biochemistry Department. Aziza Othmana University Hospital, Tunis, Tunisia.

OBJECTIVE: There is often an urgent need to start cancer treatment. Therefore, protocols with alternative timing to start COS have been proposed in fertility preservation. Is random start COS as effective as conventional start COS in fertility preservation?

DESIGN: We conducted a retrospective study.

MATERIALS AND METHODS: The study included 104 patients recently diagnosed with cancer and in preparation for gonadotoxic therapy, from January 2017 to January 2019.

Patients were evaluated within 24-48h after the referral, clinically, by ultrasound (antral follicular count) and by an AMH dosage. The underlying conditions were mainly: Hodgkin’s Lymphoma (46% patients), Breast cancer (30%), Rectal cancer (3%), and various other pathologies (Ovarian, Gastric cancer, T Lymphoma, etc.). AMH levels ranged from 0,2ng/ml to a maximum of 10,5ng/ml. All 104 patients underwent IVF cycles using GnRH antagonist protocol. 65 patients underwent an early follicular start COS (Group 1), whereas 9 had a random (late follicular or luteal) start (Group 2). The addition of Letrozole was compulsory in case of estrogen-sensitive tumors and E2 levels, closely monitored.

Oocyte retrieval was done transvaginally in 65% of cases and was transurethral in 35%. Oocyte or embryo vitrification were proposed to the patients based on marital status and preference.

We chose to compare the outcome of random-start versus conventional start COS.

RESULTS: Our patients’ age ranged from 14 to 41 years, with a mean of 26 in both groups. As for status, 73% were single, and 27% married. Mean AMH levels were similar in both groups (2.34 +/- 0.7 in Group 1; 2.29 +/- 0.9 in Group 2). All patients followed an antagonist protocol. There was no significant difference in the duration of stimulation (10.6+/-2 days in case of early follicular start COS versus 10.13+/- 2 days in random-start COS; p=0.5).

Furthermore, the total number of oocytes retrieved upon pick-up was similar in both groups (8.06+/-3 in Group 1 versus 7.37+/-2 in Group 2; NS). As for the maturity rate, no significant difference was noted (76% oocyte maturity rate in early follicular start COS and 73% in random-start COS).

CONCLUSIONS: Random start COS seems as effective as conventional start COS in fertility preservation. The main advantage is that Random-start can minimize delays and allow more patients to undergo fertility preservation, and yet still proceed with cancer treatment within 2 weeks.

ANDROGEN EXCESS

O-103 Tuesday, October 15, 2019 10:45 AM

PREGNANCY-RELATED ECONOMIC BURDEN OF POLYCYSTIC OVARY SYNDROME (PCOS). Carrie Riesenberg, MD, a Anika Jagasia, BA, b Ricardo Azziz, MD, MPH, c University of California, Los Angeles, CA; d University of Pennsylvania, Philadelphia, PA; e University at Albany, SUNY, Albany, NY.

OBJECTIVE: PCOS is the most common endocrine abnormality of reproductive-aged women, affecting approximately 6-10% of unselected reproductive-aged women (~4-6 million women in the U.S.) depending on the criteria used (National Institutes of Health [NIH], Rotterdam or the Androgen Excess and PCOS Society). The cost of initial evaluation and treatment of reproductive-aged women with PCOS, excluding those associated with pregnancy, has previously been shown to represent a significant financial burden to our health care (~$4.36 billion in 2004 dollars, 5.39 billion in current dollars). The goal of the present study was to define, using current definitions and prevalence or incidence data, the minimal excess economic burden of pregnancy in women with PCOS in the U.S.

DESIGN: Systematic literature review and economic burden analysis.

MATERIALS AND METHODS: We performed a systematic review of the published literature to identify studies evaluating the epidemiology of PCOS in pregnancy and its clinical consequences and costs. We selected the three most consistently reported and prevalent pregnancy related health outcomes associated with PCOS to generate our cost analysis: gestational diabetes (GDM), pregnancy-induced hypertension (PIH) and preeclampsia. We linked published cost data for the aforementioned health consequences to their excess incidence attributable to PCOS in order to calculate overall estimated health care-related economic costs.

RESULTS: We estimate that there were 254,463 PCOS-related births in the U.S. in 2017. After accounting for baseline risk, we estimate that an excess 27,177 of these births were complicated by GDM, 16,286 by PIH, and 7,354 by preeclampsia as a result of PCOS. We estimate the mean excess annual cost of pregnancy-related care for women with PCOS in the U.S. due to GDM to be $53,563,896, PIH to be $149,831,200 and preeclampsia to be $84,291,548.

CONCLUSIONS: A conservative estimate of the excess cost of pregnancy-related complications attributable to PCOS in the U.S. exceeds $287 billion in current dollars.


O-104 Tuesday, October 15, 2019 11:00 AM

SEVERE ENDOMETRIOSIS IN RHESUS MACAQUES CONSUMING A WESTERN-STYLE DIET (WSD) AND CHRONICALLY TREATED WITH ANDROGEN. Ov D. Slayden, PhD, a Cecily V. Bishop, PhD, b Emily Mishler, MS, c Lauren Drew Martin, DVM, c Heather M. Sidener, DVM, DACLAM, c Jon D. Hennebold, PhD, a

FERTILITY & STERILITY®
OBJECTIVE: To evaluate the effects of chronic mild hyperandrogenemia and/or consumption of a western-style diet (WSD) on the rate of endometriosis in rhesus macaques.

CONCLUSIONS: These data support the hypothesis that T in the presence of an obesogenic diet increases the risk for advanced endometriosis. Moreover, androgen alone drives cell proliferation in endometriotic cells obtained from chronically treated T+ WSD animals.


SUPPORT: NIH P50-HD071835 (RLS/JDH), and NIH P51-OD011092 (ONPRC).

TABLE 1. Frequency and stage of endometriosis (n=10/group).

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>T WSD</th>
<th>WSD + T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adhesions</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Stage I</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Stage II</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Stage III</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Stage IV</td>
<td>0</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Total Cases</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

O-105 Tuesday, October 15, 2019, 11:15 AM

POSTPARTUM WEIGHT RETENTION IN WOMEN WITH PCOS AND CONTROLS. Iris Tienlynn Lee, MD, a Snigdha Alur-Gupta, M.D., b Anuja Dokras, M.D., M.P.H., Ph.D. c

aUNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM, bUniversity of Pennsylvania Perelman School of Medicine, Philadelphia, PA.

OBJECTIVE: To evaluate whether women with PCOS are more likely to retain weight after delivery compared to women without PCOS.

RESULTS: A total of 7692 women were included (5.6% with PCOS). On average, women with PCOS were older (median age 32 versus 31 years), had fewer prior deliveries (median of 1 versus 2), and were more likely to be White (54.31% versus 36.07%) (p<0.001 for all) compared to controls. Women with PCOS had higher prepregnancy BMI (26.4 vs. 24.7 kg/m²; p=0.001) as well as higher prevalence of gestational diabetes (13.9% versus 6.32%, p<0.001) and hypertension (13.02% versus 8.66%, p=0.002) compared to controls. At each of the four postpartum time points, women with PCOS had a higher BMI than controls. However, total weight gain during pregnancy was lower in the PCOS group (12.50 kg ± 13.29 kg, p=0.015). The percentage of women who surpassed Institute of Medicine (IOM) guidelines for pregnancy weight gain based on BMI was similar between groups (43.4% PCOS versus 46.85% controls, p=0.158). At six weeks postpartum, the amount of weight retained by women with PCOS (2.95 kg, -0.77-6.07 kg) was lower than controls (3.96 kg, 0.76-7.32 kg). The likelihood of retaining five or more kilograms at this time was lower in the PCOS group (32.91% versus 40.95%, aOR 0.79, 95% CI 0.63-0.99). The proportion of high weight retainers at three (28.17% versus 38.41%), six (>35.41% versus 32.16%) and 12 (27.08% versus 28.32%) months was not significantly different between the PCOS group and controls, although approximately 20% of the cohort had an increase in BMI category at the end of 12 months. Postpregnancy BMI category did not differentially affect postpartum weight retention in either group.

CONCLUSIONS: Women with PCOS were more likely than controls to be obese prior to pregnancy but had less weight gain in pregnancy. Early nutritional counseling is needed to prevent pregnancy weight gain above the IOM guidelines. This is offered to obese pregnant patients in our health system, and our study also highlights the need for continued nutritional counseling during the postpartum period given the proportion of women with high weight retention and increase in BMI category 12 months after delivery.
ultrasound) and at least one patent fallopian tube. Women underwent OI with either CC or letrozole for up to 5 cycles. Male partners were required to have a semen analysis with sperm concentration of at least 14 million/ml. Chi-Square/Fisher exact, Student’s t, and logistic regression were utilized as necessary the OR for live birth were reduced, 0.55 (0.34, 0.89) with MetS and 0.60 (0.43, 0.85) with VHBMI. Pregnancy complications occurred in 42.5% with CC and 41.5% with letrozole. In the presence of MetS the OR for live birth were reduced, 0.55 (0.34, 0.89) with MetS and 0.60 (0.43, 0.83) with VHBMI in the CC group. The odds for LGA were higher after adjusting for VHBMI also (both OI agents). VHBMI increased the odds (1.76 [1.25, 2.48]) for Pre-E (CC and letrozole). MetS was not associated with Pre-E in either group.

CONCLUSIONS: MetS and VHBMI lowered the odds of fecundity with CC. MetS was associated with higher odds of gestational diabetes and LGA infants after adjusting for VHBMI with both agents. MetS did not correlate with spontaneous pregnancy or with either agent. VHBMI in contrast was associated with greater odds for Pre-E with either. Incidence of pregnancy complications is high following OI for oligoovulation in PCOS, in part because of MetS and/or VHBMI.

SUPPORT: The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD): U10 HD077680, U10 HD39005, U10 HD38992, U10 HD27049, U10 HD38998, U10 HD055942, HD055944, U10 HD55936, and U10HD55925. This research was made possible by the funding by American Recovery and Reinvestment Act. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NICHD or NIH.

O-107 Tuesday, October 15, 2019 11:45 AM

OXIDATIVE DAMAGE IS PRESENT IN LIPOPOLYSACCHARIDE (LPS) TOLERANT MONONUCLEAR CELLS (MNC) OF OBESE WOMEN WITH POLYCYSTIC OVARY SYNDROME (PCOS).

Anthony J. Acton, Jr., B.S. a University of Illinois at Chicago College of Medicine, Chicago, IL; bIndiana University School of Medicine, Indianapolis, IN.

OBJECTIVE: In PCOS, lipid-induced oxidative stress promotes inflammation. In vitro exposure to lipid+LPS suppresses inflammation in LPS tolerant MNC of obese women with PCOS. We examined the effect of MNC exposure to lipid alone versus lipid+LPS on IL-6 mRNA and secretion, and on the mRNA and protein of p47phox, the key component of the ROS producing enzyme NADPH oxidase, in women with PCOS compared with women without androgen excess.

METHODS: 20 PCOS (10 lean; 10 obese) and 20 controls (10 lean; 10 obese) ages 18-40. MNC isolated from fasting blood samples were cultured with palmitate under pre- (0.4 mM) and post-prandial (0.2 mM) conditions with or without LPS. IL-6 and p47phox mRNA was quantified by RT-PCR. IL-6 secretion was measured by ELISA in culture supernatants. p47phox protein was quantified by Western blotting. Androgens were measured by RIA from blood samples drawn at 0, 24, 48 and 96 hours after HCG administration. Insulin sensitivity was measured by 18F-D-glucose uptake.

RESULTS: In response to lipid+LPS, the change from baseline (Δ) between pre- and post-prandial conditions increased in lean and obese women with PCOS and obese controls, and was significantly different (p<0.001) compared with controls. A separate analysis in lean controls in response to lipid alone revealed a significant increase in MetS defined by International Diabetes Federation criteria. Overweight/obese = HbA1c (> 52 kg/m²), and Very high BMI (VHbmi) > 35 kg/m². Pregnancy complications included pre-eclampsia (Pre-E), gestational diabetes (GDM), preterm delivery, large for gestational age (LGA) and intrapartum growth restriction (IUGR).

RESULTS: Prevalence of HiBMI was 83.5%, VHbmi 50.8%, and MetS 34.5%. For VHbmi 47% had MetS compared to 21% when BMI < 35 kg/M². The odds for clinical pregnancy (fetal heart rate) were 0.59 (0.38, 0.90) with MetS and 0.60 (0.43, 0.83) with VHbmi in the CC group. Similarly the OR for live birth were reduced, 0.55 (0.34, 0.89) with MetS and 0.61 (0.43, 0.85) with VHbmi. Pregnancy complications occurred in 42.5% with CC and 41.5% with letrozole. In the presence of MetS the OR for GDM was 0.66 (p<0.0001); protein: r=0.60, p<0.0001; and was inversely correlated with ISOGTT (mRNA: r=-0.57, p<0.0004; protein: r=-0.58, p<0.0002). In women with PCOS after lipid+LPS, p47phox secretion was inversely correlated with AUC (T=0.47, p<0.05) and directly correlated with ISOGTT (r=0.51, p<0.04).

CONCLUSIONS: In PCOS, lipid-induced increases in IL-6 and p47phox are independent of obesity. Oxidative capacity is preserved in the face of LPS tolerance manifested by a two-fold increase in p47phox despite IL-6 suppression when obesity accompanies PCOS. LPS tolerance may be potentiated by hyperandrogenism to limit insulin resistance.

References: 1. Gonzalez F, Sia CL, Abdelghani OA, Melvin, RM, Garrett TJ. Lipid-induced reactive oxygen species generation is related to ovarian hyperresponsiveness to HCG stimulation in normal weight women with polycystic ovary syndrome: Lipopolysaccharide-induced NFkB suppression is linked to hyperandrogenism in PCOS. Fertil Steril. 2018; 110 (3 Suppl):c8–e9.


O-108 Tuesday, October 15, 2019 12:00 PM

SCREENING FOR ANDROGEN EXCESS IN WOMEN: ACCURACY OF SELF-REPORTED EXCESS BODY HAIR GROWTH AND MENSTRUAL IRREGULARITY.

Dysfunction. Jessica L. Chan, MD, MSCE, a Marita Pall, MD, PhD, b Uche Ezech, MD, b Ruchi Mathur, MD, a Erica T. Wang, MD, M.A.S., b Margaretta D. Pisarska, MD, a Ricardo Azziz, MD, MPH, c Cedars-Sinai Medical Center, Los Angeles, CA; dUniversity at Albany, SUNY, Albany, NY.

OBJECTIVE: To test the use of a simple telephone questionnaire to identify women at increased risk for polycystic ovary syndrome (PCOS) and other androgen excess (AE) disorders.

DESIGN: Prospective community-based cohort study.

MATERIALS AND METHODS: Women 14-45 years of age were recruited by advertisements seeking women either with irregular menstruation and/or excess body hair, or as healthy controls. A brief telephone screening was undertaken using a questionnaire consisting of 3 questions and subjects were asked to self-assess the presence or absence of male-like body hair and menstrual irregularity. Based on this screening, women with self-assessed irregular menses and/or excess body/facial hair were labeled as having possible androgen excess (Poss-AE); those self-assessed with regular menses and no excess body/facial hair were labeled as probable non-AE (Non-AE). All subjects were then examined directly; the evaluation included a health questionnaire, assessment of hirsutism using the modified Ferriman-Gallway (score), ultrasound evaluation of the ovaries, and measurement of DHEAS, total and free testosterone, TSH, prolactin and 17-hydroxyprogesterone. A luteal phase progesterone level was performed in eumenorrheic subjects to confirm ovulation. All women evaluated were not on hormonal medications in the prior 3 months.

RESULTS: The study was completed in 206/298 (69%) of eligible women in the Poss-AE cohort and in 139/192 (73%) of eligible women in the Non-AE cohort. The Poss-AE cohort was significantly older (p<0.001) and had a higher mean BMI (32.8±5 kg/m² vs. 27.6±4 kg/m², p<0.0001) than the Non-AE cohort. The Poss-E cohort had a mean free testosterone (5.2±3.7 vs. 2.4±1.9 pg/mL, p<0.001), higher total testosterone (40.9±25.8 vs. 26.5±14.3 pg/mL, p<0.001) and DHEAS FERTILITY & STERILITY®
(241.1±118.6 vs. 193.3±98.9, p<0.05) than the Non-AE cohort. Of the Poss-AE and Non-AE women, 83% and 16%, respectively, presented with PCOS according to the updated 2018 International Consortium guidelines. The sensitivity, specificity, PPV and NPV of the telephone questionnaire to predict PCOS was 88%, 77%, 84% and 81%, respectively. The sensitivity, specificity, PPV and NPV of the telephone questionnaire to predict hirsutism (mFG ≥ 4) was 8%, 80%, 81% and 80%, respectively. The sensitivity, specificity, PPV and NPV of the telephone questionnaire to predict oligo-oovulation was 98%, 87%, 84% and 98%, respectively.

CONCLUSIONS: A simple telephone questionnaire, based on self-assessment of body hair and menstrual status, can be used with high predictive value to identify women at risk for AE disorders, including PCOS, and to detect healthy controls. This approach could be an important tool for the undertaking of needed epidemiologic studies of AE and PCOS.

O-109 Tuesday, October 15, 2019 10:45 AM
THE EFFECT OF HIGH HUMIDITY ON EMBRYO CULTURE MEDIA OXIDATION. Carmela Albert, PhD, Raquel Del Gallego, PhD, Lucia Alegre, PhD, Zaloa ZL, Larraategui, PhD, Julian Marcos, Sr, PhD, Belén Aparicio-Ruiz, PhD, Marcos Meseguer, PhD, IVIRMA, Valencia, Spain; cIVIRMA Global, Valencia, Spain; dEMBRYOLOGIST, BILBAO, Spain; eIVIRMA Global, Valencia, Spain, Tel Aviv, Israel.

OBJECTIVE: Oil overlay has supported the successful use of a dry incubator to culture human embryos, preventing changes in the pH and temperature. However, dry conditions may affect the osmolality due to the evaporation of the culture media. The use of humid conditions avoids osmolality changes. Our aim in this study was to know how culture conditions might affect embryo culture related to an oxidative stress profile.

DESIGN: Retrospective multicentric study including a total of 7,544 embryos from 1,043 patients undergoing egg donation and autologous IVF treatment.

MATERIALS AND METHODS: Embryos were cultured in a time-lapse incubator system Geri® (Geneva, Australia). Out of its 6 patient-individual chambers, 3 of them worked under a dry atmosphere (DC) and 3 under humid conditions (HC). Retrospectively, blastocyst and good morphology blastocyst rate were evaluated.

For the oxidative stress profiling, a total of 125 spent embryo culture media from the Geri Dishes® were analyzed using the TCL (Thermochemiluminescence) Analyzer (Carmel Diagnostics, Kriyati-Tivon, Israel). Its mechanism of action included oxidation leading to the production of light energy counted as photons emitted per second (cps). The use of sequential vs. single-step culture medium was taken into account when HC and DC were compared. Data was analyzed with ANOVA and Chi-squared tests (SPSS software).

RESULTS: No statistical differences were found in terms of embryo development. We obtained a very similar blastocyst rate when the embryos were culture under HC: 71.3% vs DC: 71.0%. Likewise, high quality embryo rate (classified as A or B according to the ASEBIR criteria) was very similar 38.1% in HC vs 37.7% in DC. Regarding the oxidative stress profile, no significant differences were found between groups HC and DC in single-step medium. However, the results showed a trend towards a higher oxidative stress level in media cultured under DC: 127.8±40.6 cps vs. HC: 106.9±44.1 cps. On the other hand, sequential medium did show a significant oxidative status difference (p < 0.05) between media collected on day 3 (75.5±20.4 cps) and media collected on day 5/6 (105.8±39.2 cps). Moreover, no significant differences were found between the oxidative status of media coming from sequential collected on day 5/6 and single-step media. These results were quite interesting as they may depict how the oxidative metabolism in the embryos increase after day 3, when the maternal to zygotic transition takes place.

CONCLUSIONS: In a previous study, our results strongly suggested that culture conditions with a high humidity atmosphere promoted embryo development. However, in an attempt to increase the sample size to confirm these findings, no statistically significant differences have been found. According to the oxidative status of the spent media, DC seem to affects the media oxidation. A larger sample size would be required to confirm this trend.

O-110 Tuesday, October 15, 2019 11:00 AM
PUTRESCINE SUPPLEMENTATION PROMOTE THE MATURATION OF OOCYTES AND IMPROVE THE QUALITY OF OOCYTES AND THE POTENTIAL OF EMBRYOS DEVELOPMENT. Wei Wu, MD, Lingbo Cai, PhD, Yuting Ling, Master, Johnh Liu, PhD, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China; tOttawa Hospital Research Institute, Ottawa, ON, Canada.

OBJECTIVE: To investigate the mechanisms of promotion the maturation of oocytes and improvement the quality of eggs and the potential of embryos development through exogenous addition of putrescine in the treatment of diminished ovarian reserve(DOR).

DESIGN: A self-controlled paired design was used to select a total of 136 immature eggs in the ovulation-promoting process in patients undergoing in vitro fertilization.

MATERIALS AND METHODS: The even number of immature eggs of the same patient, were paired and randomly assigned to the experimental group or control group. Putrescine was added to the in vitro maturation (IVM) medium of immature eggs in the experimental group, and the control group was a conventional IVM group. After 24 to 48 hours culture, the first polar body of the maturation oocyte was biopsied and then the oocytes were subjected to whole genome amplification. Next Generation Sequencing technology was used to detect changes in whole genome copy number and mitochondrial copy number content of oocytes/polar bodies.

RESULTS: 136 GV eggs were randomly assigned to the control group (IVM group) and the experimental group (IVM+putrescine group). The maturation rate of the experimental group was 66.18%, which was higher than the 57.35% of the control group. The mitochondrial content of mature eggs in the IVM+putrescine group was 22.33% higher than that in the IVM group. The aneuploidy rate in the IVM+putrescine group was slightly higher than that in the IVM group, but the difference was not statistically significant.

CONCLUSIONS: Putrescine can promote the in vitro maturation rate of GV and can also increase the content of mitochondria in oocytes, thereby improving the quality of oocytes and promoting the development potential of embryos.

SUPPORT: The National Key Research and Development Program of China (2017YFC1001602; 2017YFC1001300)

O-111 Tuesday, October 15, 2019 11:15 AM
HUMAN BLASTOCYSTS DERIVED FROM MONOPRONUCLEAR ZYGOTES: A BIOLOGICAL MODEL FOR THE STUDY OF PLOIDY, EUPOLOIDY, TOPOGRAPHY AND HETERO-PARENTAL INHIBITION. Noelia Grau, PhD, Nuria Soler, MSc, Ana Gonzalez-Picazo, MSc, Xavier Vendrell, PhD, María José Escribá, PhD, Pilar Gáminz, PhD, IVIRMA-Valencia, Valencia, Spain; 1Universidad de Valencia, Valencia, Spain; 1IVI Foundation, Valencia, Spain; 1Sistemas Genómicos, Paterna, Spain; 1IVIRMA Valencia, Valencia, Spain.

OBJECTIVE: To describe the ploidy and euploidy, chromosomal concordance between different regions of the trophectoderm (TE) and also between TE and inner cell mass (ICM). Besides, we aimed to identify chromosomal inheritance (paternal/maternal) of haploid, diploid and polyploid blastocysts derived from monopronuclear (MPN) zygotes. Additionally, it will be discussed the eventual “rescue” of these blastocysts for reproductive purposes.

DESIGN: Prospective experimental study that includes 910 ICSI cycles from April 2016 to December 2018. 1081 MPN zygotes (1.2%) were obtained. A total of 199 zygotes reached the blastocyst stage (18.5%, blastocyst rate). Seventy-six blastocysts were assigned to three experimental series, according to the genetic analysis performed (ploidy, topography and parental inheritance).

MATERIALS AND METHODS: The study was carried out in 3 series. Series 1: 26 blastocysts were fixed by FISH (chromosomes X, Y, and 18) to assess ploidy. Series 2: 35 blastocysts were biopsied in three samples, two from TE (TE1 and TE2) and ICM. TE1 let us to determinate ploidy by FISH (chromosomes X, Y, 18); TE2 and ICM were used for 24-chromosomes study by NGS. Series 3: 15 blastocysts were biopsied as described in Series 2. TE1: study of 24 chromosomes by NGS. TE2: study of 24 chromosomes and SNPs (single nucleotide polymorphisms) by SNP-array of 750K in a “trio” format (simultaneous study of paternal/maternal/TE2 DNAs) and bioinformatic analysis. R-package for statistical analysis. The rest of the embryo was used for ploidy determinations by FISH (chromosomes X, Y, 18).
RESULTETS: 80.5% of MPN-derived blastocysts were diploid, 8% mosaic and 11.5% haploid (P<0.01). Diploid blastocysts showed a normal sex ratio (1:1); 50% diploid blastocysts were aneuploid. In relation to chromosomal topography, results showed different patterns, according to the chromosomal instability grade. In the two green compartments (TE and ICM) was perfectly matched when both compartments were euploid or whole-chromosomal aneuploid (trisomies and monosomies). Incomplete matching between compartments was observed in complex (>3 chromosomes involved), segmental or mosaic samples, which were more frequently observed in those from TE. 70% MPN-derived blastocysts showed two copies of both parental genomes. In relation to parental inheritance, 40% of blastocysts were diploid heterozygous.

CONCLUSIONS: The MPN experimental model confirms the chromosomal correlation between ICM and different regions of TE, in cases of euploidy or pure aneuploidy. The chromosomal instability associated to segmental aneuploidy seems to be confined equally to both TE and ICM compartments. A high percentage of MPN-derived blastocysts showed two copies of both parental and euploid genomes. These data re-open debate about the success rates of IVM oocytes, if fertilized, may lead to abnormal embryos and an increased risk of spontaneous miscarriages. Consequently, immature oocytes are usually discarded.

The aim of our study was to perform a detailed cytogenetic analysis of in vitro matured oocytes and compare with the chromosome constitution of oocytes which were mature (metaphase II; MII) at the time of retrieval.

DESIGN: Prospective non-randomized study.

MATERIALS AND METHODS: The oocytes examined were generated by sixteen young and healthy oocyte donors participated in the study. The average age was 28.3 years (range 21-29 years). Production of 343 oocytes were included (22 MII and 21 GV). Oocytes identified to be at the GV stage were cultured individually in 25 μl of Gemi® Geri® medium in a time-lapse incubator for up to 50.0 hours to achieve IVM and to determine the time needed for polar body (PB) extrusion. Biopsy of the 1st PB was performed once these oocytes matured to MII. Similarly, mature MII oocytes (n=22) underwent 1st PB biopsy. The cytogenetic constitution of IVM and mature oocyte-PB pairs was assessed using a well validated next generation sequencing (NGS) strategy for the identification of chromosome and chromatin errors arising during female meiosis.

RESULTS: Sixty-two percent of GV oocytes matured in vitro to MII after an average culture of 26.1 hours (95% CI 23.2-29.0). A total of 35 oocyte-PB pairs underwent NGS analysis. Of these, 13 originated from GV and 22 that were at the MII stage at retrieval. The overall euploidy rate observed was very similar between the two groups, i.e. 76.9% for the oocyte-PB pairs which were retrieved at the GV stage and 78.4% for the mature MII oocyte-PB pairs. The majority of abnormalities (60%) scored were due to unbalanced chromatin predivision, with the remaining 40% arising due to whole chromosome non-disjunction. No difference in IVM culture length was observed between normal and abnormal GV oocytes that reached the MII stage (26.1 hrs. [95% CI 22.3-30.9] vs. 25.93 hrs. [95% CI 17.4-34.5]).

CONCLUSIONS: To our knowledge, this is the first study to describe the use of NGS for cytogenetic analysis of in vitro matured human oocytes. Our findings suggest that GV oocytes, matured to MII in vitro, segregate their chromosomes in a manner equivalent to those that mature within the follicle. The fact that aneuploidy is not increased following IVM supports the idea that an attempt should be made to “rescue” immature oocytes, rather than discarding them. Further work is required to understand the basis of the poorer outcomes associated with IVM oocytes, but these results indicate that the cause is not cytogenetic in nature.
COMPARISON OF EMBRYO SPECIFIC TIME-LAPSE DISH FOR INDIVIDUAL CULTURE VERSUS AN EMBRYO SPECIFIC DISH FOR GROUP CULTURE. Rebecca Holmes, PhD, a Jaime Weinberg, BS, b Laurie Kalaghan, BS, b Brett Goode, BS, b William B. Schoolcraft, MD, c Jason E. Swain, PhD. d aCCRM Boston, Chestnut Hill, MA; bCCRM Boston, Boston, MA; cColorado Center for Reproductive Medicine, Lone Tree, CO; dCCRM Fertility Network, Lone Tree, CO.

OBJECTIVE: There are many different types of embryo culture dishes and incubators available. Dishes for time lapse incubators are very different to traditional dishes. Testing of any new dish or incubator must be extensive in order to validate the new system. The objective of this study was first to compare outcomes following sibling oocyte splits in an established culture system (embryo-specific microdrop dishes and dry benchtop incubator) to a time-lapse incubator along with its specially designed dish. The time-lapse specific dish was then tested in the benchtop incubator using sibling oocyte splits.

DESIGN: Prospective randomized trial.

MATERIALS AND METHODS: A time-lapse incubator chambers (Geri, K systems G210) and a K systems G210 were utilized to culture all embryos. In Phase I, all embryos were grown in groups A: in mini-GPS dishes (Life Global) in a K systems G210 incubator or B: Geri (Serono) dishes inside a dry chamber of Geri (Serono) incubator. All embryos were grown in Sage sequential media with 10% v/v complex protein under 4 mL Paraffin oil (Life Global) at 5% O2. All embryos were treated identically except for the dish and incubator.

Embryos were observed and media exchanged following 24h, 72h and 120h. In Phase II, to control for the impact of the culture dish, all embryos were grown in Geri dishes and placed either in the G210 (group C) or the Geri non-humidified chamber (Group D).

RESULTS:

CONCLUSIONS: Culture in the Geri dish and the Geri time-lapse system yielded more blastocysts overall and more good quality blastocysts than in mini-GPS dishes in the K systems G210. Fertilization was increased in the Geri incubator, although not significant. No changes in cleavage embryos at day 3 was apparent. More good quality embryos were observed on day 5, 6 and 7 in the Geri incubator with Geri dish.

To determine whether the incubator or the dish were responsible for these increases, the Geri dish was used to grow all embryos in Phase II and half of the oocytes placed in the K systems G210 and half in the Geri incubator. While the n is low, more good quality embryos were observed in the Geri incubator. The Geri incubator is an effective incubator yielding good quality blastocysts. More studies are required to determine if a single step media gives the same results.

References: none

SUPPORT: none

O-114 Tuesday, October 15, 2019 12:00 PM

Oocyte # 104 101 101 101
% Fertilization 68.3% 80.2% 82.9% 82.9%
% Good Cleavage Rate 80.3% 84.9% 72.4% 72.4%
% Total Blasts on D5 53.5% 65.4% 41.4% 41.4%
% Blastcs >= 3BB D5 23.9% 33.3% 20.7% 20.7%
% Total Blasts D6 67.6% 74.1% 62.1% 62.1%
% Blastcs >= 3BB D6 45.1% 59.3% 37.9% 37.9%
% Total Blasts D7 69.0% 76.5% 62.1% 62.1%
% Blastcs >= 3BB D7 52.1% 61.7% 44.8% 44.8%

O-115 Tuesday, October 15, 2019 10:45 AM

RETAINED PREGNANCY TISSUE AFTER MISCARRIAGE ASSOCIATED WITH HIGH RATE OF CHRONIC ENDOMETRITIS. Dana B. McQueen, M.D., M.A.S., Kruti P. Maniar, M.D., Anne Hutchinson, M.D., Rafael Contino, BS, Jared C. Robins, MD, Lia A. Bernardi, MD, Mary Ellen Pavone, MD, MSC; Northwestern University, Chicago, IL.

OBJECTIVE: To compare the prevalence of chronic endometritis in women undergoing hysteroscopic resection of retained pregnancy tissue (RPOC) after pregnancy loss to women with unexplained recurrent pregnancy loss (RPL).

DESIGN: Cohort study.

MATERIALS AND METHODS: Institutional Review Board approval was obtained. Women undergoing hysteroscopic resection of RPOC between 6/2008 and 12/2018 were included. In addition, women with unexplained RPL undergoing endometrial sampling between 1/2016 and 12/2018 were included. Unexplained RPL was defined as two or more pregnancy losses with a TSH level under 4 mL/l, negative antiphospholipid antibodies and normal uterine anatomy. Data on pregnancy history, time since last pregnancy loss and gestational age at time of loss were collected. H&E and immunohistochemical staining for CD138 were performed on all slides. A single pathologist blinded to patient history recorded the number of plasma cells per high power field (HPF). Chronic endometritis was defined as 1 or more plasma cells/10 HPF in addition to stromal changes (spindling, edema, foci of breakdown, presence of other inflammatory cells, and pigment deposition). In order to detect a 25% difference in the rate of chronic endometritis with 80% power and alpha of 0.05, a sample size of 49 women was needed in each group.

RESULTS: Endometrial samples from a total of 100 women were evaluated (50 women undergoing resection of RPOC and 50 women with unexplained RPL). The mean age was similar between groups, 36.4 (SD 4.7) vs 35.2 (SD 4.1) years, P = 0.18. The mean number of prior pregnancy losses was 1.9 (SD 1.0) in the RPOC group vs. 3.1 (SD 0.9) in the RPL group, P = 0.0001. By H&E staining, chronic endometritis was present in 60% (30/50) of women undergoing resection of RPOC vs. 14% (7/50) of women biopsied for RPL, P < 0.0001. By CD138 staining, chronic endometritis was present in 62% (31/50) of women undergoing resection of RPOC vs. 30% (15/50) of women biopsied for RPL, P = 0.002. In a subgroup analysis that only included women with RPL, chronic endometritis was present in 71% (20/28) of women with both RPL and RPOC vs. 24% (12/50) of women with RPL alone, P < 0.0001 (H&E). Among women with RPL without
suspected RPOC, an implantation site or placental site nodule was reported in three women, and all three of these women had chronic endometritis.

CONCLUSIONS: Following miscarriage, retained pregnancy tissue is associated with a high prevalence of chronic endometritis. A hysteroscopy to evaluate for retained pregnancy tissue may be warranted in women with RPL who are diagnosed with chronic endometritis. Further research is needed to determine if resection of retained tissue is sufficient to treat RPOC associated chronic endometritis, or if additional antibiotic treatment is necessary.

SUPPORT: Friends of Prentice Grant

O-117 Tuesday, October 15, 2019 11:15 AM

DIRECT CORRELATION BETWEEN β-hCG LEVELS AND TROPHECTODERM MORPHOLOGY QUALITY IN SINGLE EUPLOID EMBRYO TRANSFER CYCLES. Carlos Hernandez-Nieto, MD, a Joseph A. Lee, BA, a Marlena Duke, MSc, ELD, a Daniel E. Stein, MD, b Alan B. Copperman, MD, b Benjamin Sandler, M.D., b Tanmoy Mukherjee, MD, a Reproductive Medicine Associates of New York, New York, NY; cTichan School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: Embryonic trophectoderm (TE) cells play a key role in apposition, adhesion, and invasion of the maternal endometrium during early implantation. Blastocysts are morphologically graded (expansion stage (EXP); inner cell mass (ICM); trophectoderm (TE) cells) to better understand embryonic competence and improve selection at transfer. Data is scarce regarding the relationship of embryo TE quality and early levels of β-hCG, a biochemical marker of early embryo implantation and placentation. Previously, we demonstrated that embryo TE quality does not correlate with major adverse perinatal outcomes or placental weight at delivery. However, patients who had transfer of embryo(s) with a low TE grade experienced placental histological changes. (Herlihy et al. 2017) This study included patients who underwent a single, euploid frozen embryo transfer (FET) and assessed the correlation between embryo TE grade and early β-hCG levels.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: This study included patients who underwent a single, euploid FET cycle and obtained a positive pregnancy test (serum β-hCG 5 mIU/mL) from 2013 to 2019. The β-hCG measurement was analyzed 9 days after FET using an electrochemiluminescence immunoassays (Immulite 2000; Siemens and/or Cobas e-601; Roche). Only cases that had a first β-hCG measurement on day 9 after ET were included in the analysis. Blastocyst morphology was assessed using a center-specific, modified Gardner’s scoring system. ANOVA, χ² tests, univariate, multivariate linear regression and a mixed effects model with a random intercept model were used to evaluate serum β-hCG levels with regard to TE grade.

RESULTS: A total of 2,934 single, euploid FET cycles were included in the analysis. Cohorts were segregated by TE grade: (TE-A: n=1,235; TE-C: n=643). β-hCG values were significantly different among cohorts (TE-A: 155.5±97; TE-B: 133.7±80; TE-C: 94.1±73, p<0.0001) and early pregnancy loss (EPL) was significantly higher in embryos with low TE grades (TE-A:14.6%; TE-B:15.3%; TE-C: 19.2%; p<0.01) There was a significant correlation between TE grade and mean β-hCG levels (R²: 0.06, p<0.001). After adjusting for age, BMI, endometrial thickness at ET, ICM grade, EXP grade, and day of biopsy, the correlation between high TE grade and high β-hCG levels remained significant (R²:0.12, P<0.0001).

CONCLUSIONS: After adjusting for clinical parameters, embryonic expansion, and inner cell mass grade; our data showed euploid embryo TE grade correlates with β-hCG levels at first pregnancy test measurement. The ultrastructural appearance of the TE cells in euploid embryos might represent a surrogate marker of embryo’s capacity to properly adhere and invade the endometrium during the early implantation process. Further studies focusing on syncytiotrophoblast and endometrial cellular and molecular interactions could help reproductive specialists to better understand the mechanisms related to early placentation physiology.


SUPPORT: none

O-118 Tuesday, October 15, 2019 11:30 AM

PATERNAL CONTRIBUTIONS IN EARLY EMBRYONIC GENE EXPRESSION: ROLE IN EARLY PREGNANCY LOSS. Vidhu Dhawan, MD, a Manoj Kumar, Ph.D, a Neena Malhotra, MD FRCOG, a Neeta Singh, MD, a Vatsla Dadhwal, MD, a Rima Dada, MD, Ph.D. a All India Institute of Medicine at Delhi.

FERTILITY & STERILITY®
OBJECTIVE: The dynamic interplay of the vulnerable sperm genome and extragenomic cargo with the early embryonic development in spontaneous and assisted conceptions has been brought to surface. The suite of sperm transcripts retained in the spermatooza and the complex epigenetically marked sperm genome synergistically function to influence early embryonic development. Dysregulated gene expression and disrupted genomic integrity resulting in early pregnancy loss needs to be further elucidated.

DESIGN: A case control study.

MATERIALS AND METHODS: Male partners of females who experienced recurrent pregnancy loss (RPL, N=75) and recurrent implantation failures (RIF, n=75) and 75 healthy fertile controls were recruited for the study and semen samples were obtained. Gene expression analysis of the genes critical for embryonic development and DNA damage repair pathway (P<0.05). qPCR analysis after normalisation with $β$-actin and GAPDH. Functional assessment of semen included cardial biomarkers of oxidative stress by reactive oxygen species (ROS), DNA damage by DNA fragmentation index (DFI) and 8-OhD levels as well as telomere length in sperm DNA.

RESULTS: The relative gene expression of FOXG1 (P=0.048), SOX3 (p=0.03), RPS6, RBM9 and RPL10A (P=0.001) was seen to differ significantly between RPL patients and controls, while expression of $FOXG1$ (P=0.02), RPS6, RBM9 and TOMMT (p<0.001), RPL10A (P=0.039) and RPS17 (P=0.002) in RIF patients as compared to controls. The levels of ROS, DFI and 8-OHdG were found to be significantly higher as compared to controls and telomere length was found to be significantly different in both RPL and RIF patients with respect to controls. The odds of occurrence of RPL and RIF was 12.41 and 12.68 times greater with DFI>31 (OR 12.41, (6.53-23.55) and 13.68 (6.52-28.71)] respectively. The odds of occurrence was 12.68 and 18.87 time greater with DFI>31 [OR 12.68 (6.28-21.22) AND 18.87 (5.43-27.67)] respectively.

CONCLUSIONS: The orchestration of selective paternal transcripts as well as genomic integrity and telomere length is a critical determinant of early embryonic development and embryo viability. The derangements in sperm functional characteristics and gene expression has the potential to produce adverse transgenational fetal effects and health of future progeny. The adoption of sperm RNA expression can be established as an integral part of clinical diagnostic measures among other seminal biomarkers.

TABLE 1: Relationships between low day 5 hCG level (<5 IU/L) and transfer outcome.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Risk ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implantation failure</td>
<td>100</td>
<td>89.3</td>
<td>70.9</td>
<td>100</td>
<td>undefined</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Biochemical pregnancy loss</td>
<td>43.7</td>
<td>92.8</td>
<td>39.2</td>
<td>93.9</td>
<td>6.48 (4.32-9.74)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>75.0</td>
<td>89.7</td>
<td>3.8</td>
<td>99.9</td>
<td>25.10 (2.64-238.42)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Early SAB</td>
<td>11.8</td>
<td>94.3</td>
<td>31.1</td>
<td>83.0</td>
<td>1.83 (1.15-2.93)</td>
<td>0.017</td>
</tr>
<tr>
<td>Late SAB</td>
<td>20.0</td>
<td>94.3</td>
<td>3.1</td>
<td>99.2</td>
<td>4.04 (0.46-35.09)</td>
<td>0.174</td>
</tr>
<tr>
<td>All pregnancy losses</td>
<td>30.0</td>
<td>93.1</td>
<td>61.2</td>
<td>78.5</td>
<td>2.84 (2.10-3.85)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>


SUPPORT: This work is supported by All India Institute of Medical Sciences (AIIMS) internal funds. The authors declare no competing interests.
OBJECTIVE: Spontaneous recurrent pregnancy loss (RPL) is most often investigated from the women’s perspective. However, recent evidences suggest the involvement of male factor as a plausible cause particularly in idio-pathic RPL. Despite being transcriptionally and translationally quiescent, spermatozoa undergo maturation during transit through epididymal and female reproductive tract. Many proteins and regulatory RNAs associated with the exosomes (epididymosomes and prostasomes) are known selectively transfer their cargo to the sperm thereby modify sperm function. However, the proteome profile of exosomes in general and RPL in particular is largely unknown. Therefore, the main objective of the present study is to identify and understand the possible paternal factors responsible for early pregnancy loss through differential proteomic analysis of seminal exosomal proteins.

DESIGN: Prospective case-control study involving consented participants comprising of fertile donor (n = 21) and partners of spontaneous idiopathic recurrent pregnancy loss patients (n = 21).

MATERIALS AND METHODS: Seminal exosomes were isolated by ultracentrifugation and characterized by western blot, transmission electron microscopy, and nanoparticle tracking analysis followed by label free liquid chromatography mass spectrometry (LC-MS/MS) and bioinformatics pathway analysis (Ingenuity Pathway Analysis: IPA, Qiagen) and STRING protein-protein interaction (PPI) analysis.

RESULTS: A total of the 998 proteins were detected in the data set (Control: 939 and RPL: 935). Of the 447 differentially expressed proteins 385 underexpressed and 62 overexpressed in RPL while 63 and 59 proteins were exclusive to control and RPL, respectively. Immune response (HSA:168256 ; false discover rate p=2.67e-28), signalling proteins (HSA:376176 ; false discover rate p=3.04e-22), chromatin packaging and remodeling (GO:0031497; false discover rate p=2.78e-05), protein folding and apoptosis (HSA:100951; false discover rate p=5.93e-06) were the major pathways impaired in RPL as revealed by STRING-PPI analysis. Pathway analysis by IPA showed developmental, hereditary and immunological disorders were the top diseases while cell death and survival, cellular assembly and organization, DNA replication, recombination and repair, gene expression were the major functions that were deregulated in RPL spermatozoa. Overexpression of HNRNPC and HNRNPU deregulated in RPL may be responsible for defective chromatin organization and shortening of telomere-length while underexpression of RUVBL1 may be responsible for altered centrosome function leading to abnormal embryo development.

CONCLUSIONS: The result of this pilot study implies the importance of exosomes in sperm maturation and function, particularly in RPL. Further validation alongside the proteome profiling of spermatozoa may lead to identification of candidate biomarkers for determination of male factors in RPL.

SUPPORT: Higher Education Department, Government of Odisha, A University of Education Grant Commission and Department of Science and Technology, Government of India

ETHICS

O-121 Tuesday, October 15, 2019 10:45 AM

FERTILITY & STERILITY

Table 1.

<table>
<thead>
<tr>
<th>All Sites</th>
<th>West Coast</th>
<th>East Coast</th>
<th>Non-mandated States</th>
<th>Mandated States</th>
<th>Non-academic</th>
<th>Academic</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=number of IVF websites</td>
<td>N=203</td>
<td>N=66</td>
<td>N=133</td>
<td>N=85</td>
<td>N=119</td>
<td>N=112</td>
</tr>
<tr>
<td>Direct link to the practice’s clinic summary report (CSR) on SART.org website</td>
<td>103 (50.5%)</td>
<td>31 (46.9%)</td>
<td>70 (52.6%)</td>
<td>41 (48.2%)</td>
<td>62 (52.1%)</td>
<td>58 (51.8%)</td>
</tr>
<tr>
<td>Supplemental success rates reported by live birth per transfer, retrieval and cycle per each age category</td>
<td>7 (9.5%)*</td>
<td>3 (12.5%)*</td>
<td>3 (6.1%)*</td>
<td>5 (16.1%)*</td>
<td>2 (4.7%)*</td>
<td>2 (6.5%)*</td>
</tr>
<tr>
<td>Disclaimer statement when quoting IVF success rates</td>
<td>106 (51.9%)</td>
<td>35 (53%)</td>
<td>69 (51.9%)</td>
<td>40 (47.1%)</td>
<td>66 (55.5%)</td>
<td>56 (50%)</td>
</tr>
</tbody>
</table>

*percentage reflects number of clinics that reported supplemental success rates by live birth per transfer, retrieval and cycle per each age category divided by number of clinics that reported any supplemental success rates
OBJECTIVE: Historically, a large percentage of IVF clinics did not adhere to Society for Assisted Reproductive Technology (SART) guidelines for online advertising. New website guidelines, effective January 2018, are clear in expectations requiring a link to clinics’ success rates on the SART site and statistical explanations alongside explicit rules about presenting supplemental data in its entirety specifying that “no partial presentation is allowed”. SART emphasizes that “adherence to this advertising policy is a requirement for membership in SART”. This study examined if SART member IVF centers adhere to this new SART advertising policy.

DESIGN: Cross-Sectional Evaluation.

MATERIALS AND METHODS: 203 IVF center websites were examined. Univariate analysis was used for descriptive data and Fisher’s exact test was used to compare categorical data between subgroups.

RESULTS: Only 50.5% of clinics provided a link to the SART website and, similarly, only 51.9% provided the required disclaimer statement regarding their outcome statistics. Disturbingly, only 9.5% of websites followed SART requirements about the presentation of supplemental data. There were no significant differences between academic and non-academic centers, those in mandated vs non-mandated states, or East versus West Coast clinics in any of the above areas (table 1).

CONCLUSIONS: Only half of surveyed websites adhere to SART’s core guidelines surrounding reporting with lower compliance percentages in other areas. Consideration for additional education could be considered and enforcement of guidelines should be enhanced.

SUPPORT: None

O-123 Tuesday, October 15, 2019 11:15 AM

INFERTILITY IN THE DIGITAL AGE: AN OPPORTUNITY FOR REI PHYSICIANS TO COMBAT THE SPREAD OF MISINFORMATION AND FILL SUPPORT GAPS IN INFERTILITY CARE ONLINE. Emily A. Jacobs, MD, Ginny L. Ryan, MD, MA. University of Iowa Carver College of Medicine, Iowa City, IA.

OBJECTIVE: To examine infertility related content posted on Instagram, including content of posts and identity of content posters.

DESIGN: Retrospective content analysis.

MATERIALS AND METHODS: Data from Instagram were obtained on April 20, 2019. One author queried 42 popular hashtags, including both medical and lay person terminology, related to infertility diagnosis, treatment and procedures. The total number of posts from each hashtag was recorded. Each of the top ten posts (as determined by Instagram’s internal algorithm) for the 42 hashtags was then analyzed to qualitatively identify the content of each post. The post category was determined by the lead author based on the content of the post and the overall message it sent to its readers. The number of likes and comments were also recorded for each post. Lastly, data on the individual and promotional posts who were also recorded by analyzing that poster’s Instagram profile.

RESULTS: A total of 5,814,691 posts were tagged with the 42 unique hashtags queried for this study. 315 of the 420 “top posts” met inclusion criteria. Of the hashtags, #PCOS had the highest number of posts associated with it (2,000,000 posts). From the 315 included posts, 271 unique posters were identified. 239 of these posters were non-healthcare related individuals (88%) and 32 (12%) were healthcare related persons. There were 14 self-identified US physicians. All but one had verified credentials. By far, the most common type of post for non-healthcare related individuals was related to their infertility journey (60%). In contrast, the majority of posts created by healthcare-related individuals were educational (41%).

When comparing US verified physician posting versus all other posters, US physicians were more likely to post educational (33% vs 9%, p = 0.0006) and promotional posts (33% vs 1%, p < 0.0001) and less likely to post about a personal infertility journey (5% vs 58%, p < 0.0001). There was no significant difference in ‘likes’ between the two groups (194±200 for US physicians vs 430±787 for all other posters, p = 1.71). There was a significant difference in the number of comments between the two groups, with fewer comments in response to US physicians than all other posters (12±16 vs 36±51, p = 0.015).

No infertility postings by verified US physicians contained medical advice or medical questions. In contrast, 5% and 2% of postings by all other individuals gave medical advice or asked a medical question, respectively. Some of the medical advice given included taking 40mg/day of black cohosh for ovulation induction, using cannabis suppositories to shrink fibroids, and recommending supplements to increase fertility (who were often sold by the poster).

CONCLUSIONS: Instagram and other social media platforms have the potential to be highly influential in the infertility population. Physicians, particularly board-certified reproductive endocrinologists, should consider taking steps towards having a stronger presence online to combat the spread of misinformation that currently dominates these highly used platforms, and to help bridge gaps in access to infertility care.

O-124 Tuesday, October 15, 2019 11:30 AM

ADVANCING LAWS TO PERMIT SURROGACY IN US STATES: CHALLENGES & SOLUTIONS FOR ART PROVIDERS & OTHERS. Robert Klitzman, MD. Columbia University, NY, NY.

OBJECTIVE: To understand how to advance legalization of surrogacy, through data addressing opponents’ concerns.

DESIGN: Analysis of state laws & discussions with state policymakers & others.

MATERIALS AND METHODS: N/A

RESULTS: Many prospective parents face legal barriers to hiring traditional or gestational surrogates, posing critical questions of whether ART providers & others can address these obstacles & if so, how. A few US states (e.g., California) allow paid gestational surrogacy, upholding legal contracts that prohibit birth mothers from keeping the baby. Yet following the Baby M case, & largely due to fears of exploiting women as surrogates, US states range widely in whether they permit, prohibit, or limit surrogacy & how they enforce such laws. Recently, traditional surrogacy is allowed (since it is not explicitly banned) in 16 states; permitted by statute without much detail in 5; permitted by statute with restrictions in 2; permitted only if unpaid in 4; permitted but with unenforceable contracts in 9; practiced, though contracts are banned, in 2; not practiced because contracts are banned in 4; & unpredictable in 9. Gestational surrogacy is allowed by law in 3 states; allowed (since not explicitly banned) in 22; allowed by statute without much detail in 7; permitted with restrictions in 6; allowed with unenforceable contracts in 1; supported but with no law in 6; practiced, though contracts are prohibited in 5; & not practiced since contracts are prohibited in Washington, DC. States differ in how much surrogates can be paid (e.g., whether more than basic expenses); whether surrogates can change their minds & if so, in when; whether court approval & state residency are needed; & whether an intended parent must provide gametes.

Advocates have unsuccessfully tried altering laws in NY & elsewhere. Opponents tend to draw on conservative Christian arguments (and wariness of much ART) or feminist concerns that most surrogates will be poor & thus taken advantage of. Yet no data exist about these claims. Crucial questions thus arise of why women choose to be surrogates - e.g., who surrogates in fact are & how they see these issues. Anecdotally, many such women are middle class, fully grasp the risks & benefits, having given birth to their own children & feel that the rewards are worth it. Data on gestational surrogates are thus essential – e.g., on their socioeconomic status, motivations & views of their experiences – how they perceive & experience it & whether they view it, retrospectively, favorably or regretfully – to assess whether claims of exploitation are correct. Such data, if they reveal few concerns, can prompt other states to permit surrogacy, assisting many parents. These data can also be vital in educating patients, providers & the public at large about these issues. ART providers could thus help by collecting such data. Widening use of electronic medical records can facilitate collection of some of these data. Providers could also work closely with patient groups on these goals.

CONCLUSIONS: ART providers & others can advance legislation of paid gestational & other surrogacy & thus aid patients through collection of key data.

O-125 Tuesday, October 15, 2019 11:45 AM

EVALUATING THE SART CLINIC SUMMARY REPORTS – IS IT ONLY ABOUT THE LIVE BIRTH RATES? WHAT ABOUT THE SIGNIFICANT MORBIDITY/MORTALITY RISK FACTORS ASSOCIATED WITH MULTIPLE GESTATIONS?. Carrie Riestenberg, MD, a Alin Lina Akopians, MD, PhD, a Deborah E. Johnson, MA, a Zachary Haimowitz, BS, b Hal C. Danzer, MD, c Mark W. Surrey, MD, a Jason A. Barritt, PhD. a University of California, Los Angeles, Los Angeles, CA, b Southern California University of Iowa, Iowa City, IA.

OBJECTIVE: To examine infertility related content posted on Instagram, including content of posts and identity of content posters.

DESIGN: Retrospective content analysis.

MATERIALS AND METHODS: Data from Instagram were obtained on April 20, 2019. One author queried 42 popular hashtags, including both medical and lay person terminology, related to infertility diagnosis, treatment and procedures. The total number of posts from each hashtag was recorded. Each of the top ten posts (as determined by Instagram’s internal algorithm) for the 42 hashtags was then analyzed to qualitatively identify the content of each post. The post category was determined by the lead author based on the content of the post and the overall message it sent to its readers. The number of likes and comments were also recorded for each post. Lastly, data on the individual and promotional posts who were also recorded by analyzing that poster’s Instagram profile.

RESULTS: A total of 5,814,691 posts were tagged with the 42 unique hashtags queried for this study. 315 of the 420 “top posts” met inclusion criteria. Of the hashtags, #PCOS had the highest number of posts associated with it (2,000,000 posts). From the 315 included posts, 271 unique posters were identified. 239 of these posters were non-healthcare related individuals (88%) and 32 (12%) were healthcare related persons. There were 14 self-identified US physicians. All but one had verified credentials. By far, the most common type of post for non-healthcare related individuals was related to their infertility journey (60%). In contrast, the majority of posts created by healthcare-related individuals were educational (41%).

When comparing US verified physician posting versus all other posters, US physicians were more likely to post educational (33% vs 9%, p = 0.0006) and promotional posts (33% vs 1%, p < 0.0001) and less likely to post about a personal infertility journey (5% vs 58%, p < 0.0001). There was no significant difference in ‘likes’ between the two groups (194±200 for US physicians vs 430±787 for all other posters, p = 1.71). There was a significant difference in the number of comments between the two groups, with fewer comments in response to US physicians than all other posters (12±16 vs 36±51, p = 0.015).

No infertility postings by verified US physicians contained medical advice or medical questions. In contrast, 5% and 2% of postings by all other individuals gave medical advice or asked a medical question, respectively. Some of the medical advice given included taking 40mg/day of black cohosh for ovulation induction, using cannabis suppositories to shrink fibroids, and recommending supplements to increase fertility (who were often sold by the poster).

CONCLUSIONS: Instagram and other social media platforms have the potential to be highly influential in the infertility population. Physicians, particularly board-certified reproductive endocrinologists, should consider taking steps towards having a stronger presence online to combat the spread of misinformation that currently dominates these highly used platforms, and to help bridge gaps in access to infertility care.
OBJECTIVE: In 1992, HR 4773, the Fertility Clinic Success Rate and Certification Act, also known as the Wyden bill, was passed mandating public reporting of fertility clinic pregnancy success rates. Currently, >90% of ART clinics in the USA report to SART. The CDC, SART and ASRM work together to publish annual reports of clinic’s pregnancy outcomes. SART warns that “Accurate and complete reporting of ART success rates is complicated. Clinics may have differences in patient selection, treatment approaches, and cycle reporting practices which may inflate or lower pregnancy rates relative to another clinic. This report is best understood in consult with your physician.” Furthermore, “success rates should not be used to compare treatment centers.” In spite of this, patients rely on this information to decide which center they will ultimately choose for their fertility treatment. The objective of this study was to compare the ranking of live birth rate (LBR), singleton live birth rate (SLB),r and weighted ‘risk score’ ranking based on risk factors for morbidity/mortality associated with multiple gestation in clinics reporting ≥ 1000 total cycles annually. 

DESIGN: Cross-sectional evaluation.

MATERIALS AND METHODS: The 2017 SART Preliminary Data report was reviewed for all reporting ART clinics. Those clinics reporting ≥ 1,000 total cycles annually were included in our analysis, for a total of 62 clinics. LBR, SLB, LBR, twin and triplet rates were recorded for each of the clinics. A weighted ‘risk score’ was then calculated for each clinic in the following manner: twin rate x 8 + triplet rate x 21. The weighted ‘risk score’ assigned to twin and triplet gestations was derived from published relative risk data of premature and low birth weight of twin and triplet gestations compared to singlets, as these have been shown to be the principal risk factors for morbidity/mortality in multiple gestation pregnancies. All clinics were subsequently ranked into quartiles with regards to LBR and ‘risk score’.

RESULTS: Of the 153 clinics in the highest quartile with respect to LBR, only one clinic also ranked in the lowest quartile of ‘risk score’. Of the remaining 14 clinics, 5 ranked in the highest ‘risk score’ quartile and 5 in the second highest ‘risk score’ quartile. Therefore, <30% of the clinics ranking in the highest quartile for LBR also ranked in the top two quartiles for safety. 

CONCLUSIONS: Our study showed that out of the 62 highest volume ART clinics reporting to SART, two thirds of those in the top quartile for LBR and SLB ranked in the bottom two quartiles with respect to weighted ‘risk score’, with one third ranking in the highest ‘risk core’ quartile. Only one clinic was in the top quartile in both fields. This is a manifestation of the incentive to achieve a higher LBR, commonly acknowledged to be the most referenced statistic reported by SART, at the cost of a higher risk of multiple gestation. Though not intended to be a tool for clinic comparison and ranking, SART is clearly used in this manner. We argue that more attention should be brought to the balance of success and risk in order to optimize patient outcomes and encourage increased responsibility among ART clinics.

SUPPORT: None

O-126 Tuesday, October 15, 2019 12:00 PM

INSTITUTIONAL POLICIES ON POSTHUMOUS REPRODUCTION USING OOCYTES AND EMBRYOS: PRELIMINARY RESULTS FROM A CROSS-SECTIONAL STUDY. Emma C. Trawick, M.D., a Amani Sampson, B.A., a David L. Keefe, M.D., a Arthur L. Caplan, Ph.D., a Kara N. Goldman, M.D., b Gwendolyn P. Quinn, Ph.D. b Northwestern University, Feinberg School of Medicine, Chicago, IL; New York University School of Medicine, Department of Obstetrics and Gynecology, New York, NY; New York University School of Medicine, Department of Population Health, Division of Medical Ethics, New York, NY; New York University Feinberg School of Medicine, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Chicago, IL.

OBJECTIVE: Posthumous assisted reproduction (PAR) raises complicated legal and ethical issues. ASRM recommends that assisted reproductive technology (ART) and fertility preservation (FP) programs develop written policies regarding PAR, though little is known about such policies and how they have been implemented. Our objective was to assess the presence and content of policies toward PAR using oocytes and embryos among Society for Assisted Reproductive Technology (SART) member clinics in the U.S.

DESIGN: Cross-sectional questionnaire-based study.

MATERIALS AND METHODS: Our study consists of three phases of communication: email-, postal mail-, and phone-based survey. We report on the first phase of anonymous email survey responses. Surveys were emailed to ASRM-member medical directors of all SART member clinics (n = 332) during March and April 2019 using a modified Dillman Method; contact information was acquired from SART and ASRM membership database. The survey included 23 multiple-choice and 3 opened-ended questions assessing practice characteristics (practice type, location, IVF cycle volume), presence of a clinic policy towards PAR, and the content of such policy. Descriptive data are presented as %, with Fisher’s exact test used where appropriate, and thematic content analysis was applied to open-ended responses.

RESULTS: The first phase of the study received 39 clinic responses (12% response rate). Respondents were distributed across the U.S.; average volume of IVF cycles per year ranged from < 250 to > 1500. More than one-third (35.9%, n = 14) of clinics reported participating in any cases of PAR over the past five years, and 51% (n = 2) reported participation in more than five cases. Participation in cases of PAR was not significantly associated with practice type or IVF cycle volume (p > 0.05). 57.9% (n = 22) had written policies towards PAR using oocytes or embryos, while 36.8% (n = 14) reported they did not have a policy. Practice type, IVF cycle volume, FP volume, and prior participation in cases of PAR were not significantly associated with the presence of a policy (p > 0.05). Of those with a policy, 52.4% (n = 11) reported they had used that policy, 66.7% (n = 10) without a policy reported they had considered adopting one, and 60.0% (n = 9) reported they had received a request for PAR services. Only 44% (n = 15) of clinics specified that patients not expected to survive to use oocytes due to terminal illness were eligible for oocyte cryopreservation, while 50.1% (n = 17) did not specify. Open-ended comments suggested need for case-by-case appraisal and firm consent policies regarding gamete disposition.

CONCLUSIONS: Our preliminary results suggest that SART programs are receiving an increasing number of requests for PAR services, but many SART programs lack PAR policies, and those with policies do not always follow ASRM recommendations. As PAR cases become more common, clinicians should be equipped to manage the complexities of PAR. More data are needed as this study continues, and future research is needed to understand barriers to the creation and implementation of these increasingly needed policies.

O-127 Tuesday, October 15, 2019 10:45 AM

ORAL HYOSCINE BUTYL BROMIDE PLUS CERVICAL LIDOCAINE 5% CREAM IN REDUCING PAIN DURING HYSTEROSALPINGOGRAPHY. Ahmed M. Abbas, MD, a Yehia Ali, MD, b Tarek Farghaly, MD, a Mohamed Khalaf, MD. aDepartment of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; bDepartment of Obstetrics and Gynecology, Faculty of Medicine, Qena, Egypt.

OBJECTIVE: Infertility is defined as the failure of a couple to conceive during 12 months of regular unprotected intercourse. Tubal abnormalities account for 30-40% of the causes of female infertility. Hysterosalpingography (HSG) is a diagnostic procedure in the evaluation of infertile women and considered to be the traditional and the gold standard in the assessment of the patency of the fallopian tubes. The major disadvantage of HSG is pain. Our objective is to evaluate the analgesic effect of combining oral Hyoscine Butyl Bromide (HBB) with cervical lidocaine cream in alleviating pain during HSG.

DESIGN: Randomized double-blinded controlled trial (clinicaltrials.gov: NCT02710305).

MATERIALS AND METHODS: The study included reproductive-aged infertile women scheduled for HSG. Eligible women were recruited and randomized (1:1) to HBB plus lidocaine or Placebo group. All women received oral 20 mg HBB or placebo tablets 30 minutes before HSG, and then 4 ml of lidocaine 5% cream or placebo was applied to the anterior cervical lip, followed by 2 ml placed in the cervical canal using a sterile needleless syringe. The study outcomes were the mean pain score reported during speculum placement, cervical tenaculum placement, injection of the dye, 5 minutes and 30 minutes post-procedure using a 10-cm Visual Analogue Scale (VAS). A 2 cm difference in VAS score between both groups was considered a clinically significant difference. Other outcomes included the number of women who asked for additional analgesics and the adverse effects of the study medications. Mann Whitney test and Fisher’s exact test were used for the analysis of the outcomes. Multivariate regression analysis was
O-128 Tuesday, October 15, 2019 11:00 AM

THE DEVELOPMENT OF A SYSTEM TO AUTOMATICALLY EVALUATE THE NUMBER OF PRONUCLEI USING DEEP LEARNING TECHNOLOGY. Yuta Kida, M.S., a Noritaka Fukunaga, Ph.D., a Sho Sanami, Ph.D., b

RESULTS: One hundred forty women were enrolled and randomized to HBB and lidocaine arm (n=70) or placebo (n=70). Both groups were similar in age, parity, BMI, duration of infertility and the prior mode of delivery without statistically significant differences. Women in the HBB plus lidocaine group were more likely to report lower VSAS scores during injection of the dye, 5 minutes and 30 minutes post procedure (median: 3 vs. 6, p<0.0001; 2.5 vs. 5, p<0.0001; 1.5 vs. 3, p<0.0001, respectively). Moreover, nine women asked for additional analgesics in the placebo group versus 7 women in the study group (p=0.02). No difference in the rate of adverse effects. The following variables were not predictors of pain: nulliparity (p=0.48), previous cesarean deliveries (0.28), dysmenorrhea (p=0.13), and chronic pelvic pain (p=0.42) and prior HSG (p=0.45).

CONCLUSIONS: Utility of oral HBB 30 minutes before HSG plus cervical lidocaine 5% cream significantly alleviated the induced pain during and 30 min after the HSG procedure.

SUPPORT: None

O-129 Tuesday, October 15, 2019 11:15 AM

LOW ENDOMETRIAL VOLUME IS NOT ASSOCIATED WITH DIMINISHED LIVE BIRTH FOLLOWING TRANSFER OF A SINGLE THAWED EUPLOID BLASTOCYST. Shelby A. Neal, MD, a Richard Thomas Scott, Jr., MD, a Linea R. Goodman, MD. a, 1

OBJECTIVE: Three-dimensional ultrasound (3D US) facilitates reproducible assessment of endometrial volume (EV)1, but whether or not EV is associated with pregnancy outcomes in women undergoing in vitro fertilization (IVF) is unclear2. The objective of this study is to evaluate the association between EV and pregnancy outcomes following transfer of a single thawed euploid blastocyst.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: All patients planning to undergo a single thawed euploid blastocyst transfer between April and December 2017 at a large IVF center were eligible for inclusion. Subjects underwent endometrial preparation according to a standardized protocol. On the day prior to transfer, 3D US was performed for assessment of EV. Patients then underwent transfer of a single thawed euploid blastocyst.

EV was classified into four quartiles according to the 25th, 50th and 75th percentiles. The primary outcome was live birth. Secondary outcomes included clinical pregnancy (presence of a gestational sac on ultrasound), miscarriage (pregnancy loss after documentation of gestational sac), and ectopic pregnancy. Analysis of variance was used to compare continuous variables and chi square or Fisher’s exact test was used for categorical variables. Multivariate logistic regression was performed to account for potential confounders.

RESULTS: A total of 638 subjects consented to participation and completed the study. There were no differences amongst EV quartiles by age at retrieval, age at transfer, or body mass index. EV was directly associated with gravidity, parity and endometrial thickness (all P<0.01). Table 1 shows pregnancy outcomes by EV quartile. When accounting for potential confounders, there were no associations between EV and live birth [aOR 0.97 (0.90-1.05)], clinical pregnancy [aOR 1.00 (0.92-1.02)] or miscarriage [aOR 1.07 (0.95-1.21)]. There was a non-significant trend between low EV and ectopic pregnancy [aOR 1.59 (0.96-2.63), P=0.07].

CONCLUSIONS: EV is not associated with clinical pregnancy, miscarriage or live birth following transfer of a single thawed euploid blastocyst. It is possible that low EV confers an increased risk for ectopic pregnancy; however this association did not reach statistical significance and warrants further investigation.

<table>
<thead>
<tr>
<th>Quartile of EV (ml)</th>
<th>Q1: &lt; 3.7 (n=152)</th>
<th>Q2: 3.7-4.8 (n=180)</th>
<th>Q3: 4.9-6.2 (n=150)</th>
<th>Q4: ≥ 6.3 (n=156)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical pregnancy, n (%)</td>
<td>111 (73.0%)</td>
<td>139 (77.2%)</td>
<td>116 (77.3%)</td>
<td>117 (75.0%)</td>
</tr>
<tr>
<td>Miscarriage, n (%)</td>
<td>13 (8.6%)</td>
<td>9 (5.0%)</td>
<td>13 (8.7%)</td>
<td>17 (10.9%)</td>
</tr>
<tr>
<td>Ectopic pregnancy, n (%)</td>
<td>5 (3.3%)</td>
<td>3 (1.7%)</td>
<td>0 (0%)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Live birth, n (%)</td>
<td>96 (62.2%)</td>
<td>130 (72.2%)</td>
<td>102 (68.0%)</td>
<td>99 (63.5%)</td>
</tr>
</tbody>
</table>

Table 1
COMPARISON OF SINGLETON AND TWIN PREGNANCY OUTCOMES IN WOMEN WITH A CONGENITAL UNICORNUATE UTERUS AFTER IN VITRO FERTILIZATION-EMBRYO TRANSFER.

**TABLE.** The comparison between singleton-pregnancy and twin-pregnancy

<table>
<thead>
<tr>
<th>Pregnancy outcomes</th>
<th>Singleton-pregnancy group(n=277)</th>
<th>Twin-pregnancy group(n=59)</th>
<th>P-value</th>
<th>OR (95%-CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscarriage, % (n)</td>
<td>20.6% (57/277)</td>
<td>11.9% (7/59)</td>
<td>0.122</td>
<td>1.925 (0.830-4.463)</td>
</tr>
<tr>
<td>Preterm delivery, % (n)</td>
<td>13.0% (36/277)</td>
<td>57.6% (34/59)</td>
<td>&lt;0.001</td>
<td>0.110 (0.059-0.205)</td>
</tr>
<tr>
<td>Term birth, % (n)</td>
<td>65.3% (181/277)</td>
<td>28.8% (17/59)</td>
<td>&lt;0.001</td>
<td>4.658 (2.517-8.619)</td>
</tr>
<tr>
<td>Perinatal mortality, % (n)</td>
<td>1.8% (4/217)</td>
<td>15.7% (16/102)</td>
<td>&lt;0.001</td>
<td>0.101 (0.033-0.311)</td>
</tr>
<tr>
<td>Live birth, % (n)</td>
<td>76.9% (213/277)</td>
<td>76.3% (45/59)</td>
<td>0.101</td>
<td>1.035 (0.534-2.007)</td>
</tr>
<tr>
<td>Birth weight, (g)</td>
<td>3068 ± 514</td>
<td>2260 ± 476</td>
<td>&lt;0.001</td>
<td>0.986 (0.534-1.74)</td>
</tr>
<tr>
<td>Low birth weight, % (n)</td>
<td>11.7% (25/213)</td>
<td>58.1% (50/86)</td>
<td>&lt;0.001</td>
<td>0.096 (0.53-1.74)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Singleton-pregnancy could obtain better pregnancy outcomes than twin-pregnancy in women with a unicor-nuate uterus after IVF-ET. Therefore, reducing the incidence of twin pregnancy in women with a unicor-nuate uterus is clinically necessary.

SUPPORT: The science and technology project of Health and Family Planning Commission of Hunan Province (No. C20180809) and the Citic-Xiangya Research Fund (No. KYX201703)

O-131 Tuesday, October 15, 2019 11:45 AM

**UTE RINE SUBSEPTATIONS AN INDICATION FOR SURGICAL CORRECTION IN INFERTILITY PATIENTS: A COMPARISON OF FOUR SYSTEMS.** Mary Emily Christiansen, MD, Irene Peregrin-Alvarez, MD, Robert Roman, MD, Roberto Levi D’Ancona, MD, Jennifer Gordon, MD, Laura Detti, MD. The University of Tennessee Health and Science Center, Memphis, TN; University of Tennessee Health Science Center, Memphis, TN; UTHSC, Memphis, TN.

OBJECTIVE: In this study we sought to evaluate uterine subseptations using four proposed methods: the AFS-10 mm (1988/2003), the ESHRE-ESGE (2013), the ASRM (2016), and our group’s 5.9 mm cut-off length (2017), to identify the classification method which allows the most accurate diagnosis and indication for surgical incision

DESIGN: This was a retrospective cohort study at a University center.

MATERIALS AND METHODS: Patients being evaluated for infertility or recurrent pregnancy loss were included in the study if they were diagnosed with a uterine subseptation, defined as having a length ≥ 3 mm, as this was the minimum length measured in our population. Patients diagnosed with subseptate uteri were evaluated with 2-D and 3-D ultrasound in accordance with the four different methods. The diagnosis of uterine septum according to each method’s specifications was then compared among the four groups: AFS, ESHRE-ESGE, ASRM, and 5.9-mm cut-off. We compared distributions using the non-parametric Mann-Whitney U test with a p value <0.05 defining statistical significance. We used SPSS v24 for Windows (Chicago, Illinois).

RESULTS: 125 women had uterine subseptations and all four diagnostic systems identified septate uteri in our database. The 5.9-mm cut-off diagnosed 89 septate, and 36 normal uteri and was the most inclusive while the ASRM cut-off was the most restrictive one. Subseptations were inconsistently diagnosed by the ESHRE-ESGE classification, as some subseptations longer than 10 mm would be classified as normal uteri. Five/24 had one previous early loss and 19/24 had suffered recurrent early pregnancy loss. The 5.9-mm system was the most sensitive, while the ASRM the least sensitive) in predicting pregnancy loss (71.2% vs. 9.5%).

CONCLUSIONS: The proposed 5.9-mm cut-off was the most sensitive in identifying subseptate uteri and in predicting early pregnancy loss. Conversely, the AFS-10 mm and the ASRM were too restrictive, potentially missing treatment for dangerous subseptations. When dealing with such a catastrophic outcome as a pregnancy loss, it is important to find the most sensitive system to diagnose a subseptation, and the 5.9-mm system had the highest sensitivity to diagnose a subseptation and its risk of early pregnancy loss. The current study bridges the gap undermining other studies: it correlates the diagnosis of septate uterus with obstetric outcomes and provides an objective analysis of the morphometric changes of the septate compared to the normal uterus. SUPPORT: None

FERTILITY & STERILITY®

e55
MATERIALS AND METHODS: Women <45 years undergoing AM, LM or RALM for symptomatic leiomyomata were included. Pre-operative pelvic MRI or US was performed based on physician preference. Baseline demographics were recorded for all patients, including the number, location and dimensions of all leiomyomata on MRI or US. Total leiomyomata volumes were calculated based on recorded dimensions. Primary operative outcomes of interest were total operating time, leiomyomata weight and estimated blood loss (EBL). Spearman’s correlation was used to evaluate the correlation between leiomyomata volume and operative outcomes. Receiver-operator-characteristic (ROC) curves were constructed for outcomes showing statistical significance.

RESULTS: A total of 117 patients were included; there was no difference in the demographics or leiomyomata characteristics of patients undergoing MRI or US in the AM (n=69), LM (n=13) or RALM (n=35) groups. The mean age and leiomyomata volume of patients undergoing LM was 36.7±7.1 years and 152.1±90.9 mL, respectively. The was a strong positive correlation between MRI leiomyomata volume and operating time (r=0.90; P<0.001) and leiomyomata weight (r=0.89; P<0.02). Patients in the RALM group had a mean age and leiomyomata volume of 36.9±4.1 years and 242.4±136.1 mL, respectively. A significant positive correlation between MRI leiomyomata volume and operating time (r=0.83; P=0.03) and leiomyomata weight (r=0.79; P=0.01) was noted in the RM group as well. These correlations were non-significant in the LM and RALM groups when using US leiomyomata volume. MRI leiomyomata volume was also predictive of LM and RALM conversion to laparotomy (area-under-the-curve=0.92). These correlations were positive but non-significant in AM group. No correlation was observed between MRI and US leiomyomata volume and EBL in all groups.

CONCLUSIONS: Pre-operative pelvic MRI in patients undergoing LM or RALM strongly correlates with operating time and leiomyomata weight and predicts conversion to laparotomy.

Support: None

IVF OUTCOME PREDICTORS 1

O-133 Tuesday, October 15, 2019 10:45 AM

GONADOTROPIN-SPECIFIC FOLLICULAR STEROIDOGENESIS IN OVARIAN STIMULATION: EVIDENCE FROM THE MENOPUR IN GnRH ANTAGONIST SINGLE EMBRYO TRANSFER - HIGH RESPONDER (MEGASET-HR) TRIAL. Fady I. Sharara, M.D., a Fady D. Foster, Ph.D., b Anshul Sinha, B.Tech, b Gaurang S. Daftary, MD, MBA, b Patrick W. Heiser, Ph.D., b Virginia Center for Reproductive Medicine, Reston, VA; b Ferring Pharmaceuticals, Inc, Parsippany, NJ.

OBJECTIVE: To evaluate gonadotropin related differences in follicular endocrine physiology in predicted high responder women undergoing assisted reproductive technology.

DESIGN: Multicenter, randomized, assessor-blind, non-inferiority trial.

MATERIALS AND METHODS: Ovulatory women aged 21-35y, BMI <35 kg/m 2 and serum anti-Mullerian hormone (AMH) ≥5 ng/mL (N=620) were randomized 1:1 to a 150 IU start dose of HP-hMG or rFSH in a GnRH antagonist cycle; 75 IU dose adjustments were allowed on/after stimulation day 6. Central laboratory serum hormones were measured on stimulation days: 1, 6, day of/after trigger. Log transformation was performed and displayed with/without modeling as a function of both the number of follicles and follicles ≥12 mm to account for site of steroidogenesis. Birth outcomes resulting from fresh/frozen transfers within 6 months of randomization were collected.

RESULTS: Demographics for the HP-hMG and rFSH arms were similar. The primary non-inferiority end-point of ongoing pregnancy was met, but a higher average number of oocytes/patient was retrieved in the rFSH (22.2) vs. the HP-hMG arms (15.1). Cumulative live birth rates were similar, but OHSS and cumulative early pregnancy loss rates were significantly higher in subjects who received rFSH. Although serum estradiol (E2) concentrations were significantly elevated on day 6 and day of trigger in the HP-hMG group, serum E2 adjusted by follicle number was instead higher in the HP-hMG group on the day of trigger. Progesterone levels remained higher in the rFSH group independent of model. Androstenedione and testosterone levels were significantly higher regardless of adjustment, in the HP-hMG group on the day of trigger (table).

CONCLUSIONS: Data suggest that gonadotropin specific follicular steroidogetic responses exist. After accounting for ovarian response, HP-hMG drives higher androgen and estradiol with lower progesterone levels at the end of stimulation. Additional investigation will determine whether changes in ovarian follicle steroid output might be linked to the differences in safety parameters observed.

Support: Ferring Pharmaceuticals

IN VITRO FERTILIZATION WITH PERSONALIZED BLASTOCYST TRANSFER VERSUS FROZEN OR FRESH BLASTOCYST TRANSFER: A MULTICENTER, RANDOMIZED CLINICAL TRIAL. Carls Simon, MD, PhD,a Carlos Gomez, M.Sc., Sergio Canbanillas, MD, Ph.D., a Ivar K. Vladimirov, M.D., Ph.D., a Gemma Castillón, M.D., Ph.D., a Juan Giles, M.D., Ph.D., a Fazilet Kubra Boyumakalin, M.D., MSc, a Necati Findikli, Ph.D., a Israel Ortega, M.D., Ph.D., a Carmen Vidal, M.D., Ph.D., a Alexandra Izquierdo, M.D., Ph.D., a Susana Portela, M.D., a Nilo Franz, M.D., a Sagiri Taguchi, M.D., Ph.D., a Elena Labarta, M.D, Ph.D., a Francisco Colucci Coelho, M.D., Ph.D., a Shari Mackens, M.D., a Xavier Santamaria, M.D., Ph.D., a Elkin Muinoz, M.D., Ph.D., a Saul Guillermo Barrera Sr., M.D., Ph.D., a Manuel Fernandez-Sanchez, M.D., Ph.D., a Marcos Ferrando, M.D., a Antonio Pellicer, M.D., Ph.D., a Ben W. Mol, M.D., Ph.D. Prof., a Diana Valbuena, M.D., Ph.D., a University of Valencia, Igenomix Foundation-INCLIVA, Valencia, Spain; b Igenomix SL, Patera, Spain; c IVI-RMA Valencia, Valencia, Spain; d SBALAGROM-Sofia, Sofia, Bulgaria; e IVI-RMA Barcelona, Barcelona, Spain; f Bahceci Health Group-Fulya IVF Centre, Istanbul, Turkey; g IVI-RMA Madrid, MADRID, Spain; h IVIRMA Valencia, Valencia, Spain; i ProcesTec, Madrid, Spain; j IVI-RMA Vigo, Vigo, Spain; k Nilo Franz Reproductive Medicine, Porto Alegre, Brazil; l Oak Clinic, Japan, Osaka, Japan; m IVI-RMA, Valencia, Spain; n Centro de Infertilidad e Medicina Fetale del Norte Fluminense, Campos dos Goytacazes, Brazil; o Universitat Ziekenhuis Brussel, Jette, Belgium; p IVI-RMA Vigo, Vigo, Spain; q Nilo Frantz Reproductive Medicine, Porto Alegre, Brazil; r University of Valencia, Igenomix Foundation-INCLIVA, Valencia, Spain; s IVI-RMA Sevilla, Sevilla, Spain; t IVI-RMA Bilbao, Bilbao, Spain; u Monash University, Monash Medical Centre, Department of Obstetrics and Gynaecology, Melbourne, VIC, Australia.

<table>
<thead>
<tr>
<th>DAY 6</th>
<th>TRIGGER DAY</th>
</tr>
</thead>
<tbody>
<tr>
<td>rFSH</td>
<td>HP-hMG</td>
</tr>
<tr>
<td>5279</td>
<td>4984</td>
</tr>
<tr>
<td>5041</td>
<td>5527</td>
</tr>
<tr>
<td>Testosterone nmol/L</td>
<td>1.2</td>
</tr>
<tr>
<td>Estradiol nmol/L</td>
<td>2622</td>
</tr>
<tr>
<td>Progesterone nmol/L</td>
<td>2407,2867</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>trigger day</th>
<th>rFSH</th>
<th>HP-hMG</th>
<th>ADJ rFSH</th>
<th>ADJ HP-hMG</th>
</tr>
</thead>
<tbody>
<tr>
<td>7594</td>
<td>9789</td>
<td>9510</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7763,8051</td>
<td>9258,10351</td>
<td>6951,7667</td>
<td>9692,10713</td>
<td></td>
</tr>
<tr>
<td>Testosterone nmol/L</td>
<td>2.0</td>
<td>2.4</td>
<td>1.9</td>
<td>2.5</td>
</tr>
<tr>
<td>Estradiol nmol/L</td>
<td>1.9,2.1</td>
<td>2.3,2.6</td>
<td>1.8,2.0</td>
<td>2.4,2.7</td>
</tr>
<tr>
<td>Progesterone nmol/L</td>
<td>8823,10382</td>
<td>7576,9011</td>
<td>7631,9049</td>
<td>8805,10494</td>
</tr>
</tbody>
</table>

ADJ: adjusted
Value
95% Confidence Interval
OBJECTIVE: To determine the effectiveness of personalized embryo transfer (pET) versus frozen embryo transfer (FET) or fresh embryo transfer (ET) in infertile patients undergoing IVF at their first appointment. In pET, embryo transfer is performed within the optimal window of implantation identified by the endometrial receptivity array (ERA).

DESIGN: Multicenter randomized clinical trial. Participants aged ≥ 37 years scheduled for IVF with elective blastocyst transfer at the first appointment were randomized to undergo pET, FET or ET.

MATERIALS AND METHODS: Setting: 16 reproductive medicine centers in Europe, America and Asia with a common reference genetic laboratory. Patient(s): We recruited 569 women, and 458 were randomly assigned to pET (N=148), FET (N=154), or ET (N=156) groups.

Intervention(s): The ERA test was performed using hormone replacement therapy guiding embryo transfer in the pET arm. Blastocyst vitrification was performed in the pET and FET arms. Blastocyst transfer in all groups.

Main outcome measure(s): The primary outcome was live birth. Secondary outcomes were pregnancy and implantation rates as well as clinical miscarriage, biochemical pregnancy, and obstetric and neonatal outcomes. We performed intention-to-treat and per protocol analyses.

RESULTS: In the per protocol analysis, live birth rates at the first embryo transfer were 45 of 80 (56.2%) in the pET group, 39 of 92 (42.4%) in the FET group, and 43 of 94 (45.7%) in the ET group (pET versus FET relative risk [RR] 1.35, 95% confidence interval (CI) 0.97-1.86; p=0.09; pET versus ET RR 1.26, 95% CI 0.91-1.74; p=0.17). Cumulative live birth rates after 12 months were 57 of 80 (71.2%) in the pET group, 51 of 92 (55.5%) in the FET group and 46 of 94 (48.9%) in the ET group (pET versus FET RR 1.47, 95% CI 1.01-2.13; p=0.04; FET versus ET RR]1.71, 95% CI 1.17-2.49; p=0.003).

Pregnancy rates at the first embryo transfer in the pET, FET and ET were 72.5%, 54.3% and 58.5% respectively (RR 1.56, pET versus FET, 95% CI 1.01-2.29, p=0.03; pET versus ET RR 1.49, 95% CI 1.02-2.15, p=0.03). No differences between groups were found for clinical miscarriage, biochemical pregnancy or any other secondary outcomes. Obstetrical outcomes, type of delivery and neonatal outcomes were similar in all groups.

CONCLUSIONS: In this RCT, we found a statistically significant improvement in cumulative live birth rates in pET compared to FET and ET. Pregnancy and implantation rates after pET over FET and ET at first attempt as well as in cumulative rates were significantly higher. These findings indicate the potential of pET with the ERA test at the first appointment that should be confirmed in larger randomized clinical trials. (ClinicalTrials.gov NCT 01954758).


SUPPORT: The study was supported by Igenomix.
DIMINISHED OVARIAN RESERVE (DOR) IS ASSOCIATED WITH REDUCED EUPLOID RATES VIA PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) INDEPENDENT OF AGE: EVIDENCE FOR CONCOMITANT REDUCTION IN OOCYTE QUALITY WITH QUANTITY. Eleni A. Greenwood, MD, MSc,1 Charles E. McCulloch, PhD,2 Marcelle I. Cedars, MD,3 Mitchell P. Rosen, MD, HCLD4 1University of California San Francisco, San Francisco, CA; 2UCSF, San Francisco, CA; 3University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: Controversy surrounds whether an age-adjusted reduction in ovarian reserve is accompanied by diminished oocyte quality. We sought to determine whether women with DOR (quantitatively) had lower rates of euploid blastocysts via PGT-A testing, as a proxy for oocyte quality. DESIGN: Retrospective cohort. MATERIALS AND METHODS: Results from all day 5 and 6 blastocyst trophectoderm biopsies for PGT-A between 2010-2019 at a single academic center. Infertility diagnoses were grouped as DOR (assigned DOR on the basis of age-adjusted mature oocyte (M2) yield, signed DOR on the basis of age-adjusted mature oocyte yield, this relationship remained (Table). No differences were identified in rates of live birth or ongoing pregnancy between patients with and without DOR after SET of a euploid blastocyst (n=944 transfers) (56.8% vs 54.8%, respectively; p=0.88).

CONCLUSIONS: Blastocysts from women with DOR are less likely to be euploid than those from women without DOR, after adjustment for age. Given the concomitent reduction in euploid rates with quantity of oocytes observed in this study, quantitative ovarian reserve assessments (i.e. follicular machinery) may yield insight into relative ovarian aging.

Average euploid rates per cycle, by DOR vs non-DOR; and impact of DOR diagnosis on euploid rates, adjusted for age

<table>
<thead>
<tr>
<th>Clinician-diagnosed</th>
<th>DOR</th>
<th>Non-DOR</th>
<th></th>
<th>Lowest 1/4 M2 Yield</th>
<th>DOR</th>
<th>Non-DOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>42.8%</td>
<td>54.8%</td>
<td>45.1%</td>
<td>57.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-37</td>
<td>50.3%</td>
<td>50.2%</td>
<td>43.5%</td>
<td>51.4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>38-40</td>
<td>27.5%</td>
<td>40.8%</td>
<td>34.0%</td>
<td>38.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>41-42</td>
<td>22.4%</td>
<td>25.6%</td>
<td>28.9%</td>
<td>21.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>29.0%</td>
<td>44.9%</td>
<td>38.2%</td>
<td>43.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOR*</td>
<td>aOR 0.76 (95% CI 0.65, 0.90)</td>
<td>p&lt;0.01</td>
<td>aOR 0.80 (95% CI 0.68, 0.93)</td>
<td>p&lt;0.01</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Impact of DOR diagnosis on euploid rate, adjusted for age
significantly impacted by a delay in blastocyst development, with both implantation (D5 = 73.6%; D6 = 60.9%; D7 = 39.5%) and live birth rates (D5 = 68.5%; D6 = 55.2%; D7 = 37.0%) being significantly decreased (P<0.0001). Even when compared to a cohort of maternal age-matched counterparts (mean maternal age = 37.6 ± 3.6 years), women achieved poorer live birth outcomes with the SET of a D7 euploid blastocyst (37%) compared to a D5 or D6 euploid blastocyst SET (63%; n = 1,314; P<0.0001).

CONCLUSIONS: Aneuploidy rates and reproductive success were significantly associated with the appropriate timing of blastulation and identification of the ICM. Increased maternal age was associated with a delay in blastocyst development. However, even with maternally aged-matched counterparts, significantly compromised developmental potential was observed for D7 euploid blastocysts compared to D5 or D6 euploid blastocysts. Biochemical, metabolic and epigenetic processes that could impact embryo viability, independent of chromosome number, are potential contributors to the observed halving of the live birth rate for D7 euploid blastocysts. Despite poorer outcomes, these data still suggest that with appropriate patient counseling, extended culture to D7 for blastocyst biopsy is a viable clinical option for poorer prognosis patients.

SUPPORT: None.

O-138 Tuesday, October 15, 2019 12:00 PM

PROTOCOL MATTERS: A PROPENSITY GROUP ANALYSIS SHOWS THAT PROGESTERONE ELEVATIONS ON DAY OF TRIGGER DURING FRESH IVF-ET AFFECT LIVE BIRTH RATES DIFFERENTLY ACCORDING TO STIMULATION PROTOCOL. Chantall Bartels, MD,a James Grady, PhD,b Chao Ran Hu, M.S.,c Grow R. Daniel, MD,c aCenter for Advanced Reproductive Services, University of Connecticut, Farmington, CT; bUniversity of Connecticut, Farmington, CT.

OBJECTIVE: To assess the influence of trigger day progestrone (P) levels on live birth rate (LBR) after fresh embryo transfer when using different ovarian stimulation protocols, either gonadotropin-releasing hormone (GnRH) agonist suppression or GnRH antagonist.

DESIGN: Retrospective propensity score matching

MATERIALS AND METHODS: eIVF is a multicenter database that has collected over 122,548 patient IVF cycles, 2004-2018. We use logistic regression with protocol types, namely GnRH agonist suppression and GnRH antagonist, to identify co-variates and perform propensity score matching. The two protocol cohorts were matched for age, smoking status, P level on day of trigger (ng/mL) was 1.0 +/- 0.45 between the mean and one standard deviation.

RESULTS: The two propensity groups where similar with respect to matched covariates and performed Chi-square was used to regress the outcome live birth against protocols type and progesterone level and the (protocol / progesterone) interaction. Chi-square p-value 0.45 0.0001.

CONCLUSIONS: Elevated serum P levels on day of trigger during ovarian stimulation with the GnRH agonist suppression protocol. This data suggests that protocol should be considered when recommending a freeze-all approach in the setting of elevated P levels on the day of trigger.

SUPPORT: None

LGBTQ

O-139 Tuesday, October 15, 2019 10:45 AM

REPRODUCTIVE FUNCTION IN A TRANSGENDER MOUSE MODEL FOLLOWING CESSATION OF TESTOSTERONE. Molly B. Moravek, MD, MPH,a Hadrian M. Kinneer, BA,b Varshini Padmanabhan, MS,c Arielle Shikanov, PhD,c aUniversity of Michigan, Ann Arbor, MI; bUniversity of Rochester Medical Center, Rochester, NY; cUniversity of Michigan, Ann Arbor, MI.

OBJECTIVE: While pregnancy is certainly possible in transgender men previously on gender-affirming testosterone (T), very little is known about overall fecundability, and thus fertility preservation is recommended prior to starting T. Studies of T-exposed ovaries at the time of gender-affirming surgery reveal aberrations in ovarian histology and follicle appearance, but functional studies have not been performed. We have established a mouse model to study the effects of gender-affirming T therapy on reproduction. The objective of the current pilot study was to examine fertility following T cessation in our mouse model, with the hypothesis that reproductive function would be fully restored.

DESIGN: Translational animal study.

MATERIALS AND METHODS: Ten 8–9 week old female C57BL/6 mice were injected with T enanthate 0.45mg and 5 control (C) mice were injected with vehicle twice weekly for 6 weeks, then all injections were stopped. Daily vaginal cytology and weekly serum hormone analysis was performed. Once cyclicity resumed, mice were divided into two groups: 1) sacrificed after 3–4 estrous cycles and ovaries harvested or 2) 14 weeks breeding 1:1 with male C57BL/6 mice. Offspring resulting from group 2 were sacrificed on day of life (DOL) 26 and organs harvested. Descriptive statistics were calculated and confidence intervals calculated via modified Wald method or using a t-distribution, as appropriate.

RESULTS: All T-treated mice stopped cycling after 1–2 T injections and 8/9 resumed cycling 7–15 weeks following T cessation (one mouse sacrificed early for vaginal prolapse). Control mice cycled regularly throughout. Despite resumption of cyclicity, T-treated mice sacrificed after 3–4 estrous cycles (n=4) exhibited ovarian stromal hyperplasia and lack of corpora lutea on histologic examination. In the breeding arm, 50% of T-treated (2/4) and 50% of control mice (1/2) produced offspring. We observed a similar sex ratio (50% female in T group, 95% CI: .24 .76; 57% in control, 95% CI: .33 .79) and litter size (4.5 in T vs 4.7 in C) between groups. Mean weight on DOL 4 was 2.44g (95% CI: 1.89, 3) in T offspring vs 3.29g (95% CI: 2.93, 3.64) in control offspring, and 14.75g (95% CI: 13.68, 15.82) in T offspring and 16.33g (95% CI: 13.46, 19.2) in control offspring on DOL 26. The ovaries of both T and control offspring appeared normal, both grossly and histologically.

CONCLUSIONS: Despite histologic aberrations noted in the ovaries of T-treated mice early after resumption of cyclicity, their fertility approximated that of controls, with no obvious aberrations noted in the offspring. These pilot data suggest that T-induced subfertility may be reversible following cessation and may not affect long-term reproductive function. Further, these data justify a larger study of fertility following T cessation, as well as further investigation into the molecular mechanisms underlying T-induced changes in ovarian architecture.

SUPPORT: ASRM/SREI Research Grant; University of Michigan Office of Research Grant

O-140 Tuesday, October 15, 2019 11:00 AM

REPRODUCTIVE LIFE PLANNING AND INTEREST IN FERTILITY PRESERVATION AMONG TRANSGENDER AND GENDER NON-BINARY INDIVIDUALS. Nina Vyas, MD, Alisse Singer, BA, Armen Ter-Barsegyan, MPH, Alena Kantor, BS, Christ Mann, MSW, ASW, Sylvia I. Lambrechts, MPH, MA, Molly M. Quinn, MD, University of California, Los Angeles, Los Angeles, CA.

OBJECTIVE: Professional organizations agree that all transgender persons should be counseled on the effects of their transition on their fertility
TABLE 1.

<table>
<thead>
<tr>
<th>Referral to GHP specifically for fertility preservation</th>
<th>Gender Documented at Birth</th>
<th>Average Age (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>Male</td>
<td>Intersex</td>
</tr>
<tr>
<td>Referral to GHP specifically for fertility preservation</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Those with reproductive life planning goals</td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>Those who have undergone fertility preservation</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Those who desire fertility preservation</td>
<td>26</td>
<td>20</td>
</tr>
</tbody>
</table>

as well as options for fertility preservation and reproduction prior to transition. The UCLA Gender Health Program (GHP) is a multidisciplinary medical, surgical and behavioral health team that supports transgender and gender non-binary individuals in their transition. We sought to identify characteristics of individuals who desired fertility preservation at intake to the GHP.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: When individuals establish care at the GHP, a Care Coordinator performs a telephone intake to ascertain which referrals and services they require. We obtained IRB exemption to examine this intake data for all those in the Gender Health Program from January 2018 – March 2019. The data were coded and de-identified. Descriptive statistics were then performed.

RESULTS: A total of 397 intake surveys were included in the data analysis. The average age of individuals who established care at the GHP was 29 years (SD 12.4). Forty-seven (11.8%) individuals stated they had reproductive life planning goals. Twelve (3%) had previously undergone fertility preservation, with eleven of those assigned male at birth. Forty-seven (11.8%) stated they desired fertility preservation. Of the 397, only eight (2%) endorsed presenting to the GHP for fertility preservation as their primary goal. Eleven (2.9%) stated they were interested in referral for hysterectomy with oophorectomy. None of these eleven patients who desired surgical sterilization were also interested in referral for fertility preservation (see Table 1). Neither gender identity, nor race/ethnicity was predictive of interest in fertility preservation.

CONCLUSIONS: Access to reproductive health services is desired by many transgender and gender non-binary individuals. Although forty-seven (11.8%) of individuals stated they had reproductive goals, only twelve (3%) had undergone any fertility preservation and a majority of those had sex documented as male at birth. Given the low reported rate of fertility preservation and apparent level of interest, future research should focus on barriers to receiving fertility counseling or referrals for transgender and gender non-binary individuals.

O-141 Tuesday, October 15, 2019 11:15 AM

MEDICAL ASPECTS OF FERTILITY PRESERVATION (FP) FOR TRANSGENDER ADOLESCENTS AND YOUNG ADULTS (TAYAS): A SYSTEMATIC REVIEW.
Shira Baram, MD, a Samantha Myers, B.A, b Samantha Yee, Ph.D, c Clifford Lawrence Librach, MD, c CREATE Fertility Centre, Toronto, ON, Canada; 2McMaster University, Hamilton, ON, Canada.

OBJECTIVE: Many TAYAs choose to undergo gender-affirming hormone treatment (GAHT), sex reassignment surgery (SRS) or both. While these treatment options help alleviate symptoms of gender dysphoria, there are significant fertility risks that should be considered prior to commencing the transition process. This study aimed to systematically review the current literature on risks of GAHT, FP options and outcomes specific for TAYAs, to identify gaps in the current research and future research directions.

DESIGN: Systematic review and quantitative analysis.

MATERIALS AND METHODS: We systematically searched the following electronic databases: Medline, PubMed, Embase®, and PsychINFO to identify all studies which evaluated GAHT effects, FP options and outcomes in both male to female (MiF) and female to male (FiM) TAYAs. We included peer-reviewed papers from 2001 to March 2019. We excluded abstracts, clinical reviews, opinion pieces, editorial letters, and dissertations.

RESULTS: The search identified 745 papers. After applying exclusion and inclusion criteria, 21 were included. Among topics discussed in the selected papers are GAHT effects on hormone levels, semen parameters, testicular and ovarian morphology, spermatogenesis and oocytes as well as FP outcomes. Nine studies evaluated the effects of GAHT in MiF TAYAs. Most of the data suggest significant, yet mostly reversible, effects of GAHT on semen parameters. Interestingly, 2 of the studies described reduced parameters in TAYAs with no prior GAHT. The effects on testicular morphology and spermatogenesis vary between studies, with maturation arrest being the most common abnormality (24-100%). Normal spermatogenesis was observed in 0 to 25% of cases. Eight studies evaluated the effects of GAHT in FiM TAYAs. AMH level was found to be reduced in one study, yet unchanged in another. While some studies described follicular distribution in the majority of specimens as polycystic pattern, others describe normal distribution. Two studies evaluated in vitro maturation of oocytes retrieved at the time of SRS. Maturation rate was 34-38%, 68% survived vitrification/thaw and 87-94% had a normal appearing spindle. The literature regarding outcomes of FP in TAYAs consists mainly of case reports and case series, suggesting the feasibility of the process. No studies regarding ovarian tissue cryopreservation were identified.

CONCLUSIONS: This review brings to light the paucity of data available in the literature on the reproductive effects of GAHT and outcomes of FP in TAYAs. Current guidelines recommend that FP counselling take place before commencing GAHT, and support medical therapy initiation soon after a diagnosis is established. This paradigm, creates a dilemma for reproductive specialists as there are currently little high-quality data to rely upon when counselling TAYAs. Most available data point to some degree of effect of GAHT on both the testis and ovaries, yet the extent and reversibility of that effect has not yet been thoroughly explored. Future research should include large scale cohort studies, throughout the entire FP process.

SUPPORT: CREATE Fertility Centre

O-142 Tuesday, October 15, 2019 11:30 AM

THE BURDEN OF FAMILY BUILDING AS A GAY MALE COUPLE: THE MAJORITY OF GAY MALE COUPLES SEEN AT A LARGE REPRODUCTIVE MEDICINE PRACTICE DESIRE A CHILD WITH EACH OF THEIR GENETICS.
Lisa Schuman, MSW, a Spencer S. Richlin, M.D., b Robin Mangieri, MA, a Melissa Kelleher, MSW, c Nora Bolger, RN, a Mark Leonidires, M.D., b Reproductive Medicine Associates of Connecticut, Norwalk, NY; Reproductive Medicine Associates of Connecticut, Norwalk, CT; Reproductive Medicine Associates of CT, Norwalk, CT; dRMA of Connecticut, Norwalk, CT.

OBJECTIVE: In 2012, advances in reproductive endocrinology led ASRM to recommend a single embryo transfer for patients “with a good prognosis and to recipients of embryos from donated eggs”. Progress in gay rights has led to more men seeking fertility treatment to build their families over the past decade. Often same sex male couples (SSMC) desire a child from each of their genetics, which requires a donor and a surrogate, in addition to clinic fees. As a result of the high cost for IVF using an ovum donor, surrogate, surrogacy agency, and legal representation per pregnancy, these patients typically request a double embryo transfer. The aim of our study was to verify our observation that both men typically desire a child from each partner and when counseled, the majority of these men are willing to proceed with a single embryo transfer.

DESIGN: Retrospective Analysis

MATERIALS AND METHODS: Between 2017 and 2018, 46 SSMC participated in a meeting with the clinic Medical Director which included a review of risks associated with a twin gestation. These couples also received a counseling session with one of two mental health professionals who also discussed risks involved in proceeding with a double embryo transfer. These clinicians also asked, “are you interested in having children with both of your genetics?”

RESULTS: 45 (98%) couples said they desired a child from each of their genetics. One couple said they were “not sure” if they would have more than one child. Two couples had one child when they came to the clinic. Of the forty one couples who were beginning their path to parenthood, 27 (66%) decided to pursue a single embryo transfer after completing counseling.
CONCLUSIONS: Scientific literature addressing the importance of pur- sing a single embryo transfer in regard to childhood outcome is particularly relevant when using an ovum donor (Fert. Stert. 2012; 4:838). Consideration of patient desires, including the interest to transfer two embryos for an improved chance of a successful pregnancy and concomitant costs for a sec- ond journey needs to be understood. Many clinics are only willing to transfer a single embryo created with a donor oocytes into a surrogate without further discussion. Additional consideration should be given to SSMC who face the expenses of ovum donation and surrogacy since both want to be genetic fa- thers. As surrogacy agencies and the public become more aware of the health risks associated with a twin gestation, it is likely fewer male couples will request a double embryo transfer. For now, fertility clinics should consider the financial difficulties inherent in two surrogacy journeys and counsel these men with sensitivity.

References: None

SUPPORT: None

O-143 Tuesday, October 15, 2019 11:45 AM

PREGNANCY SUCCESS RATES FOR LESBIAN COU- PLES UNDERGOING INTRAUTERINE INSEMINATION

ConMaye Jasmyn K. Johal, MD, MSc,a Eleni A. Greenwood, MD, MSc,b Sara J. Vaughn, MD,c Eleni A. Greenwood, MD, MSc,a,b Lasine Aghajanova, MD PhD,d 1Stanford University School of Medicine, Stanford, CA; 2University of California San Francisco, San Francisco, CA.

OBJECTIVE: To compare pregnancy rates in lesbian women undergoing donor sperm intrauterine insemination (IUI) to heterosexual women under- going IUI using partner or donor sperm; we hypothesized that pregnancy rates would not differ significantly between the two populations.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: This study included all IUI cycles completed at Fertility centers of University of California, San Francisco from 2009-2016 and Stanford University from 2016-2017. The primary outcome of interest was clinical pregnancy rates per cycle. Student t-test and chi square test were used for statistical analysis. Significance was accepted at p<0.05.

RESULTS: A total of 11,845 IUI cycles were included, 341 of which were lesbian women using donor sperm and 11,504 of which were heterosexual women with unexplained or male factor infertility using either partner or donor sperm. Baseline characteristics including maternal age, type of IUI cy- cle, and total motile sperm count were similar between the two groups. Lesbian women had a clinical pregnancy rate of 11% per IUI cycle similar to that of heterosexual women who had a clinical pregnancy rate of 12% (p=0.17). Among both lesbian and heterosexual women, age was inversely correlated with clinical pregnancy rate (p=0.005 and p=0.02, respectively).

CONCLUSIONS: Increasing numbers of lesbian women are attempting to achieve pregnancy using IUI with donor sperm. Lesbian women generally seek these treatments for procreative management and not for infertility. Nonetheless, they have an increased prevalence of smoking, obesity, sexually transmitted diseases and polycystic ovary syndrome compared to heterosex- ual women, which may affect their fertility and IUI success (1). Previous studies are limited with conflicting findings. More information is desperately needed and will help guide counseling, management, and treatment in this population. Despite the majority of lesbian females not having a diagnosis of infertility, in this study pregnancy rates were similar in lesbian women under- going IUI for procreative management and heterosexual women undergo- ing intrauterine insemination for unexplained or male factor infertility. Pregnancy rates for both groups were comparable to nationally reported IUI success rates (2).


O-144 Tuesday, October 15, 2019 12:00 PM

IMPORTANT DECISION-MAKING CONSIDERATIONS FOR SAME-SEX MALE COUPLES (SSMC) AND SINGLE MEN (SM) WHEN PURSUING ASSISTED REPRO- DUCTIVE TECHNOLOGIES (ART).

Shilini Hemalal, BAS, MSc Candidate,a Samantha Yee, Ph.D,a,b Mona Loutfy, MD, MPH,b Clifford Lawrence Librach, MD,c bCreAte Fertility Centre, Toronto, ON, Canada; bDalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada; cWomen’s college Hospital, Toronto, ON, Canada.

OBJECTIVE: There is an increasing trend for SSMC and SM to have children through ART. However, research on their experience accessing care is lim- ited. Our objective was to evaluate decision-making considerations throughout the ART process which are unique to SSMC and SM who have used, or are currently using, ART.

DESIGN: This study was approved by the University of Toronto REB (#32847). A 58-item anonymous online questionnaire accessible through Survey Monkey was administered in order to collect quantitative data. This initial study includes only those undergoing ART in Canada.

MATERIALS AND METHODS: Data collection began in 08/2018 using convenience sampling techniques to recruit participants and is still ongoing. To date, 72 completed surveys have been used for this analysis.

RESULTS: The sample consisted of 63 partnered men and 9 SM, of which 21 had a child using ART, and 51 were actively pursuing ART at the time of filling out the survey. There were a similar number of Canadian (n=32, 44.4%) and international intended parents (n=39, 54.2%) who completed the survey. The majority (n=48, 66.7%) were in their 30s at the time of pur- suing ART. The sample cohort was predominantly Caucasian (n=50, 69.4%) and had a high socioeconomic status; 80.6% were university graduates and the median individual income before tax was $79,500 CAD ($59,360 USD).

With respect to the decision to pursue parenthood, the majority of partici- pants (n=63, 87.5%) had ‘a deep desire to have a child’ and felt that having a child was ‘a natural next step in their life’ (n=50, 69.4%). Common resources for learning about ART were internet search (58.3%), social media platforms (41.7%), friends (38.9%), and attending seminars, workshops, and conferences (33.4%) focused on men pursuing parenthood. Twenty-five participants (34.7%) ‘never’ experienced social stigma regarding their family building journey needs to be understood. Many clinics are only willing to transfer a single embryo created with a donor oocytes into a surrogate without further consideration. Additional consideration should be given to SSMC who face the expenses of ovum donation and surrogacy since both want to be genetic fa- thers. As surrogacy agencies and the public become more aware of the health risks associated with a twin gestation, it is likely fewer male couples will request a double embryo transfer. For now, fertility clinics should consider the financial difficulties inherent in two surrogacy journeys and counsel these men with sensitivity.

References: None

SUPPORT: None
MALE REPRODUCTION AND UROLOGY: CLINICAL

O-145 Tuesday, October 15, 2019 10:45 AM

THE PREVALENCE OF Y-CHROMOSOME MICRODELETIONS IN OLIGOZOOSPERMIC MEN: A SYSTEMATIC REVIEW AND META-ANALYSIS OF NORTH AMERICAN AND EUROPEAN STUDIES. Taylor P. Kohn, MD, MPH.a Jaden R. Kohn, MD, MPH,a Robert M. Coward, MD.a Johns Hopkins University School of Medicine, Baltimore, MD; b Johns Hopkins University School of Medicine, Department of GYN/ OB, Baltimore, MD; c University of North Carolina, Chapel Hill, NC.

OBJECTIVE: European and North American guidelines recommend Y-chromosome microdeletion (YCM) screening in azoospermic and oligozoospermic men with sperm concentrations < 5 million sperm/mL; however, numerous studies have suggested that YCM are rare when sperm concentrations are > 1 million sperm/mL. We systematically reviewed and meta-analyzed European and North American studies to determine the prevalence of complete YCM in oligozoospermic men with sperm concentrations of > 1–5 million sperm/mL versus azoospermic men with sperm concentrations of > 1–5 million sperm/mL.

RESULTS: Thirty-seven studies were identified during systematic review (n = 2,492 oligozoospermic men). All complete YCM in oligozoospermic men were AZFb microdeletions. Eighteen studies contained data conducive to meta-analysis (n = 10,866 men). Comparing the pooled estimated prevalence by sperm concentration, complete YCM were significantly more common in men with sperm concentrations of > 0–1 million sperm/mL (5.0% [95% CI: 3.6–6.8%] vs. > 1–5 million sperm/mL (0.8% [95% CI: 0.5–1.3%]; p < 0.001). YCM were similar in men with sperm concentrations > 1–5 million sperm/mL and > 5–20 million sperm/mL (0.8% [95% CI: 0.5–1.3%] vs 0.5% [95% CI: 0.2–0.9%]; p = 0.14).

CONCLUSIONS: In Europe and North America, the majority of YCM occur in men with sperm concentrations ≥ 1 million sperm/mL, with less than 1% identified in men with > 1 million sperm/mL. Male infertility guidelines for North America and Europe should reconsider the sperm concentration screening thresholds to recommend.

SUPPORT: None.

O-146 Tuesday, October 15, 2019 11:00 AM

THE EFFECT OF ADVANCING PATERNAL AGE ON PREGNANCY AND NEONATAL OUTCOMES FOLLOWING A SINGLE EUFROZION FROZEN EMBRYO TRANSFER IN A DONOR OOCYTE MODEL. Sydney Chang, MD, a Dmitry Gounko, MA, b Joseph A. Lee, BA, c Nathan Bar-Chama, MD, d Alan B. Copperman, MD, e Lucky Sekhon, MD.a 1. Icahn School of Medicine at Mount Sinai, New York, NY; b Reproductive Medicine Associates of New York, New York, NY; c University of North Carolina, Chapel Hill, NC; d Johns Hopkins University School of Medicine, Baltimore, MD; e University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: Advanced maternal age is a significant determinant of oocyte quality and a risk factor for adverse obstetric outcome. Less is known about the effect of paternal age on in vitro fertilization (IVF) and neonatal outcomes. Population-based studies have suggested that advanced paternal age is associated with preterm birth and low birth weight.1 Previously, our center demonstrated no association between paternal age and impaired fertilization, blastulation, or increased embryonic aneuploidy.2 While chromosomal copy number variants are largely derived from errors in oocyte meiosis, there is evidence showing a positive correlation between paternal age and de novo germline mutation rates.3 We hypothesize that a higher prevalence of de novo mutations in embryos derived from men with advancing paternal age could be associated with early pregnancy loss (EPL), lower ongoing pregnancy/live birth (OP/LB) rates, and adverse perinatal outcomes. Using a donor oocyte derived euploid embryo, in a frozen embryo transfer (FET) model, this study sought to elucidate the relationship between paternal age and pregnancy/perinatal outcomes.

DESIGN: Retrospective, cohort study.

MATERIALS AND METHODS: The study included patients undergoing a single euploid FET of donor oocyte-derived embryos from 2012 to 2019. Oocyte donors were ≤ 35 years of age. Paternal age was treated as a continuous variable. The primary outcome of the study was OP/LB rate. Secondary outcomes included clinical pregnancy (CP) rate, EPL rate, gestational age (GA) at delivery, and neonatal birth weight. Data were evaluated using multivariate linear regressions with generalized estimating equations.

RESULTS: A total of 303 single euploid FET cycles from 187 patients were included in this study. Paternal age ranged from 27.6 to 66.7 years (44.5 ± 6.5). There was no statistically significant association between paternal age, CP rate (OR 1.01 [95% CI 0.96–1.07], p = 0.62), OP/LB rate (OR 0.99 [95% CI 0.94–1.05], p = 0.75), or EPL rate (OR 1.00 [95% CI 0.96–1.07], p = 0.96) after controlling for oocyte age, BMI, endometrial thickness at transfer, embryo morphology grade, and days required for blastulation. No association between paternal age and birth weight (β = 8.17, p = 0.91) was observed after controlling for GA, fetal sex, and BMI. Paternal age was not associated with GA at delivery (β = −0.02, p = 0.83).

CONCLUSIONS: In a large, homogeneous cohort of single, euploid FETs derived from donor oocytes, paternal age was not associated with pregnancy or perinatal outcomes. Our results are encouraging, as they did not demonstrate a link between paternal age and preterm delivery or birth weight. While research in this area does not address other multifactorial diseases such as schizophrenia and autism that have been associated with advanced paternal age,4 As the diagnostic capabilities of preimplantation genetic testing expand to include the detection of de novo mutations and higher resolution detection of copy number variants, future studies might investigate the impact of paternal age on the embryonic genome, pregnancy outcomes, and newborn health and development.


SUPPORT: None.

O-147 Tuesday, October 15, 2019 11:15 AM

THE EFFECT OF TETRAHYDROCANNABINOL ON TESTOSTERONE AMONG MEN IN THE UNITED STATES: RESULTS FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY. Richard Jacob Fantus, MD,a Taylor P. Kohn, MD, MPH.a Ranjith Ramasamy, MD.a University of Chicago, Chicago, IL; b Johns Hopkins University School of Medicine, Baltimore, MD; c University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: Smoking tetrahydrocannabinol (THC) causes central suppression of gonadotropins resulting in testosterone deficiency. Emerging literature suggests that this effect may not occur, and that men using THC may actually have increased testosterone (T). Given this discrepancy, we sought to determine the association between different levels of THC use and T levels using a nationally representative cohort.

DESIGN: This is a retrospective review of a cross-sectional data set, the National Health and Nutrition Examination Survey (NHANES). A survey designed by the center for disease control (CDC) to determine the health of the United States.

MATERIALS AND METHODS: All men ages 18-80 years who answered the substance use questionnaire and underwent laboratory testing for T were included. THC use was self-reported and categorized by number of times used monthly. Multivariate modeling, controlling for confounders identified on univariate analysis, was then used to determine the relationship between THC use and T levels.

RESULTS: Among the 5,146 men who met inclusion criteria, 1477 (28.7%) endorsed smoking THC at least once in their lifetime, 509 endorse smoking in the last year (15.7%), and 625 (12.1%) reported smoking the last month. Men T level of the last month was 450 ± 185 ng/dL. Univariate analysis revealed that men who reported smoking THC in the last year on average had a higher T (497) compared to those who did not report using THC (414 ng/
CONCLUSIONS: Analysis of a nationally representative cohort suggests that there is a dose-dependent effect of THC on T levels. While there is an increase in T in all THC users, increased amounts of THC usage appear to have a detrimental effect on serum testosterone levels. Future prospective work using specific doses of THC and studies elucidating the mechanism of the association is required to corroborate these findings.

**Table.** The effects of THC use on testosterone when controlling for age, body mass index, exercise level, alcohol use, and race

<table>
<thead>
<tr>
<th>THC use within last year</th>
<th>Difference in T Level (ng/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>—</td>
</tr>
<tr>
<td>Once a month</td>
<td>49.96</td>
</tr>
<tr>
<td>2-3 times a month</td>
<td>66.77</td>
</tr>
<tr>
<td>4-8 times a month</td>
<td>52.18</td>
</tr>
<tr>
<td>9-24 times a month</td>
<td>41.81</td>
</tr>
<tr>
<td>25-30 times a month</td>
<td>33.44</td>
</tr>
</tbody>
</table>

* Controlling for age, body mass index, exercise, alcohol use, race, comorbidities, study years.

**Linear/Quadratic trend significant.

**O-148 Tuesday, October 15, 2019 11:30 AM**

**Utilizing the YO® Home Sperm Test Novice Users’ Obtained Accurate Results As Compared to Trained Technicians.** Nathan Bar-Chama, MD, b Lev Rabinovich, PhD, b Stan Honig, MD, c Ichacn School of Medicine at Mount Sinai, New York, NY; b Medical Electronic Systems, Caesarea Industrial Park, Israel; c Yale University, New Haven, CT.

**Objective:** Home sperm testing is emerging as an option for men to assess their fertility in a convenient and private environment. This study evaluated the ability of untrained users (NOVICE) to obtain accurate YO Home Sperm Test (YO) results compared to trained technicians (TRAINED).

**Design:** Double-blind multi-center prospective study.

**Materials and Methods:** The YO home sperm test is an FDA approved OTC device to measure Motile Sperm Concentration (MSC). Results are reported as a LOW MSC of <6x10⁶/mL or MODERATE/ NORMAL MSC of ≥6x10⁶/mL. This MSC cut-off is based on the WHO 5th edition reference values for semen analysis. Statistical analysis was based on positive (PPA) and negative percent agreement (NPA) between NOVICE and TRAINED user’s results. Positive results were defined as below the MSC cut-off and negative results above it, indicating absence of the condition being tested. Analysis was performed using MedCalc statistical software.

316 patients (NOVICE users) were enrolled in the study conducted at 3 sites. NOVICE users were comprised of 292 males with a mean age of 26.9 (19-61) and 24 females with a mean age of 35.0 (20-58). Ethnic breakdown was White 68%, Black 15%, Latino 11%, Asian 3% and Others 3%. Educational level was high school 23%, tech school 5%, college 58% and post graduate 14%. English, the first language in 218 cases (69%) was the second language in 98 (31%) of users. After semen collection, the NOVICE user was provided a YO kit to perform the test on either a Galaxy or iPhone up-loaded with the YO app. The NOVICE user conducted the test following only the instructions provided in the kit and on the YO app. Once the NOVICE user completed the test, a blinded laboratory professional (TRAINED) ran the same sample on the same Smartphone.

**Results:** The NOVICE vs. TRAINED users demonstrated a PPA of 96.7%, an NPA of 98.7% with 97.7% accuracy for all sites combined. The inter-site coefficients of variation (CV) were <2%.

**Conclusions:**

- 316 untrained users (NOVICE) of the YO Home Sperm Test demonstrated a high level of agreement and accuracy determining Motile Sperm Concentration above and below 6x10⁶/mL compared to trained technicians (TRAINED).
- The capability to accurately determine Motile Sperm Concentration at home may enable couples to appreciate earlier and more privately if a male factor is impacting their ability to conceive.

Reference: None.

**Support:** Medical Electronic Systems.
University of Central Florida, Clermont, FL; a PUR Clinic, Clermont, FL; b Keiser University, Cooper City, FL.

OBJECTIVE: To assess the efficacy of Ultrasound Guided Targeted Cryoaulation (UTC) of the peri-spermatic cord as a salvage treatment for patients who failed microsurgical denervation of the spermatic cord (MDSC) for the treatment of chronic scrotal content pain (CSP).

DESIGN: Retrospective review of 279 cases (221 patients: 58 bilateral) undergoing UTC between Nov 2012 to July 2016, performed by two fellowship trained microsurgeons.

MATERIALS AND METHODS: UTC was performed using a 16-gauge cryo needle (Endocare, HealthThronics, Austin, TX). Branches of the genitofemoral, ilioinguinal and inferior hypogastric nerves were cryoaulated medial and lateral to the spermatic cord at the level of the external inguinal ring. Level of pain was measured preoperatively and postoperatively using the Visual Analog Scale (VAS) and Pain Index Questionnaire (PIQ-6) (QualityMetric Inc., Lincoln, RI).

RESULTS: Median age was 43 years, operative duration 20 minutes, and post-operative follow-up 36 months (24 to 60). Subjective VAS outcomes: 75% significant reduction in pain (11% complete resolution and 64% ≥ 50% reduction in pain). Objective PIQ-6 outcomes: 53% significant reduction at 1 month (279 cases), 55% at 3 month (279 cases), 60% at 6 month (279 cases), 63% at 1yr (279 cases), 65% at 2yrs (275 cases), 64% at 3yrs (232 cases), 59% at 4yrs (128 cases) and 64% at 5 yrs (53 cases) post-op. Complications: two wound infections, four penile pain cases (resolved in a few months).

CONCLUSIONS: Ultrasound Guided Targeted Cryoaulation of the peri-spermatic cord is a safe potential treatment option for the salvage management of persistent CSP in patients who have failed MDSC.

SUPPORT: None.

MENTAL HEALTH

O-151 Tuesday, October 15, 2019 10:45 AM

THE IMPACT OF KLINEFELTER SYNDROME ON QUALITY OF LIFE - A MULTICENTRE STUDY. Sebastian Franik, MSc, MD, a Kathrin Fleischer, MD, PhD, a Barbara Kortmann, MD, PhD, a; Kathleen D’Hauwers, MD, PhD, b Joanna IntHout, PhD, c Claire Bouvattier, MD, b Jolanta Słowińska-Helzer, MD, PhD, b Solange Grunenwald, MD, b Tim van de Geit, MD, PhD, d Audrey Cartault, MD, d Annette Richter-Unruh, MD, PhD. d Ute Thyen, MD, PhD. e Hedi Claasen - van der Grinten, MD, PhD. f Resident in Obstetrics and Gynaecology, Nijmegen, Netherlands; g Department of Obstetrics and Gynaecology, Radboudumc, Nijmegen, Netherlands; h Department of Pediatric Endocrinology, Radboudumc, Nijmegen, Netherlands; i Department of Obstetrics and Gynaecology, Radboudumc, Nijmegen, Netherlands; j Department of Urology, Nijmegen, Netherlands; k Department of Health Evidence, Nijmegen, Netherlands; l Department of Pediatric Endocrinology, Paris, France; m Department of Andrology and Reproductive Endocrinology, Medical University of Lodz, Lodz, Poland; n Department of Endocrinology and Metabolic Disease, Toulouse, France; o VU medisch centrum, Amsterdam, Netherlands; p Department of Pediatrics, Toulouse, France; q Department of Pediatric Endocrinology, Bochum, Germany; r Department of Pediatrics, Lübeck, Germany; s Department of Pediatric Endocrinology, Radboudumc, Nijmegen, Netherlands.

OBJECTIVE: Klinefelter syndrome (KS) is associated with an increased risk of lower socioeconomic status and a higher risk for morbidity and mortality, which may have a significant impact on quality of life (QOL). The objective of this study is to investigate QOL in a large European cohort of men with KS and associate QOL with socioeconomic status, prevalence of somatic disease and mental illness, testosterone supplementation and age of diagnosis.

DESIGN: This study was part of the European dsd-LIFE study, a non-interventional, clinical, cross-sectional study.

MATERIALS AND METHODS: Participants were recruited in 14 clinical study centres in 6 European countries which participated in the European dsd-LIFE study. 218 men with KS were eligible for inclusion. Male normative data from the European Social Surveys (ESS) was used for comparison. Clinical data, related to quality of life, social activity and health status were collected.

RESULTS: The WHO physical domain score of men with KS (66.2 ± 19.4; n = 206) was significantly lower compared to the healthy reference population (75.5 ± 16.2; n = 1324; p < 0.001). The WHO psych domain score of men with KS (n = 206) was significantly lower (63.0 ± 17.9) compared to the healthy reference population (67.8 ± 15.6; n = 1324; p < 0.05). The WHO environment domain score of men with KS (69.7 ± 14.9; n = 206) was comparable to the healthy reference population (70.5 ± 20.7; n = 1324; p = 0.5). The WHO social domain score of men with KS (59.1 ± 22.1; n = 206) was significantly lower compared to the healthy reference population (68.2 ± 13.8; n = 1324; p = 0.001). A significant reduction in pain (11% complete resolution and 64% ≥ 50% reduction in pain). Objective PIQ-6 outcomes: 53% significant reduction at 1 month (279 cases), 55% at 3 month (279 cases), 60% at 6 month (279 cases), 63% at 1yr (279 cases), 65% at 2yrs (275 cases), 64% at 3yrs (232 cases), 59% at 4yrs (128 cases) and 64% at 5 yrs (53 cases) post-op. Complications: two wound infections, four penile pain cases (resolved in a few months).

CONCLUSIONS: Ultrasound Guided Targeted Cryoaulation of the peri-spermatic cord is a safe potential treatment option for the salvage management of persistent CSP in patients who have failed MDSC.

SUPPORT: None.
OBJECTIVE: To determine whether infertility centers that offer in-center stress reduction modalities (SRM) have higher live birth rates compared to centers without such services.

DESIGN: Retrospective cohort study comparing LBR among a sample of SART-affiliated fertility clinics with and without in-center SRM. Information on in-center availability of massage therapy and acupuncture were collected through standardized “secret shopper” phone conversations with clinic staff and/or navigation through each center’s website.

MATERIALS AND METHODS: The LBR from SART-affiliated fertility clinics from 6 states (NY, NJ, MA, PA, AZ, WA) were collected. Cycles utilizing gestational carriers were excluded, as were centers without finalized SART data or with unknown SRM treatments. Information regarding in-center acupuncture or massage was gathered via the centers’ websites or anonymous phone conversations with center staff. The primary outcome was LBR in the primary outcome per egg retrieval cycle. LBR was weighted based on the number of cycles performed in each age group for each center. The mean LBR was compared between centers who offer in-center SRM and those who do not stratified by SART maternal age group (<35, 35-37, 38-40, 41-42, >42) using student’s t-test; p<0.05 determined significance.

RESULTS: Ninety-four centers in 6 states (NY, NJ, MA, PA, AZ, WA) were identified using the SART website; 9 centers were excluded due to non-finalized 2016 data and 16 centers were excluded due to unavailable SART information. Of the 69 fertility clinics included, 16 offered acupuncture and/or massage therapy in-center. LBR was significantly higher in women ages <35 (41.8% vs 37%, p-value 0.02) and 35-37 (32.8% vs 13.7%, p-value 0.04) in clinics offering SRM compared to those who do not (Table).

<table>
<thead>
<tr>
<th>SART Age category</th>
<th>Live Birth Rate with SRM (n=16)</th>
<th>Live Birth Rate without SRM (n=55)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>41.8</td>
<td>37.0</td>
<td>0.02</td>
</tr>
<tr>
<td>35 - 37</td>
<td>32.8</td>
<td>13.7</td>
<td>0.04</td>
</tr>
<tr>
<td>38 - 40</td>
<td>20.5</td>
<td>10.0</td>
<td>0.17</td>
</tr>
<tr>
<td>41 - 42</td>
<td>11.1</td>
<td>5.5</td>
<td>0.20</td>
</tr>
<tr>
<td>&gt;42</td>
<td>4.2</td>
<td>2.0</td>
<td>0.30</td>
</tr>
</tbody>
</table>

CONCLUSIONS: To our knowledge, this is the first study to examine the impact of stress reduction modalities including massage and acupuncture on SART-reported LBR among affiliated clinics. LBR was found to be significantly higher for women ages <35 and 35-37 among clinics that offer these complementary therapies. This suggests that incorporating alternative medical treatments, such as acupuncture and massage, may improve IVF outcomes for younger patients. It is possible that older patients have less of a benefit due to the profound relationship between age and fertility; however, expanding this analysis to include more centers may similarly suggest a benefit for a broader patient population, and help to ascertain the true utility of SRM.
RESULTS: The study included 6,656 eligible patients. Among the PGT-A group, 19.1% of those without a delivery in the first cycle did not return for a second cycle compared to 13.3% in the non-PGT-A group (P=0.02) (Table 1). The proportion not returning after subsequent cycles did not differ (all P≥0.14). The cumulative incidence of live birth after up to six IVF cycles was similar in the PGT-A (76.1%, 95% CI: 67.3–82.6%) and non-PGT-A (72.9%, 95% CI: 71.2–74.5%).

CONCLUSIONS: Couples utilizing PGT-A were more likely than those who did not to terminate treatment after the first unsuccessful IVF cycle. In subsequent cycles, those using PGT-A were just as likely as those who did not to terminate treatment prior to achieving a live birth. Although it is accepted that PGT-A improves the likelihood of live birth per transfer, it is likely many couples did not return to care due to a lack of euploid embryos or due to the stresses of fertility treatment independent of PGT-A.

SUPPORT: None.

O-156 Tuesday, October 15, 2019 12:00 PM

HAIR CORTISOL AS A NEW BIOMARKER OF UNDERLYING CHRONIC STRESS, ANXIETY AND DEPRESSION IN INFERTILITY: A PILOT STUDY. Diana C. Santa-Cruz, MSc, a Rafael Caparros-Gonzalez, PhD, a Juan A. Garcia-Velasco, MD, PhD. b 1IVI-RMA Madrid, Madrid, Spain; 2Universidad de Jaen, Jaen, Spain.

OBJECTIVE: To study the viability of hair cortisol levels as a biomarker of chronic stress and explore its relationship with perceived anxiety levels and depressive symptoms.

DESIGN: Prospective, observational, cross-sectional study.

MATERIALS AND METHODS: A total of 50 non-smoking women, with body mass index of 19-30 kg/m2 and no previous fertility treatments, undergoing IVF were eligible for the study. Interested patients were asked to give a sample of their hair in their second consultation with the doctor and twelve weeks later. Study exclusion criteria included subjects with any recognized psychiatric or immune health condition; no drugs, alcohol consumption or high caffeine consumption. To reduce the confounding effect of risk variables, patients diagnosed with Cushing disease, asthma, on steroid medication, diabetes or other conditions known to influence cortisol levels, were excluded. The State-Trait Anxiety Inventory (STAI) and Depresssion Subscale (DEP) from Symptom Checklist 90-R (SCL-90-R) were used to assess anxiety and depression respectively at second appointment (T1) and twelve weeks after (T2). A score ≥40 on the State Anxiety scale (S-Anxiety) was used to detect clinically significant anxiety. SCL-90-R scores of DEP 2.0 were used to detect depression. Non-parametric, student t-tests, Chi-Square and Shapiro-Wilk normality tests were used where appropriate and a p<0.05 was considered to be significant.

RESULTS: The mean age was 36.2 (8.4) prior starting treatment. No patient was receiving psychological therapy or were on psychiatric medication at the time of the treatment. Overall patients had more Trait Anxiety at T1 (mean: 29.8, p<0.001) than T2 (mean: 24.4, p<0.001), while there was a mild difference in terms of depression (mean: 0.8 vs 1.5, p<0.001) from T1 to T2. Cortisol levels increased from T1 to T2 (mean: 239.2 vs 246.9, p <0.001). On T2, 52% of women had a positive pregnancy test, and their cortisol levels were reduced from T1 to T2 (mean: 357.2 vs 151.1, p<0.001) while women who had a negative result had higher cortisol levels at T2 (mean: 106.5 vs 378.6, p<0.001). Regarding correlation only frequent physical exercise showed a significant association to lower cortisol secretion at T1 but not at T2 (0.03 vs 0.09, p<0.05). Neither age, infertility diagnosis, anxiety levels had any significant association with cortisol.

CONCLUSIONS: We have shown that hair cortisol is a promising new biomarker to evaluate chronic stress in infertility patients. Cortisol secretion interacted with stress to accelerate the development of depressive symptoms, especially in those patients with a negative pregnancy test. Replication of these findings in a larger population will allow further explorations of the possible physiological mechanisms underlying stress and treatment outcomes.

PEdiatric and Adolescent gynecology

O-157 Tuesday, October 15, 2019 10:45 AM

ADOLESCENTS AND ECTOPIC PREGNANCY: TRENDS IN EMERGENCY DEPARTMENT UTILIZATION BETWEEN 2006-2014. Emma Giuliani, MD, a Monica W. Rosen, MD, b Elisabeth H. Quint, MD, b Erica E. Marsh, MD, a Yolanda R. Smith, MD, a 1Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI; 2University of Michigan, Ann Arbor, MI.

OBJECTIVE: Ectopic pregnancies (EP), if not promptly diagnosed and treated, are associated with significant morbidity and mortality and can negatively impact future fertility in young women. A substantial portion of the work-up and management of EP occurs in the Emergency Department (ED). To better understand this condition in adolescents, we investigated trends in ED utilization for EP in girls aged 13 to 19 years old over a 9-year period.

DESIGN: Retrospective cross-sectional study.

MATERIALS AND METHODS: The Nationwide Emergency Department Sample (NEDS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality, was queried for all ED visits in adolescents between 13 and 19 years old with a primary or secondary diagnosis (ICD-9-CM) of EP from 2006 to 2014. Parameters assessed included national estimated numbers of ED visits, ED charges adjusted for inflation, hospital geographic locations, patient’s demographic characteristics, and methotrexate (MTX) administration (SAS 9.4 - Cary, NC).

RESULTS: Approximately 75% of adolescents who presented to the ED for EP between 2006 and 2014 were 18 or 19 years old. While the number of ED visits for EP in adolescents remained fairly stable between 2006 and 2010 (3,264 versus 3,180), there was a 17.0% drop in 2011 (2,707) and another 17.9% drop in 2014 (2,221). In the most recent year analyzed, 2014, the majority of ED visits for EP in adolescents were seen in metropolitan areas (52.4%), in the southern regions (38.4%), in patients with Medicaid insurance (57.1%) and those in the lowest quartile for household income based on zip code (35.5%). Average ED charges per visit for EP progressively increased from $5,301 in 2006 to $9,066 in 2014, while total ED charges for this condition remained relatively stable ($17.2M in 2006 versus $20.1M in 2014). Overall, admission rates decreased from 43.7% to 18.4% through the years analyzed. Admission rates were higher in 16 and 17 years old adolescents living in metropolitan areas and in the western states. Finally, the percentage of ED visits associated with MTX administration increased from 1.7% in 2006 to 6.9% in 2014.

CONCLUSIONS: The number of ED visits for EP in adolescents decreased substantially between 2006 and 2014, which aligns with lower teenage pregnancy rates recorded by the CDC and easier access to emergent and non-emergent contraception as made available by government initiatives.

Vol. 112, No. 3, Supplement, September 2019

# Table 1. Comparing women who had PGT-A to women who did not have PGT-A in their first cycle

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Did not return for treatment N/Total N (%)</th>
<th>Did not return for treatment N/Total N (%)</th>
<th>Did not return for treatment N/Total N (%)</th>
<th>Did not return for treatment N/Total N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6,656</td>
<td>273</td>
<td>NA</td>
<td>6,383</td>
</tr>
<tr>
<td>2</td>
<td>4,483</td>
<td>174</td>
<td>41/215 (19.1)</td>
<td>663/4,972 (13.3)</td>
</tr>
<tr>
<td>3</td>
<td>2,470</td>
<td>108</td>
<td>21/129 (16.3)</td>
<td>572/2,934 (19.5)</td>
</tr>
<tr>
<td>4</td>
<td>1,427</td>
<td>58</td>
<td>22/80 (27.5)</td>
<td>357/1,726 (20.7)</td>
</tr>
<tr>
<td>5</td>
<td>816</td>
<td>38</td>
<td>11/49 (22.5)</td>
<td>259/1,037 (25.0)</td>
</tr>
<tr>
<td>6</td>
<td>507</td>
<td>18</td>
<td>6/24 (25.0)</td>
<td>156/645 (24.2)</td>
</tr>
</tbody>
</table>

*P compares PGT-A with no PGT-A.

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Cycle cohort</th>
<th>Did not return for treatment N/Total N (%)</th>
<th>Cycle cohort</th>
<th>Did not return for treatment N/Total N (%)</th>
<th>Cycle cohort</th>
<th>Did not return for treatment N/Total N (%)</th>
<th>Cycle cohort</th>
<th>Did not return for treatment N/Total N (%)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6,656</td>
<td>NA</td>
<td>273</td>
<td>NA</td>
<td>6,383</td>
<td>NA</td>
<td>663/4,972</td>
<td>13.3</td>
<td>0.02</td>
</tr>
<tr>
<td>2</td>
<td>4,483</td>
<td>174</td>
<td>41/215</td>
<td>673/5,087 (13.3)</td>
<td>663/4,972</td>
<td>13.3</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2,470</td>
<td>108</td>
<td>21/129</td>
<td>572/2,934 (19.5)</td>
<td>572/2,934</td>
<td>19.5</td>
<td>0.37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1,427</td>
<td>58</td>
<td>22/80</td>
<td>357/1,726 (20.7)</td>
<td>357/1,726</td>
<td>20.7</td>
<td>0.14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>816</td>
<td>38</td>
<td>11/49</td>
<td>259/1,037 (25.0)</td>
<td>259/1,037</td>
<td>25.0</td>
<td>0.69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>507</td>
<td>18</td>
<td>6/24</td>
<td>156/645 (24.2)</td>
<td>156/645</td>
<td>24.2</td>
<td>0.93</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
over the same time period. The drop in admission rates suggests an opportunity to shift the low-acuity cases of EP from the ED to the less expensive outpatient clinics. Additionally, adolescents who utilized the ED for EP more frequently belonged to the lowest income quartile and had Medicaid coverage which presents potential disparities in access to care and highlights a need for improved pediatric and adolescent gynecology outpatient services.

O-158 Tuesday, October 15, 2019 11:00 AM
PARENT COMPREHENSION FOLLOWING VIDEO-BASED EDUCATION FOR PEDIATRIC FERTILITY PRESERVATION. Nicole Handa, BS,1 Courtney J. Harris, MD,2 Kristine S. Corkum, MD,2 Aminata Bangoura, BS,2 Shaina M. Goff,1 Monica M. Laronda, PhD,1 Erin E. Rowell, MD,2,4 Northwestern University Feinberg School of Medicine, Chicago, IL;1 Department of Pediatric Surgery, Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL;2 Stanley Manne Children’s Research Institute, Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL;4Division of Pediatric Surgery, Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL.

OBJECTIVE: Decisions about whether to pursue fertility preservation (FP) can be particularly difficult in the pediatric patient population because parents are making decisions for their children. Additionally, the therapies for prepubertal children and surgical FP are experimental. Parents often cite lack of knowledge about infertility risk and experimental nature of options as barriers in deciding whether to pursue FP. This study was designed to gauge comprehension of FP video-based educational tools and to assess parent attitudes towards the tools.

DESIGN: This was a prospective randomized survey-based study completed 2018-2019 at a single tertiary care children’s hospital with Institutional Review Board approval.

MATERIALS AND METHODS: Participants were parents of pediatric patients (0-18 years old) admitted to a general surgery floor. Parents of children with a diagnosis putting them at risk for infertility or who had previously undergone FP were excluded. Participants completed pre-assessment questions, viewed two publicly available videos about FP, and completed post-assessment questions. Video A was colorful, animated, and used simple vocabulary. Video B was mostly black-and-white, more detailed, and used more complex vocabulary. Participants were randomized into two groups, each viewing the videos in a different order. Survey questions included participants’ FP knowledge, comprehension, and video preference. Statistics were gathered using chi-squared analyses and Wilcoxon rank sum tests.

RESULTS: 45 participants completed the survey. The average age was 37.5 years old; the majority were female (76%) and had completed high school/GED or above (98%). At baseline, 64% of participants indicated that they knew nothing about options for children at risk for infertility. After watching both videos, baseline knowledge scores improved in 73% of all participants and 61% felt they knew some or a lot about FP. There was no difference in the number of participants that improved from baseline between the two groups (p = 0.946). After viewing both videos, 87% of participants correctly answered >50% of the comprehension questions with no difference after video A compared to video B (p = 0.832). However, 70% of participants reported a preference for video A because it was interactive, colorful, and concise.

CONCLUSIONS: After utilizing FP video-based educational tools, parents experienced an increase in FP understanding, including the risk of infertility and options available for children, with preference for videos that are colorful and interactive. Our work indicates that video-based educational tools are an effective way to increase parent knowledge of FP options in the pediatric setting.

O-159 Tuesday, October 15, 2019 11:15 AM
FACTORS ASSOCIATED WITH CHOOSING FERTILITY PRESERVATION IN A PEDIATRIC, ADOLESCENT AND YOUNG ADULT POPULATION. Megan R. Sax, MD,1 Tara Schafer-Kaliskoff, MA,2 Brycen Ferrara, BS,2 Olivia Jaworek Frias, MSN, RN, CNL,2 Lesley Breach, MD,2 Karen Burns, MD, MS,1 Andrew C. Strine, MD,1 Julie Sroga Rios, MD,4 University of Cincinnati and Cincinnati Children’s Medical Center, Cincinnati, OH;1 Cincinnati Children’s Hospital medical center, Cincinnati, OH;2 Cincinnati Children’s Hospital Medical Center, Cincinnati, OH;4Division of Pediatric Urology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

OBJECTIVE: To determine patient characteristics associated with the decision to pursue fertility preservation prior to gonadotoxic therapy in a female pediatric, adolescent, and young adult patient population.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This IRB-approved study involved analysis of patient data in the Comprehensive Fertility Care and Preservation Program patient registry at Cincinnati Children’s Hospital Medical Center from 10/1/2013 through 11/6/2018. All female patients who received a fertility consult from this group were included in the analysis. Demographics, clinical diagnosis, and treatment characteristics were compared between patients that selected fertility preservation versus those that declined. Continuous variables were analyzed by student’s t-test and categorical variables were analyzed using Chi-square test. Results with p < 0.05 was considered statistically significant.

RESULTS: Of the 447 total fertility consults, 320 (71.5%) patients were eligible for fertility preservation options prior to gonadotoxic treatments, and one-third chose to pursue a fertility preservation intervention. In patients with a high-risk fertility assessment, 52.5% opted for fertility preservation. Patients receiving high risk gonadotoxic therapy and those planning bone marrow transplant (BMT) were more likely to choose fertility preservation. A higher proportion of non-English speaking patients/families declined fertility preservation than selected it (Table 1).

CONCLUSIONS: BMT, high fertility risk assessment, and non-English as primary language but not pubertal status or previous cancer treatment were significant factors affecting patient/family choice for fertility preservation in pediatric, adolescent and young adult setting. Based on these results, it is unclear whether a language barrier or cultural beliefs are affecting the decision making in non-English speaking participants. Further research is needed answer this and to better characterize barriers to fertility preservation in this population.

O-160 Tuesday, October 15, 2019 11:30 AM
WHO SEES FERTILITY SPECIALISTS? CANCER TREATMENTS AND SEEKING FERTILITY SERVICES IN ADOLESCENTS AND YOUNG ADULTS (AYA) WITH CANCER. Christina Lam, MD,4 Alexa CO Medica, MD,5 Kelsey Pinson, MD,4 Ksenya Shliakhtsitsava, MD,4 Brian W. Whitcomb, PhD,5 H. Irene Su, MD, M.S.C.E.6 University of California San Diego, La Jolla, CA;5University of California, San Diego, La Jolla, CA;4UT Southwestern, Dallas, TX;6University of Massachusetts, Amherst, Amherst, MA.

OBJECTIVE: Clinical guidelines endorse infertility risk counseling in newly diagnosed AYA cancer survivors and referral to fertility specialists in those who express interest. Limited empiric data exist on whether cancer treatment gonadotoxicity is related to patients seeking fertility services, which would suggest appropriate referrals to care. We hypothesized that AYA cancer survivors with planned gonadotoxic treatments are more likely to undergo infertility risk counseling (counseling) and fertility preservation procedures (FP procedures).
**DESIGN:** Cross-sectional.

**MATERIALS AND METHODS:** Female AYA survivors who were ages 18-39, diagnosed with cancer at ages 15-35, completed primary cancer treatment, had at least one ovary were recruited from cancer registries, clinics and advocacy groups between 2015 and 2018 to the parent Reproductive Window study on ovarian function. Participants completed a web-based questionnaire on infertility risk counseling and preservation procedures prior to cancer treatment, as well as demographic, cancer, and reproductive characteristics. Cancer treatments were abstracted from primary records. Log-binomial regression models were used to test associations between gonadotoxic treatments (alkylating chemotherapy [AC], abdominopelvic radiation therapy [RT], total body irradiation [TBI]) and fertility services (counseling and FP procedures) utilization, adjusting for confounding.

**RESULTS:** 578 survivors, mean age 33.1 (SD 4.7) years and 73.8% white, met eligibility criteria and were diagnosed with cancer at a mean age of 26.1 (SD 5.8) years. The most common cancers were breast (27.7%), thyroid (19.7%), and Hodgkin lymphoma (17.3%). Gonadotoxic treatment exposures were 49.5% to AC, 7% to >7 g/m² of cyclophosphamide equivalent dosing (CED), 4.3% to RT and 1.4% to TBI. Overall, 23.5% had counseling and 14.7% underwent FP procedures. In bivariable analysis, older age at diagnosis, infertility before cancer, cancer type, AC and CED, and RT were significantly associated with increased counseling. In adjusted analysis, age (aRR 1.09 [1.05-1.12]), CED <7 g/m² vs. none (aRR 1.71 [1.27-2.28]), and CED ≥ 7 g/m² vs. none (aRR 1.89 [1.09-3.27]) remained significantly associated with counseling. For FP procedures, white race, AC, CED and RT were associated in bivariable analysis. In adjusted analysis, undertaking FP procedures was more likely with older age (aRR 1.09 [1.05-1.31]), white race (aRR 1.88 [1.1-3.2]), receipt of <7g/m² CED vs. none (aRR 1.66 [1.10-2.49]), receipt of >7 g/m² CED vs. none (aRR 2.93 [1.64-5.23]), and RT (aRR 2.45 [1.36-3.30]).

**oophorectomy**, or had sonographic abnormalities (e.g. ovarian cyst) on post-oophorectomy ultrasound. Data collected included: age, race, comorbidities, age of menarche, surgeon specialty, ultrasound findings and bilateral ovarian volumes prior to surgery, indication for surgery, surgical pathology, and ultrasound findings and ovarian volume of remaining ovary following surgery. Descriptive analysis of ovarian volume of the remaining ovary following oophorectomy calculated on ultrasound were compared to known age-matched standard volumes at the time of post-operative ultrasound.

**RESULTS:** The average age of patients at time of oophorectomy was 10.8 years (2 days – 18 years). Twenty-four (25%) were < 10 years of age and 72 (75%) were > 10 years. Average time from surgery to post-operative ultrasound was 12.1 months (0 – 19 months). Average ovarian volume < 10 years was 2.5 ml and > 10 years was 13.7 ml. Sixty (63%) of patients had post-operative volumes greater than age-matched standards and 29 (30.2%) had smaller volumes. Of those with increased volume, average was 15.3 ml (< 10 years) and 15 ml (> 10 years). Sixty (62.5%) patients had volumes more than 10% larger than the age matched standards, and 50 (52.1%) patients had volumes more than 50% larger. Of the those with increased post-operative ovarian volume (n=60, 83.3%) had volumes > 50% larger than age-matched standards.

**CONCLUSIONS:** Ovarian enlargement occurs in the contralateral ovary following unilateral oophorectomy in the pediatric and adolescent population which supports the concept of compensatory ovarian hypertrophy that has been previously demonstrated in non-human models. This knowledge is important to the future clinical management of young females who have undergone unilateral oophorectomy.

References: Astrahan AH (1920) On the cause of the hypertrophy of the surviving A ovary after semispaying (albino rat) and on the number of ova in it. A Dev Dyn 28:59–79.


**SUPPORT:** None.

**PRACTICE MANAGEMENT**

**O-163 Tuesday, October 15, 2019 10:45 AM**

**CURRENT STATUS OF REPRODUCTIVE LABORATORY PROFESSION: WORKLOAD, WELLNESS, EARNINGS AND JOB SATISFACTION.** T. Arthur Chang, PhD, HCLD, ELD, 1 Ching-Chien Chang, PhD, HCLD, 1 Liesl Nel-Themaat, PhD, HCLD, 1 Scott E. Smith, PhD, HCLD, 1 Shane Zozula, B.S., T.S. (ABB), 1 Y. Tina Su, PhD, 1 University of Texas Health Science Center, San Antonio, TX; 2 Reproductive Biology Associates, Atlanta, GA; 3 University of Colorado Anschutz Medical Campus, Aurora, CO; 4 Abington IVF & Genetics, Abington, PA; 5 Ovation Fertility, Newport Beach, CA; 6 Affiliation not provided.

**OBJECTIVE:** To investigate the current workplace status among reproductive laboratory professionals in the U.S., including trends in earnings and comparison to benchmarks, work environment, job satisfaction, and wellness.

**DESIGN:** Retrospective analysis of multiple years of Society of Reproductive Biologists and Technologists (SRBT) Salary and Job Satisfaction Surveys with comparable publications and benchmarks.

**MATERIALS AND METHODS:** Data collection for survey data 2001-2018 were analyzed to determine longitudinal trends of salary among reproductive lab personnel. Variables including work environment, benefits, salary of various job titles, clinic setting, gender, job satisfaction and burnout, as well as off-site consulting, were analyzed. Key compensation numbers were compared with national earnings data from U.S. Bureau of Labor Statistics, and similar clinical lab and biotechnology sector wage surveys.

**RESULTS:** Total of 1,737 responses were analyzed. Overall, survey responses showed satisfaction with their current jobs and optimism on job market projections. However, the majority of survey responses also indicated significant stress (89% answered medium to extremely high level of stress), burnout (60% had 10 or more hours of overtime work (72.8%)). Most common benefits received were health and dental insurance, paid time-off, retirement plan, and support for conference attendance and certification. In 2018, the average annual clinical workload processed by each hands-on personnel included 108 fresh oocyte retrievals, 82 FETs, 79 biopsies for PGT, and 167 andrology tasks. Throughout the past two decades, nominal compensation (non-inflation adjusted) of reproductive lab professionals steadily increased throughout most of the survey period, with numbers higher than the national average for college/advanced degree workers. Such earnings were higher than most clinical lab specialties as well, with exception in a couple biotechnology sectors. Director earnings increased trending higher to advanced degree workers nationwide. Non-director categories showed a more significant salary growth than nationwide college/advanced degree workers and lab directors. Data from recent years revealed a wider distribution in salary range, which may reflect the volatility due to short supply of senior embryologists. Recent data also demonstrated an increasing portion of bonus in the compensation structure, which may indicate a broader utilization of bonus/incentives across all clinical settings, and possibly a contributing factor to the wider range of compensation among lab personnel. Gender-related difference in compensation remains significant despite an overall smaller gap than nationwide college/advanced degree workers.

**CONCLUSIONS:** The salary trend of reproductive lab profession show a steady increase throughout the period, a good indication compared to national labor wage and related clinical lab wage benchmarks. However, work-related stress, burnout, overtime duties, and gender pay gap remain issues to be resolved. Potential factors and impacts on these trends warrant further investigation.

**O-164 Tuesday, October 15, 2019 11:00 AM**

**DOES THE OPERATOR PERFORMING THE EMBRYO TRANSFER SIGNIFICANTLY INFLUENCE THE CYCLE OUTCOME?** Federico Cirillo, MD, EFRM ESHRE/EBCOG, 1 Pasquale Patrizio, M.D., 2 Emanuela Morenghi, Prof, 2 Michela Bacconi, Prof, 3 Elena Zannoni, MD, 4 Luca Cafari, MD, 5 Camilla Ronchetti, MD, 6 Annamaria Baggiani, MD, 7 Paolo Emanuele Levi Setti, MD, 8 Humanitas Research Hospital, Rozzano (Milan), Italy; 9 Yale Fertility Center, New Haven, CT; 10 Biostatistics Unit, Humanitas Research Hospital., Rozzano (MI), Italy; 11 Department of Statistics, Computer Science, Applications, University of Florence, Florence, Italy.

**OBJECTIVE:** Although embryo transfer (ET) is recognized to be an operator dependent technique, it is still unclear whether there are factors that can influence a correlation between success and operator. This study sought to analyze whether Ongoing Pregnancy Rate (OPR) is associated to the operator and whether there is a learning curve to become proficient.

**DESIGN:** Retrospective comparative analysis including all the fresh ET performed between 1996 and 2016 at a University-affiliated Center. Only embryo transfers performed by the surgeon on duty on that day were included. For operators with previous experience, the number of previous procedures was their entering threshold.

**MATERIALS AND METHODS:** A logistic regression model with a random intercept for the surgeon was specified, accounting for the heterogeneity among surgeons. To investigate the role of experience on OPR, a two-step procedure was implemented: a logistic regression for every surgeon to estimate a linear term expressing the relationship between experience and OPR. Then the estimated slopes were compared through meta-analysis techniques.

**RESULTS:** We included in the analysis 19,829 fresh ET performed by 32 operators. The random effects logistic model included: woman age, FSH, number of oocytes retrieved, fertilization rate, year of the procedure, number and stage of transferred embryos. The likelihood-ratio test for the heterogeneity among operators was highly significant (p-value = 0.0066). From the results, the best operator the difference between intercepts varied from a coefficient of -0.205374 to a coefficient of 0.1458145; this result can constitute a very big burden. Performing a random effects meta-analysis on these slopes, we found that the overall estimate was near zero, with a total pooled effect = 0.000 (-0.001 - 0.001). No evidence arose of an increase in OPR according to the operator’s experience. The I² of the heterogeneity among slopes was 43.7%. From our data, some operators perform worse than the
mean and do not improve with additional transfers. This observation can be explained because ET is generally performed by a single operator who learn on his own, with little opportunity of comparison.

CONCLUSIONS: This study shows that the operator factor can affect OPR but there is no significant increase in the outcome with experience. In future a very useful method could be the digital simulator, which could help operators to ameliorate without practicing on real patients.

SUPPORT: None.

O-165 Tuesday, October 15, 2019 11:15 AM

ONLINE PATIENT REVIEWS ARE INFLUENCED BY TYPE OF PHYSICIAN-BASED INFERTILITY PRACTICE. Ricci Allen, BA, BS, MSc, a Shrutil Agarwal, DO, a Mark P. Trollee, MD, a University of Central Florida College of Medicine, Orlando, FL. b UCF College of Medicine/FICA Consortium of Greater Orlando, Kissimmee, FL. c Fertility CARE: The IVF Center, University of Central Florida College of Medicine – Associate Professor, Winter Park, FL.

OBJECTIVE: In the field of reproductive endocrinology and infertility (REI), physician online presence plays a large marketing role with success rates and procedures reported on clinic/hospital websites and patient assessments on physician rating sites. Compared to other specialties, REI clinics place a strong emphasis on optimizing patient-centered care in order to enhance their experience, increase treatment compliance and patient wellbeing while minimizing anxiety and depression during their often extended treatment cycles. The objective of this study is to determine if patient online ratings are influenced by infertility insurance coverage. We hypothesize that patient reviews of physicians will be more positive in areas where health insurance mandates fertility coverage given that financial burden on patients is often cited as a major stressor of their experience.

DESIGN: Retrospective Cohort Study.

MATERIALS AND METHODS: Online physician ratings submitted between 2016-2019 from popular websites (Vitals, RateMD, Healthgrades) were recorded for REI specialists in the U.S. registered through SART and CDC. Overall rankings of physicians were compared based on infertility insurance coverage, clinic location, and type of clinical practice (university/hospital vs. private practice). Infertility insurance coverage was determined as covered if state health insurance mandates type of coverage for fertility treatment and not covered if the state does not mandate fertility coverage.

RESULTS: Data was collected from 1,097 REI specialists. An average rating of 4.09 out of 5 was found for physicians in states with mandated insurance coverage and an average rating of 4.08 out of 5 was found for those without insurance coverage (p = 0.762). The average rating for physicians based within a university/hospital practice was 3.96 compared to 4.13 for physicians in a private practice setting (p = 0.011). Among regions in the U.S., the South scored significantly higher mean average rating (p<0.01) than the Northeast and Midwest region. There was no significant difference (p>0.05) between West and South region (see Table).

CONCLUSIONS: A statistically significant higher rating was found for physicians in private practice compared to those affiliated with a university/hospital. No difference was found between the average rating in states with mandated insurance coverage for infertility treatment compared to states without insurance coverage. Furthermore, the South region had significantly higher mean average ratings compared to other regions in U.S except the west.

<table>
<thead>
<tr>
<th>Region</th>
<th>N</th>
<th>Mean Average Rating +/- standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northeast</td>
<td>327</td>
<td>3.99 +/- 0.930*</td>
</tr>
<tr>
<td>West</td>
<td>241</td>
<td>4.14 +/- 0.95</td>
</tr>
<tr>
<td>South</td>
<td>354</td>
<td>4.22 +/- 0.85*</td>
</tr>
<tr>
<td>Midwest</td>
<td>175</td>
<td>3.91 +/- 1.01*</td>
</tr>
</tbody>
</table>

*p = 0.01 – 0.049; *p = 0.765


O-166 Tuesday, October 15, 2019 11:30 AM

FREQUENCY AND CLAIMS BASIS FOR LAWSUITS OVER LOST, DISCARDED AND DAMAGED FROZEN EMBRYOS OVER A 10 YEAR PERIOD. Gerard Letterie, MD, a Dov Fox, JD, DPhil, LL.M. b Seattle Reproductive Medicine, San Diego, CA. c Professor of Law and Director of the Center for Health Law Policy and Bioethics at the University of San Diego, San Diego, CA.

OBJECTIVE: Cryopreservation technology has opened options to preserve fertility and maximize family building options. These opportunities create liability risks for providers not directly related to clinical practice and quality controls but also for maintenance of laboratory equipment and environment. Insights into how best to deliver care and assure optimal outcomes may be gained from a first-ever review of an increasing body of recent case law brought over embryos that have been lost, damaged discarded, mis-implanted or contaminated. Our objectives are to review claims, basis of claims and frequency of lawsuits over lost frozen or damaged frozen embryos.

DESIGN: Retrospective review of case law in state and federal courts over a 10 year period.

MATERIALS AND METHODS: Case law was researched from January 1, 2009 to April 22, 2019. Bloomberg, Westlaw and Lexis Nexis databases were searched to provide coverage of state court dockets regarding allegations and basis of claims made. Bloomberg Law included all federal court dockets. Cross-referenced terms included embryo, fertilized oocyte, cryopreserved embryo, discarded, lost and damaged embryo/s and implanted embryos. Data extracted included claims arising in federal and state courts.

RESULTS: A total of 131 cases were identified: 121 and 10 lawsuits in the state and federal court dockets respectively. 87 cases involved the recent cases in California and Ohio in 2018-19. Allegations for these relate to frozen embryo losses. In the remaining 44 cases, the majority (37) were brought across a broad range of allegations including: personal injury; breach of contract or warranty; product liability; professional negligence; unfair business practices and miscellaneous tort. A minority of cases (7) were brought for medical malpractice. The locations of these 44 cases included New York, Delaware, Illinois, Arizona and North Dakota.

CONCLUSIONS: The frequency of suits for damaged, lost or destroyed embryos is low with the exception of the recent events in California and Ohio. The basis of the claims is seldom for medical malpractice. These findings suggest that insurance coverage directed to claims outside of medical malpractice may be warranted given the expanding inventories of frozen oocytes, embryos and sperm and varying basis for claims. SUPPORT: None.

O-167 Tuesday, October 15, 2019 11:45 AM

IMPROVED MONITORING OF HUMAN EMBRYO CULTURE CONDITIONS USING A DEEP LEARNING-DERIVED KEY PERFORMANCE INDICATOR (KPI). Manoj Kumar Kanakasabapathy, MS, a Prudhvi Thirumalaraju, BS, a Raghav Gupta, BTech, a Rohan Pooniwalla, BTech, b Hemanth Kandula, BS, c Irene Souter, MD, c Irene Dimitriadis, MD, c Charles L. Bormann, PhD, c Hadi Shafiee, PhD, c “Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; c Massachusetts General Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: The clinical outcome of an in-vitro fertilization (IVF) cycle is perhaps the best indicator of system efficiency with ongoing pregnancy rates providing the most robust marker of embryo quality. Several early developmental stage markers are widely used to monitor culture conditions, however, their association with clinical outcomes is unclear. The objective of this study was to determine whether the use of an artificial intelligence (AI) algorithm, trained to predict in-vitro human embryo developmental fate, can be effectively used as a key performance indicator (KPI) for monitoring the performance of the embryo culture system.

DESIGN: Retrospective cohort study using a pre-developed deep neural network. The deep neural network (AI) analyzed embryos images acquired at 70 hours post insemination and provided a score (KPI score) taking into account all embryos within a given group.

**Materials and Methods:** A total of 876 embryos were cultured in 6 different lots of media (Medium A-F: C210/C210, Irvine Scientific) under identical conditions at 37°C, 5% O2 and 5% CO2 with oil overlay (Ovoil, Vitrolife). The percentage of 2 pronucleus (2PN) zygotes at the 4-cell stage on Day 2, 6-cell to 10-cell, ≥7-cells and those predicted to develop into high quality blastocyst stages using an AI-based generated KPI on Day 3 of embryo development was compared with ongoing pregnancy rates using a regression analysis. The low threshold value for ongoing pregnancy rates in the Massachusetts General Hospital (MGH) fertility clinic is set at 50%.

**Results:** The AI-based generated KPI for predicting high quality blastocyst formation had the highest association with ongoing pregnancy rates (R²=0.9063). This was the only cleavage stage KPI examined that was able to detect changes in our embryo culture environment that resulted in the pregnancy rates dropping below the threshold of 50%.

**Conclusions:** The most important aspect of quality assurance analysis is the identification of KPIs that will provide meaningful insight into laboratory functioning. This study demonstrated the power of using AI predictions in monitoring the performance of the embryo culture environment.


**Support:** This work was partially supported by the Brigham Precision Medicine Developmental Award (Brigham Precision Medicine Program, Brigham and Women’s Hospital) and R01AI118502, R01AI138800, and R21HD092828 (National Institute of Health).

O-168 Tuesday, October 15, 2019 12:00 PM

EMBRYO TRANSFER MANEUVERS AND MANIPULATIONS – THE EFFECT ON IN VITRO FERTILIZATION (IVF) OUTCOMES.

**Materials and Methods:** This study included all women undergoing IVF/ICSI with a subsequent Day 3 or Day 5 ET at a single academic hospital (MGH) from 1/2013 to 1/2018. The first ET during the study period was included from each patient. A ‘trial followed by transfer’ method was used in 416 patients. Objective: To determine the effect of maneuvers performed on the embryo transfer (ET) catheter during ET on in vitro fertilization (IVF) outcomes.

**Design:** Retrospective cohort study.

**Materials and Methods:** This study included all women undergoing IVF/ICSI with a subsequent Day 3 or Day 5 ET at a single academic hospital (MGH) from 1/2013 to 1/2018. The first ET during the study period was included from each patient. A ‘trial followed by transfer’ method was used in 416 patients. Objective: To determine the effect of maneuvers performed on the embryo transfer (ET) catheter during ET on in vitro fertilization (IVF) outcomes.

**Design:** Retrospective cohort study.

**Materials and Methods:** This study included all women undergoing IVF/ICSI with a subsequent Day 3 or Day 5 ET at a single academic hospital (MGH) from 1/2013 to 1/2018. The first ET during the study period was included from each patient. A ‘trial followed by transfer’ method was used in 416 patients. Objective: To determine the effect of maneuvers performed on the embryo transfer (ET) catheter during ET on in vitro fertilization (IVF) outcomes.
The negative influence on key miRNAs and gene transcription levels, in addition to the uterine microenvironment and was predictive of reproductive outcome. Lastly, an increased abundance of SERPING1, a protein associated with downstream synthesis of prostaglandins like PGE2. Decreased expression of AFC or other laboratory parameters after the PRP procedure, therefore IVF-ICSI and embryo banking at cleavage stage. Markers of ovarian reserve and IVF outcomes in patients with POI.

OBJECTIVE: Premature ovarian insufficiency (POI) affects 1% of reproductive age women. There are currently no effective treatment options that allow women with POI to conceive with their own eggs. Autologous platelets have been used as a source of proteins for healing and tissue regeneration for more than two decades, and platelet-rich plasma (PRP) is reported to promote the development of isolated human primordial and primary follicles to the preantral stage. In this study, we aimed to investigate the effects of intravaginal injection of autologous PRP on ovarian reserve and IVF outcomes in patients with POI.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Women (age range 20-48) diagnosed with POI based on ESHRE criteria (amenorrhea or oligomenorrhea for at least four months and increased follicle-stimulating hormone (FSH) > 25 IU/l measured twice with a four-week interval) were recruited for the study. Antral follicle counts (AFC), anti-mullerian hormone (AMH), and FSH levels were determined at baseline. PRP was prepared from peripheral blood using routine techniques. PRP injection was performed transvaginally, under ultrasound guidance, into at least one ovary using a 35 cm 17 G single lumen needle. Cyclic estrogen (4 mg estradiol daily on days 1-25) and progesterone (200 mg progesterone daily on days 16-25) were used to induce vaginal bleeding after PRP treatment. On the 2-4th days of induced menses after the procedure, AFC, AMH, and FSH levels were re-assessed. Patients with at least one antral follicle were started on ovarian stimulation for IVF-ICSI and embryo banking at cleavage stage. Markers of ovarian reserve (AFC, FSH, AMH), and IVF laboratory outcome parameters (number of MII oocytes, 2PN embryos, cleavage stage embryos) were followed.

RESULTS: At the time of this submission, a total of 70 patients (mean age ± SD: 40.8 ± 4.8) with the diagnosis of POI were included in the study. PRP treatment resulted in improved AFC (2.6 ± 1.3 vs 0.9 ± 0.8; p < 0.01), increased AMH levels (2.00 vs 1.08; p = 0.01), and lower serum FSH (32.6 ± 9.6 vs 37.4 ± 11.2; p = 0.06) levels. Total number of MII oocytes, 2PN and cleavage embryos obtained were 2.38 ± 1.58, 2.00 ± 1.47, and 1.94 ± 1.08, respectively. In 24 patients (34.2%), no changes were observed in terms of AFC or other laboratory parameters after the PRP procedure, therefore IVF-ICSI was not attempted. Another 24 patients (34.2%) failed to respond to stimulation or had fertilization failure. In 21 patients (30%), at least one cleavage stage embryo was obtained and embryo banking was performed. Importantly, spontaneous pregnancy occurred in six patients (7.1%, mean age ± SD: 39.5 ± 5.8) one or two cycles after the PRP procedure. At the time of this report, one of these pregnancies had resulted in missed abortion while the others were ongoing.

CONCLUSIONS: In women with POI, intravaginal injection of autologous PRP might be considered as an alternative experimental treatment option. Further studies with larger sample size and randomized prospective study design will be necessary to determine whether this intervention truly results in improved clinical outcomes.

O-170 Tuesday, October 15, 2019 11:00 AM

MINIMALLY INVASIVE UTERINE ASPIRATION 24 HOURS AHEAD OF EMBRYO TRANSFER CHARACTERIZES THE COMPROMISED RIF UTERINE MICROENVIRONMENT AND IS PREDICTIVE OF REPRODUCTIVE OUTCOME. Jason C. Parks, BS, Blair R. McCallie, BS, Mary E. Haywood, PhD, Taylor Pini, PhD, William B. Schoolcraft, MD, Mandy G. Katz-Jaffe, Ph.D., Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Repeat implantation failure (RIF) is particularly challenging to treat in ART, resulting in limited success even when adequate preparation of the endometrium is established and a transfer is performed with a high grade euploid blastocyst. The objective of this study was to utilize a multidisciplinary approach to decipher the complexity of RIF through investigations of the maternal molecular components ahead of an embryo transfer.

DESIGN: Research study.

MATERIALS AND METHODS: Patients were recruited with IRB consent 24 hours prior to a programmed frozen embryo transfer (FET) with a euploid blastocyst. Uterine secretions were collected by gentle aspiration (~2-5ul) under ultrasound guidance and grouped according to reproductive outcomes: Failed euploid FET (RIF patients, ≥3 prior IVF failures) and Positive live birth FET (maternally age-matched patients; mean 36.6 ± 3.8 years). Total RNA (n = 22) was sequenced using the NGS platform and the raw reads were aligned to hg38 using GSNAP and analyzed with edgeR (FDR cutoff of 5%; P ≤ 0.01). Metabolite analysis (n = 20) was performed by UHPLS-MS (Thermo) using MassMatrix and Maven (Princeton Univ). Proteomic analysis (n = 6) involved FASP digestion and LC-MS/MS, with protein identifications generated by Mascot (v 2.6) and Scaffold (v 4.8.9) (α ≥ 0.05; fold change ≥ 1.5 or <0.5).

RESULTS: A unique uterine microenvironment was observed for RIF patients and negative implantation outcomes 24 hours prior to an embryo transfer (P < 0.05). An interplay of several biological processes were evident in RIF failed aspires with a focused interest on 13 significantly reduced transcripts, 7 significantly increased maternal miRNAs, 12 significantly decreased amino acids and 16 proteins of significantly altered abundance (P < 0.05). Specific examples included decreased expression of PLA2G4D (P < 0.001), which regulates the eicosanoid pathway, thereby impacting downstream synthesis of prostaglandins like PGE2. Decreased expression of TET1 (P < 0.0001), an epigenetic regulator required for DNA methylation. Increased expression of miR-17, a known negative regulator of VEGFA, required for successful implantation (P < 0.01). Decreased quantities of arginine, essential for blastocyst activation and trophoderm motility (P < 0.05). Lastly, an increased abundance of SERPING1, a protein associated with inflammation, which regulates the eicosanoid pathway, thereby impacting downstream synthesis of prostaglandins like PGE2. Decreased expression of TET1 (P < 0.0001), an epigenetic regulator required for DNA methylation. Increased expression of miR-17, a known negative regulator of VEGFA, required for successful implantation (P < 0.01). Decreased quantities of arginine, essential for blastocyst activation and trophoderm motility (P < 0.05). Lastly, an increased abundance of SERPING1, a protein associated with inflammation, which regulates the eicosanoid pathway, thereby impacting downstream synthesis of prostaglandins like PGE2. Decreased expression of TET1 (P < 0.0001), an epigenetic regulator required for DNA methylation. Increased expression of miR-17, a known negative regulator of VEGFA, required for successful implantation (P < 0.01). Decreased quantities of arginine, essential for blastocyst activation and trophoderm motility (P < 0.05). Lastly, an increased abundance of SERPING1, a protein associated with inflammation, which regulates the eicosanoid pathway, thereby impacting downstream synthesis of prostaglandins like PGE2. Decreased expression of TET1 (P < 0.0001), an epigenetic regulator required for DNA methylation. Increased expression of miR-17, a known negative regulator of VEGFA, required for successful implantation (P < 0.01). Decreased quantities of arginine, essential for blastocyst activation and trophoderm motility (P < 0.05). Lastly, an increased abundance of SERPING1, a protein associated with inflammation, which regulates the eicosanoid pathway, thereby impacting downstream synthesis of prostaglandins like PGE2. Decreased expression of TET1 (P < 0.0001), an epigenetic regulator required for DNA methylation. Increased expression of miR-17, a known negative regulator of VEGFA, required for successful implantation (P < 0.01). Decreased quantities of arginine, essential for blastocyst activation and trophoderm motility (P < 0.05). Lastly, an increased abundance of SERPING1, a protein associated with inflammation, which regulates the eicosanoid pathway, thereby impacting downstream synthesis of prostaglandins like PGE2. Decreased expression of TET1 (P < 0.0001), an epigenetic regulator required for DNA methylation. Increased expression of miR-17, a known negative regulator of VEGFA, required for successful implantation (P < 0.01).
REVIEW.

Inez Roest, BSc, a Nienke van Welie, M.D., b

Tuesday, October 15, 2019 11:45 AM

who did not have an ERA before their first FET. The differences in implan-
tation rate and the clinical pregnancy rate. A two-sample t-test was
used to compare continuous outcomes between groups, and Chi-square
testing was used to compare proportions between the two groups.

RESULTS: The implantation rate for patients that underwent ERA vs. no
ERA prior to FET was 64.6% vs. 60.5% (p = 0.71). The clinical pregnancy
rate for ERA vs. no ERA prior to FET was 56.5% vs. 52.8% (0.56). The
live birth rate for ERA vs. no ERA prior to FET was 52.2% vs. 51.1%
(p = 0.9). The single embryo transfer rate was 96% for the ERA group vs.
98% for the non-ERA group.

CONCLUSIONS: Performing an ERA prior to first time FET with a
euploid blastocyst did not increase the live birth rate compared to patients
who did not have an ERA before their first FET. The differences in implan-
tation and clinical pregnancy rates between the two groups were also not sta-
tistically significant. Our findings warrant an adequately powered
randomized controlled trial to determine the efficacy of ERA prior to the
transfer of a euploid blastocyst.

O-173 Tuesday, October 15, 2019 11:45 AM

SAFETY OF OIL-BASED CONTRAST MEDIUM FOR
HYSTEROSALPINGOGRAPHY: A SYSTEMATIC
REVIEW. Inez Roest, BSc; a Nienke van Welie, M.D., b
Velja Mijatovic, M.D., PhD, b Kim Dreyer, M.D., PhD, b
Caroline A. M. Koks, M.D., PhD, a Ben W. Mol, M.D., Ph.D. Prof. a
Department of Reproductive Medicine, Maxima Medical Center, Eindhoven/Veld-
hoven, Veldhoven, Netherlands; bDepartment of Reproductive Medicine,
Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam; Netherlands;
Monash University, Monash Medical Centre, Department of Obstetrics and
Gynaecology, Melbourne, VIC, Australia.

OBJECTIVE: A hysterosalpingography (HSG) with oil-based contrast in-
creases pregnancy rates in women with subfertility. However, there have been
some concerns regarding complications, most importantly the risk of in-
trauterine and extrauterine complications, pelvis infections, and thyroid
dysfunction. Here, we present a clear overview on the frequency of
the reported complications.

DESIGN: A systematic review and meta-analysis.

MATERIALS AND METHODS: We searched electronic databases up to
March 2018 as well as textbooks (published before 1960) and reference lists
to identify eligible studies. There were no language or publication date restric-
tions. We performed a systematic review and meta-analysis of relevant RCTs,
cohort studies and case reports/series. We looked at women and their offspring.

RESULTS: We included 120 studies, published between 1928 and 2017, of
which 76 case reports/series. The 44 cohort studies reported on 20,438
HSG's. Intravasation occurred in 1.9% (389/20,438), no treatment was
needed in the majority of cases. Embolisation occurred in 0.1% (24/ 20,438),
all of which were due to intrauterine or extrauterine complications; five
caused by peritonitis (last report in 1950) and one caused by an oil-embolism
(1955), which occurred in a 45-year old woman who received an HSG for
another indication than subfertility. Among the cohort studies published
since 1970, 22 studies reported on 7027 HSG's, intravasation occurred in 1.5% (102/7027) and embolisation in 0.2% (13/7027), without fatal
complications.

In the 76 case reports/series, published since 1928, reported on a total of 204
intravasations and 27 embolisations, with locations in the lungs, cerebrum
and retina. There have been seven deaths described in the case reports/series;
one caused by anaphylactic shock and one caused by an oil-embolism in a
woman of 60 years who received an HSG for a different indication than sub-
fertility. The other five deaths were caused by infection after the HSG and/or
a subsequent laparotomy. The latest fatal infection occurred in 1950.

CONCLUSIONS: HSG with oil-based contrast for tubal testing is a safe
procedure, when performed in a modern setting with antibiotic prophylaxis
when indicated.

SUPPORT: Guerbet, France.

O-174 Tuesday, October 15, 2019 12:00 PM

NATIONAL TRENDS IN EMBRYO TRANSFER
TRAINING. Dana B. McQueen, M.D., M.A.S.
Jared C. Robins, MD, Eve C. Feinberg, M.D. Northwestern
University, Chicago, IL.

OBJECTIVE: To evaluate national trends in embryo transfer training for
Reproductive Endocrinology and Infertility Fellows.

DESIGN: Cross Sectional study.

MATERIALS AND METHODS: Institutional Review Board approval
was obtained. Reproductive Endocrinology and Infertility (REI) Fellowship
program directors and fellows were surveyed to assess their experience with
live embryo transfers performed by fellows and potential barriers to fellow-
ship training in live embryo transfer.

RESULTS: Anonymous surveys were sent to 51 REI fellowship program
directors and 142 fellows. Responders included 25 program directors and 47
fellows (10 first-year, 14 second-year and 23 third-year fellows). 35% prac-
ticed in the Midwest, 35% in the North East/Mid Atlantic, 18% in the South
West/South East and 18% in the West/Northwest. Among all 72 responders,
19% (14/72) reported that no live embryo transfers were performed by fel-
lovers in their program, 16% (4/25) of program directors and 21% (10/47) of
fellows. 70% (7/10) of first year fellows, 43% (6/14) of second year fellows
and 44% (10/23) of third year fellows had performed < 10 live embryo trans-
fers at the time of survey. The median number of live embryo transfers per-
formed during fellowship was 20 (range 0-370, mean 65.1, SD 95). On a
scale of 1-10, the program directors’ reported level of comfort with fellows
performing live embryo transfer was 8.1 in the Midwest, 8.5 in the North
East/Mid Atlantic, 6.9 in the South West/South East and 5.9 in the West/
Northwest. Barriers to live embryo transfers performed by fellows included:
attentive live physician acceptance (50%, 36/72), perceived patient acceptance
(44%, 32/72), physician-patient relationship (42%, 30/72), history of difficult
transfer (25% 18/72), perceived fellow skill (21%, 15/72), concerns
regarding competition with private practice (18%, 13/72), and lack of simu-
lator training (8%, 6/72). There was no agreement regarding the number of
live embryo transfers that should be performed prior to graduation from
fellowship, with program directors reporting a range of 0 to 100 (median
25, mode 25) and fellows reporting a range of 0 to 250 (median 30, mode 50).

CONCLUSIONS: There are significant differences between fellowship
programs regarding the availability of live embryo transfer training, with
nearly half of third year fellows reporting < 10 live embryo transfers. Data
suggests that embryo transfers performed by fellows have similar live birth
rates to embryo transfers performed by attending physicians. However, per-
ceptions among fellowship program directors regarding physician and pa-
tient acceptance likely influence experience during fellowship training.
Efforts should be made to address these barriers and set minimum standards
for number of transfers performed during fellowship.

REPRODUCTIVE BIOLOGY: ANIMAL AND EXPERIMENTAL
STUDIES

O-175 Tuesday, October 15, 2019 10:45 AM

HIGH-FAT DIET CAUSES DYSREGULATION OF
OVARIAN ENDOTHELIN-2 EXPRESSION ACROSS
THE ESTROUS CYCLE. Natalie M. Hohos, PhD,
Emily M. Elliott, BS, Malgorzata E. Szakm-Wikiel, MD Uni-
VERSITY OF COLORADO - ANSCHUTZ MEDICAL CAMPUS, Aurora, CO.

OBJECTIVE: We have previously shown that high-fat diet (HFD) feeding
in female mice leads to abnormal estrous cyclicity, subfertility, and aberrant
ovarian expression of genes important in ovulatory function, regardless of
obese phenotypel,2. We found that a gene critical to normal ovulation, endo-
theclin-2 (Edn2), is significantly downregulated in animals exposed to HFD.
Edn2’s ovarian expression increases sharply right before ovulation. However,
it is unknown how Edn2’s ovarian expression increases. Here, we present a
clear overview on the frequency of

Edn2's ovarian expression increases sharply right before ovulation. However,

how that expression is impacted by HFD. We aimed to evaluate ovarian

Edn2’s expression across the estrous cycle and

fertility. Here, we present a clear overview on the frequency of

INHERITED ETILOGIES OF FERTILITY
DIFFICULTIES.
expression throughout the estrous cycle in HFD exposed mice and compare it with chow fed controls.

DESIGN: Prospective laboratory animal study.

MATERIALS AND METHODS: 5-week-old C57Bl/6f mice were fed a standard chow or 60% HFD for 10 weeks. Estrous cyclicity was evaluated daily for the last two weeks of feeding and ovaries were collected in each of the four estrous cycle stages (N = 9/group/stage). T-test and chi-square tests were used for statistical analysis, as appropriate.

RESULTS: After 10 weeks of diet, HFD mice weighed more than chow controls (28.8 ± 0.7g, 21.1 ± 0.2 g < 0.0001). HFD mice also had a higher prevalence of abnormal estrous cycles compared to chow controls (58.3% and 21.6% p = 0.0018). In chow controls, Edn2 was expressed as expected with basal levels during diestrus and proestrus, increased 11.6-fold during estrus, and decreased back to basal levels during metestrus. In the HFD mice, Edn2 was dysregulated across the entire estrus cycle (table 1), and when Edn2 expression was examined across all cycle stages in HFD mice, there was no characteristic peak of Edn2 expression in estrus with the lowest levels of Edn2 observed. Endothelin converting enzyme (Ece, cleaves Edn2 pre-peptide to active form) transcript expression levels were found to be uniformly upregulated in the HFD exposed mice across all stages of the estrous cycle (table 1).

CONCLUSIONS: Our data suggest that Edn2 and its post-translational regulation is dysregulated across the estrous cycle in HFD-fed mice. Work is currently underway to examine ovarian protein Edn2 levels across the estrous cycle to confirm our gene expression data. Future research should investigate mechanisms behind dysregulated Edn2 expression with HFD feeding. Collectively, this work will allow us to better understand how HFD leads to ovulatory dysfunction and to develop strategies targeting HFD-induced ovulation defects.


SUPPORT: Colorado NORC Pilot Grant (P30DK048520) to MES-W.

O-176 Tuesday, October 15, 2019 11:00 AM

REGULATION OF EMBRYONIC DEVELOPMENT BY PLATELET-ACTIVATING FACTOR IS MOST LIKELY VIA THE INTRINSIC APOPTOSIS PATHWAY. Tracy Oyugi, BS, a Lindsay Michele Grasso, BS, MS, a Charlotte Leblang, BA, MS, a Lauren Tyler, BS, a Arnav Lal, na Jonathan L. Blalock, BS, b Shawn Zimmerman, PhD, HCLD, c Renee J. Chosed, PhD, c William E. Roudebush, PhD d University of South Carolina School of Medicine Greenville, Greenville, SC, b Vios Fertility Institute, Swansea, IL.

OBJECTIVE: Platelet-activating factor (PAF) is a potent signaling phospholipid produced by preimplantation embryos and is required for development and implantation. The mechanistic process(es) by which PAF regulates embryo development has not been fully elucidated. In other physiological systems, PAF modulates apoptotic activity, both by inhibition and activation. Apoptosis is initiated via two different cellular pathways: extrinsic and intrinsic. Each pathway leads to programmed cell death but is initiated by different signals (e.g. aneuploidy; DNA damage) and utilizes caspase-8 and caspase-3 activities in different steps. The sea urchin is a time-honored model for investigational studies in developmental biology and is beneficial for understanding similar events for human embryos. Therefore, this study utilized the sea urchin to investigate the effect of PAF on early embryo development including apoptosis activity.

DESIGN: Prospective, randomized controlled experimental laboratory animal study utilizing the sea urchin (Lytechinus varieatus) model.

MATERIALS AND METHODS: Two-cell stage sea urchin embryos were cultured (20 embryos/replicate; 6 replicates per treatment group) in synthetic sea water (50mL) and in the presence or absence (control) of 10^-7M PAF, and 10^-3M lyso-PAF (biologically inactive form of PAF). Following a 24-hour culture period at 22°C, embryo development was recorded, and apoptotic activity was assessed by monitoring cleavage of 30mM DEVD-AMC and 50mM IETD-AMC peptide substrates of caspase-3 and caspase-8 respectively. Cleavage of the peptide substrates by sea urchin embryonic extracts were determined by detecting absolute fluorescence (absolute fluorescence units; AFU) over time (once/minute; 30 minutes).

RESULTS: The PAF group (57.2%) had significantly (P<0.01) more gastrula stage embryos than the control (11.1%) or lyso-PAF (5.0%) groups. There was a significant difference (P<0.05) in caspase-3 enzyme activity between sea urchin embryos cultured in PAF (17.872 AFU/minute) versus controls (8.764 AFU/minute) and versus lyso-PAF (31.787 AFU/minute). Therefore, PAF treated sea urchin embryos extracts cleaved the caspase-3 specific peptide substrate differently than either control or lyso-PAF treated sea urchin embryos. No significant differences were found between PAF (32.909 AFU/minute), lyso-PAF (32.622 AFU/minute) or control (24.236 AFU/minute) groups regarding caspase-8 enzyme activity. Therefore, exposure of sea urchin embryos to PAF did not yield any effect on caspase-8 activity towards the peptide substrate.

CONCLUSIONS: Exogenous PAF induced advanced stages of development in sea urchin embryos. Sea urchin embryos exposed to PAF affected caspase-3 but not caspase-8 protease activities suggesting a greater involvement of the intrinsic pathway for initiating apoptosis. Thus, PAF’s impact on enhanced embryo development may result from intracellular cues to modulate apoptotic activities via the intrinsic pathway. Additional studies will further elucidate the mechanism by which PAF regulates apoptosis during early embryonic development.

O-177 Tuesday, October 15, 2019 11:15 AM

OCYOTE SPECIFIC TRANSCRIPTION REGULATORS, NOBOX AND FIGLA, ARE IDENTIFIED AS KEY CONTRIBUTORS TO THE DECLINE IN FECUNDITY ASSOCIATED WITH OVARIAN AGING. Jennifer E. Russ, BS, Jason C. Parks, BS, Blair Robertson, BS, Mary E. Haywood, PhD, William B. Schoolcraft, MD, Mandy G. Katz-Jaffe, Ph.D., Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Advanced maternal age (AMA; ≥35 years) is associated with a decline in fecundity that is largely attributed to loss of oocyte number and quality. The aim of this study is to explore at a molecular level the relationship between aging, ovarian environment and oocyte quality.

DESIGN: Longitudinal research study.

MATERIALS AND METHODS: Young outbred CD1 female mice (3-4 months old; Young) and naturally aged outbred CD1 female mice (10-12 months old; Aged) were super-ovulated and oocytes collected (n = 10 group) for quantitative immunofluorescence of endoplasmic reticulum (ER) stress indicators, pIRE1 and ATP6. Total RNA was isolated from un-stimulated ovaries (n = 6 per group), sequence libraries were prepared using the TrueSeq Total RNA library kit (Illumina) and sequenced on the Illumina NovaSEQ 6000. Differentially expressed genes (DEGs) were generated using edgeR with an FDR cutoff of 5% (q value <0.01) and Student’s t-test significance at p<0.001, followed by Ingenuity Pathway Analysis (Qiagen).

RESULTS: Oocyte numbers significantly declined with natural aging (Young: Aged = 4.6, Young = 12.9; p<0.0001). Total RNA sequencing revealed 281 significant DEGs in Aged versus Young ovaries (120 increased and 161 decreased; p<0.0001). Unsupervised hierarchical clustering of the 281 DEGs cleanly separated the ovaries according to female age. Enriched pathway analysis revealed signaling pathways including Citrulline-Nitric Oxide Cycle, VEGF Family Ligand Receptor Interactions, and HIF1alpha signaling. Nitric oxide is a common signaling molecule in these pathways, and has been shown to maintain diplotene arrest in pre-ovulatory oocytes. Aged ovaries displayed a significant decrease in nitric oxide gene expression.

10705
O-178 Tuesday, October 15, 2019 11:30 AM
SAFE AND EFFICIENT DETECTION OF EGG MATURITY WITHOUT CUMULUS CELL REMOVAL BY NON-INVASIVE TOMOGRAPHY. Rebecca L. Krisher, PhD, a Deirdre M. Logsdon, MS, a Benjamin B. Goheen, BS, a O-178

OBJECTIVE: Currently, eggs must be denuded to assess maturity. However, maintenance of the cumulus cell investment is critical to support oocyte quality during maturation. A novel tomography device using near-infra-red light has been developed to detect the first polar body without removing cumulus cells. Our objective was to determine the effect of tomographic imaging for polar body detection on mouse oocyte developmental competence and subsequent embryo quality.

DESIGN: Prospective research study. The experimental design consisted of three treatment groups: control eggs (C), standard IVF/IVC protocol; n=135), imaged eggs (I; n=45), and eggs that were treated identically to I but not exposed to tomography (NI; n=63). Two replicates were performed.

MATERIALS AND METHODS: In vivo matured mouse (outbred CF1, n=8 females) eggs were collected following ovarian stimulation. A subset of oocytes was randomly selected and immediately placed into fertilization medium containing sperm (C). The remaining eggs were placed into two imaging dishes, consisting of 50 µL drops of MOPS buffered medium under oil. Both dishes were moved to a heated stage on the imaging system. Eggs in one dish were imaged (I; 8-10 eggs/microdrops); oocytes in the second dish (NI) served as an environmental control. Presence or absence of the polar body was recorded for each egg. After imaging, both I and NI groups were placed into sequential culture medium.

RESULTS: It required 93 seconds on average to image each oocyte and determine if it contained a polar body (range, 40-150 sec/oocyte). Tomography evaluation revealed that 78% of the eggs were mature. After IVF, C had fewer (p<0.01) 2PN zygotes than either I or NI (60%, 87%, 76%, respectively). The percentage of mature eggs (78%) was slightly underestimated compared to the percentage of successfully fertilized zygotes (87%). There were no differences in blastocyst development or hatching between treatments (C, 64% and 5%; I, 67% and 0%; NI, 75% and 67%, respectively). There were no differences in ICM or total cell number between treatments. Although NI tended (p=0.08) to have fewer TE cells than C (NI, 83±6.5; C, 100.8±6.1), the percentage of ICM cells was increased (p<0.05) in I (12.3±1.1%) compared to C (8.9±0.7%). The expression of 89 genes related to blastocyst viability (BMP15, DNM3TA, FOXO3A, GLUT1, GRP78, NANOG, PASG, PLAC8) did not differ between treatments, although expression of ATF4 was decreased (p<0.05) in I and NI compared to C. CONCLUSIONS: Assessment of cumulus enclosed mouse eggs to determine maturity using near-infra-red tomography does not have any negative effects on fertilization, blastocyst development or embryo quality. This data suggests that tomography could be used to safely make clinical decisions about the most appropriate fate of each retrieved egg prior to cumulus removal, thereby improving quality of the oocyte cohort.

O-179 Tuesday, October 15, 2019 11:45 AM
THE PLASMINOGEN ACTIVATOR SYSTEM IN THE PRIMATE ENDOMETRIUM DURING THE OVARIAN CYCLE AND MENSTRUATION. Reem Sabouni, MD, a Esra Demirel, MD, a, b David F. Archer, MD. c aEVMS/ Jones Institute for Reproductive Medicine, Norfolk, VA; bNorth Shore University Hospital & Long Island Jewish Medical Center, Manhasset, NY; cEastern Virginia Medical School, Norfolk, VA.

OBJECTIVE: The endometrium undergoes dynamic morphologic changes reflecting hormonal fluctuations. The plasminogen activator system (PAS) is an enzymatic cascade involved in hemostasis and matrix turnover that is activated by tissue plasminogen activator (tPA) and inhibited by plasminogen activator inhibitors-1 (PAI-1). Evidence supports PAS’s role in remodeling the endometrium in human endometrial cancers, yet little is known on the dynamic alterations of these enzymes within a controlled ovarian cycle. This study seeks to characterize the expression of PAI-1 and tPA in the primate endometrium during an artificial cycle.

DESIGN: Animal in vivo experiment.

MATERIALS AND METHODS: Endometrial biopsy samples were obtained from 4 adult cycling female rhesus macaques monkeys during an artificial cycle controlled with estrogen and progesterin implants at 3 separate time points: menstrual, proliferative and secretory. The tissue sections were stained via immunohistochemistry (IHC) with specific PAI-1 and tPA antibodies using immunofluorescence and IHC were captured with standardized settings with 4 representative images of stroma, gland and vasculature from each tissue. Four separate areas of stroma, gland or vasculature were analyzed from different parts of each slide. Values were expressed as integrated optical density and analyzed using Image-J software. Statistics were performed on means ± standard deviation of n=4/group and subjected to ANOVA with Tukey’s multiple comparison test at p<0.05.

RESULTS: Stromal PAI-1 was highest in the secretory phase (184.7±9.1), then proliferative (151±5.6) and menstrual phase (88.4±18.6) with a statistically significant difference between secretory phase compared to the proliferative and menstrual phases (p<0.0001). Glandular PAI-1 was highest in the secretory phase (99.6±36.9), followed by proliferative (48±9.8) and menstrual phase (44.1±3.1). Vascular PAI-1 was highest in the secretory phase (127.7±23), followed by proliferative (89±16.3) and menstrual phase (61.9±4.7). Statistically significant differences were seen between secretory compared to proliferative and menstrual phases for the gland (p<0.1) and vasculature (p<0.001). Stromal tPA was highest in the secretory phase (181±17.6), then proliferative (169.6±10.7) and menstrual phase (145±33). Glandular tPA was highest in the secretory phase (123±20.7), then menstrual (113±29) and proliferative phases (71±15). Vascular tPA was highest in the secretory phase (119.9±26.6), followed by menstrual (109±29) and proliferative phase (94.5±6.6). The differences between the menstrual phases for tPA were not statistically significant.

CONCLUSIONS: PAI-1 was noted to be significantly expressed in the secretory phase in the stroma, gland and vasculature supporting its possible role in the endometrial decidualization. High PAI-1 levels in the secretory stroma may reflect protease activity with the onset of menses. Comparing expression of PAI-1 and tPA demonstrates that PAI-1 appears to have a more dynamic expression within the monkey endometrium suggesting a larger role in endometrial remodeling.

O-180 Tuesday, October 15, 2019 12:00 PM
THE ROLE OF GLYPHOSATE IN INFERTILITY: THE MECHANISTIC LINK. Charalampos Chatzicharalampous, MD, PhD, Zeina A. Yahoufi, BS, David Bai, BS, Awoyinfolu Awojumike, MD, Husam Abu-Soud, PhD Wayne State University, Detroit, MI.

OBJECTIVE: In light of the recent Roundup lawsuit, glyphosate has been widely accepted as a significant environmental toxin that may affect humans in various ways including cancer and infertility. Exposure to even low doses of glyphosate-based herbicides during pregnancy has been found to impair fertility, cause intrauterine growth restriction and induce fetal malformations. In this study...
we sought to determine the underlying mechanism by which glyphosate negatively impacts oocyte quality, fertilization rates as well as embryo development.

**DESIGN:** Experimental case-control study of mouse oocytes and pronuclear embryos, exposed in vitro to increasing glyphosate concentrations and followed through day 5 of development. We utilized multiple assays including reactive oxygen species (ROS) generation and zinc depletion to examine the possible underlying detrimental mechanisms.

**MATERIALS AND METHODS:** Metaphase II mouse oocytes (n=200) were retrieved from 8-10 week female mice and a subset (n=100) were fertilized using IVF. The oocytes as well as the fertilized mouse embryos were then exposed to increasing concentrations of glyphosate (0-200 μM) for 2h - 4h as per protocol. The oocytes were divided into four groups that were treated as follows: Group A: ROS detection assay, Group B: Zinquin ethyl ester assay, Group C: fixed, stained and scored based on the spindle structure (microtubule morphology - MT and chromosomal alignment - CH) as indicators of the oocyte’s capacity to sustain exposure. All groups were compared to Group 4: untreated controls.

Exposed embryos were incubated for up to 120 hours post fertilization and evaluated for full and hatching blast rate conversion. They were photographed and graded daily based on their appearance and development using published embryo grading protocols. A subset of the treated embryos (n=10 for each concentration) were treated, in a similar fashion as the oocytes, in order to evaluate for ROS overproduction and zinc depletion. Confocal microscopy was used to assess the embryos. Statistical analysis was performed using t-test, ANOVA and chi-square. A p-value <0.05 was considered statistically significant.

**RESULTS:** Oocytes treated with increasing glyphosate concentrations >50 μM were found to have poor scores for MT and CH and that difference was statistically significant as compared to controls (p<0.05). Embryos followed to 96 hours post fertilization (early blastocyst) and 120 hours (full and hatching blastocyst) after glyphosate exposure (0-200 μM) were assessed and those exposed to glyphosate concentrations >100 μM showed significantly increased arrest rates and poor morphology scores compared to controls. ROS overproduction as well as zinc depletion was evident in embryos treated with high glyphosate concentrations. These observations were statistically significant compared to untreated controls (p<0.05).

**CONCLUSIONS:** This work suggests the possible underlying mechanisms by which glyphosate negatively affects reproductive health in the mouse model. Possible fertility implications in humans will require further research.

**SUPPORT:** None.

**ART LAB: TECHNOLOGY**

O-181 Wednesday, October 16, 2019 10:45 AM

**SHORTER TELOMERE LENGTH OF WHITE BLOOD CELLS IS ASSOCIATED WITH HIGHER RATES OF ANEUPLOIDY IN WOMEN UNDERGOING IN VITRO FERTILIZATION.** Brent M. Hanson, MD, 1 Xin Tao, Ph.D, 2 Yiping Zhan, Ph.D, 2 Julia G. Kim, MD, MPH, 2 Emily K. Osman, MD, 2 Ashley W. Tieg, MD, 2 Shelby A. Neal, MD, 2 Richard Thomas Scott, Jr., MD, 3 Emre Seli, M.D. 4

**OBJECTIVE:** Telomeres are tandem repeats of the sequence TTAGGG located at the ends of chromosomes. Telomere shortening is a key mechanism of cell senescence and aging. Telomere shortening has been associated with decreased oocyte quality through disruption of chromosome alignment and spindle structure. In this study, we sought to evaluate whether the telomere length of cumulus cells (CC) or white blood cells (WBC) in an infertile population shows reproductive aging.

**DESIGN:** Prospective cohort study.

**MATERIALS AND METHODS:** Women undergoing IVF between July 2017 and December 2018 were recruited for the study under Institutional Review Board approval. Blood and CC were collected at the time of oocyte retrieval. Genomic DNA was isolated and stored at -80°C. Telomere DNA length was measured by quantitative real-time PCR and normalized to AluYa5 sequence as an endogenous control for each sample. Linear regression was applied to determine if telomere length (TL) of WBC or CC was associated with patient age, number of oocytes retrieved, number of mature (M2) oocytes retrieved, blastulation rate, aneuploidy rate, serum anti-mullerian hormone (AMH), and serum estrogen (E2) level on day of hCG or GnRH administration.

**RESULTS:** TL data was available for WBC samples from 156 individuals and for CC samples from 142 patients. Data was available for both tissue types from 13 patients (age range 25.7 to 45.0 years, mean 35.0 ± 4.0 years).

As expected, WBC telomere length declined with increasing age (p=0.006). In contrast, CC TL was equivalent in patients of all ages and failed to show anticipated age-related shortening. As such, CC TL was unrelated to any index of ovarian performance including number of oocytes retrieved (p=0.95), M2 oocytes retrieved (p=0.81), blastulation rate (p=0.98), aneuploidy rate (p=0.30), AMH level (p=0.32), or mid-cycle E2 level (p=0.77). Consistent with these data, CC TL was not associated with patient age (p=0.99). While WBC TL declined with increasing maternal age, it was a poor predictor of quantitative ovarian performance [total oocytes retrieved (p=0.47), number of M2 oocytes retrieved (p=0.30), AMH level (p=0.13), E2 level (p=0.36), and blastulation rate (p=0.48)]. However, TL of WBC samples was associated with embryonic competence as evidenced by aneuploidy rate (p=0.02), with shorter TL associated with higher aneuploidy.

**CONCLUSIONS:** The TL of CC was not associated with patient age or any index of ovarian or embryonic performance. Declining WBC TL was associated with increasing maternal age and increasing rates of embryonic aneuploidy. Further studies are necessary to determine if changes in peripheral somatic cell TL are truly prognostic for aneuploidy rate within a given maternal age group or if this finding is simply reflective of a simultaneous change which occurs with age.

**Reference:** None.

**SUPPORT:** None.

---

O-182 Wednesday, October 16, 2019 11:00 AM

**NON-INVASIVE OOCYTE SELECTION INCREASES CLINICAL PREGNANCY RATE: A PROSPECTIVE STUDY OF 108 PATIENTS.** Inge Van Vaerenbergh, PhD, 1 Tom Adriaenssens, MSc, 2 Nazli Akin, MSc, 3 Wim Coucke, PhD, 4 Ileena Mateizel, PhD, 4 Greta Verheyen, PhD, 4 Eilen Van Hecke, Msc, 4 André Rosenthal, Prof, 4 Johan Smits, MD, PhD, Prof, 4 "Folicile Biology Laboratory, Vrije Universiteit Brussel, Brussels, Belgium; 4Quality of Laboratories, ScienSano, Brussels, Belgium; 4Centre for Reproductive Medicine, UZ Brussel, Brussels, Belgium; 4Fertiga, Lede, Belgium.

**OBJECTIVE:** To compare clinical pregnancy outcome by non-invasive cumulus testing using gene expression in combination with embryo morphology versus morphology alone in eSET patients.

**MATERIALS AND METHODS:** Planned fresh transfers of day-3 ICSI eSET. Patients were stimulated with GnRH antagonist and HP-HMG. Oocytes underwent single denudation after pick-up. The cumulus cells were analysed with QRT-PCR for three predictive genes CAMK1D, EFNB2 and SASH1 (Corona Test) and two control genes. The analysis resulted in a single score for each oocyte. The score was used to select and transfer a single day 3 embryo with excellent or good morphology. The control group was matched (blinded for outcome) under the same conditions as the intervention group (same age, same number of embryos, same stimulation protocol).

The primary outcome was clinical pregnancy (fetal heartbeat confirmed by endovaginal ultrasound at 7 weeks), with stratification for age and number of excellent/good quality embryos (QGE). Secondary outcome included cumulative pregnancies from frozen embryo transfers. Outcomes were compared among treatment arms using one-tailed chi-square test.

**RESULTS:** A total of 108 patients underwent the Corona Test and were matched with 108 control patients nearest in time to the treated cases. There was an 80% increase in clinical pregnancy rates on day 3 eSET (61% Corona Test group vs 34% control group). The cumulative pregnancy rate in the Corona Test group was 79% and 50% in the control group. In our center, outcome for the same patient population with day-5 blastocyst transfer is 50% with eSET and 71% cumulatively.

**CONCLUSIONS:** Using Corona Test as a non-invasive test to select a day 3 embryo could almost double the clinical pregnancy rates on day 3 and shows an increase compared to the day 5 blastocyst transfer. These data indicate that morphology selection supported by non-invasive cumulus testing can drastically increase pregnancy rates.

---
OBJECTIVE: Cytoplasmic maturation, fertilization, embryogenesis and placentaion all rely on sufficient energy production and therefore mitochondrial biogenesis. Reactive oxygen species which are potentially harmful to the developing embryo are a side-product of the mitochondrial oxidative phosphorylation integral to energy production. This study’s objective was the assessment of predictive value of mitochondrial DNA (mtDNA) copy number in the context of reproductive potential in the human blastocyst.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: mtDNA content in 700 euploid human embryos following single embryo transfer were used to assess this question, determining if the implantation outcome is associated with mtDNA copy number. Additionally, 78 euploid paired sibling cycles (two consecutive transfer cycles performed on the same patient, using euploid embryos from the same cohort, where the first cycle failed to result in implantation and the second cycle resulted in sustained implantation) were included to assess whether or not within a given cohort the mtDNA content was predictive. Relative mtDNA copy number was determined using targeted amplification followed by quantitative real-time PCR (qPCR) for 2 mitochondrial loci (16S and MajArc) relative to a multicopy nuclear genome locus (AluYb8). A logistic regression model was used to determine whether mtDNA content was associated with the odds of achieving pregnancy. Covariates were maternal age and day of biopsy. A ROC curve was created to determine if there were threshold values above which there was a meaningful change in clinical outcomes. Finally, a paired analysis was done to determine if the pregnancies which occurred in the second transfer cycle after a failed first euploid transfer were more likely to have lower mitochondrial concentrations.

RESULTS: The range of maternal age was 21.8-45.3, and the sustained implantation rate at 9th gestational week was 65.3%. mtDNA copy number was not associated with sustained implantation rates (p=0.74), and there was no threshold value above or below which ongoing implantation was more or less likely. There was also no correlation between mtDNA copy number and maternal age (p=0.45). In addition, in women who underwent a second single embryo transfer following a failed transfer (n=39), there was no association between relative mtDNA levels of sibling embryos in the 2nd transfer relative to the 1st transfer and ensuing implantation and delivery rates (p=0.67).

CONCLUSIONS: Neither the 700 euploid single embryo transfers nor the set of 78 paired transfers suggest that mtDNA copy number analysis is a predictive biomarker of euploid human embryo reproductive competence. In addition, no relationship between blastocyst mtDNA copy number and female age was identified. These data do not support the clinical utilization of mtDNA copy number in clinical decision making when selecting which embryo to transfer.

Support: This study was funded by IWT/VLAIO and Vrije Universiteit Brussel IOFPOC26.

O-183 Wednesday, October 16, 2019 11:15 AM

mtDNA CONTENT IS NOT ASSOCIATED WITH EMBRYONIC REPRODUCTIVE COMPETENCE. Richard Scott, III, B.S. a Li Sun, Ph.D.aby Yiping Zhan, Ph.D. b Diego Marin, M.S. b,a Xin Tao, Ph.D.b Enure Seli, M.D. a,b Yale School of Medicine, New Haven, CT; bThe Foundation for Embryonic Competence, Basking Ridge, NJ; cFoundation for Embryonic Competence, Basking Ridge, NJ; dIVI-RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: To apply Artificial Intelligence (AI) technology on time-lapse (TLM) embryo images and morphokinetic parameters to predict live birth.

DESIGN: The morphokinetic parameters (n=131, ICIS only), with known live birth data from single blastocyst transfers, and 131 TLM images of embryos at 111.5 hours post ICSI were used to train (70%), validate (15%), and blindly test (15%) for prediction of live birth by an AI feature-extraction system. Inclusion criteria involved recipients from our oocyte donation program with single blastocyst transfer and non-PGT.

MATERIALS AND METHODS: Absolute and interim cleavage time points (t2 to t8) were used, along with 33 independent numerical variables extracted from standardized TLM images as an input data. The artificial neural network (ANN) architecture associated with the genetic algorithm was used to produce a predictable output of live birth. The efficacy of prediction of live birth was quantified and assessed using ROC curves, AUC and confusion matrices (True Positive - TP, True Negative - TN, False Positive - FP, and False Negative - FN).

RESULTS: Overall accuracy of prediction of live birth by AI using morphokinetic data was 96.2% (126/131; TP= 37, TN= 69, FP= 1, FN= 4, AUC= 0.946). In the training dataset, the accuracy was 95.5% (86/91, AUC= 0.96), and in the blind test dataset, accuracy was 100% (20/20, AUC= 0.961). The overall accuracy of live birth by AI using image analysis was 90.1% (100/111, TP= 39, TN= 61, FP= 7, FN= 4, AUC= 0.91). In the training dataset, the accuracy was 89% (81/91, AUC 0.887), and in the blind test dataset, accuracy was 95% (19/20, AUC=0.67-0.94). The combination of morphology and morphokinetics, the AUC for positive were similar (0.96) but for negative live birth were less predictive (0.65).

CONCLUSIONS: This is the first time that AI is used to evaluate human embryo quality using morphokinetic and morphological assessment in a data set of single embryo transfers from an oocyte donation program with known live birth. Our data suggests that AI can be used to enhance the efficacy of embryo selection performed by the standard morphology or the existing algorithms of morphokinetics. Applying AI in conjunction with morphokinetic or image analysis has the potential for being the platform of embryo selection, with similar predictive abilities when treated independently although its combination may not improve the performance of AI.

Support: Agencia Valenciana de Innovación, Generalitat Valenciana.

O-185 Wednesday, October 16, 2019 11:45 AM

A DEEP LEARNING FRAMEWORK OUTPERFORMS EMBRYOLOGISTS IN SELECTING DAY 5 EUPLOID BLASTOCYSTS WITH THE HIGHEST IMPLANTATION POTENTIAL. Eduardo Hariton, MD, MBA,a Irene Dimitriadis, MD,a Manoj Kumar Kanakasabapathy, MS,b Prudhi Thirumalaraaju, BS,b Raghav Gupta, BTech,b Rohan Poonivala, B Tech,b Irene Souther, MD,a Sarah T. Rice, MS,b Pragati Bhowmick, MD,a Leslie B. Ramirez, PhD,a Carol Lynn Curchoe, PhD, TS (ABB),a Jason E. Swain, PhD,a Lynn M. Boechnlein, BS,b Charles L. Bormann, PhD,a Hadi Shafiee, PhD.b aMassachusetts General Hospital, Harvard Medical School, Boston, MA; bBrigham and Women’s Hospital, Harvard Medical School, Boston, MA; cExtend Fertility, New York, NY; dSan Diego Fertility Center, San Diego, CA; eCCRM Fertility Network, Lone Tree, CO; fDivision of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of Wisconsin, Madison, WI.

OBJECTIVE: To evaluate the performance of an artificial intelligence-based approach, using a deep convolutional neural network (CNN) combined with a genetic algorithm (GA), in selecting top quality day 5 euploid blastocysts compared to those selected by highly trained embryologists.

DESIGN: Historical Prospective Double-Blinded Multi-Center Cohort Study.

Overall clinical pregnancy (n=108) (%) 61 34 <0.0001
Overall cum. clinical pregnancy (n=108) (%) 79 50 <0.0001
Clin. preg. Age <35 (n=66) (%) 62 35 0.0014
Clin. preg. Age [35-38] (n=43) (%) 60 33 0.0047

Support: This study was funded by IWT/VLAIO and Vrije Universiteit Brussel IOFPOC26.
MATERIALS AND METHODS: Using a dataset of 3,469 embryos, the deep CNN model was trained and tested to primarily classify images of embryos captured at 113 hours post insemination (hpi). A non-overlapping set of 97 euploid embryo images with known implantation outcomes was then used to compare CNNs against existing embryology experts. We included a total of 15 highly trained embryologists from multiple centers in the US to that of the CNN. Only euploid embryos that had undergone preimplantation genetic testing for aneuploidy (PGT-A) were included to remove the bias introduced by chromosomal abnormalities.

RESULTS: The CNN performed with an accuracy of 75.3% while the embryologists performed with an average accuracy of 67.4% (min-max: 64.5%-70.2%) in differentiating euploid embryos based on their implantation outcome. The CNN performed with a sensitivity and specificity of 84.2% (CI: 72.1% to 92.5%) and 62.5% (CI: 45.8% to 77.3%), respectively. The positive predictive value (PPV) and negative predictive value (NPV) of the network were 76.2% (63.8% to 86.0%) and 73.5% (55.6% to 87.1%), respectively. A one sample t-test revealed that the CNN significantly outperformed embryologists in predicting embryo implantation of euploid embryos using a static image obtained at a single time-point (113 hpi) (P<0.0001).

CONCLUSIONS: The trained artificial intelligence framework outperformed trained embryologists in identifying PGT-A euploid embryos destined to implant. A large randomized controlled trial is warranted to confirm that the developed CNN can improve in-vitro fertilization outcomes by prospectively selecting embryos with higher implantation potential than those selected with the current methods.

SUPPORT: This work was partially supported by the Brigham Precision Medicine Developmental Award (Brigham Precision Medicine Program, Brigham and Women’s Hospital) and R01AI118502, R01AI138800, and R21HD092828 (National Institute of Health).

O-186 Wednesday, October 16, 2019 12:00 PM
THE ASSOCIATION BETWEEN RAPIDLY DIVIDING EMBRYOS AND EMBRYONIC EUPLOIDY DETECTED VIA NEXT GENERATION SEQUENCING (NGS). Jenna Friedenthal, MD, Dmitry Gounko, MA, Joseph A. Lee, BA, Lawrence Grunfeld, MD, Alan B. Copperman, MD. Icahn School of Medicine at Mount Sinai, New York, NY; Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Previous research has suggested that rapid embryo development may be a strong predictor of outcomes [1]. Rapid cell division of the early embryo was thought to be “chaotic,” and cleavage stage embryos with >8 cells thought to have poor developmental potential. However, others have found that early cleavage embryos have higher implantation rates [2]. Studies evaluating the relationship between cleavage development and embryonic aneuploidy [3] are limited by use of older technologies. Thus, our goal was to assess whether rapid cell division of an early embryo is correlated with copy number aneuploidy and embryonic competence.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The study included patients at a single academic center who underwent in vitro fertilization and had at least one embryo that reached cleavage stage from 2016 to 2019. Day 3 embryos were divided into 3 groups: slow (< 6 cells), intermediate (6-8 cells), and fast (≥8 cells). Our primary outcome was euploidy as diagnosed by trophectoderm (TE) biopsy for preimplantation genetic testing for aneuploidy (PGT-A). All tested embryos were evaluated using NGS. Secondary outcomes included number of blastocysts, biopsied blastocysts, ongoing pregnancy/live births (OP/ LB), and clinical losses (CL). Data were analyzed using students ANOVA, chi square tests, and a multivariate logistic regression, with p<0.05 considered significant.

RESULTS: A total of 40,916 Day 3 embryos from 3,565 patients were assessed in this study. In an adjusted analysis, there were significant differences between slow (n=5,651), intermediate (n=23,907), and fast (n=11,358) Day 3 embryos that developed to blastocysts (30.30%; 77.50%; 80.08%, p<0.0001) and that were biopsied (9.68%; 46.89%; 52.22%, p<0.001). Euploidy was similar among groups (47.71%; 49.07%; 50.76%, p=0.07). A sub-analysis of intermediate vs fast embryos showed a higher rate of euploidy in the fast group (p=0.04). After adjusting for confounders, and using the intermediate group as a control, fast Day 3 embryos were significantly associated with increased odds of reaching blastocyst stage (OR 1.13, CI 1.06-1.20, p = 0.0001) and having blastocysts that were eligible for TE biopsy (OR 1.18, CI 1.12-1.24, p <0.0001). After controlling for confounders, we found no association between fast growing Day 3 embryos and odds of euploidy (OR 1.04, CI 0.97-1.11, p = 0.23). There was no association between fast growing Day 3 embryos and odds of OP/LB (OR 0.97, CI 0.82-1.14, p = 0.69) or CL (OR 1.02, CI 0.77-1.35, p = 0.09).

CONCLUSIONS: Rapidly dividing cleavage embryos perform as well as, if not better than, intermediate or slow growing cleavage embryos. Prior studies of rapidly dividing embryos may have witnessed an artifact of maternal dysynchrony and not necessarily implantation failure related to embryonic competence. Our study demonstrated that rapidly dividing embryos have high rates of euploidy and clinical potential. Morphokinetic measurements combined with genomic and non-genomic markers provide the ideal support to optimize embryo selection and improve patient outcomes.


SUPPORT: None.

ENDOMETRIOSIS

O-187 Wednesday, October 16, 2019 10:45 AM
CORRELATION BETWEEN FOLLICULAR LEVELS OF INTERLEUKIN 6 (IL-6) AND ANTI-MULLERIAN HORMONE (AMH) AND ICSI OUTCOME IN WOMEN WITH PROVEN ENDOMETRIOSIS. Jihadia Feriel Kacem Berjeb, Associate Professor, Marouen Braham, Associate professor, Cirine Ben Mila, Associate Professor, Fethi Zhioua, Pr, Affiliation not provided.

OBJECTIVE: Investigating a potential correlation between follicular AMH and IL-6 in women with endometriosis and thus a potential influence of the inflammatory process in endometriosis on ICSI outcome.

DESIGN: A matched case-control study was conducted in the Reproductive Medicine center at Aziza Othmana Hospital in Tunis. The study population included a total of seventy-five patients; twenty-five patients with proven endometriosis and fifty patients diagnosed with other causes of infertility, each undergoing an ICSI cycle between March and August 2018.

MATERIALS AND METHODS: All patients followed a controlled ovarian stimulation protocol for an ICSI cycle. The follicular fluid was collected from 75 patients at the time of oocyte retrieval, and then stored at -80°C until assay. AMH and IL6 concentrations in follicular fluid were determined by electrochemiluminescence immunoassay. Comparisons of data between the two groups were performed with t student test and with chi 2 test. Correlations were assessed with the Pearson correlation test.

RESULTS: Two groups were formed; an endometriosis group and a control group. Both groups were comparable regarding clinical parameters and those of the ovarian stimulation. As for the biological parameters measured in the follicular fluid, IL-6 levels showed a statistically significant increase in the “endometriosis” group compared to the “control” one (162.32 vs 19.93; p=0.02). The follicular AMH levels were comparable between the two groups (2.22 vs 2.71; p=0.41). No correlation was shown between the follicular levels of IL6 and AMH (r = 0.01, p = 0.3). The comparison of ICSI outcomes between the “endometriosis” group and the “control” group showed that the fertilization rate (69.90% vs 62.98%; p=0.05) the Top embryos rate (41.71% vs 37.64%; p<0.05) and the pregnancy / transfer rate (38.09% vs 34%; p=0.05) were comparable between the two groups. The miscarriage rate was higher in women with endometriosis (37.5% vs 18.75%; p<0.05).

CONCLUSIONS: The higher miscarriage rate in women with endometriosis suggests that the endometrial receptivity is the target of the deleterious effect of the inflammatory process. Further investigations are needed to confirm such a theory.

SUPPORT: This study was funded by the research department of Aziza Othmana Hospital in Tunis.
OBJECTIVE: One conundrum in endometriosis arising from a recent study is that, while endometriotic epithelial and stromal cells supposedly co-exist, the two cellular components seem to take independent developmental trajectory. This is due to the finding that, while cancer-associated somatic mutations were found to be enriched in the epithelial component, the stroma does not carry much. Given that endometriotic lesions are fundamentally wounds undergoing repeated tissue injury and repair that ultimately progress to fibrosis, we hypothesized that the stromal component of endometriotic lesions may recruit other cells and turn them into mesenchymal cells. One possible candidate cell is endometrial cell. Essentially, endometrial cells in lesions transdifferentiate into mesenchymal cells, likely induced by transforming growth factor β1 (TGF-β1) released by activated platelets, contributing further to lesional fibrosis. This study was undertaken to test this hypothesis.

DESIGN: Laboratory study using human tissues, in vitro experimentation using an human umbilical vein endothelial cell line HUVEC.

MATERIALS AND METHODS: Immunofluorescent analysis of 30 each ovarian endometrioma (OE) and deep endometriosis (DE) tissue samples, using antibodies against CD31 and fibroblast-specific protein 1 (FSP-1), was performed. Immunohistochemistry analysis of CD31, FSP-1 and α-smooth muscle actin (α-SMA) was also performed. Masson trichrome staining was used to evaluate the extent of lesional fibrosis. In in vitro experiments, we evaluated morphological changes, gene and protein expression levels, migratory and invasive propensity, cellular contractility, and collagen production for HUVEC co-cultured with vehicle, activated platelets or thrombin only. We used A83-01, a TGF-β1 inhibitor, to neutralize TGF-β1.

RESULTS: Endometriotic lesions clearly exhibited signs consistent with EndoMT especially in OE lesions. Activated platelets, through the induction of TGF-β1 signaling pathway, induced EndoMT in HUVECs, resulting in increased migratory and invasive propensity, cellular contractility, and collagen production. Prolonged exposure of HUVECs to activated platelets induced increased expression of α-SMA, desmin and F-actin indicating further transdifferentiation into smooth muscle-like cells. Neutralization of TGF-β1 abolished these changes. OE lesions had significantly higher staining levels of CD31, but lower α-SMA and FSP-1 staining, concomitant with lower lesional fibromuscular content than that of DE lesions. The staining levels of CD31 correlated negatively with the staining levels of α-SMA, as well as the extent of lesional fibrosis.

CONCLUSIONS: EndoMT contributes to fibrogenesis in endometriosis. Because of EndoMT, the endometriotic stroma is constantly replenished by endometrial cells and other cells. These cells generally have much lower mutation rates than that of the endometriotic epithelium. Thus, we provide an explanation for the above mentioned conundrum of apparent independent developmental trajectories taken by endometriotic epithelium and stroma.

O-189 Wednesday, October 16, 2019 11:15 AM

SOMATIC CANCER DRIVER MUTATIONS IN ENDOMETRIOSIS LESIONS CONTRIBUTE TO SECONDARY CANCER RISK. Kenneth Ward, MD; Rakesh Chettier, MD; Hans M. Albertsen, PhD; Terry Morgan, MD, PhD; Todd Williams, MD; Predictive Laboratories Inc, Salt Lake City, UT; Juean Biosciences, LLC, Salt Lake City, UT; Oregon Health Sciences University, Portland, OR.

OBJECTIVE: To determine whether cancer driver mutations contribute to the development and progression of endometriosis and endometriosis associated cancers.

DESIGN: Endometriosis lesions might arise as an autotransplant, as a hematoma, through metaplasia, or as a neoplasm. Some endometriosis lesions are progressive, invasive, and possibly metastatic, and cancers sometimes arise in endometriosis lesions. Recent studies have shown that somatic mutations accumulate during the clonal evolution of individual endometriosis lesions. We conducted whole exome sequencing to investigate the presence of known cancer driver mutations in endometriosis lesions and to correlate these mutations with long term outcomes.

MATERIALS AND METHODS: 276 women (age 12 to 95) operated on at OHSU between 2003 and 2014 with a confirmed histologic diagnosis of endometriosis were consecutively enrolled. Exome sequencing was performed on DNA extracted from formalin-fixed paraffin-embedded tissue samples exhibiting endometriosis histology to varying degrees. Within a 5 to 16 year follow-up interval, 55/276 (20%) of these women had a subsequent diagnosis of cancer at OHSU. Whole exome sequencing (WES) was performed using Ion Proton Instrument with the AmpliSeq Exome Capture Kit. All missense, truncating (stop-gain, stoploss, splicing and frameshifts), and synonymous variants listed in the IntOGen database were considered (20,302 TIER1 cancer driver mutations). Tier 1 cancer driver genes have epidemiologic, functional and evidence to support their role in oncogenic transformation.

RESULTS: 113 Tier 1 cancer driver mutations (4 splicing, 15 stopgain and 94 missense) were seen in tissue from 66 women. 24% of the 276 surgical samples show at least one cancer driver mutation; 7.3% carried at least 2 cancer driver mutations, a single sample was observed to have 9 cancer driver mutations, and one sample had multiple deletions (runs of homozgyosity) including a hemizygous driver mutation. The TP53 gene had the highest rate of cancer driver mutations with 5 mutations detected. 14.7% of the women without a detected driver mutation had a diagnosed cancer during the follow-up interval while 24 of the 66 (36%) women with endometriosis lesions harboring a cancer driver mutation developed a cancer during the follow-up interval ([p=0.01, odds ratio = 3.3, 95% confidence limits 1.8-6.2]). The majority of the cancers developing in these 18 women were cancers known to be associated with endometriosis. Of note, the mean age of endometriosis diagnosis for the 18 women with a somatic driver mutation who developed cancer was 53.2, and the age at diagnosis was 36.3 for those with no cancer to date (Wilcox p=0.0001).

CONCLUSIONS: Somatic cancer driver mutations are common in endometriosis lesions. When a cancer driver mutation is present in an endometriosis lesion, the risk of a secondary cancer appears to be elevated.

SUPPORT: Juean Biosciences, LLC.
inflammatory disease, but genetic evidence suggest that the initiation of endometriosis is linked to the structural features of the cell. This non-hormonal pathogenic model suggest that it may be possible to prevent endometriosis by inhibiting EMT and by stabilizing mesothelial barrier integrity.

SUPPORT: J uneau Biosciences, LLC.

O-191 Wednesday, October 16, 2019 11:45 AM

ENDOMETRIOSIS DOES NOT IMPACT LIVE BIRTH RATES IN FROZEN EMBRYO TRANSFER (FET) OF EUPLOID BLASTOCYSTS. Lauren A. Bishop, MD, a Kate Davey, MD, b Justin C. Gunn, BS, c Eric A. Widra, M.D., d Rhianna D. Saunders, MD, e Alan H. Decherney, MD, f Breonna Slocum, MD, g Micah J. Hill, DO, h NIH, Bethesda, MD; c Shady Grove Fertility, Washington D.C., DC; 3 Edward Hébert School of Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD; 4SGFertility, Washington, DC; 6Walter Reed National Military Medical Center, Bethesda, MD; 7Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD; 5MedStar Georgetown University/Washington Hospital Center, Washington, DC; 7National Institute of Child Health and Human Development, NIH, Bethesda, MD.

OBJECTIVE: One explanation proposed for subfertility among women with endometriosis is impaired endometrial receptivity. We sought to test this hypothesis by comparing pregnancy and live birth (LB) outcomes in women with endometriosis versus two control groups without suspected endometrial factor: (1) non-infertile patients who underwent ART in order to test embryos for a single gene disorder and (2) couples with isolated male factor infertility.

DESIGN: Retrospective Cohort.

MATERIALS AND METHODS: FETs of PGT-A normal blastocysts performed from January 2016 through March 2018 were included in the analysis. Patients with endometriosis were compared to those with male factor infertility and non-infertile patients using PGT-M for a single gene disorder. Endometriosis was confirmed surgically in 90% of the endometriosis cohort. Patients with multiple infertility diagnoses and those using gestational carriers or donor oocyte were excluded from the analysis. All blastocysts vitrified and warmed for transfer were grade BB or better. Comparisons were done with multigroup chi-square and P<0.05 was considered statistically significant.

RESULTS: 472 euploid FET cycles were available for analysis, 59 transfers occurred in patients with endometriosis, 362 transfers in patients with male factor infertility, and 51 transfers in non-infertile patients. There was no difference in patient age in each treatment group and age was not associated with live birth in euploid embryo transfers. An equal number of embryos were transferred in each group. Patients with endometriosis had similar rates of clinical pregnancy (CP) and spontaneous abortion (SAB) when compared to male factor and non-infertile patients. There was no difference in LB in patients with endometriosis (63%) compared to patients with male factor (51%) and non-infertile patients (53%). While the study was only powered to detect a 20% decrease in LB, the 63% LB rate in endometriosis patients did not suggest a negative effect.

CONCLUSIONS: Whether endometriosis primarily affects IVF outcomes via oocyte quality or the endometrium is debated. By controlling for embryo quality using euploid FET cycles, we found no difference in pregnancy outcomes in patients with endometriosis compared to those with male factor and non-infertile patients.

O-192 Wednesday, October 16, 2019 12:00 PM

NON-INVASIVE DIAGNOSIS OF ENDOMETRIOSIS: USING MACHINE LEARNING INSTEAD OF THE OPERATING ROOM. Kathryn L. Shaia, MD, MHA, a Chaitanya R. Acharya, PSM, PhD, b Stephanie Smeltzer, MD, c Herbert K. Lyerly, MD, d Kelly S. Acharya, MD, e 8 Division of Reproductive Endocrinology and Infertility, Duke University Medical Center, Durham, NC; 9 Duke Center for Applied Therapeutics, Department of Surgery, Durham, NC.

OBJECTIVE: Endometriosis affects an estimated 1 in 10 women during their reproductive years, and up to 30% to 50% of women with endometriosis may experience infertility. Classically, endometriosis is a surgical diagnosis, and excision or ablation of endometriosis is known to be technically challenging with little added benefit for patients undergoing in vitro fertilization (IVF). However, the presence of an endometriosis diagnosis may impact clinical recommendations during fertility treatment. A previous study developed classifiers for prediction of endometriosis in a cycle-phase specific manner by using margin tree classification within one dataset. Our aim was to build on this research by utilizing machine learning to predict and independently validate the presence or absence of endometriosis, regardless of cycle phase and other uterine pathology, through endometrial biopsy (EMB) samples.

DESIGN: Retrospective cohort analysis of publicly available genomic data.

MATERIALS AND METHODS: We trained Random Forest classifiers on ten gene-expression based modules, derived from spectral decomposition of the discovery dataset (n = 148) to predict the presence of endometriosis. These classifiers were validated in an independent gene expression dataset (n = 37) of eutopic EMB samples obtained from patients with and without endometriosis.

RESULTS: We identified a 280-gene predictor of endometriosis using Random Forests that was found to predict the presence of endometriosis, regardless of the endometrial phase and other pathology, with an accuracy of 84% (area under ROC = 0.84; p-value: 6.14e-05), with a negative predictive value of 86% and a positive predictive value of 81%. We reduced model over-fitting by performing 10-fold cross-validation of our discovery data.

CONCLUSIONS: Using machine learning, we developed a new genomic signature with the ability to accurately predict the presence of endometriosis from an EMB sample regardless of cycle phase or other pathology. Ongoing work is interrogating the findings in the IVF population, and the role played by DNA methylation in regulating expression of key genes and pathways in our predictive model. In a move towards personalized, noninvasive medicine, the EMB diagnosis of endometriosis could provide meaningful clinical information without subjecting patients to the risks and expense of surgery.


SUPPORT: None.

TABLE 1.

<table>
<thead>
<tr>
<th>Gene Set</th>
<th>Description</th>
<th>Gene Set Size</th>
<th>Expected Count</th>
<th>Observed Count</th>
<th>Fold Enrichment</th>
<th>P Value</th>
<th>FDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>GO:0005887</td>
<td>Integral plasma membrane</td>
<td>1596</td>
<td>65.6</td>
<td>126</td>
<td>1.92</td>
<td>3.58E-13</td>
<td>2.75E-10</td>
</tr>
<tr>
<td>GO:0044430</td>
<td>Cytoskeletal part</td>
<td>1620</td>
<td>66.6</td>
<td>127</td>
<td>1.91</td>
<td>4.86E-13</td>
<td>2.75E-10</td>
</tr>
<tr>
<td>GO:0009986</td>
<td>Cell surface</td>
<td>782</td>
<td>32.1</td>
<td>67</td>
<td>2.08</td>
<td>9.24E-09</td>
<td>1.36E-06</td>
</tr>
<tr>
<td>GO:0098590</td>
<td>Plasma membrane region</td>
<td>1175</td>
<td>48.3</td>
<td>86</td>
<td>1.78</td>
<td>1.08E-07</td>
<td>0.0002</td>
</tr>
<tr>
<td>GO:0033102</td>
<td>Extracellular matrix</td>
<td>496</td>
<td>20.4</td>
<td>43</td>
<td>2.11</td>
<td>3.99E-06</td>
<td>0.0006</td>
</tr>
<tr>
<td>GO:0030054</td>
<td>Cell junction</td>
<td>1268</td>
<td>52.1</td>
<td>83</td>
<td>1.59</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

e80 ASRM Abstracts Vol. 112, No. 3, Supplement, September 2019
O-193 Wednesday, October 16, 2019 10:45 AM

METABOLIC SYNDROME (Mets): FECUNDABILITY AND ADVERSE PREGNANCY OUTCOMES IN UNEXPLAINED INFERTILITY. Sushila Arya, MD, a Karl R. Hansen, MD PhD, b Michael P. Diamond, MD, c Robert A. Wild, MD, M.P.H. PhD, d NICHD’s Reproductive Medicine Network, eUniversity of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma city, OK; e Augusta University, Augusta, GA.

OBJECTIVE: To determine the association of Mets with fecundability and pregnancy complications after ovarian stimulation—intrauterine insemination (OS-IUI) for unexplained infertility.

DESIGN: Secondary analysis of a randomized clinical trial (RCT) investigating clinical pregnancy, live birth, and multiple pregnancy rates with OS-IUI for couples with unexplained infertility.

MATERIALS AND METHODS: This secondary analysis included all 900 couples undergoing OS-IUI treatment as part of The Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation (AMIGOS) clinical trial. Briefly, this trial enrolled women at 12 sites, age 18–40 with at least one patient fallopian tube and regular menses who underwent OS-IUI with letrozole, clomiphene citrate (CC) or gonadotropins for up to four treatment cycles. Male partners were required to have a semen analysis with at least 5 million sperm/mL. Couples undergoing OS-IUI treatment as part of The Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation—unexplained infertility were excluded if it was not possible to determine ruptured versus non-ruptured ectopic pregnancy.

RESULTS: Prevalence of Hi BMI was 51.09%, VHBMI 10.4%, and Mets 17.6%. BMI or Mets was not associated with clinical pregnancy or live birth rates. Pregnancy complications occurred in 40.18% overall (CC 30.0%, letrozole 41.4% and gonadotropins 46.9%). For CC and letrozole, the odds for any pregnancy complication with Mets were 2.72 (1.27, 5.82). With MetS, 22.7% had Pr-E and 27.3% had GDM vs. 5.2% and 8.3% without Mets. When given gonadotropins, MetS was not associated with complications, however multiple pregnancies were more common (33% of triplet pregnancies had Pr-E). For those with VHBMI, the odds of a complication were 4.30 (1.17, 15.79), and 65% had MetS. The overall odds for a complication with MetS present were 3.10 (1.44, 6.67) adjusting for HiBMI and multiple pregnancies.

CONCLUSIONS: Mets did not influence fecundability. However, it is significantly associated with pregnancy complications beyond the risk conferred by obesity alone. MetS potentiates pregnancy complications, as does VHBMI, with OS-IUI for patients with unexplained infertility.

Walaa G. Hozayen, PhD, a Kamel M. A. Hassanin, PhD, b Kamal A. Abdalla, MD, c Noha A. Abdalla, B.Sc. d Odessa Reproductive Medicine Center, Helotes, TX; e Biochemistry Division, Chemistry Department, Faculty of Science, Beni-Suef University, Beni-Suef, Egypt; f Biochemistry Department, Faculty of Veterinary Medicine, Minia University, Minya, Egypt; g Department of Obstetrics & Gynecology, Faculty of Medicine, Minya University, Minya, Egypt.

OBJECTIVE: Study the use of the aromatase inhibitor, letrozole, for the treatment of ectopic pregnancy compared to methotrexate.

MATERIALS AND METHODS: A series of 42 consecutive patients with undisturbed ectopic pregnancy were counseled regarding the treatment options including surgical treatment (control group), medical treatment with the methotrexate (study group 1) or letrozole (study group 2). Each group included 14 patients. Primary outcome was complete resolution of ectopic pregnancy determined by serum hCG levels below laboratory immunoassay detection. Secondary outcomes included changes in the biochemical parameters of ovarian reserve, Anti-Mullerian Hormone (AMH), as well as hematological and hormonal changes associated with the two medical treatments compared to surgical treatment.

RESULTS: Complete resolution of ectopic pregnancy occurred in equal number of patients, 12 out of 14 (86%) in each of the two study groups. The two patients who failed methotrexate treatment had to undergo surgery after becoming hemostatically unstable, while in the letrozole group, one patient had to go to surgery when she became hemostatically unstable, while in the second patient, a decision to do surgery was due to failure of hCG level to decline four days after letrozole treatment. Treatment with methotrexate was associated with higher levels of liver enzymes, and lower levels of platelets (the differences in both parameters were statistically significant). The decline in hCG levels was faster in the letrozole group, when compared to the methotrexate group. Three months after treatment, AMH levels were lower in the methotrexate group when compared to the letrozole and the surgery group. However, the decline in the hCG and AMH levels were not statistically significant.

CONCLUSIONS: Up to our knowledge, this is the first report in the literature on the success of letrozole in medical treatment of ectopic pregnancy. In the absence of estrogen priming, progesterone may not exert its physiological function due to a negative effect on progesterone receptors. It is hypothesized that by inhibiting the estrogen synthetase (the aromatase enzyme), the progesterone would not exert its physiological function in maintaining pregnancy, including ectopic pregnancy. The small sample size and non-randomized design of our study would limit our conclusion about letrozole success in treating ectopic pregnancy. However, the promising high resolution rate and better safety profile that letrozole has over a chemo therapeutic agent like methotrexate, should encourage studying the letrozole as a promising medical treatment for ectopic pregnancy through more definitive randomized clinical trials, that are adequately powered. Furthermore, letrozole may also be a safer alternative instead of surgical approach in managing early pregnancy loss, and pregnancy termination when medically indicated and ethically appropriate. In our study, a long follow up is intended to compare ovarian reserve in the two study groups and the surgery control group.


SUPPORT: None.

O-195 Wednesday, October 16, 2019 11:15 AM

REPRODUCTIVE OUTCOMES FOLLOWING A RUPTURED ECTOPIC PREGNANCY. Barry E. Perlman, DO, a Kavitha Krishnamoorthy, MD, b Ruchi Karsalia, BS, b Debra Heller, MD, c Rutgers New Jersey Medical School, Newark, NJ; d Rutgers New Jersey Medical School, Newark, NJ.

OBJECTIVE: Ectopic pregnancies account for 2% of all pregnancies in the United States. Subsequent pregnancy outcomes following ruptured versus non-ruptured ectopic pregnancy have been poorly reported in the literature. Non-peer reviewed websites have reported that ruptured ectopic pregnancies are damaging for future fertility; however, only one single study has reported no difference. As rupture of an ectopic pregnancy could lead to hemoperitoneum, inflammation, and scar formation, we hypothesized that ruptured ectopic pregnancies will decrease future fertility. Therefore, the primary objective of this study is to determine if fewer subsequent intrauterine pregnancies occur following surgical excision of a ruptured tubal ectopic compared to surgical excision of a non-ruptured ectopic pregnancy.

DESIGN: Retrospective cohort study at a University-affiliated hospital.

MATERIALS AND METHODS: All patients undergoing salpingectomy for a tubal ectopic pregnancy from 1/1991-12/2016 were considered. Patients were excluded if: it was not possible to determine ruptured versus non-ruptured status; if the patient had documented contraceptive use or no sexual
activity within 12 months of the procedure; or if the patient had insufficient follow-up, defined as less than 2 visits within 12 months of the procedure. All data was statistically analyzed using Fisher exact tests.

RESULTS: A total of 1,171 tubal ectopic pregnancies were identified, 77 of which met inclusion criteria. Ruptured ectopic pregnancies did not result in a significant decrease in subsequent intrauterine pregnancy rate nor a significant increase in future ectopic pregnancy rate during the 12-month follow-up period. 10 out of 27 (37%) patients with ruptured ectopic pregnancy had an intrauterine gestation within 12 months, while 17 out of 50 (34%) patients with a non-ruptured ectopic achieved an intrauterine pregnancy within 12 months (p = 0.8070). 4 out of 27 (15%) cases with a ruptured ectopic and 7 out of 50 (14%) cases with a non-ruptured ectopic had a subsequent ectopic pregnancy within 12 months (p = 0.99).

CONCLUSIONS: Ruptured ectopic pregnancy did not adversely affect the intrauterine pregnancy rate nor recurrent ectopic pregnancy rate 12 months following the rupture, compared to non-ruptured ectopic pregnancies.


O-196 Wednesday, October 16, 2019 11:30 AM

PROGESTIN THERAPY FOR WOMEN WITH COMPLEX ATYPICAL HYPERPLASIA: LEVONOR-GESTREL INTRAUTERINE DEVICE VERSUS SYSTEMIC THERAPY.

Rachel S. Buchtelbaum, MD, Marcia A. Ciccone, MD, David J. Nusbaum, BS, Alan H. DeCherney, MD, Enrique F. Schisterman, PhD. a National Institute of Child Health and Human Development, NIH, Bethesda, MD; bUniversity of Utah, Salt Lake City, UT.

OBJECTIVE: For women with complex hyperplasia with atypia (CAH) who do not undergo hysterectomy, either for fertility preservation or due to poor surgical candidacy, the effectiveness of the levonorgestrel-releasing intrauterine device (LNG-IUD) compared to systemic therapy has not been well studied. We sought to examine differences in treatment response between the LNG-IUD and systemic therapy in women with CAH.

DESIGN: A retrospective observational study at a tertiary care center between 2003-2018.

MATERIALS AND METHODS: Time dependent analyses of complete response (CR) and progression to cancer were performed for LNG-IUD vs. systemic therapy. A propensity score inverse probability of treatment weight (IPTW) model was used to create a weighted cohort that differed based on treatment type but was similar with respect to other characteristics. An interaction-term analysis was performed to examine the impact of body habitus on treatment response, and an interrupted time-series analysis was employed to assess changes in treatment patterns over time.

RESULTS: Among 245 women with CAH, 69 (28.2%) had the LNG-IUD and 176 (71.8%) received systemic therapy. Mean age and body mass index were 36.9 years and 40.0 kg/m², respectively. In the patient level analysis (Table 1), women who received the LNG-IUD were three times more likely to have CR and had a 75% lower likelihood of progression to cancer compared to those who received systemic therapy (both, P < 0.001). In particular, women with class III obesity derived significant benefit from the LNG-IUD vs. systemic therapy (CR rates, 70.3% vs. 40.6%; HR 4.34, 95% CI 2.75-6.86, P < 0.001) compared to those with class I-II obesity (95.3% vs. 53.5%, HR 1.85, 95% CI 1.16-2.97, P = 0.010). In the cohort level analysis, LNG-IUD use significantly increased after 2007 (6.3% to 82.7%, 13.2-fold increase, P < 0.001), and this increase was associated with an increasing number of women who achieved CR (32.9% to 81.4%, 2.5-fold increase, P = 0.005).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Progestin route</th>
<th>Adjusted-HR (95%CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete</td>
<td>Systemic</td>
<td>46.7%</td>
<td>1</td>
</tr>
<tr>
<td>response</td>
<td>LNG-IUD</td>
<td>80.7%</td>
<td>3.14 (2.35-4.21)</td>
</tr>
<tr>
<td>Overall</td>
<td>Systemic</td>
<td>57.0%</td>
<td>1</td>
</tr>
<tr>
<td>response</td>
<td>LNG-IUD</td>
<td>80.9%</td>
<td>2.07 (1.61-2.66)</td>
</tr>
<tr>
<td>Cancer</td>
<td>Systemic</td>
<td>15.7%</td>
<td>1</td>
</tr>
<tr>
<td>response</td>
<td>LNG-IUD</td>
<td>4.1%</td>
<td>0.25 (0.12-0.52)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Our study suggests that the LNG-IUD may be more effective than systemic therapy with oral progestins for women with CAH who opt for non-surgical treatment, particularly in morbidly obese women.

O-197 Wednesday, October 16, 2019 11:45 AM

PRECONCEPTION A1C AND TIME TO PREGNANCY.


CONCLUSIONS: Our study suggests that the LNG-IUD may be more effective than systemic therapy with oral progestins for women with CAH who opt for non-surgical treatment, particularly in morbidly obese women.

PRECONCEPTION A1C AND TIME TO PREGNANCY, PREGNANCY LOSS, AND LIVE BIRTH.


CONCLUSIONS: Our study suggests that the LNG-IUD may be more effective than systemic therapy with oral progestins for women with CAH who opt for non-surgical treatment, particularly in morbidly obese women.

PRECONCEPTION A1C AND TIME TO PREGNANCY, PREGNANCY LOSS, AND LIVE BIRTH.

OBJECTIVE: Reproductive aged women are increasingly at risk of comorbid conditions resulting from obesity and sedentary lifestyles. Past research indicates that increasing A1c in healthy populations is positively associated with markers of inflammation and the development of diabetes in the future. It is unknown if increasing A1c in healthy women during the preconception period impacts reproductive success. Our goal was to examine the relationship of preconception A1c and time-to-pregnancy (TTP), pregnancy loss, and live birth.

DESIGN: Prospective cohort from the Effects of Aspirin in Gestation and Reproduction trial included 1,228 healthy women ages 18-40 years with a history of one or two pregnancy losses attempting spontaneous conception, and no known diagnosis of infertility, diabetes, or PCOS.

MATERIALS AND METHODS: A1c was measured using high performance liquid chromatography (Tosoh Bioscience) at the baseline visit prior to pregnancy. Pregnancy was detected with hCG and ultrasound. Feasibility odds ratio (FOR) and 95% confidence intervals (CI) were estimated using discrete Cox proportional hazards regression models, accounting for left truncation and right censoring. Weighted log-binomial regression models were used to estimate relative risk (RR) and 95% CIs for live birth and pregnancy loss. Models were adjusted for age, BMI, race, income, and treatment arm.

RESULTS: Preconception A1c results were available for 1,194 participants. The lower 10th percentile consisted of A1c values of 3.8-4.6% (n = 121), the middle group A1c of 4.7-5.5% (n = 975), and upper 90th percentile A1c was 5.5-7.5% (n = 98). Increasing preconception A1c was associated with longer TTP (FOR 0.74; 95% CI 0.57, 0.96) in unadjusted models, however, there was no association in adjusted models after accounting for BMI and other markers of obesity and insulin resistance (FOR 0.92; 95% CI 0.69, 1.22). Preconception A1c was not associated with differences in live birth (RR 1.03; 95% CI 0.84, 1.25) or pregnancy loss (RR 0.74; 95% CI 0.49, 1.12).

CONCLUSIONS: Among healthy women, we observed no association of A1c with live birth rate or pregnancy loss. The association of A1c and TTP appeared to be influenced by BMI, a strong risk factor for both diabetes and
infertility. It is expected that increased adiposity contributes to alterations in glucose metabolism, inflammation, and lowered reproductive efficiency. Our data supports current guidelines that reserve preconception A1c assessment in patients with risk factors for diabetes.

O-198 Wednesday, October 16, 2019 12:00 PM

A LONGITUDINAL ASSESSMENT OF OVARIAN RESERVE AFTER MYOMECTOMY. Devora Aharon, MD,1,2 Lucky Sekhon, MD,1 Joseph A. Lee, BA,1,2 Mackenzie Naert, BA,1 Ahmed Kerr, MD,1 Charles Ascher-Walsh, MD,1 Alan B. Copperman, MD,1,2 Icahn School of Medicine at Mount Sinai, New York, NY;1 Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Myomectomy is the preferred treatment option for symptomatic fibroids in women desiring fertility-sparing treatment. However, the effect of myomectomy on ovarian reserve is largely unknown. There is evidence to show that other treatments for fibroids including uterine artery embolization and hysterectomy may diminish ovarian reserve. Additionally, the use of a tourniquet transiently decreases blood supply to the ovaries, which may impact ovarian reserve. This study sought to determine whether open and minimally invasive myomectomy are associated with immediate and/or long-term changes in serum anti-Mullerian hormone (AMH).

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Patients undergoing minimally invasive (robot-assisted or laparoscopic) or open abdominal myomectomy by one primary surgeon from May 2018 through March 2019 were included. A Penrose drain tourniquet was used for all open myomectomies. Vasopressin was injected into the myoma subsersa for all minimally invasive myomectomies (MIS). Baseline data collected included age, BMI, and race. Surgical data collected included surgical approach, additional procedures, estimated blood loss (EBL), length of procedure, and weight of fibroids removed. Serum AMH was collected prior to the procedure. Follow-up serum AMH levels were measured at 2 weeks, 3 months, and 6 months after the procedure. To achieve 80% power to detect a 15% difference in mean AMH level, with p < 0.05, a minimum of 43 subjects needed to be recruited. Paired t-tests were used to detect the mean difference between baseline AMH and 2 week, 3 month, and 6 month AMH respectively. Univariate linear regression was used to detect the effect of surgical approach and covariates on the percent difference in AMH from baseline to each follow-up time point. All follow-up visits will be completed by September 2019, therefore a preliminary analysis was conducted for the purpose of this abstract.

RESULTS: A total of 56 patients were included in the study. 32 had open myomectomies and 24 had minimally invasive myomectomies. A significant decrease in serum AMH was found between baseline and 2 weeks post-operatively (n=42) (b=0.26 ± 0.75 (95% CI 0.03-0.49) p=0.029). This transient effect was no longer significant after 3 months (n=20) and 6 months (n=14). Linear regression showed a significantly greater decrease at 2 weeks post-operatively in the open compared to MIS group (b=-0.56, p=0.039). No significant differences in AMH were seen between open and MIS groups at 3 and 6 months. Surgical factors such as EBL, length of surgery, and fibroid weight were not significantly associated with post-operative changes in serum AMH level.

CONCLUSIONS: AMH levels appear to undergo a transient decline in the immediate post-operative period after myomectomy, with a more pronounced effect with an open compared to MIS approach. The use of a tourniquet might cause a more significant decrease in AMH in the immediate post-operative period, but does not appear to have a sustained effect. Patients can be reassured that undergoing a myomectomy does not have a long-term impact on ovarian reserve, regardless, of the approach.

Reference: None.

SUPPORT: None.

FERTILITY & STERILITY®

O-199 Wednesday, October 16, 2019 10:45 AM

HOW OPEN IS THE WINDOW OF OVARIAN FUNCTION AFTER CANCER TREATMENT? Brian Kwan, PhD,1,2 Shaylyn S. Stark, MPH,1 Mary D. Sammel, ScD,1 Brian W. Whitcomb, PhD,1 Andrew C. Dietz, MD, MSCR,1 Elena Martinez, PhD,1 Loki Natarajan, PhD,1 R. Irene Su, M.D., M.S.C.E.,1 University of California San Diego, La Jolla, CA;1 UNIVERSEITY OF PENNSYLVANIA HEALTH SYSTEM, PHILADELPHIA, CA;2 University of Massachusetts, Amherst, Amherst, MA;4 University of California San Diego Moomes Cancer Center, San Diego, CA;4 University of California, San Diego, Family and Preventive Medicine and Public Health, La Jolla, CA.

OBJECTIVE: The remaining window of ovarian function after cancer treatment is clinically important, yet largely unknown. This study estimated the trajectory of AMH over two decades following cancer treatment in female survivors of adolescent and young adult cancers (AYA survivors). We hypothesized that AMH levels would initially rise, then plateau and finally fall over time after cancer treatment, and trajectories would vary by treatment gonadotoxicity.

DESIGN: Cross-sequential.

MATERIALS AND METHODS: Female AYA survivors who were ages 18-39, were diagnosed with cancer at ages 15-35, completed primary cancer treatment and had at least one ovary were recruited from cancer registries, clinics and advocacy groups between 2015 and 2018. Followed for 18 months, participants collected dried blood spots (DBS) and answered questionnaires every 6 months. DBS were assayed for AMH levels (LOD 0.03 ng/mL, inter- and intra-assay CV <10%) using the picoAMH assay (Ansh-Labs, Webster, TX). Cancer treatment data were abstracted from primary records. Functional Principal Component Analysis (FPCA) modeled AMH trajectory over time since treatment. Principal components were compared by gonadotoxicity (low, moderate, high) and age at diagnosis (<25, 25 to <35, ≥35) groups.

RESULTS: 763 survivors, mean age 33.3 (SD 4.7), contributed 1968 AMH levels at a median of 6.5 years post-treatment (IQR 2.0-9.1). The most common cancers were breast (27%), lymphoma (25%) and thyroid (18%). By treatment gonadotoxicity, 30% were low, 62% were moderate, and 8% were high. For the overall trajectory, post-treatment AMH levels began high, rose to plateau at 2.5 years, and maintained levels began to fall at 10 years. FPCA showed that trajectories differed significantly by gonadotoxicity group (p<0.001) and age at cancer diagnosis (p<0.05). The low group displayed rising levels until 2.7 years post-treatment, then maintained at similar levels until 10 years post-treatment before levels began to fall. The moderate group trajectory was similar, but the magnitude of peak AMH recovery was approximately two-thirds of the low group. In contrast, the high group displayed a quick recovery (plateau by 1.5 years) and no appreciable time interval during which AMH was maintained before a steep fall of levels. Younger age at diagnosis was associated with higher levels of AMH at plateau, but similar maintenance intervals prior to fall of levels, compared with older age at diagnosis. The predicted trajectories showed overlapped among groups.

CONCLUSIONS: Using the hybrid longitudinal and cross-sectional design, with the FPCA approach, we show novel data on the trajectory of AMH beyond the first 5 years after cancer treatment. The AMH trajectories suggest that for low and moderate toxicity groups, the duration during which AMH stays plateaued appears long, in contrast to a narrow window in the high toxicity group. These trajectories aid in counseling AYA survivors on their family building plans.

SUPPORT: NIH HD080952-05.

O-200 Wednesday, October 16, 2019 11:00 AM

IN SEARCH OF THE CRYSTAL BALL - HOW MANY EGGS TO A LIVE BIRTH? A 2-STEP PREDICTION MODEL FOR EGG FREEZING COUNSELING BASED ON INDIVIDUAL PATIENT AND CENTER DATA. Serena H. Chen, M.D.,1 Yajing Angela Xie, Ph.D,1 Natalie A. Cekleniak, MD,2 Debra A. Keegan, MD,1 Mylene WM. Yao, MD,1 Division of Reproductive Medicine, IRMS at St Barnabas, Livingston, NJ;1 Unility Inc., Los Altos, CA.

OBJECTIVE: We aim to develop a two-step egg freezing counseling tool that provides personalized expected live birth (LB) rates before oocyte retrieval (Pre-OR) and adjusts the expectations after oocyte retrieval (Post-OR), when the oocyte yield is known.

MATERIALS AND METHODS: We applied machine learning (ML) to a retrospective IVF-LB outcomes data set. Due to limited LB outcomes from egg freezing itself, this large, diverse IVF patient population served as proxy for women considering egg-freezing to preserve fertility potential.

MATERIALS AND METHODS: We applied the boosted tree method and cross-validation to train and test Pre- and Post-OR models in predicting LB outcomes. The dataset comprises linked IVF-ET data from 1,166 IVF cycles started at our center in 2015 for women under 42. Both Pre- and Post-OR
models use clinical predictors such as age, BMI, AMH, day 3 FSH, any clinical infertility diagnosis, reproductive history, and semen analysis, but only the Post-OR model uses the oocyte yield. Models with optimal discrimination (AUC) and prediction accuracy relative to an age-control model were selected. As this approach not only relies on oocyte live birth rates or per-embryo aneuploidy rates, however, it does assume 1) clinical predictors have the same relative impact on LB rates in IVF patients and women without infertility diagnosis and 2) the freeze-thaw survival rates of oocytes and blastocysts are similar.

RESULTS: Model Evaluation: The AUC for the Pre-OR, Post-OR and age-control models were 67%, 73%, and 57%, respectively. Compared to age-control, AUC improved by 17% (Pre-OR) and 28% (Post-OR). Prediction accuracy, measured by the posterior log of odds ratio compared to age-control (i.e. “how many times more accurate compared to age-control”) is improved by 25-folds (Pre-OR) and 67-folds (Post-OR) using natural log scale. Based on the Pre-OR model, 84% of our IVF patients have a personalized LB rate over 32% from transfer(s) of embryo(s) generated from one IVF-COH cycle. Relevance for Egg Freezing Counseling - Example 1: Based on the Pre-OR model, a 30 year old woman (BMI 26, AMH 3.5 ng/mL, no infertility) has 69-70% (95% CI) LBR per egg-freezing cycle (per cycle here on) which would be adjusted if oocyte yield is less than expected. For example, if her oocyte yield were 5-9 oocytes (less than the expected 10-15), her expected LBR per cycle would decrease to 48-53% (95% CI), Example 2: Based on the Pre-OR model, a 36 year old woman (BMI 28, AMH 2.5 mg/mL, no infertility) has 52-53% (95% CI) LBR per cycle. However, if her oocyte yield were > 15 oocytes (higher than expected), her expected LBR per cycle would increase to 60% (95% CI).

CONCLUSIONS: We have developed a two-step egg freezing counseling tool that sets expectations about LB outcomes before and after knowing the actual oocyte yield while personalizing LB expectations to each woman’s reproductive health profile and maximizing transparency with ML-based models validated against our center’s IVF outcomes. User experience testing is required to optimize how to best convey LB expectations provided by the models.

SUPPORT: Each organization funded its own research efforts.

O-201 Wednesday, October 16, 2019 11:15 AM

CHEMOTHERAPY CAUSES PRIMORDIAL FOLLICLE DEATH IN THE HUMAN OVARY VIA MULTIPLE APOPTOTIC PATHWAYS AND NOT BY “BURN OUT.” Shiny Titus, Ph.D., Kutluk H. Oktay, M.D., Ph.D., Yale University School of Medicine, New Haven, CT.

OBJECTIVE: It has been proposed that gonadotoxic chemotherapy results in the “burn out” of primordial follicle reserve by activating PI3K/PTEN/Akt signaling pathway. Others have challenged this concept and put forward DNA damage and apoptosis as the main mechanism of follicle loss. We conducted this study to answer this controversy and conclusively determine the mechanism of chemotherapy-induced damage to ovarian reserve in women.

DESIGN: Ovarian cortical pieces from organ donors aged ≤32 years were xenografted subcutaneously to SCID mice (n=12 mice/tissue from 4 donors each). After 10 days, the mice were given an injection of cyclophosphamide (75mg/kg) or the vehicle. The tissues were recovered 12 hours later.

RESULTS: The number of primordial follicle, tertiary follicle, and corpus luteum significantly decreased in the CP-alone group compared with the control group. The deleterious effects of CP were significantly rescued when oral metformin was given if the follicular counts were significantly higher in the CP + metformin group than CP-alone group (number of primordial follicle: 16.7±6.3 vs. 9.6±4.7; p=0.004; tertiary follicle: 5.4±1.1 vs. 2.6±1.8, p=0.002; corpus luteum: 8.2±1.5 vs. 5.6±1.3, p=0.029). The other two specific mTOR inhibitors, sirolimus and everolimus, also exhibited similar protective effects on the ovarian follicular counts against CP damage. The serum level of anti-mullerian hormone, a reliable objective marker of reproductive health profile and maximizing transparency with ML-based models, was used to assess phosphorylation of the anti-apoptotic Bcl2 (p-Bcl2) (p=0.0003) accompanied by enhanced colocalization of the pro-apoptotic BAD-Bcl2 complex (p=0.006) in the primordial follicles, confirming that cyclophosphamide induces follicle death via apoptosis.

CONCLUSIONS: This single cell transcriptomic and immunohistochemical analysis of human primordial and primary follicles prove that gonadotoxic chemotherapy agents do not cause follicle activation; they rather create a pro-apoptotic state resulting in massive loss of ovarian reserve. Future research on pharmacological fertility preservation should target preventing DNA damage and apoptosis rather than follicle activation.

SUPPORT: This work was supported by R01 HD061259 from NICHD.

O-202 Wednesday, October 16, 2019 11:30 AM

METFORMIN: A NOVEL OPTION OF FERTILITY PRESERVATION DURING CYCLOPHOSPHAMIDE-CONTAINING CHEMOTHERAPY. Chu-Chun Huang, MD, Mei-Jou Chen, MD, PhD, Sheen-Uan Chen, MD, PhD, Hong-Neng Ho, MD, PhD, Yu-Shih Yang, MD, PhD, Department of Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan; National Taiwan University Livia Shangwu Yan Scholar, Taipei, Taiwan; Taipei Medical University, Taipei, Taiwan; Department of Obstetrics and Gynecology, Fu Jen Catholic University Hospital, New Taipei, Taiwan.

OBJECTIVE: Cyclophosphamide (CP) could cause premature follicular activation and depletion, and finally premature ovarian failure, through the imbalanced activation of mTOR signaling pathway. Whether metformin, a widely prescribed anti-diabetes agent with mTOR inhibitory effect, could preserve fertility during CP treatment is still unknown.

DESIGN: A murine study.

MATERIALS AND METHODS: The female C57BL/6 mice aged 6-8 weeks were randomized into five groups (n=8 per group), including the control group with no any medical treatment, the CP-alone group (75mg/kg, i.p. weekly), the treatment groups which CP was co-administered with either oral metformin (50mg/kg/day) or two specific mTOR inhibitors (sirolimus 0.67mg/kg/day or everolimus 0.167mg/kg/day). After four weeks of treatment, five mice per group were sacrificed to collect the ovarian tissue and serum, and three mice per group were mated with male breeders 8 weeks after the end of treatment. The data were analyzed by one-way analysis of variance, the chi-square test or Fishers exact test where appropriate. A P value of < 0.05 was considered statistically significant.

RESULTS: The number of follicular, tertiary follicle, and corpus luteum significantly decreased in the CP-alone group compared with the control group. The deleterious effects of CP were significantly rescued when oral metformin was given if the follicular counts were significantly higher in the CP + metformin group than CP-alone group (number of primordial follicle: 16.7±6.3 vs. 9.6±4.7; p=0.004; tertiary follicle: 5.4±1.1 vs. 2.6±1.8, p=0.002; corpus luteum: 8.2±1.5 vs. 5.6±1.3, p=0.029). The other two specific mTOR inhibitors, sirolimus and everolimus, also exhibited similar protective effects on the ovarian follicular counts against CP damage. The serum level of anti-mullerian hormone, a reliable objective marker of ovarian reserve, was significantly decreased in the CP-alone group and increased in CP + metformin group (Control vs. CP-alone vs. CP + metformin: 5.8±0.3 vs. 2.1±1.0 vs. 4.6±1.2 ng/mL, p<0.0001). The number of the offspring was also significantly decreased in the CP-alone group and increased in the CP + metformin group (Control vs. CP-alone vs. CP + metformin: 6.7±1.2 vs. 1.0±1.0 vs. 4.0±2.0, p=0.004). The IHC stain showed that the expression of phospho-mTOR protein and TUNEL protein within mice ovaries were increased when treated with CP and were significantly decreased when co-treatment was accompanied.

CONCLUSIONS: This is the first research showing that metformin could preserve ovarian function and fertility in mice treated with CP. The underlying mechanism might be related to both the mTOR inhibitory and anti-apoptotic effects of metformin. It could be a safe, effective and also economic fertility preserving agent during CP-containing chemotherapy thus showing promising potential in future clinical research and application.

SUPPORT: This study was supported by grants MOST 105-2314-B-002-109-MY3 (H.N. Ho), MOST 102-2311-B-002-093-MY3 and 105-2628-B-002-043-MY4 (M.J. Chen), and MOST 105-2628-B-002-031-MY3 (C.C. Huang) from the Ministry of Science and Technology of Taiwan and the National Taiwan University Hospital (107-004058, 108-004336).
WORLD WIDE UPDATE: RESULTS WITH CRYOPRESERVED OVARIAN TISSUE TRANSPLANT. Sherman Silber, MD, a Yuting Fan, M.D., a Sierra Goldsmith, B.S. a Infertility Center of St. Louis, Chesterfield, MO; University of Michigan, Ann Arbor, MI.

OBJECTIVE: There have been many scattered case reports, with a confusing literature therefore, on results with ovarian cryopreservation for cancer patients. There have been only three other series reported, with differing and changing techniques. Our objective was to report a consistent series, and to mine from the literature the number of babies, and whether the procedure (after 22 years) should still be labeled as “experimental”.

DESIGN: Patients who have had ovary freezing, and came back later years to re-implant their frozen tissue, were studied monthly post-op for many years for ovarian function, pregnancy, and live birth. In addition, the scattered world literature was scanned to determine the total number of live births.

MATERIALS AND METHODS: 115 patients, age 2 to 35 years, had frozen ovary cortex stored at our center since 1997. 15 of them up till now have had the tissue thawed and re-implanted. Three were leukemia, one was multiple sclerosis, two were premature ovarian failure, and the rest were solid tissue cancers. All were menopausal for at least 3 years. The technique for re-implantation was the same in all cases. After thaw of cortical tissue, three to five slices were quilted into one piece with 9-0 nylon interrupted sutures. The dead cortex was removed in entirety, and the quilted slices were sutured to the underlying medulla with 9-0 nylon interrupted sutures after hemostasis was achieved with micro-bipolar forceps and irrigation with pulsatile heparinized media to avoid adhesions. All transplants were orthotopic so that the patient could be conceived spontaneously. Patients were followed monthly for hormones, return of menses, and pregnancy, and delivery. In addition, the literature was reviewed to try to tabulate the number of live births to date in the world.

RESULTS: Of the fifteen patients who had their frozen tissue re-implanted, none underwent IVF, all pregnancies were spontaneous from intercourse. 15 healthy babies were delivered to 10 of the 15 women (66%). Two women had 4 babies from the thawed, transplanted tissue. Two of the three with leukemia had a total of 4 healthy babies. In the literature, we counted a total of 170 babies in addition to our 15, making a total of 185. Live baby pregnancy rate in the literature ranged from a low of 31% to our 77.7% (95% CI, 65.10, 90.22), FIGO 3, 77.7% (95% CI, 65.10, 90.22), FIGO 4, 68.1% (95% CI, 59.08, 75.18), and FIGO 5, 74.0% (95% CI, 67.21, 80.85). Similar results were seen in women with a primary fibroid volume of either < or ≥ 56.2 cm³ (median) and uterine volume of either < or ≥ 356.5 cm³ (median). Overall AEs for elagolix+E2/NETA excluded hot flushes (20.0%), nausea (9.4%), headache (9.4%), night sweats (8.6%), and fatigue (6.1%).

CONCLUSIONS: Ovarian cryopreservation for cancer patients should no longer be labeled ‘‘experimental’’.

FIBROIDS

ARE GENDER DYSPHORIA PATIENTS COUNSELED ON FERTILITY PRESERVATION PRIOR TO INITIATING HORMONAL THERAPY? Ross G. Everett, MD MPH a Bryce A. Baughman, MD, BA a Johnathan Doolittle, MD, Jay I. Sandlow, MD. Medical College of Wisconsin, Milwaukee, WI.

OBJECTIVE: National guidelines recommend counseling patients with gender dysphoria on the impacts of hormone or surgical therapy on their fertility prior to beginning either intervention. In this study, we aim to identify the compliance to these guidelines at our institution.

DESIGN: Retrospective, single institution chart review.

MATERIALS AND METHODS: Utilizing ICD codes, we identified patients with a diagnosis of gender dysphoria [GD] treated at our institution between 2008-2018. Various parameters regarding medication regimen, surgical intervention, fertility counseling, and fertility preservation were obtained through retrospective review. Patient demographics and interventions were compared. All data was analyzed in a standard statistical fashion utilizing Stata software.

RESULTS: Upon review, 269 patients met inclusion criteria. Of these, 114 (42.4%) had a chromosomal sex of female and 155 (57.6%) were chromosomal males. Race was divided as 75.5% White, 16.7% Black and 7.8% other. The average age was 30.9 (S.D.±13.7). Regarding management of GD, 63.6% had been managed by Endocrinology, 118 (43.9%) by Genetics, and 25 (9.3%) had seen Urology, 74 patients (27.5%) ultimately pursued some surgical intervention. 97 patients (36.1%) were on hormonal therapy for GD prior to evaluation at our institution and were excluded from subsequent analysis. Another 26 patients did not have record of pursuing hormonal therapy to date. Of the remaining 146 patients, 96 (65.8%) had documented counseling regarding fertility. On chi-square tests, age was the only demographic found to be significantly different between those counseled on fertility and those not. Additionally, on multinomial logistic regression, individuals ≤30 years were significantly more likely to be counseled regarding fertility than those 31-50 years (RR 2.45, p=0.049) and those 51+ years (RR 5.47, p=0.013). Factors such as race, chromosomal sex, and managing specialty were not found to be predictive. Among those patients ≤30 years of age, 71 of 98 (72.5%) were counseled regarding fertility preservation.

CONCLUSIONS: Compliance with national guidelines to counsel GD patients on fertility preservation is best among younger patients, most notably those less than or equal to 30 years of age. This appears consistent among patients of both chromosomal sexes and across different managing specialties. Further research is needed regarding other risk factors for poor counseling as well as to predict those patients who will be interesting in fertility preservation.


FERTILITY & STERILITY
**SUBLINGUAL MISOPROSTOL 400 VS. 200 MCG FOR REDUCING BLOOD LOSS DURING ABDOMINAL MYOMECTOMY: A RANDOMIZED DOUBLE-BLIND CLINICAL TRIAL.** Ahmed M. Abbas, MD, a Hammam Ramadan, MSc,b Shymaa Ali, MSc,c Yehia Ali, MSc,d Mohammed Khairiy Ali, MD,e Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; Department of Obstetrics and Gynecology, Faculty of Medicine, Arsan University, Arsan, Egypt; Department of Obstetrics and Gynecology, Faculty of Medicine, Suez University, Suez, Egypt; Department of Obstetrics and Gynecology, Faculty of Medicine, Qena, Egypt.

OBJECTIVE: Uterine leiomyomas are the most frequent benign gynecologic pelvic tumor in women, which originate from smooth muscle cells of the uterus. Interleukin-6 and preoperative bleeding points are the main concerns for blood transfusion and iron therapy are major challenges with abdominal myomectomy. Our objective is to compare the effectiveness of preoperative sublingual misoprostol 200 vs. 400 mcg for reducing blood loss during and after abdominal myomectomy.

**DESIGN:** A randomized, double-blind, clinical trial (ClinicalTrials.gov: NCT02709564).

**MATERIALS AND METHODS:** Patients with documented uterine fibroids on pelvic imaging and scheduled for abdominal myomectomy were invited to participate in our study. We included women aged (18-50 years) with five or less symptomatic subserous or intramural fibroids, Preoperative hemoglobin level is >8 g/dl, and uterine size is less than 24 weeks gestation. The eligible women were randomized (1:1) to either (group A) received two tablets of sublingual misoprostol 400 mcg at 3 hours and 1 hour before the surgery (group B) received one tablet of sublingual misoprostol 200 mcg and one placebo tablet at the previously mentioned schedule. The primary outcome was the difference in the mean amount of intraoperative blood loss during myomectomy. The secondary outcomes included the change of hemoglobin (HB) before and 24 hours after surgery, duration of surgery, post-operative blood transfusion and the side effects of the drug. Mann Whitney test and Fisher’s exact test were used for the analysis of the outcomes.

**RESULTS:** Eighty women were enrolled and randomized (n=40 in each arm).

No difference between both groups regarding age, parity, BMI, type, number, size of fibroids and the total uterine size. Estimated blood loss was significantly lower in the misoprostol 400 mcg group (373.3±55.6 vs. 560.0±105.2 ml, p<0.001).

Moreover, the reduction in HB level was significantly lower in the misoprostol 400 mcg group (0.8±0.18 vs. 1.7±0.38 g/dl, p<0.001). The operative duration was significantly shorter in the misoprostol 400 mcg group (91.3±57.7 vs. 111.2±6.3 minutes, p<0.001). Seven cases required a blood transfusion in the misoprostol 200 mcg group versus two cases in the other group (p=0.03). No difference between both groups reading the side effects of misoprostol.

**CONCLUSIONS:** Sublingual misoprostol 400 mcg is an effective and safe method for reduction of blood loss and need for blood transfusion during abdominal myomectomy.

**SUPPORT:** None.

**O-208**

Wednesday, October 16, 2019 11:30 AM

**VITAMIN D LONG-TERM TREATMENT DECREASES HUMAN UTERINE LEIOMYOMA SIZE THROUGH SPECIFIC MOLECULAR MECHANISMS IN A XENOGRAFT ANIMAL MODEL.** Ana Corachán, MS,a Hortensia Ferrero, PhD,b Julia Escrig, MD,c Javier Monleón, MD,d Amparo Faus, Lab Technician,e Irene Cervelló, PhD,f Antonio Pellegrini, MD,g IVI Foundation - University of Valencia, Valencia, Spain; IVI Foundation - Instituto de Investigación Sanitaria INCLIVA, Valencia, Spain; Servicio de Ginecología, Hospital Universitario y Politécnico La Fe, Valencia, Spain; IVI Foundation, Valencia, Spain; IVI Foundation Innovation - Reproductive Medicine IIS La Fe, Valencia, Spain.

OBJECTIVE: Uterine leiomyomas (LM) are benign estrogen-dependent tumors, composed of smooth muscle cells interspersed in an abundant extra-cellular matrix (ECM). In women, an increased risk of LM is associated with Vitamin D (VitD) deficiency. Our group have demonstrated in vitro the anti-proliferative action of VitD on human LM primary cells, elucidating the potential role of VitD as a possible therapy to shrink LM. In this study, we aim to corroborate in vivo the VitD effect at both short and long terms in a xenograft mouse model through specific mechanisms: cell proliferation, ECM degradation and apoptosis.

**DESIGN:** Preclinical study of human uterine LM treatment with VitD in an animal model.

**MATERIALS AND METHODS:** Human LM fragments (4mm²) were implanted intraperitoneally in ovariectomized NOD-SCID mice (hormonally supplemented). One week after, we established 3 groups: control, VitD 0.5 μg/kg/day and VitD 1 μg/kg/day. Treatments were delivered by micro-osmotic pumps. At the end of the treatments, LM were collected and measured macroscopically, proliferation was analyzed by immunohistochemistry (Ki67), apoptosis by Western Blot (WB) (CASPASE 3) and TUNEL assay, and ECM formation by Masson staining. LM were analyzed in vivo by PET/CT imaging.

**RESULTS:** At 6 weeks of treatment, LM size was significantly decreased in the VitD groups compared with the control group. At 12 weeks, LM size was further reduced in the VitD group with higher dose. LM proliferation was significantly decreased in the VitD groups compared with the control group. VitD treatment also induced an increase in ECM deposition, as evidenced by Masson staining. Lastly, apoptosis was increased in the VitD groups compared with the control group.

**CONCLUSIONS:** Vitamin D treatment is an effective therapy for reducing LM size through specific molecular mechanisms, including cell proliferation, ECM degradation and apoptosis. Further studies are needed to determine the long-term effects of VitD treatment on LM in vivo.
monitoring showed a statistically significant reduction of $^{18}$F-FDG uptake in both VitD-treated groups ($p<0.05$), indicating a reduction in LM size. Likewise, macroscopic LM size diminished significantly in VitD $1 \mu$g/kg/day dose group ($p=0.025$). Besides, the high dose of VitD significantly decreased cell proliferation in LM size, while at long term VitD significantly reduces LM size by cell proliferation inhibition and ECM degradation and apoptosis increase, without side effects. Our data strongly suggest that long-term treatment with VitD could be considered as an effective adjuvant treatment for uterine LM in women.

CONCLUSIONS: VitD short-term treatment is only capable to maintain human uterine LM size, while at long term VitD significantly reduces LM size by cell proliferation inhibition and ECM degradation and apoptosis increase, without side effects. Therefore, this study provides evidence that long-term treatment with VitD could be considered as an effective adjuvant treatment for uterine LM in women.

**OBJECTIVE:** Outpatient hysteroscopic myomectomy can be usually performed in case of single submucosal myoma with largest diameter up to 2 cm. The volume of the myoma has a critical role in outpatient myomectomy because larger myomas require a longer resection time and, thus, these procedures may be less tolerated by patients. One of the major advantages of preoperative therapy is to decrease the volume of uterine myomas. This prospective study compared outpatient hysteroscopic myomectomy performed by using the Versapoint system in patients who received 3-month preoperative treatment with leuprolide acetate (LA), ulipristal acetate (UPA) or who did not receive any preoperative hormonal therapy.

**DESIGN:** Single-center prospective non-randomized study.

**MATERIALS AND METHODS:** This study included patients of reproductive age requiring outpatient resection of single FIGO type 0-1 myoma with largest diameter < 2 cm. Exclusion criteria were: previous surgical treatment of uterine myomas, previous administration of hormonal therapies for uterine myomas, additional endometrial conditions requiring hysteroscopic treatment (such as uterine polyps), additional surgical procedures performed by other approaches (such as laparoscopy), suspicion of malignancy. Study patients underwent either preoperative treatment with UPA (5 mg/day; group UPA) or LA (11.25 mg/ml, group LA) for 3 months or immediate surgery (without preoperative hormonal therapy, group S). The choice of receiving preoperative treatment was based on patients’ preference. Hysteroscopic myomectomy was performed by using the Versapoint system. The primary objective of the study was to compare the rate of complete resections in the three study groups. The secondary objective of the study was to compare the operative results between the study groups. The tertiary objective of the study was to assess the characteristics of the myomas and the endometrium in patients treated with UPA and LA. Data were analyzed according to intention to treat.

**RESULTS:** 138 patients were included in the study. The percentage decrease in the volume of uterine myomas was higher in patients receiving LA than in those treated with UPA ($p=0.015$). Before surgery, myoma volume was lower in group LA and in group UPA than in group S ($p=0.026$ and 0.043, respectively). The percentage of complete resection was significantly higher in group LA (83.0%; 39/47) than in group UPA (60.5%; 23/38; $p=0.020$) and in group S (62.2%; 33/53; $p=0.021$). The volume of fluid infused was significantly lower in group LA than in group S ($p<0.005$). There was no significant difference in the volume of fluid absorbed between the three study groups ($p=0.341$). Concerning the characteristics of the endometrium, completely atrophic endometrium was significantly more frequent in the LA group compared with the other study groups. The texture of the myoma was rubbery or soft more frequently in the UPA group than in the other groups.

**CONCLUSIONS:** Compared with UPA or no treatment, LA improves the rates of complete resection in patients undergoing outpatient hysteroscopic myomectomy.
OBJECTIVE: To explore the influence of body weight on ovarian response and related clinical outcomes after individualized follicle-stimulating hormone (FSH) dosing versus fixed starting dosing of 150 IU FSH in women undergoing in vitro fertilization (IVF).

DESIGN: Randomized, assessor-blind, controlled trial; 1326 women undergoing their first ovarian stimulation cycle were randomized: 1:1 to follitropin delta or follitropin alfa. In the follitropin delta group, women with anti-Müllerian hormone (AMH) <15 pmol/L received fixed daily doses of 12 μg and women with AMH ≥15 pmol/L received individualized doses, based on AMH level and body weight. Women randomized to follitropin alfa received a fixed starting dose of 150 IU, regardless of their AMH and body weight.

MATERIALS AND METHODS: Oocytes retrieved 36±2 hours after triggering follicular maturation were inseminated by IVF or intracytoplasmic sperm injection. Good-quality blastocysts (≥3 BB) was based on Gardner-Schoolcraft classification (1999). Blastocyst transfer was performed on day 5, and ongoing pregnancy was confirmed by ultrasound at 10-11 weeks after transfer. Data were evaluated descriptively by calculating the mean number of oocytes, good-quality blastocysts, and the ongoing pregnancy rate for nested subgroups of women based on increasing body weight.

RESULTS: Exposure to serum FSH showed an inverse relationship with body weight for both follitropin delta and follitropin alfa. In women with AMH <15 pmol/L, the ovarian response in terms of number of oocytes did not show any body weight dependence. In women with AMH ≥15 pmol/L treated with follitropin alfa, the number of oocytes decreased from an overall mean of 13 oocytes to a mean of 10 oocytes with increasing body weight. In the individualized follitropin delta group, the number of oocytes was not affected by body weight. Accordingly, the number of good-quality blastocysts decreased with increasing body weight in women with AMH ≥15 pmol/L in the follitropin alfa group, from an overall mean of 2.3 to a mean of 2.0, whereas body weight did not affect the number of good-quality blastocysts in the individualized follitropin delta group. The ongoing pregnancy rate after fresh transfer tended to decrease with increasing body weight in the follitropin alfa group but not in the individualized follitropin delta group.

CONCLUSIONS: With fixed starting doses of FSH, ovarian response and related clinical outcomes after individualized follicle-stimulating hormone dosing versus fixed starting dosing of 150 IU FSH in women undergoing in vitro fertilization (IVF) were not shown to be body weight dependent. In women with AMH ≥15 pmol/L, received individualized doses, based on AMH level and body weight. Women randomized to follitropin alfa received a fixed starting dose of 150 IU, regardless of their AMH and body weight. Accordingly, the number of good-quality blastocysts decreased with increasing body weight in women with AMH ≥15 pmol/L in the follitropin alfa group, from an overall mean of 2.3 to a mean of 2.0, whereas body weight did not affect the number of good-quality blastocysts in the individualized follitropin delta group. The ongoing pregnancy rate after fresh transfer tended to decrease with increasing body weight in the follitropin alfa group but not in the individualized follitropin delta group.

SUPPORT: The study was funded by Ferring Pharmaceuticals, Copenhagen, Denmark.

### Table: The predictive factors for the EPL

<table>
<thead>
<tr>
<th>Parameters</th>
<th>β</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MA</td>
<td>0.723</td>
<td>2.061 (1.721-2.467)</td>
</tr>
<tr>
<td>GATUS</td>
<td>0.650</td>
<td>1.916 (1.050-3.497)</td>
</tr>
<tr>
<td>GSD</td>
<td>0.664</td>
<td>0.515 (0.382-0.694)</td>
</tr>
<tr>
<td>CRL</td>
<td>1.272</td>
<td>0.280 (0.194-0.405)</td>
</tr>
<tr>
<td>EHR</td>
<td>1.719</td>
<td>0.179 (0.144-0.223)</td>
</tr>
<tr>
<td>YSD</td>
<td>0.632</td>
<td>0.532 (0.410-0.690)</td>
</tr>
<tr>
<td>Constant</td>
<td>7.339</td>
<td></td>
</tr>
</tbody>
</table>

### SUPPORT: The Science and Technology Project of the Health and Family Planning Commission of Hunan Province (No. C20180289) and the Citic-Xiangya Research Fund (No. KYX-M-201703).

---

**O-213 Wednesday, October 16, 2019 11:15 AM**

**THE IMPACT OF AGE BEYOND PLOIDY: OUTCOME DATA FROM 9,101 EUPLOID SINGLE EMBRYO TRANSFERS.** Andrea Reig, M.D., Richard Thomas Scott, Jr., MD, Emre Seli, M.D. Yale University - Bridgeport Hospital, Bridgeport, CT; IVI-RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: Rate of embryonic aneuploidy increases significantly with increasing female age and is the primary cause of lower pregnancy and live birth rates observed in older reproductive age women. This study evaluates single euploid embryo transfers to eliminate the impact of aneuploidy on reproductive efficiency. It then seeks to determine if an age-related decline in reproductive efficiency persists indicating that other factors may contribute to impaired outcomes in aging women.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 9,101 single embryo transfers that had undergone pre-implantation testing for aneuploidy (PGT-A) and cryopreservation were included. These were divided into five groups according to the age of the woman at the time of oocyte retrieval: <35 years old (n=4,858 embryos transferred), 35-37 years old (n=2,272), 38-40 years old (n=1,665), 41-42 years old (n=330), and ≥42 years old (n=249). Biochemical (positive serum ß-hCG 10 days after transfer), clinical (visualized gestational sac), and live birth rates were calculated for each group as percentage of embryos transferred into the uterus serosa (GATUS, 1.6% vs. 3.1%, p=0.001) and related clinical outcomes after individualized follicle-stimulating hormone (FSH) dosing versus fixed starting dosing of 150 IU FSH in women undergoing in vitro fertilization (IVF). The probability of EPL was: exp(β(1 + exp(β))), where x = 7.339 + (0.723 × MA) + (0.650 × GATUS) - (0.664 × GSD) - (1.272 × CRL) - (1.719 × EHR) - (0.632 × YSD).

Conclusions: The MA, GATUS and GSD, CRL, EHR, YSD on day 27-29 were the probability factors of EPL after IVF. The multinomial logistic model could be used to calculate the probability of EPL and thus, proper early treatment could be applied to the high-risk patients.

### Table: Outcomes of 9101 single euploid embryo transfers

<table>
<thead>
<tr>
<th>Age group</th>
<th>% of embryos transferred</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>81%</td>
</tr>
<tr>
<td>35-37</td>
<td>86%</td>
</tr>
<tr>
<td>38-40</td>
<td>95%</td>
</tr>
<tr>
<td>41-42</td>
<td>96%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>p value</th>
<th>Live birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.0001</td>
<td>0.0144</td>
</tr>
</tbody>
</table>

---

**O-216 Wednesday, October 16, 2019 11:00 AM**

**PREDECESSORS OF EARLY PREGNANCY LOSS FOR 7,261 INFERTILE PATIENTS AFTER IN-VITRO FERTILIZATION.** Yan Ouyang, MD./Ph.D.a, Xihong Li, MD./Ph.D.a, Yuyao Mao, Master,a Pei Cai, Master.b aReproductive and Genetic hospital of Citic-Xiangya, Changsha, China; bCentral South University, Changsha, China.

OBJECTIVE: Due to the patients undergo in vitro fertilization (IVF) have a high rate of early pregnancy loss (EPL), our study aims to investigate the predictors of EPL for those patients in order to facilitate early treatment for the high-risk patients.

DESIGN: Prospective study.

MATERIALS AND METHODS: All participants underwent IVF treatment at our reproductive center between January and December 2017. During this period, 7,286 women were identified with a singleton pregnancy by the first routine TVS at day 27-29 after IVF. The gestational sac diameter (GSD), crown-rump length (CRL), embryonic heart rate (EHR) and yolk sac diameter (YSD) were measured and recorded. Meanwhile, the clinical characteristics were also collected. The first trimester pregnancy outcome of these women was noted at 12 weeks of gestation. Twenty-five cases were lost at follow-up. There were 966 cases of spontaneous miscarriage ≤12 weeks of gestation, which were assigned as EPL. And 6,205 women with an ongoing pregnancy for >12 weeks of gestation. Multinomial logistic regression analysis was used to identify the probability predictive factors of EPL.

RESULTS: Compared with the ongoing pregnancy group, the maternal age (MA), duration of infertility and transfer cycle were significantly higher, and the day14 human chorionic gonadotrophin and the endometrium thickness on transfer day were significantly lower in the EPL group (P < 0.001).

In addition, the GSD (18.5±3.6 vs. 13.2±4.8 mm), CRL (3.5±0.9 vs. 1.2±1.6 mm) and YSD (3.6±0.4 vs. 2.6±1.5 mm) were significantly greater in the ongoing pregnancy group than the EPL group (P < 0.01). There was a higher likelihood of cardiac activity being present in the ongoing pregnancy group (99.2% vs. 39.0%, P < 0.001). However, the presence of intrauterine hematoma (16.0% vs. 18.8%, p = 0.026) and a gestation approximate to the uterine serosa (GATUS, 1.6% vs. 3.1%, p = 0.001) were detected more often in the EPL group.

Finally, GATUS, MA, GSD, CRL, EHR and YSD were identified by multinomial logistic regression model after stepwise screening. The multinomial logistic model could be used to calculate the probability of EPL and thus, proper early treatment could be applied to the high-risk patients.

### Table: Predictive factors of EPL

<table>
<thead>
<tr>
<th>Parameters</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MA</td>
<td>0.723</td>
</tr>
<tr>
<td>GATUS</td>
<td>0.650</td>
</tr>
<tr>
<td>GSD</td>
<td>0.664</td>
</tr>
<tr>
<td>CRL</td>
<td>1.272</td>
</tr>
<tr>
<td>EHR</td>
<td>1.719</td>
</tr>
<tr>
<td>YSD</td>
<td>0.632</td>
</tr>
<tr>
<td>Constant</td>
<td>7.339</td>
</tr>
</tbody>
</table>

SUPPORT: The Science and Technology Project of the Health and Family Planning Commission of Hunan Province (No. C20180289) and the Citic-Xiangya Research Fund (No. KYX-M-201703).
transferred, and then compared using a Chi-square for trend. Similarly, the clinical pregnancy rate was also analyzed for trend as a percentage of biochemical pregnancies, and the live birth rate as a percentage of clinical pregnancies, in order to detect at what stage increasing age has the greatest impact.

CONCLUSIONS: The implantation rate as a percentage of embryo transfers negatively correlated with oocyte age, with the percentage of embryos transferred ranging from 73.1% in the oldest group to 81.5% in the youngest (p<0.0001). This difference was consistent throughout clinical pregnancy rates (57.4% - 67.5%; p<0.0001), and live birth rates (50.5% - 58.5%; p=0.01). Interestingly, the proportion of clinical pregnancies which were lost did not change with age, strongly suggesting that factors contributing to decline in reproductive potential with age have their impact prior to the establishment of a clinical pregnancy.

CONCLUSIONS: Age-related diminution in reproductive efficiency is largely overcome by selection of euploid embryos for transfer. However, an age-related decrease in implantation, clinical pregnancy, and live birth rates persists indicating that aneuploidy is not the only factor contributing to reproductive senescence. The additional factors, which remain to be defined, seem to impact the reproductive process prior to implantation as the inability of progressing to delivery after implantation was not impacted by age.

O-214 Wednesday, October 16, 2019 11:30 AM
THREE-DIMENSIONAL ULTRASOUND DIAGNOSIS OF ADENOMYSOSIS IS NOT ASSOCIATED WITH DIMINISHED LIVE BIRTH FOLLOWING SINGLE-THAWED EUPOLOID BLASTOCYST TRANSFER: A PROSPECTIVE COHORT STUDY. Shelby A. Neal, MD, a Scott J. Morin, MD, a Marie D. Werner, MD, a Ndeye-Aicha Gueye, MD, a Paul Pirtea, MD, a George Patounakis, MD, PhD, a Richard Thomas Scott, Jr, MD, a Linnea R. Goodman, MD, a IVI-RMA New Jersey, Basking Ridge, NJ; IVI-RMA Northern California, San Francisco, CA; IVI-RMA Pennsylvania, Allentown, PA; IVI-RMA Florida, Lake Mary, FL; 'University of North Carolina, Raleigh, NC.

OBJECTIVE: To evaluate the impact of adenomyosis, diagnosed using three-dimensional ultrasound (3D US), on pregnancy outcomes following single thawed euploid blastocyst transfer.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Patients planning to undergo a single thawed blastocyst transfer between April and December 2017 at a large IVF center were eligible for inclusion. Exclusion criteria were body mass index ≥ 40 kg/m², uterine anomalies, history of myomectomy, use of a gestational carrier, and communicating hydrosalpinx. Consenting patients underwent endometrial preparation according to a standardized protocol. On the day prior to embryo transfer, 3D US was performed and images were analyzed for adenomyosis. Subjects with adenomyosis and those without adenomyosis were linked to the Massachusetts Cancer Registry. Main outcomes of interest were treatment patterns, number of oocytes retrieved, number of oocytes fertilized with or without ICSI, number of embryos transferred, implantation rates, and clinical intrauterine gestation (CIG). We used generalized estimating equations to account for multiple pregnancies per woman with a log link and a Poisson distribution to estimate relative risks (RR) and 95% confidence intervals (CI) a priori adjusted for maternal age and cycle year. To investigate mechanism of association, we stratified by autologous/donor gametes and compared autologous embryo quality between women with and without cancer history.

RESULTS: Among women who utilized ART, 587 (1,273 ART cycles) were childhood and young-adult cancer survivors. In crude models, women cancer survivors undergoing ART were more likely to use donor gametes (RR:1.27 (1.01-1.61)) compared to women with no history of cancer, although this attenuated after adjustment for age and cycle year (RR:1.04 (0.82-1.30)). We saw no difference in number of oocytes retrieved (RR:1.02 (0.96-1.09)) or proportion of oocytes fertilized (RR:0.97 (0.94-1.01)) between autologous cycles with and without a history of cancer, however cancer survivors had higher total FSH administered (3735.9 IU/mL; RR:1.14 (1.09-1.19)) compared to cycles with no history of cancer (3362.2 IU/mL). Among autologous cycles, cycles to women with a history of cancer were less likely to result in CIG (RR:0.71 (0.64-0.78)) compared to cycles without a history of cancer; this relationship was strongest among autologous cycles (RR:0.64 (0.57-0.72)) but absent from donor cycles (RR:1.06 (0.91-1.23)). When restricted to cycles with embryos transferred, there was no difference in CIG between cycles with and without a history of cancer (RR:0.98 (0.90-1.08)). Among autologous single embryo transfers, no significant difference was seen in the proportion of good quality embryos transferred at the cleavage (RR:1.13 (0.91-1.42)) or blastocyst (RR:1.20 (0.98-1.47)) stage in cancer survivors compared to women with no history of cancer.

CONCLUSIONS: Cancer survivors may require more FSH and potentially different ART protocols compared to women with no history of cancer. Our analyses further suggest that cancer may influence ovarian stimulation response, given that autologous cycles to cancer survivors were less likely to result in CIG among cycle starts but not among embryo transfers. Future studies should investigate stimulation protocols to maximize successful implantation and CIG among women starting ART cycles who have a history of cancer.

SUPPORT: NIH R01HD067270.

O-216 Wednesday, October 16, 2019 12:00 PM
ENDOMETRIAL COMPACTION (DECREASED THICKNESS) IN RESPONSE TO PROGESTERONE RESULTS IN HIGHER ONGOING PREGNANCY RATE. Eran Zilberberg, M.D., a Dan Nayot, M.D., b Ramsey Genco Smith, B.Sc., a James Meriano, M.Sc., a Eran Barzilay, M.D. Ph.D., a Jigal Haas, M.D., a Robert F. Casper, M.D. b Trio Fertility, Toronto, ON, Canada; bTRIO Fertility, Staff Physician, Toronto, ON, Canada; bTRIO Fertility, Toronto, ON, Canada; aDepartment of Obstetrics and Gynecology, Samson Assuta Ashdod University Hospital, Ashdod, Israel;
OBJECTIVE: For a pregnancy to occur, implantation of an embryo into a receptive endometrium is crucial. There are few methods to reliably assess the receptivity of the endometrium during an in-vitro fertilization (IVF) cycle. Some methods are invasive such as endometrial biopsy for histologic dating or for the Endometrial Receptivity Array (ERA) and cannot be done in the cycle of interest. Other non invasive methods that can be performed in the treatment cycle include ultrasound (US) for endometrial pattern & thickness or for sub-endometrial waves. We have previously shown a significant increase in ongoing pregnancy if the endometrium became thinner (compacted) during the progesterone phase in hormonally replaced (HRT) frozen embryo transfer (FET) cycles with untested embryos. The objective of the present study was to evaluate whether endometrial compaction was also associated with improved ongoing pregnancy rates in fresh IVF cycles and in FET cycles involving euploid embryos after preimplantation genetic testing for aneuploidies (PGT-A).

DESIGN: A retrospective observational cohort study.

MATERIALS AND METHODS: We retrospectively evaluated cycles from 3 cohorts: 271 HRT cycles with untested single blastocyst FET, 250 HRT single FET cycles of euploid embryos, after PGT-A, and 370 cycles of single fresh embryo transfers after controlled ovarian hyperstimulation. We evaluated recorded digital US images of the endometrium using imaging software and measured endometrial thickness. We calculated the change in endometrial thickness from the end of the estrogen stage/trigger day to the day of embryo transfer. We divided the patients into two groups: 1) cycles with a compaction rate of 10% or greater; 2) cycles with no change or an increase in thickness. The primary outcome was ongoing pregnancy defined as visualization of fetal cardiac activity at 12 weeks gestation or later.

RESULTS: Similar to our previous findings in HRT cycles with untested single blastocyst transfers, we found a significantly higher ongoing pregnancy rate in the euploid embryo cohort and in the fresh embryo transfer cohort with a 10% or greater compaction of the endometrial lining thickness.

Ongoing pregnancy:

<table>
<thead>
<tr>
<th># of cycles</th>
<th>Compacted</th>
<th>Not Compacted</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frozen Embryo Transfer</td>
<td>271</td>
<td>43/83</td>
<td>45/188</td>
</tr>
<tr>
<td>Euploid embryo FET</td>
<td>250</td>
<td>47/99</td>
<td>49/151</td>
</tr>
<tr>
<td>Fresh Transfers</td>
<td>370</td>
<td>52/130</td>
<td>61/240</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Compaction of the endometrial lining results in a better ongoing pregnancy rates in FET cycles with euploid embryos and in fresh embryo transfers. Our results suggest that an US measurement in the estrogen phase and again in the progesterone phase demonstrating endometrial compaction may be a new non-invasive determinant of endometrial receptivity in IVF cycles.

MALE FACTOR

O-217 Wednesday, October 16, 2019 10:45 AM

A MICROFLUIDIC SPERM-SORTING DEVICE REDUCES THE PROPORTION OF SPERM WITH DOUBLE STRAND DNA FRAGMENTATION.

Aida Pujol Masana, PhD,a Agustín García-Peiró, Sr., PhD,b Rafael Lafuente, PhD,c Karinna Lattes, MD, MSc,d Rita Vassena, DVM, PhD,e Daniel Mataró, MD, PhD,f CIRH (Centro de Infertilidad y reproducción Humana), Barcelona, Spain; fClinica EUGIN, Barcelona, Spain; gAffiliation not provided.; hCIRH (Centro de Infertilidad y Reproducción Humana), Barcelona, Spain; iClinica EUGIN, Barcelona, Spain.

OBJECTIVE: To determine whether the use of the microfluidic sperm sorting device Fertile Chip diminishes the proportion of sperm with double strand DNA fragmentation (dsSDF) compared to swim up.

DESIGN: This is a matched cohort study of samples from nine patients. All were diagnosed with 60% or more dsSDF in their spermatozoa, as assessed by a neutral COMET. The study was approved by the local IRB. The number of patients included was calculated to detect a difference of 20% in the proportion of dsSDF between study groups, with an alpha risk of 0.05 and a beta risk of 0.05.

MATERIALS AND METHODS: One semen sample of each participant was collected for the study. After a basic sperm analysis, a part was frozen and a part was split into two further aliquots; one aliquot was processed using Fertile Chip and then frozen, and the other was processed using swim up and then also frozen. The three frozen aliquots were analysed by neutral COMET assay for the detection of dsSDF.

RESULTS: The nine patients included in the study had a mean age of 38.9 years (range 34 – 53) and their mean BMI was 26.78 kg/m² (range: 20.9 – 32.84). Five of them had a history of miscarriage (range: 1-7). Their basic semen characteristics were: the mean volume was 2.88 ml (range: 1-4); the mean concentration was 94.13 M/ml (range 5.98 - 321.4) and the mean percentage of motile sperm (+b forms) was 37.77% (range 20.9 – 59.8). Processing semen samples using swim up did not change the percentage of spermatozoa with dsSDF (64.8% in the raw samples and 65.1% post swim up). On the other hand, microfluidic sorting of the fresh semen sample using Fertile Chip lowered the percentage of dsSDF to 34.9%; a reduction of 45.2% (p<0.001).

CONCLUSIONS: The selection of spermatozoa using Fertile Chip diminishes significantly the percentage of spermatozoa with dsSDF, either compared to the fresh ejaculate or after swim up. Fertile Chip can be used in patients with a high proportion of spermatozoa carrying dsSDF to perform ICSI. Although this study did not evaluate reproductive results, it is reasonable to expect an improvement of clinical variables in this kind of patients.

SUPPORT: None.

O-218 Wednesday, October 16, 2019 11:00 AM

A STEP TOWARDS THE AUTOMATION OF INTRACYTOPLASMIC SPERM INJECTION (ICSI): REAL TIME CONFIRMATION OF OOCYTE PENETRATION BY ELECTRICAL RESISTANCE REAL TIME CONFIRMATION OF OOCYTE PENETRATION BY ELECTRICAL RESISTANCE

Amir Mor, MD PhD,a,b Man Zhang, MD, Ph.D.a,c Eemc Esencan, M.D.d Burcin Simsek, Ph.D.,e Stephanie M. Nichols-Burns, Ph.D.d, Yifei Liu, Ph.D.b, Jonathan Lo, MSc.f Dawn A. Kelk, Ph.D., HCILD.g Xiao-Bing Gao, PhD.h Emre Selç, M.D.i Yale School of Medicine, New Haven, CT; jUniversity of Pittsburgh, Pittsburgh, PA; kYale University, New Haven, CT.

OBJECTIVE: Automated (robotic) intracytoplasmic sperm injection (ICSI) requires confirmation of plasmatic membrane penetration. Visual assessment using image processing algorithms have been developed but remain unreliable. We hypothesized that an increase in electrical resistance upon oocyte plasmatic membrane piercing during ICSI can serve as an objective tool to confirm oocyte penetration.

DESIGN: Experimental study.

MATERIALS AND METHODS: Oocyte membrane piercing with the ICSI pipette was performed by advancing the pipette towards mature (metaphase II) oocytes collected from 6 to 12-week-old mice and immature (germinal vesicle stage and metaphase I) oocytes donated by women who underwent oocyte retrieval. Electrical resistance at the ICSI pipette tip was measured using a conventional electrophysiological setup that includes an electrical resistance meter and two electrical wires located in the lumens of the holding and ICSI pipettes. Our mouse experiments included four groups: a study group, two negative and one positive penetration control groups. In the study group, egg penetration was determined visually by three investigators through 2D light microscopy. The first negative penetration control group consisted of oocytes that were not perforated. In the second negative control group, the ICSI pipette tip was advanced to the perivitelline space and the absence of oocyte penetration was confirmed by applying fluid pressure to demonstrate oocyte compression and zona pellucida expansion. In the positive penetration control group, the plasmatic membrane was ruptured after the application of pressure through the pipette tip (confirming that the tip was inside the egg and not in the perivitelline space). A biopsy oocyte experiment included two groups: non-viable (germinal vesicle normal (viable) and fragmented (non-viable) oocytes, as determined visually by two investigators through 2D light microscopy. In all experiments, median resistance changes and their ranges were calculated.

RESULTS: In mouse oocytes, significant electrical resistance (R in MΩ) increases were detected in all positive penetration control group cases (n=11). ΔR = 8.2 (3.0 – 106.0), P < 0.001. In these cases, rupturing the
membrane, by positive pressure, led to an immediate resistance drop to around the extracellular resistance values. In the two negative penetration control groups (n=19), no significant resistance changes were detected. In the study group (n=45), resistance increase was detected after visual observation for 10 min; ΔR = 6.5 ± 1.7 (0.1 – 191.7), P < 0.001. In human oocytes, a marked increase in resistance was observed in all visually normal (viable) oocytes (n=28); ΔR = 2.2 (0.9 - 6.7), P < 0.001. In the fragmented/non-viable oocytes (n=6), no significant change in resistance was detected.

CONCLUSIONS: An electrical resistance increase can serve as a reliable tool to confirm oocyte penetration, independent of optical visualization. Following further validation and safety assessment, this technology can potentially be integrated into manual or robotic ICIS systems.


O-219 Wednesday, October 16, 2019 11:15 AM

SIMPLE VITRIFICATION OF A SMALL NUMBER OF TESTICULAR SPERMATOZOA USING RAPID-I CARRIERS IN NON-OBSTRUCTIVE AZOSPERMIA. Yozo Nagao, MS, Keiko Tanaka, MS, Hitomi Osubo, BS, Shigetoshi Mizumoto, PhD., Takeshi Kurasaki, M.D., Ph.D., Masao Murakami, PhD. KURAMOTO Women’s Clinic, Fukuoka, Japan.

OBJECTIVE: Testicular sperm extraction (TESE) combined with ICSI has made biological fatherhood possible for many men with non-obstructive azospermia (NOA), the most severe form of male infertility. For the men with a limited number of testicular spermatozoa, efficient sperm storage is crucial to avoid complications related to repeated TESEs in cases of failed ICSI cycles. However, reports on ideal carriers and techniques for cryopreservation of spermatozoa in azoospermic men have been rarely reported. Therefore, the aim of this study is to evaluate the sperm viability and penetration rate of cryo-vitrification of a small number of spermatozoa using Rapid-i carriers (ESHRE 2011) was evaluated for men with NOA and a small number of testicular spermatozoa.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Vitrification of a small number of spermatozoa was performed for 14 men with NOA following conventional (3 men) or micro-dissection (11 men) TESE from February 2012 to January 2019. Vitrification was performed by 1-10 spermatozoa were aspirated into an ICSI pipette and added to 1.5 μL of cryoprotective solution (K-SISC, Cook Medical) on a Rapid-i carrier strip (Vitrilife), which was placed in LN₂ vapor (2 min), inserted into a pre-cooled LND salmon sperm cryopreservation medium with rapid freezing of sperms in glycerol and to survey the effect of cryo-vitrification in azoospermic men with NOA and a small number of testicular spermatozoa.

RESULTS: In total, 409 spermatozoa (78% motile) were vitrified. The average number of vitrified spermatozoa per patient was 29.2 ± 3.4. During ICSI (22 cycles), 219 spermatozoa were warmed; the sperm recovery rate was 87%. The average number of warmed spermatozoa per patient was 11.9 ± 1.8. The motile sperm rate per recovered spermatozoa was 49%. The fertilization rate was 31%. Of the warmed ET cycles (17 cycles), clinical pregnancy rate per ET, live delivery rate per ET (not including 2 ongoing pregnancies), and miscarriage rate per pregnancy were 41%, 18%, and 29%, respectively.

CONCLUSIONS: In this study, we report 87% sperm recovery rate and the first successful use of warmed spermatozoa for ICSI-ET with our modification of the Rapid-i protocol in men with NOA and a small number of spermatozoa following TESE. Our approach shortens the laborious and time-consuming search for warmed individual spermatozoa from hours to minutes. Thus, in addition to avoiding repeated TESEs, this method may provide benefits in men with a small number of spermatozoa, such as improving ICSI outcomes and avoiding the risk of finding no sperm on the day of oocyte retrieval. Although NOA is relatively rare in the overall population, follow-up studies with a larger cohort are warranted to validate the efficacy of the approach.

O-220 Wednesday, October 16, 2019 11:30 AM

COMPARISON OF CRYOPROTECTANT FREE VITRIFICATION OF HUMAN SPERMATOZOA IN A NEW SEMEN SIMULANT WITH RAPID FREEZE OF SPERMATOZOA IN GLYCEROL. Soundarya Janani Senthil Kumar, MBBS, M.Sc. N. Sanjeeva Reddy, MD (Obstetrics and Gynaecology), DGO; Manjula Daniel G, PhD; Sridhara Namboori Srinivasan, MBBS, M.Sc Clinical Embryology, PhD Research Scholar. 1. Clinical Embryology Sri Ramachandra Institute of Higher Education and Research, Chennai, India; 2. Professor and Head, Department of Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, India; 3. Assistant Professor, Department of Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, India; 4. Lecturer, Department of Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, India.

OBJECTIVE: Seminal fluid contains materials with cryoprotectant properties. However, ROS and free radicals generated by the spermatozoa and seminal leukocytes within the seminal fluid may have a detrimental role in the protection of spermatozoa during cryopreservation. The purpose of this study was to formulate a new medium simulating the seminal fluid and to compare the effects of vitrification of spermatozoa in the newly prepared semen simulant medium with rapid freezing of sperms in glycerol and to survey the effect of cryo-vitrification over cryopreservation of spermatozoa.

RESULTS: In total, 409 spermatozoa (78% motile) were vitrified. The average number of vitrified spermatozoa per patient was 29.2 ± 3.4. During ICSI (22 cycles), 219 spermatozoa were warmed; the sperm recovery rate was 87%. The average number of warmed spermatozoa per patient was 11.9 ± 1.8. The motile sperm rate per recovered spermatozoa was 49%. The fertilization rate was 31%. Of the warmed ET cycles (17 cycles), clinical pregnancy rate per ET, live delivery rate per ET (not including 2 ongoing pregnancies), and miscarriage rate per pregnancy were 41%, 18%, and 29%, respectively.

CONCLUSIONS: The total motility, viability and the sperm chromatin integrity was comparatively better in the sperms vitrified in the semen simulant. The current work assumes that the main cause of damage in the rapid freezing group was osmotic shock, because it requires cryoprotective agent (CPA). On the other hand, CPA was not used in vitrification and the speed of cooling is high, avoiding extracellular ice formation. In conclusion, vitrification in the semen simulant medium has great potential for human sperm cryopreservation and does not require CPA. Due to the cost effectiveness and inhouse preparation, vitrification in the semen simulant could be an effective alternative for commercial media.

O-221 Wednesday, October 16, 2019 11:45 AM

SURGICAL SPERM EXTRACTION VS. SEMEN CENTRIFUGATION: METHOD OF SPERMATOZOA RECOVERY DOES NOT CORRELATE WITH EUPLOIDY RATES IN PATIENTS WITH CRYPTOZOSPERMIA. Carlos Hernandez-Nieto, MD. Joseph A. Lee, BA; Martha Luna-Rojas, MD; Tamar Alkon, MD; Christine Britton-Jones, PhD, HCLD; Natan Bar-Chama, MD; Alan B. Copperman, MD; Benjamin Sandler, MD. Reproductive
OBJECTIVE: Cryptozoospermia is defined as spermatozoa not identified in the ejaculate, but observed in pellet following centrifugation (World Health Organization). Fertility specialists differ in opinion whether there might be benefits to surgically retrieving sperm in these patients. Previous studies have described a correlation between testicular extracted sperm and spermatic aneuploidy in patients with non-obstructive azospermia (1). However, there are currently no peer reviewed publications associating rates of embryonic ploidy with Cryptozoospermia. The aim of this study was to evaluate the rate of embryonic euploidy in blastocysts derived from testicular versus ejaculated sperm in cryptozoospermic patients.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: The study included couples who suffer from Cryptozoospermia and underwent an autologous IVF cycle(s) with pre-implantation genetic testing (PGT-A) from 2014 to 2019. Only cases where oocyte insemination was conducted with intra-cytoplasmic sperm injection (ICSI) were evaluated. Cohorts were separated based on the source of sperm (Ejaculated vs. Testicular (Tese)). Demographic and clinical embryology parameters were compared. Student’s t-test, Wilcoxon rank test, chi-square test, and multivariate logistic regression models were used for data analysis.

RESULTS: Of the 87 IVF/PGT-A cases on cryptozoospermia patients (mean age, 34.4 years; 74 cases (n= 47, blastocysts) utilized ejaculated sperm while 13 cases (n = 99 blastocysts) utilized testicular sperm. No significant differences were found in demographic and stimulation parameters among cohorts. No differences between the ejaculated and testicular cohorts were found in fertilization (63.2%; 61.1%, p=0.32); blastulation (64.5%; 66.6%, p=0.69); and rate of embryo euploidy (49.7%; 51.2%, p=0.76) respectively. No differences were found in rate of cycle cancellation due to unavailable embryos for TE biopsy (18.9% vs 7.6%, p=0.32). After adjusting for female and male age, BMI, AMH, and number of biopsied embryos, there were no association with utilizing surgical extracted sperm and lower odds of embryo euploidy (OR 0.69, CI 95% 0.11-4.3, p=0.69).

CONCLUSIONS: Normal chromosomal composition is a primary driver of embryonic competence and reproductive success in patients undergoing ART. In our review of the literature, this is the first study analyzing the euploidy rate on a large cohort of embryos in patients with Cryptozoospermia. Our data demonstrate that the odds of the resulting embryo being euploid is not associated with the source of sperm recovery. Regardless of the method of collection, a number of researchers have raised concerns about genetic and epigenetic risks of utilizing sperm cells prone to increased DNA integrity damage or exposed to different environmental factors (i.e. free oxygen radicals). Our study findings show that there is no genomic advantage to surgical sperm retrieval in cryptozoospermic patients. These data can be used to counsel patients who suffer from cryptozoospermia about the potential chromosomal composition of their embryos.


O-222 Wednesday, October 16, 2019 12:00 PM


OBJECTIVE: To map the level of sperm chromatin fragmentation (SCF) at different areas of the male genital tract.

DESIGN: Male partners from consenting couples had their ejaculated specimens screened for SCF with a commercially available kit. ICSI clinical outcomes were compared between those with normal and abnormal levels of SCF.

Men with abnormal SCF had the option to undergo spermatozoa retrieval from the vas deferens, epididymis, and testes to be concurrently screened for SCF.

Clinical outcomes were compared between the ejaculated and surgically retrieved (SR) spermatozoa. Encouraged by these results, men with ICSI-failed and high SCF in their ejaculate agreed to undergo surgical spermatozoa retrieval and ICSI at our center, and the results were compared to their historical ejaculated cycles.

MATERIALS AND METHODS: SCF levels were assessed by terminal deoxynucleotidyl dUTP nick-end labeling (TUNEL). A threshold of <15% was considered normal, with at least 500 spermatozoa assessed per patient. ICSI was performed in the standard fashion, and the outcome was recorded.

RESULTS: A total of 200 couples underwent 439 ICSI cycles utilizing spermatozoa with normal SCF. When these outcomes were compared with those from 122 couples who underwent 278 ICSI cycles utilizing spermatozoa with abnormal SCF (9.3±3.8 vs. 22.6±9.9%; P < 0.01), the results demonstrated that high SCF hindered implantation rates (P < 0.05).

Topographical mapping through the male genital tract showed that SCF was 20.4±9.6% in the vas deferens, 15.8±7.7% in the epididymis, and 11.4±5.7% in the testis, which was much lower compared to the ejaculated control (32.9±20%; P < 0.05).

Couples (n=25) who underwent ICSI with SR spermatozoa had lower SCF (P < 0.0001) and higher implantation, clinical pregnancy (CP), and delivery rates (P < 0.05). Epididymal spermatozoa performance was superior to both ejaculated and testicular sperm for implantation, CP, and delivery rates (P < 0.01).

Finally, couples (n=45) with a history at other medical institutions of ICSI failure with ejaculated spermatozoa were treated solely with SR spermatozoa at our center. When compared to the historical cycles, SR spermatozoa had lower fertilization rates (P < 0.05) but enhanced implantation (19.1%), CP (40.0%), and delivery rates (34.3%; P < 0.01), with epididymal spermatozoa performing even better (P < 0.001).

CONCLUSIONS: For the first time, we have demonstrated that SCF increases progressively through the testicle, to the epididymis, the vas deferens, and is highest in the ejaculate. Reproductive physicians can guide their patients toward the use of SR spermatozoa, which can enhance the success of reproductive treatments.

MALE REPRODUCTION AND UROLOGY: RESEARCH

A NOVEL MOUSE MODEL TO INVESTIGATE PLACEMENT, PROCESSING AND REMOVAL OF SPERM PROTAMINES. Samantha B. Schon, MD, MTR, a Lindsay Moritz, BS, b Sue Hammoud, Ph.D. a aUniversity of Michigan, Ann Arbor, MI; bUniversity of Michigan, Cellular and Molecular Biology Graduate Program, Ann Arbor, MI.

OBJECTIVE: Protamines, consisting of protamine 1 (P1) and protamine 2 (P2) are essential for packaging paternal DNA into the sperm nucleus. Proper histone-to-protamine exchange is critical for normal fertility with aberrations in this process associated with infertility, altered semen parameters, decreased fertilization rates in couples undergoing IVF and even decreased pregnancy rates. Despite their critical importance, our understanding of the mechanism by which protamines are processed, placed or removed from DNA remains poorly understood due to the unavailability and/or unreliability of commercially available antibodies. To circumvent these limitations, the objective of our study was to generate a novel mouse model with the endogenous P2 loci epitope-tagged and to identify novel interacting proteins to gain insight into P2 placement, processing and removal.

DESIGN: Laboratory experiments utilizing transgenic murine testes and sperm.

MATERIALS AND METHODS: Epitope-tagged P2 mice were generated via CRISPR/Cas9. Incorporation of two tags was validated with western blot and immunofluorescence (IF). Phenotypic and fertility assessments were performed using tests and epididymal weights, sperm counts, motility assessment and breeding trials. Immunoprecipitation followed by mass spectrometry (IP-MS) from whole testes using both transgenic (P2ΔΔT) and wild-type control mice was performed for identification of interacting proteins. Newly identified proteins were validated via reciprocal IP-MS, western blot and IF.

RESULTS: We demonstrate successful incorporation of both of the two tags in sperm. P2ΔΔT and P2ΔΔT mice are fertile with normal litter size and fertility parameters. IP-MS revealed over 500 interacting proteins,
number of which have been validated and are known to have enzymatic or chaperone/chromatin remodeling roles in other cell types.

CONCLUSIONS: We have successfully generated an epitope-tagged protamine 2 transgenic mouse. Through IP-MS we have further identified a number of candidate interacting proteins. Future studies will focus on continued validation of these proteins and investigation of their specific functions. This work is critical to elucidating the currently unknown mechanism by which protamines are placed, processed and removed in both sperm and the early embryo.

SUPPORT: 5K12HD065257-07 (SBS) and 1DP2HD091949-01 (SSH).

O-224 Wednesday, October 16, 2019 11:00 AM

POLYMORPHISMS IN THE HUMAN PRDM9 GENE MAY LEAD TO MEIOTIC ARREST AND AZOOSPERMIA. M. Blake Evans, DO, Sherry Ralls, BA, Mohamed Mahgoub Mohamed, MD, PhD, Alan H. DeCherney, MD, Todd Macfarlan, PhD NIH-NICHD, Bethesda, MD.

OBJECTIVE: PRDM9 is responsible for directing the location of programmed double strand breaks and subsequent crossover events between homologous chromosomes during meiosis in human gametes. Prdm9 is also essential for meiosis and fertility in mice, with PRDM9 knockout males displaying complete azoospermia. PRDM9 contains a rapidly evolving DNA binding zinc finger array that is coded by a ~84 nucleotide repeating unit mini-satellite sequence. The human A-type allele, which accounts for ~90% of the alleles in the human population, contains 1-3 repeating units. We sought to develop a strategy to effectively genotype this mini-satellite with PacBio sequencing and to determine whether PRDM9 variation, including mini-satellite length polymorphisms, is associated with infertility in the human male.

DESIGN: Observational study.

MATERIALS AND METHODS: Using a normalspermic human control, a two-step polymerase chain reaction (PCR) protocol was established to successfully amplify the PRDM9 zinc finger array mini-satellite and sequence it using both Sanger and PacBio next generation sequencing, which has the advantage of circular consensus sequencing and long reads. We next amplified PRDM9 from the genomic DNA of 48 azoospermic men and 5 controls. The samples were visually analyzed with gel electrophoresis, and potential mutant alleles that had an atypical band appearance were compared to the wild type.

RESULTS: PacBio sequencing results from the normalspermic control were found to be an identical match to the known human A allele, confirming our ability to effectively genotype the mini-satellite array in a single PacBio run. Gel electrophoresis of PCR amplified PRDM9 alleles from azoospermic men identified 6 potential mutant variants of distinct mini-satellite lengths differing from the A-allele.

CONCLUSIONS: We have developed a protocol to effectively genotype the human PRDM9 zinc finger array mini-satellite to evaluate a potential etiology of azoospermia in the infertile human male. We found 6 potential PRDM9 alleles differing from the known A-allele in a small (n=48) azoospermia cohort. Current/ongoing research includes applying our PacBio sequencing protocol to genotype all 48 azoospermic men in comparison to a control group and evaluate if there is an association between PRDM9 mini-satellite repeat length, polymorphisms, or de novo mutations and azoospermia.

O-225 Wednesday, October 16, 2019 11:15 AM

A RANDOMIZED CONTROLLED ANIMAL TRIAL: EF-FICACY OF A 4K3D VIDEO MICROSCOPE VERSUS AN OPTICAL OPERATING MICROSCOPE FOR URO-LOGIC MICROSURGERY. Russell P. Hayden, MD, a Huixing Chen, MD, a Marc Goldstein, MD, a Philip S. S. Li, MD, a Weil Cornell Medicine, New York, NY; aWeill Cornell Medicine, New York Presby-terian Hospital, New York, NY; aWeill Cornell Medical College, New York, NY.

OBJECTIVE: Operating microscopes continue to use classical optics to provide magnification whereas video microscopy utilizes an image sensor and video monitors. Early video microscopes lacked the technology to produce a comparable experience to optic-based systems. Modern 4K3D video surgical systems can theoretically outperform traditional optics in flexibility, working depth and user ergonomics. We conducted a randomized controlled trial in rats comparing the efficacy and safety of a 4K3D video microscope to a traditional operating microscope.

DESIGN: Randomized controlled animal trial.

MATERIALS AND METHODS: The FDA approved ORBEye surgical platform (Olympus/Sony), which provides 4K3D video images via light-weight eyewear, was compared to a traditional operating microscope (S3, Zeiss). Male Wistar rats weighing 250 - 357 gm were used. Each rat underwent vasovasostomy (VV) and vasoepididymostomy (VE) with a single-armed needle microsurgical technique, with laterality defined by coin toss. 16 animals were randomized just prior to incision to either operating microscope. An additional eight rats were used as shams, and another 2 were used for initial training on the ORBEye. All animals were euthanized 6 weeks post-op. Operating time per anastomosis, patency, and sperm granuloma formation were compared for each arm. Prism v7 (GraphPad Software) was used for statistical analysis.

RESULTS: 23 rats survived to week-6 post-op. VV patency rates were 57.1% and 62.5% (p = 0.9) for the S3 and ORBEye, respectively. VE patency rates were 87.5% and 75% (p = 0.9) for the S3 and ORBEye, respectively. There was no statistical difference in granuloma formation for either VV (p = 0.9) or VE (p = 0.6). Granuloma size did not differ significantly for VV (S3 7mm vs. ORBEye 10mm, p = 0.3) or for VE (2mm vs. 7mm, p = 0.2). Anastomosis time was not different between the two microscopes (VV: S3 31min vs. ORBEye 36.5min, p = 0.2; VE: 29min vs. 33min, p = 0.1).

CONCLUSIONS: Using a well-established microsurgery training model, performance of the ORBEye did not differ from a traditional operating microscope in terms of patency, granuloma formation, or operative time. Based on this data, the ORBEye appears to be noninferior for urologic microsurgery procedures. The system can be applied to microsurgery in any specialty. Further study is warranted to substantiate these results and to assess for meaningful differences in working depth and user ergonomics.

SUPPORT: The ORBEye was provided on loan from the Olympus Corporation of America.

O-226 Wednesday, October 16, 2019 11:30 AM

MALE PARTNER AGE AND THE RISK OF ISCHEMIC PLACENTAL DISEASE IN AUTOLOGOUS IVF PREGNANCIES. Anna Merport Modest, PhD, MPhil, Ai-ris Y. Collier, MD, Emily A. Seidler, MD, Laura E. Dodge, ScD, MPhil. aBeth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA; bBoston IVF; cBeth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA.

OBJECTIVE: Advanced paternal age has been extensively studied and is a known risk factor for adverse pregnancy outcomes including ischemic placental disease (IPD), defined as the obstetrical diagnosis of preeclampsia, small for gestational age (SGA), or placental abruption. Advancing paternal age has been associated with decreased fecundity, early pregnancy loss, and adverse outcomes for the offspring; however, little is known about the impact of age has been associated with decreased fecundity, early pregnancy loss, and adverse outcomes for the offspring; however, little is known about the impact of advanced paternal age on IPD. Our objective was to evaluate the association between male partner age and the risk of IPD among pregnancies 20 weeks of gestation or greater.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We identified all deliveries from January 1, 2004 to December 31, 2013 at a tertiary hospital that resulted from autologous in vitro fertilization (IVF) cycles. Cycles using donor sperm were excluded. Male partner age at the time of oocyte retrieval was categorized as <30, 30-<35, 35-<40, and 40 years or older. Couples whose male partner was 30-<35 was used as the reference group. IPD was defined as preeclamp-sia, placental abruption, SGA, or intrauterine fetal demise due to placental insufficiency. We identified pregnancies complicated by preeclampsia or placental abruption using ICD-9 codes and medical record review. We defined SGA as <10th percentile using gestational age and sex-adjusted U.S. growth curves. All IUFDS were reviewed in the medical record to determine the cause, if known. We used log-binomial regression and generalized estimating equations with an independent correlation matrix to estimate risk ratios (RR) and 95% confidence intervals (CI), accounting for multiple
pregnancies per woman. All models were adjusted for maternal age, paternal age, year of delivery, cycle number, and nulliparity.

RESULTS: We identified 1,133 deliveries from 1,023 couples. The overall incidence of IPD was 26.4%. The risk of IPD was similar across categories of male age (range: 23.0-29.4%). When compared to couples with a male partner 30–<35 years of age, the risk of IPD was 0.72 (95% CI 0.43-1.2) in the male age 30<35 group, 0.89 (95% CI 0.65-1.2) in the male age 35–<40 group, and 1.1 (95% CI 0.60-1.9) in the male age 40+ group. When evaluating subgroups of IPD, compared to couples whose male partner was 30–<35, deliveries from couples whose male partner was <30 had a lower risk of SGA (RR 0.28, 95% CI 0.10-0.76). The risk of the other individual components of IPD was similar in all of the male partner age categories.

CONCLUSIONS: There is no association between male partner age and the risk of IPD; however, the risk of SGA is lower in the youngest male age category. Larger studies are needed to confirm these findings.

O-227 Wednesday, October 16, 2019 11:45 AM

EVALUATION OF SPERM PROTEOME IN CANCER PATIENTS PRIOR TO TREATMENT. Manesh Kumar Panner Selvam, PhD,1 Ashok Agarwal, PhD,2 Peter Natesan Pushparaj, PhD,3 American Center for Reproductive Medicine, Cleveland Clinic, Cleveland, OH; Center of Excellence in Genomic Medicine, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah, Saudi Arabia.

OBJECTIVE: Cancer has an adverse effect on sperm health. Conventional semen analysis does not explain the fertility status of cancer patients. Currently, proteomics is being used as a powerful tool to identify the fertility associated molecular pathways affected in spermatozoa. The objective of this study was to evaluate the sperm proteome of cancer patients compared with healthy fertile men and infertile men.

DESIGN: Cryopreserved semen samples of cancer patients before starting cancer therapy were used in the current study. Type of cancer patients included were: Testicular cancer (n=28), Hodgkin’s disease (n=20), Lymphoma (n=8) and Leukemia (n=5). Pooled samples from the cancer patients were used for proteomic analysis. The proteome of cancer group, was compared with fertile men (n=7) and infertile men (n=9).

MATERIALS AND METHODS: Proteomic profiling of sperm (cancer patients, fertile men, and infertile men) was performed using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Proteins and peptides were identified using search programs Mascot and Sequest. Sperm proteins of cancer patient group were compared separately with fertile and infertile men groups. Differentially expressed proteins (DEPs) obtained from two different analysis were subjected to comparison analysis using ingenuity pathway analysis (IPA) software.

RESULTS: The functional bioinformatic analysis revealed that proteins associated with mitochondrial dysfunction, oxidative phosphorylation, and mitogen signaling pathways were dysregulated in cancer patients compared to fertile and infertile men. Furthermore, comparison analysis of two sets of DEPs predicted deactivation of oxidative phosphorylation and TCA cycle (Table 1).

CONCLUSIONS: Current proteomic findings indicate that the cellular pathways associated with oxidative phosphorylation and TCA cycle are affected in spermatozoa of cancer patients. Further in-depth investigation and validation of specific proteins associated with both the pathways in cancer patients are warranted.

TABLE 1. Deactivated pathways in spermatozoa of cancer patients

<table>
<thead>
<tr>
<th>Pathways</th>
<th>Z score*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cancer vs. Fertile</td>
</tr>
<tr>
<td>Oxidative Phosphorylation</td>
<td>-3.46</td>
</tr>
<tr>
<td>TCA cycle II</td>
<td>-2.45</td>
</tr>
<tr>
<td>Fatty acid β-oxidation I</td>
<td>-2.00</td>
</tr>
<tr>
<td>Glycolysis I</td>
<td>-2.24</td>
</tr>
</tbody>
</table>

*Considered significant when Z score is >2 or < -2.

Reference: None.

SUPPORT: None.

O-228 Wednesday, October 16, 2019 12:00 PM

NOVEL EX VIVO CULTURE OF NEONATAL MOUSE TESTICULAR ORGANOID MAINTAINED IN A HANGING DROPLET WITH RETINOIC ACID. Philip Xie, B.S.; Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D., The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To propose a method to sustain germ cell characteristics of neonatal germlinal epithelial cells in the form of self-organized organoids and initiate meiotic differentiation under the exposure of retinoic acid (RA).

DESIGN: We tested the feasibility of utilizing an ex vivo three-dimensional culture system maintained in a hanging droplet (HD) to sustain and induce maturation of murine neonatal testicular cells.

MATERIALS AND METHODS: After trypsinization of 5-day-old newborn mouse testicular tissue, isolated cells were cultured in medium designed for spermatogonial stem cells (SCs) composed of DMEM/F12 with GDNF, FGF2, 2-mercaptoethanol, L-glutamine, and B27 supplement in a gelatin-treated well for 3 days. Cell culture was then trypsinized and washed in SSC medium. The resulting cell pellet was resuspended in SSC medium void (control) or with 1 μM RA (HDRA). Cell suspensions were then adjusted to 40,000 cells/ml, and approximately 1,000 testicular cells were placed in each 25-μl HD. Cell characterization was performed every 3 days by germ cell stage–specific markers on an H&E-stained background.

RESULTS: After culturing neonatal testicular cells in HDs, initial aggregation was observed 48 hours after HD culture. The earliest complete self-formation of spherical organoids was observed at day 3 for both control and HDRA. In the control group, continuing and consistent expression of OCT4 (>70%) and nuclear DAZL (>75%) throughout the experiment until day 21 determined that the SCs retain stemness. In HDRA, a downregulated expression of OCT4 was recorded as early as day 3 in approximately 50% of the cells. A shift from nuclear to perinuclear positivity of DAZL in 16% of the cells in the HDRA group at day 21 confirmed differentiation in spermatocytes. Cytoplasmic VASA expression in the HDRA group confirmed meiotic/post-meiotic differentiation of the germ cells. Positive vimentin staining in 25% of the cells indicated the presence of nurturing pre-Sertoli cells in both groups.

CONCLUSIONS: The attempt to maintain germ cell characteristics of neonatal testicular cells in the form of self-organized organoids appears to be an effective strategy for studying ex vivo spermatogenesis in the long-term. With the essential supplement of RA, germlinal epithelial maturation was achieved. Once the ability to induce late-stage gametogenesis is confirmed, this technique may benefit cancer survivors who underwent gonadotoxic therapy in prepubertal age with irreversible damage of the germlinal epithelium.

NURSING

O-229 Wednesday, October 16, 2019 10:45 AM

TRIGGER PREPARATION ONLINE VIDEOS IMPROVE WORKPLACE EFFICIENCY & NURSING SATISFACTION. Viji Sundaram, MD,1 Katrina Cruz, BSN, MSN,2 Maria Farinha, BSN,1 Martha Noel, MD,1 Marcelle I. Cedars, MD,1 Heather G. Huddleston, MD,1 University of California, San Francisco, San Francisco, CA; 1University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA; 1University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: To test the hypothesis that implementation of tailored ovulation trigger injection instruction videos would (1) reduce average nursing time spent counseling a patient for trigger by 20%, (2) reduce overall calls made to the after-hours physician regarding trigger instructions, (3) increase average nursing and patient satisfaction scores.

DESIGN: Prospective Intervention Trial.

MATERIALS AND METHODS: Nine total videos were created to instruct patients on how to mix and inject specified doses of Human
Chorionic Gonadotropin (hCG): 1500 units (u), 2500u, 3300u, 5000u, and 10,000u from a 10,000u vial of hCG; 1500u, 3300u, 5000u, and 10,000u from a 5000u vial of hCG. Nurses logged total time spent counseling patients on trigger injections over a 2-week period in June 2018, prior to video implementation. Videos were emailed to all patients on the day of planned trigger starting mid-November 2018. Nurses logged time spent counseling per patient 1 month following video implementation over a 2-week period. Nursing satisfaction surveys were sent following video initiation and compared to pre-video scores. Patient surveys were sent retrospectively to gauge adequacy of information received, satisfaction, confidence, and need to page on-call physician prior to and following video implementation. Means were compared using a paired t-test for each of the measured outcomes on the patient surveys.

RESULTS: Time spent counseling patients by staff was on average 29 minutes prior to video implementation and decreased by 40% to 17.5 minutes following initiation of videos. 5 nurses completed the satisfaction survey with improved average scores from 20% pre-video to 84% post-video. 148 patients were sent a survey 1 month before and after video implementation with a response rate of 38.5% pre-video and 25% post-video. Overall trends revealed that patients completing a trigger injection for the first time reported improved scores on information received, satisfaction, and confidence, though none of these values approached significance. Patients undergoing repeat trigger injection reported significantly lower satisfaction scores following video implementation (9.44/10 to 8.36/10, p = 0.028). There was a reduction in overall calls made to the on-call physician with 10.5% calling prior to the video and 8.1% post-video.

CONCLUSIONS: Trigger videos resulted in a 40% reduction in nursing time spent counseling patients and fewer calls to the on-call physician. This improved efficiency was associated with improved nursing satisfaction and stable patient satisfaction and confidence. Practices seeking efficiency gains should consider utilization of video-based instruction.

O-230 Wednesday, October 16, 2019 11:00 AM

ELECTIVE EGG FREEZING AND MALE SUPPORT: A QUALITATIVE STUDY OF MEN’S HIDDEN ROLES IN WOMEN’S FERTILITY PRESERVATION

Marcia C. Inhorn, PhD, MPH, Daphna Birenbaum-Carmeli, PhD, Pasquale Patrizio, M.D. Yale University, New Haven, CT; University of Haifa, Haifa, Israel; Yale Fertility Center, New Haven, CT.

OBJECTIVE: Do men participate in women’s fertility preservation decisions and procedures? Emerging evidence suggests that lack of a male partner is the primary reason why women are pursuing elective egg freezing (EEF). However, this qualitative study asked women whether men played any supportive roles in their fertility preservation decisions and procedures.

DESIGN: In this binational, qualitative study, 150 women (114 in the United States, 36 in Israel) who had completed at least one cycle of EEF were interviewed by two senior medical anthropologists, one in each country, during the period from June 2014 to August 2016.

MATERIALS AND METHODS: Study participants were recruited through 4 American IVF clinics (2 academic, 2 private) and 3 in Israel (1 academic, 2 private). In-depth, semi-structured, open-ended interviews were audio-recorded, transcribed, and entered into a qualitative data analysis program ( Dedoose) for thematic analysis, along with detailed interview summaries.

RESULTS: Although 85% of women identified the lack of a male partner as their main reason for pursuing EEF, nearly two-thirds (63%) relied on some form of male support during their EEF decision making processes and procedures. Five categories of men, in order of support, included: 1) fathers (or other male father figures), 2) male partners (past or present), 3) male friends, 4) brothers, and 5) male judges (who supported EEF in divorce settlements). More than a dozen different forms of assistance were offered by men in four major categories (instrumental, financial, physical, and psychological).

CONCLUSIONS: Five different categories of men played supportive roles in women’s EEF, offering 12 forms of instrumental, financial, physical, and psychological assistance. Although one-third of women went through EEF alone or with only female support, this study reveals the “hidden” roles men play in supporting female family members, friends, and partnered. SUPPORT: US National Science Foundation, Cultural Anthropology Program, BCS-1356136.

THE EFFECTIVENESS OF EDUCATION USING VIDEOS WITH SMART PHONES AND A BOOKLET ON FERTILITY WOMEN - FOCUSED ON THE PROCESSION OF IN VITRO FERTILIZATION

Eun Hee Seo, MS, Hwayeon Cho, Master, Eunjung Jeon, master, Kyongyol Kim, MS, JiSuk Lee, BS, Hyunju Choi, BS, Mi Ok Moon, MS, Hayoung Lee, MS, Tae Ki Yoon, M.D, Ph.D. Hyeok Kim, MD, PhD. CHA University, CHA fertility center, Seoul station, Seoul, Korea, Republic of (South); CHA Fertility Center Seoul Station, Obstetrics and Gynecology, Seoul, Korea, Republic of (South).

OBJECTIVE: The purpose of this study was to develop a ‘Q&A related to in vitro fertilization’ for the first-time trial women and to produce a booklet with the contents of the existing video education ‘In Vitro fertilization’ and compare the effectiveness of education through knowledge and educational satisfaction surveys and to find a more effective educational plan for women in vitro fertilization.

DESIGN: Retrospective study.

MATERIALS AND METHODS: From September 10th, 2016 to October 25th, 2016, a total of 131 women who participated in the first trial of in vitro fertilization in the CHA Fertility Center Seoul Station, and 9 participants were eliminated those who they did not see the educational data to the end or did not respond to the questionnaire sincerely. The secret selection of educational materials was selected by the participants. The selection result was selected by a total of 122 participants; 45 pamphlets, 35 videos, and 42 videos and pamphlets. The survey tool, Knowledge Measurement Problem Question questionnaire, consisted of 17 items by the validity of the revised content of the expert group and the difficulty of the content of the general population. It modified and supplemented the education satisfaction items in web-based virtual classrooms developed by Jeong In-seong and Lim Jung-hoon (1999). The reliability of the tool was a = 0.895 for Kronbach. The participants were asked about the level of knowledge and satisfaction of education on the 7th - 8th day of menstruation, which is the next hospital visit. Data analysis was performed using SPSS WIN 21.0. The general characteristics of the participants were asked by descriptive statistics and frequency analysis. ANOVA and crossover analysis were used for homogeneity. ANOVA, Scheffe, regression analysis and correlation analysis were used respectively. Percentage of correct answer which can be an important parameter of the paper was calculated as a percentage using the right answer and the number of samples *100.

RESULTS: As a result of this study, the total score of the knowledge level items was the highest with correct answer rate of 86.83%, and followed by the booklet group with 85.49% and the video group was 82.02%. The results of the ANOVA showed that there was no significant difference in the level of knowledge among the three groups: 13.91 2.369 in the video group, 14.64 1.540 in the booklet group, and 14.74 2.165 in the booklet + video group. It was confirmed that the score of booklet + video group was high in the order of booklet group 4.14 0.534, video group 4.31 0.581, booklet + video group 4.41 0.529.

CONCLUSIONS: Based on the results of this study, it is shown that if the education needs of the participants who are in vitro are analyzed, and if systematic and standardized educational materials are produced accordingly and brochures and videos are appropriately provided, It is possible to increase education satisfaction. The purpose of this study has its meaning in conducting the study about the content and method of education for infertility women and the content and method of education provided to the participants of in vitro baby are specifically proposed.


FERTILITY & STERILITY®
O-232 Wednesday, October 16, 2019 11:30 AM

EVALUATION OF ANXIETY IN FREEZE-ALL PATIENTS. 

Nagihan Dinçer, Bsc, Ayse Salgın, Bsc, Necatı Fındıklı, Ph.D., Fazilet Kubra Boyunakul, M.D., MSc, Mustafa Bahçeçi, M.D., Ph.D, BAHÇECİ FÜLYA IVF CENTER, İSTANBUL, Turkey; Bahçeçi Health Group-Fulya IVF Centre, Istanbul, Turkey; Bahçeçi Health Group-Fulya IVF Centre, ISTANBUL, Turkey.

OBJECTIVE: To investigate the anxiety scores and depression scales of infertile women that applied to Bahçeçi Fulya IVF Center for elective frozen blast embryo transfer between February 26, 2019, and April 18, 2019.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: This study is a prospective cohort study which included 178 patients. Face to face interview in the patient’s room 1 hour ago the embryo transfer was performed and Beck Depression Inventory (BDI) with 21 items and Anxiety and Depression Scale (HADS) with 14 items were fulfilled. The age of the patients, number of previous failed trials, total follicle stimulating hormone (FSH) and human menopausal gonadotropin (HMG) doses during ovulation induction period, number of oocytes obtained after oocyte pick up, number of m2, number of frozen embryos, number of embryos remaining were recorded from the patients file. The data obtained after BDI and HADS were evaluated with SPSS 15.0 program. All these parameters were analyzed in multiple regression analysis.

RESULTS: BDI and HADS score was found to be correlated (rho:0.57 p<0.001). In the multivariate analysis no factor such as women age, number of previous failed trials, FSH and HMG doses during ovulation, number of oocytes retrieved, number of m2, number of frozen embryos, number of embryos remaining were found to have an effect the BDI and HADS. Also, the pregnancy rates were not affected according to the BDI and HADS scores stratified.

CONCLUSIONS: Anxiety scales does not affected by the patient’s ovulation induction and embryological parameters.

O-233 Wednesday, October 16, 2019 11:45 AM

CLINICAL EXPERIENCE OF NURSING TEAM IN PRE-CONCEPTION GENETIC COUNSELING AT A LARGE, DIVERSE INFERTILITY PRACTICE. 

Marlene De La Mota, BS, Elizabeth Lipov, BS, Karina Yaipen, RN, Joseph A. Lee, BA, Teresa A. Cacchiene, MS, CGC, Melissa Bell, RN, Margaret Danekyo, RN, Tanmoy Mukherjee, MD, Reproductive Medicine Associates of New York, New York, NY; Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: While ethnicity based-carrier screening was once a mainstream approach, contemporary approaches utilizing preconception counseling, expanded carrier screening (ECS), and preimplantation genetic testing (PGT-M) are now widely utilized. The modern infertility nursing team is crucial in advocating for and educating patients about contemporary reproductive options, patients will obtain a greater sense of autonomy across their family building journey.

Reference: None.

O-234 Wednesday, October 16, 2019 12:00 PM

WHAT IS THE IDEAL NUMBER OF VIALS OF DONOR SPERM TO PURCHASE FOR PATIENTS UNDERGOING DONOR SPERM INTRAUTERINE INSEMINATION (DIUI)? 

Sydney Chang, MD, Dmitry Gounko, MA, Joseph A. Lee, BA, Melissa Bell, RN, Margaret Danekyo, RN, Alan B. Copperman, MD, Tanmoy Mukherjee, MD, Icahn School of Medicine at Mount Sinai, New York, NY; Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Gamete donation has provided patients who would not otherwise have the ability to conceive the opportunity to have a healthy child via screened selected eggs and sperm. Donor sperm is a limited resource, and scarce literature exists to inform patients regarding the optimal number of vials to purchase to maximize the chances of conceiving while minimizing cost. The objective of this study is assess the number of donor sperm vials needed to achieve ongoing pregnancy (OP) for patients who are undergoing donor sperm intrauterine insemination (DIUI).

DESIGN: Retrospective, cohort study.

MATERIALS AND METHODS: The study included patients at a single academic center who underwent a natural cycle or mediated ovulation induction cycle (with clomiphene citrate or letrozole) with DIUI from 2010-2019. Exclusion criteria included gonadotropin use or imaging showing tubal pathology, uterine myomas, or polyps >0.5 cm. r-hCG was administered when ≥1 18mm follicle was visualized. DIUI was performed 36 hours later. The primary outcome was OP, A Kaplan-Meier curve was created for each SART age group to determine the cumulative probability of OP from each DIUI cycle. A second curve stratified by anti-Mullerian hormone (AMH) levels: (low <0.7 ng/mL, normal 0.7-8.4 ng/mL, high >8.4 ng/mL). Patients were censored when they dropped out or progressed to IVF.

RESULTS: A total of 913 patients were included in the study (Groups A: 257, B: 199, C: 168, D: 142, E: 147). The cumulative percent of patients that achieved OP in each cycle is shown in Table 1.

CONCLUSIONS: Until now, there has not been a personalized algorithm to predict how many vials of donor sperm should be purchased prior to attempting DIUI. Using Kaplan-Meier curves stratified by age and AMH, we developed a starting point from which clinicians can further tailor their recommendations to incorporate patient characteristics and preferences for family size. The cumulative OP rate per cycle can also be used to counsel patients about when to transition their treatment strategy to one that includes assisted
reproductive technologies. Future studies might include a financial analysis that includes time and cost as variables of both low-tech and high treatments, so that we can best inform our patients.


**SUPPORT:** None.

![Image](https://via.placeholder.com/150)

**PROFESSIONAL DEVELOPMENT**

**O-235 Wednesday, October 16, 2019 10:45 AM**

**IMPROVING THE REI FELLOWSHIP INTERVIEW EXPERIENCE: A SURVEY.** Erika P. New, MD, MPH; Papri Sarkar, MD; Ruben J. Alvero, MD; Anthony N. Imudia, MD. University of South Florida, Brandon, FL; USF, Tampa, FL; Stanford University, Palo Alto, CA; University of South Florida, Tampa, FL.

**OBJECTIVE:** The interview process for residents applying to Fellowship in Reproductive Endocrinology and Infertility (REI) is a highly competitive process with many challenges for applicants such as conflicting interview dates, the expense of traveling, and missing days from work. The goal of this study is to collect data on the current REI fellowship interview process so that it may be improved in the future.

**DESIGN:** An anonymous survey was sent to individuals who have gone through the REI fellowship interview process. In addition, fellowship program directors and coordinators were contacted by e-mail to gain information on typical interview dates for each program.

**MATERIALS AND METHODS:** The survey designed for applicants was distributed over social media and the REI fellow e-mail list-serv. Some survey questions included:

- How many days of work or vacation did you take off for Fellowship interviews?
- Did you ever miss an opportunity to interview at a program you were interested in? If so, what was the reason?
- How often did you have to travel to the same city more than once for an interview?
- How much money did you spend on average per interview?
- What recommendations do you have for how the interview process could be improved?

The fellowship program information was obtained by contacting each program using the publicly available contact information on the Accreditation Council for Graduate Medical Education (ACGME) website.

**RESULTS:** There were 44 survey respondents. Of those, 38.6% participated in the 2018 REI interview season, 29.5% in 2017 and 31.8% participated more than 2 years ago. The mean number of interviews attended was 12.6 (range of 1-22). On average 13.4 (0-30) days off work or vacation were used to interview. 67.4% of respondents missed an opportunity to interview at a program they were interested in, with most common reasons: the interview date was the same day as another interview, could not attend due to geographic location, and cost was too great. 72% traveled to the same city more than once for an interview. The average cost per interview was $478 (range $200-$1,000) and average cost per interview season was $5,660 (range $900-$15,000). Fellowship program data was available from 43 of 48 programs contacted. The 2018 interview season spanned from June 4-August 30. The most popular interview date was Monday, August 27 (5 interviews). The number of dates that had conflicting interviews scheduled were 26. Most programs offered 2 interview dates (46.5%). 30% offered 3 interview dates, 16% offered 1 date, and 6.9% offered 4 dates.

**CONCLUSIONS:** This data supports the need to coordinate the REI fellowship recruitment process between programs to reduce conflicting interview dates and mitigate cost. Recommendations from respondents include having programs notify applicants of interview offers at the same time, geographically aligning interviews by region, including a virtual component to interviews such as video interviews or interviewing at a central location, and helping applicants with costs such as hotels or flights. Encouraging collaboration between fellowship programs would increase applicant satisfaction.


**SUPPORT:** None.

**O-236 Wednesday, October 16, 2019 11:00 AM**

**THE STATE OF WOMEN IN ACADEMIC REPRODUCTIVE ENDOCRINOLOGY PROGRAMS.** Jessica Selter, MD, Emily Spurlin, MD, Paula C. Brady, MD Columbia University Medical Center, New York, NY.

**OBJECTIVE:** To identify gender differences in leadership and academic rank within academic reproductive endocrinology programs with fellowships in the United States.

**DESIGN:** Cross-sectional study.

**MATERIALS AND METHODS:** Official institutional websites of the 2017-2018 American Board of Obstetrics and Gynecology (ABOG)-accredited reproductive endocrinology fellowship programs were reviewed, and gender representation at each leadership position and academic rank (Division and Fellowship Director; Full, Associate, and Assistant Professor) was recorded. Three programs did not consistently report academic rank, so only leadership positions were recorded. Associate Fellowship Directors were rarely reported and therefore excluded. Only medical doctors (MD, DO, MBBS) who completed postgraduate training in OB/GYN were included. Private practice physicians affiliated with universities were included only if present on academic department websites with academic titles. Univariate comparisons were performed using Chi-squared tests, with significance at P < 0.05.

**RESULTS:** Among 49 ABOG-accredited reproductive endocrinology programs, 263 faculty were identified, 129 (49%) male and 134 (51%)

---

**TABLE 1. Cumulative OP rate per cycle (%)**

<table>
<thead>
<tr>
<th>Cycle</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>Low</th>
<th>Normal</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18.3</td>
<td>14.6</td>
<td>11.9</td>
<td>11.2</td>
<td>2.0</td>
<td>3.3</td>
<td>7.7</td>
<td>15.4</td>
</tr>
<tr>
<td>2</td>
<td>32.5</td>
<td>23.0</td>
<td>19.1</td>
<td>16.0</td>
<td>4.0</td>
<td>3.3</td>
<td>14.9</td>
<td>27.9</td>
</tr>
<tr>
<td>3</td>
<td>42.5</td>
<td>28.1</td>
<td>28.2</td>
<td>20.5</td>
<td>4.0</td>
<td>12.8</td>
<td>21.2</td>
<td>36.9</td>
</tr>
<tr>
<td>4</td>
<td>50.0</td>
<td>32.8</td>
<td>31.7</td>
<td>25.6</td>
<td>6.4</td>
<td>12.8</td>
<td>27.4</td>
<td>36.9</td>
</tr>
<tr>
<td>5</td>
<td>53.6</td>
<td>44.6</td>
<td>38.9</td>
<td>37.0</td>
<td>6.4</td>
<td>12.8</td>
<td>27.4</td>
<td>36.2</td>
</tr>
<tr>
<td>6</td>
<td>61.1</td>
<td>50.1</td>
<td>42.3</td>
<td>46.7</td>
<td>30.2</td>
<td>44.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>64.4</td>
<td>54.7</td>
<td>42.3</td>
<td>46.7</td>
<td>30.2</td>
<td>44.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>69.5</td>
<td>54.7</td>
<td>42.3</td>
<td>46.7</td>
<td>30.2</td>
<td>44.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>76.3</td>
<td>55.1</td>
<td>57.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>76.3</td>
<td>55.1</td>
<td>57.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
female. Division directors were 69.4% male and 30.6% female (p = 0.006). Similarly, fellowship directors were 65.3% male and 34.7% female (p = 0.03). Full professors (n = 101) were more frequently male (70.3% vs. 29.7%, p < 0.001). There was no difference in gender among associate professors (n = 60, 51.7% male vs. 48.3% female, p = 0.79), while significantly more assistant professors were female than male (n = 102, 73.5% vs. 26.5%, p < 0.001).

CONCLUSIONS: While a majority of residents in obstetrics and gynecology and half of reproductive endocrinology academic faculty are female, women are still underrepresented among leadership positions and full professors in academic reproductive endocrinology programs. More women than men are currently assistant professors, suggesting the possibility of a more equal distribution of leadership and tenure in the future.

O-237 Wednesday, October 16, 2019 11:15 AM

EVALUATION OF OFFICE HYSTEROSCOPY SIMULATION AS PART OF AN OB/GYN RESIDENCY TRAINING CURRICULUM. Jessica Selter, MD, Sally F. Vitez, MD, Eric J. Forman, MD, Samuel Zev Williams, M.D., Ph.D. Columbia University Medical Center, New York, NY.

OBJECTIVE: To evaluate the impact of an office hysteroscopy simulation on Ob/Gyn resident comfort with the procedure and performance metrics. DESIGN: One-group pretest-posttest design study. MATERIALS AND METHODS: Ob/Gyn residents at a single institution were recruited to voluntarily attend an office hysteroscopy 2-hour training session. Residents underwent testing on the Endosee procedure. They then went through a series of Endosee simulation exercises with increasing level of difficulty, and then were re-tested on the original Endosee procedure. Residents were evaluated via both objective measures by a pre/post multi-metric scoring system and subjective measures with pre- and post-surveys. The multi-metric scoring system included an overall score that incorporated procedure time, patient comfort, visualization, and precision. Univariable analysis with paired student’s t-test, wilcoxon-signed rank test, and fisher exact tests were performed as appropriate.

RESULTS: A total of 17 residents completed the office hysteroscopy simulation program. The average age was 28.8 with 87% females, and an even distribution of years of training. The distribution of intended subspecialty training included 11.7% into reproductive endocrinology, 29.4% into gynecologic oncology,11.7% into minimally invasive gynecologic surgery, and 23.5% into generalist/unknown. All residents reported little to no experience with office hysteroscopy prior to the training experience and 88% felt extremely uncomfortable with performing the office hysteroscopy procedure. Following training, there was a significant increase in subjective comfort (76% vs. 11.4%, p < 0.01) with a majority of residents reporting slight/moderate comfort with performing the procedure. Following training, all residents agreed that Endosee simulation was a good preparation for office hysteroscopy. Furthermore, there was a significant increase in residents who agreed that office hysteroscopy simulation should be integrated into OB/Gyn curriculum (68% vs. 94%, p = 0.04). After training, residents had an improved overall score (218 vs. 242, p < 0.01), decreased procedure time (116sec vs. 73sec, p < 0.01), shorter cumulative path length (24.4 vs. 17.8cm, p = 0.01) and a trend towards improved navigation percentage (61% vs. 70%, p = 0.06).

CONCLUSIONS: This study demonstrates that office hysteroscopy training using a simulator improves both subjective resident comfort and objective performance. Despite the small sample size, the overall enthusiasm regarding office hysteroscopy simulation suggests the need for a larger study group and a possible role for integrating office hysteroscopy into resident OB/Gyn curriculum.

SUPPORT: CooperSurgical provided surgical simulators for the study.

O-238 Wednesday, October 16, 2019 11:30 AM

FERTILITY KNOWLEDGE IN OBSTETRICS AND GYNECOLOGY RESIDENTS. Leah Roberts, MD,a Rashmi Kudesia, MD,b Shaliz Dolan, MD,a Marisa Rose, MD,b a Temple University Hospital, Philadelphia, PA; b CCRM Fertility Houston, Houston, TX.

OBJECTIVE: Reproductive Endocrinology and Infertility is taught in every obstetrics and gynecology (OB-GYN) residency program in the country, however, resident knowledge in this area has never been assessed by a validated instrument. The goal of this study was to evaluate fertility knowledge among current OB-GYN residents using a recently published validated instrument, the Fertility and Infertility Treatment Knowledge Score (FIT-KS).

DESIGN: Survey.

MATERIALS AND METHODS: OB-GYN residents in the United States were recruited through an email to all residency coordinators nationwide. They were asked to voluntarily respond to a short questionnaire including demographic information and the FIT-KS instrument, through an online survey platform.

RESULTS: One hundred and seventy-seven residents responded to the survey (approximately a 4% response rate). The sample was 91% female, with 69% between the ages of 26 and 30. They represented an equal distribution between all four levels of training with 40, 47, 39 and 40 respondents of each year of training. Mean score was 21.2 (73%). Several knowledge gaps were noted. In terms of understanding natural conception, 27% of respondents believed having less than nine periods a year could be normal, and 27% also responded that a male partner’s age did not impact fertility. Only 56% knew that sperm would survive for three to five days in the female reproductive tract. For risk factors, the fertility effects of moderate alcohol consumption and sexual lubricants were most commonly mischaracterized. Residents could define the common assisted reproductive technologies; however, grossly overestimate their success rates per cycle. No statistically significant differences were noted across the level of training. The majority of all residents (95%) stated that they do discuss fertility with their patients, however 18% stated they do not feel comfortable answering their patient’s questions. Residents who did not feel comfortable answering their patient’s questions mean score was 20.9 (72%), not significantly different from those residents who did feel comfortable providing fertility counseling 21.3 (73%).

CONCLUSIONS: Substantial gaps exist in fertility knowledge among OB-GYN residents, with understanding of male fertility and success


O-239 Wednesday, October 16, 2019 11:45 AM

COLLABORATIVE AND MULTIDISCIPLINARY APPROACH TO THE REI FELLOWSHIP APPLICATION. Randi H. Goldman, M.D., Christine Mullin, M.D., Esther Lopez, M.P.A., Jeanette Tomasino, Ph.D., Martina Borovica, M.B.A., Avner Hershlag, M.D., Northwell Health Fertility, Zucker School of Medicine at Hofstra/ Northwell, Manhasset, NY.

OBJECTIVE: To describe the development and implementation of a Reproductive Endocrinology and Infertility (REI) fellowship program and the process of attaining initial accreditation, with a focus on the multidisciplinary collaborative effort of the OB/GYN department, GME committee, and affiliated programs.

MATERIALS AND METHODS: This is a descriptive study completed at an academic institution that evaluates the critical aspects of establishing an REI fellowship program. We specifically explored how to utilize the broad network of interdisciplinary opportunities already established at our institution to provide a collaborative, inclusive learning environment for fellow trainees.

RESULTS: REI sub-specialists are expected to master the medical knowledge and surgical procedures involved with all aspects of reproductive health, including care for infertile women and couples, disorders that threaten fertility such as cancer and systemic disease, pediatric and adolescent gynecologic care, and fertility preservation. When designing our fellowship program, we built upon the multidisciplinary strengths of our institution by consulting with other departments and divisions. Minimally Invasive Gynecologic Surgery, Male Infertility, Endocrinology, Pediatric Endocrinology, and Genetics – disciplines that encompass the broad aspects of our field – have partnered in developing our REI fellowship program. We specifically explored how to utilize the broad network of interdisciplinary opportunities already established at our institution to provide a collaborative, inclusive learning environment for fellow trainees.

CONCLUSIONS: Although 53% of residents feel REI exposure during residency is “too light,” most (79%) trainees expect to feel comfortable completing a basic infertility workup at the end of residency, while 93% of residents who felt their REI exposure was “just right” (N=46) anticipated feeling comfortable, a statistically significant difference (p=0.001). Residents training in the Northeast felt least prepared to perform a workup vs. the rest of the U.S. (69% vs. 86%, p=0.048). Significantly fewer fellowship-aspiring residents felt their REI exposure was “just right” (32%) vs. residents who were undecided or planning to be general OB/GYNs (55%) (p=0.038).

Residents planning to pursue REI fellowship were least likely to feel their REI exposure was “just right” (18%, vs. 82% “too light”). Only 1 resident felt that their REI exposure was “too heavy.” Residents whose REI curricula included ASRM teaching modules were significantly more likely to feel their REI exposure was “just right” (62% vs. 38%, p=0.035). No differences were seen based on rotation length, university- vs. community-based programs, having a sub-specialty trained program director, or presence of an institutional REI fellowship.

CONCLUSIONS: Although 53% of residents feel REI exposure during residency is “too light,” most (79%) trainees expect to feel comfortable completing a basic infertility workup upon graduation. ASRM teaching modules may be a simple intervention to standardize REI curricula and help residents feel more content with their REI exposure during training. Importantly, adequate exposure to REI may help inform career choices of trainees.
DIFFERENTIATION OF EMBRYONIC STEM CELLS INTO MALE GERM LINE CELLS IN A BIOREACTOR USING DECELLULARIZED SEMINIFEROUS TUBULE MATRIX IMMERSED IN A CONDITIONED MEDIUM.

**O-241** Wednesday, October 16, 2019 10:45 AM

**MATERIALS AND METHODS:** Male mESCs were cultured in epiblast cell-like cell (EpilC) medium containing activin A, bFGF, and KSR for 3 days to allow differentiation into EpilC. Subsequent exposure to primordial germ cell–like cell (PGCLC) medium poised with BMP4, BMP8b, SCF, LIF, and EGF in hanging droplet (HD) allowed the formation of embryoid bodies (EBs) rich in PGCLCs. Isolated cells from 80 EBs were utilized in the bioreactor, in directed contact with DSTM, and loaded with DMEM in a gelatin-treated culture well equipped with a 0.4-μm pore size mesh inlet. 1 day after inoculation, EBs were decellularized for 3 days, and EBs were reseeded into DSTM, which was conditioned by immersion in 1% sodium dodecyl sulfate for 24 hours. Eighty 3-mm sections of DSTM, longitudinally sliced into two parts, were placed below the mesh; interstitial cells were isolated from the respective contralateral testes by differential plating and loaded above the mesh. Cell characteristics were analyzed by germ cell–specific markers on H&E-stained background.

**RESULTS:** After culturing mESCs in EpilC medium, the continuing expression of OCT4 (>90%) and the decreased positivity of Nanog (45%) indicated progression to EpilCs. EBs rich in PGCLCs expressed positive surface SSEA-1 after 6 days of culture in HD with PGCLC medium. Isolated cells of PGCLCs were derived from the digestion of EBs and layered on the DSTM. The earliest attachment of PGCLCs onto DSTMs occurred on day 3, and complete recellularization was observed at approximately day 10. Following complete recellularization, about half of all isolated cells obtained from the enzymatic digestion of recellularized tubule displayed decreased expression of OCT4, while 5% displayed nuclear DAZL positivity at day 10. In 1% of the cells, perinuclear DAZL confirmed spermatocyte differentiation at day 21. At around day 16, cytoplasmic VASA positivity in 5% of the cells suggested meiotic/post-meiotic germ line differentiation.

**CONCLUSIONS:** The timeline of our bioreactor system was comparable with in vivo spermatogenesis in the mouse, occurring in the course of 21 days. Once the ability of a 3D biocompatible scaffold to induce late-stage gametogenesis is confirmed, it will be possible to study spermatogenesis in vitro. Neogametogenesis from genotyped stem cells performed in a scaled-down microfluidic device may help to treat men afflicted with Sertoli cell–only syndrome.

**O-242** Wednesday, October 16, 2019 11:00 AM

**EFFICIENT GENERATION OF GRANULOSA CELL LIKE CELLS FROM HUMAN ENDOMETRIUM DERIVED IPS CELLS AS A SOURCE FOR AUTOLOGOUS ESTRADIOL PRODUCTION.** Jun Hyun Park, MD, PhD, HeeYon Kim, M.D., Hyun Kyung Kim, MS, SiHyun Cho, M.D., Ph.D., Yongyeon University College of Medicine, Gangnam Severance Hospital, Seoul, Korea, Republic of (South).

**OBJECTIVE:** To derive granulosa cell like cells from induced pluripotent stem cells (iPSCs) which are derived from discarded endometrial stromal cells as a novel source of autologous estradiol production.

**DESIGN:** iPSCs were driven using human endometrial cells obtained from five benign hysterectomy and stepwise granulosa cells were differentiated to successfully induce estradiol production.

**MATERIALS AND METHODS:** After pathologic confirmation, human endometrial cells free from pathologic findings were obtained from five hysterectomy specimens of benign indications. Using episomal vectors for Sox2, Oct4, cMyc and Klf4, 3 cell lines were driven per donor. Embryoid body-like (EBs) were first formed from these patient endometrium derived iPSCs and to induce primitive streak-mesendoderm and intermediate plate mesoderm lineage. Consequently estradiol(E2) producing granulosa like cells were differentiated from human embryonic stem cell (hESC) line H9 was used as control. To induce mesodermal lineage differentiation, produced EBs were supplemented with BMP4 (10 ng/ml), WNT3a (6 ng/ml), Activin A (6 ng/ml) and bFGF (5 ng/ml) for 6 days. After confirming mesodermal commitment, differentiation was further directed using BMP4 (10 ng/ml), Follistatin (25 ng/ml) and bFGF (5 ng/ml) for an additional 6 days. During the differentiation process markers indicative of granulosa cell differentiation (AMH, FOXL2, FSHR, AMHR2, LHR, CYP19A1) was performed via real-time PCR and FACS analysis. After a differentiation period of 12 days, these cells were seeded at a density of 4×10^5 per one 6-well plate and after adding aromatasecogene for an additional period of time. E2 assay was performed using ELISA.

**RESULTS:** After a differentiation process of 6 days, FACS analysis of brachury expression for H9 was 30% and 21.7% (SD +/- 3.5%) for human iPSCs. This primitive streak-mesendoderm marker, brachury showed marked expression at day 6 of differentiation and decreases up to day 12 of differentiation. Donor and cell line variabilities with regards to efficiency and time requirements were observed.

**CONCLUSIONS:** Granulosa cell line cells expressing the appropriate markers and functional for estradiol production could be successfully derived from human endometrium derived iPSCs.

**SUPPORT:** None.
RNA-seq demonstrated that several key inflammatory mediators including TNF-α, IL1a, IL1b, IL17, IL-12, CINC-1, ICAM-1, IL1ra, CXCL5, and TIMP-1 were upregulated in DE-MSMSCs as compared to VEH-MSMSCs. The RNA expression of IL-10 which is an anti-inflammatory mediator was downregulated in the cell line. q-PCR analysis confirmed the alteration of RNA expression of these inflammatory mediator genes (P<0.05).

Cytokines antibody array analysis exhibited an increased expression of CINC-1, ICAM-1, IL1ra, CXCL5,TIMP-1, and VEGF in DE-MSMSCs vs VEH-MSMSCs. q-PCR analysis demonstrated that treatment with Vitamin D3 and its analogue Paricalcitol reversed the effect of DE exposure by down-regulating those pro-inflammatory cytokines (P<0.01). Cytokines antibody array further demonstrated that vitamin D3 and Paricalcitol reversed the DE-induced upregulation of pro-inflammatory mediators including CINC-1, ICAM-1, IL1ra, CXCL5, TIMP-1, and VEGF in DE-MSMSCs.

CONCLUSIONS: Our data strongly demonstrate that developmental exposure to DE increases the risk of adult onset of UF by creating an inflammatory milieu in the myometrium. Vitamin D3 and Paricalcitol treatment are capable of reversing the effect of DE exposure-induced activation of pro-inflammatory pathways in the endometrium suggesting that vitamin D3 and its analogue as a treatment option could be useful to decrease the incidence of UF.

SUPPORT: NIH RO1 ES028615 and U54 MD007602.

O-245 Wednesday, October 16, 2019 11:45 AM

USE OF CRISPR/Cas9 SYSTEM FOR INDUCTION OF MESENCHYMAL STEM CELLS. Sercin Karahuseyinoglu, MD, Ayse Kose, MD, Gizem Nur Sahin, MS, Yagmur Ergun, MS, Student. *Asst. Prof., Istanbul, Turkey; **MS, Istanbul, Turkey; ***MS, Student, Istanbul, Turkey.

OBJECTIVE: The objective of this study is to use CRISPR/Cas9 gene editing technology in order to increase gene activation for induction of differentiation of mesenchymal stem cells obtained from human umbilical cord matrix.

DESIGN: Human umbilical cord mesenchymal stem cell line was used for differentiation via chemical induction or CRISPR/Cas9 genome activation system. Osteogenic, adipogenic, and neurogenic differentiations were established. The experiments were designed as three biological replicated and three technical replicates for each biological replicate. The efficiency of differentiation capacity was evaluated by qPCR, Western blotting and super resolution microscopy.

MATERIALS AND METHODS: Human umbilical cord mesenchymal stem cells (MSCs) were isolated from umbilical cords (PCS500010/ATCC) were first differentiated into osteocytes, adipocytes and neurons via use of chemicals. Dexamethasone, glycerol 3-phosphate, ascorbic acid in DMEM with 10% FBS were used for osteogenic induction. Dexamethasone, insulin, indomethacin, isobutyl xanthine in DMEM with 10% FBS were used for adipogenic induction. Valproic acid, potassium Chloride, butylated hydroxyanisole in DMEM with 10% FBS were used for neurogenic induction. The inductions lasted for 28 days. In another group of MSCs were induced via use of gene Cas9 viral transduction. In order to induce differentiation related transcriptional/or activator factors were activated via use of dCas9-SAM (SynergisticActivation Mediator) system. Guide RNAs (gRNAs) for PPAR-gamma, RUNX2 and SOX were designed to target the area of 0 to -200 basepair according to TSS (transcription starting site). For 48 hours gRNAs were transduced to MSCs via lentivirus that holds the plasmids and gRNAs. At the end of induction period (28 days after chemical and 2 days after CRISPR/Cas9 induction) MSCs were assessed for morphological and biochemical changes. Osteopontin and alizarin red were used for osteogenic; oil red o and adiponectin were used for adipogenic and MAP2, Neun, beta-III-tubulin were used for evaluation of neurogenic induction. qPCR, IF, and WB were used.

RESULTS: The induction of MSCs via CRISPR/Cas9 showed significantly efficient results in terms of both phenotypical and biochemical changes, by 35% for adipogenic induction, 45% for osteogenic induction and 25% for neurogenic induction (p<0.05) as depicted by qPCR analysis. Superresolution microscopy evidently elaborated the changed morphology of cells with positive stainings for osteopontin in osteogenic cells, lipid granules in adipogenic cells. The neurogenic cells showed long dendrite-like extensions that reach out to each other. These cells were positive for Neun, beta-III-tubulin and MAP2.

CONCLUSIONS: CRISPR/Cas9-SAM activation system was significantly more efficient for differentiation of human umbilical cord MSCs into different lineages. The differentiation was more rapid, did not need constant use of induction medium and did not reverse by time.

O-246 Wednesday, October 16, 2019 12:00 PM

POST-MEiotic MALE GERM CELL DIFFERENTIATION OF MOUSE EMBRYONIC STEM CELLS BY EXPOSURE TO CONDITIONED MEDIUM. Aysa Trout, B.A., Philip Xie, B.S., Alessandra Parella, M.Sc., Zeyn Rosewaks, M.D., Gianpiero D. Palermo, M.D., Ph.D., The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To determine whether the exposure of mouse embryonic stem cells (mESCs) to medium conditioned by adult peripheral or neonatal germlinal epithelial cells (mPGECs) that efficiently increases differentiation into primordial germ cell–like cells (PGC-LCs) and induces meiosis.

CONCLUSIONS: Our data show that BM-MSCs are increasingly mobilized to the circulation during marine pregnancy, are able to undergo decidualization in vitro, and are a source of Hoxa11+ nonhematopoietic decidual cells in pregnancy. These suggest that BM-MSCs play an important previously unrecognized role in pregnancy.


FERTILITY & STERILITY®
DESIGN: We tested a novel culture system utilizing a mesh interphase system to initiate meiotic differentiation of mESCs under media conditioned by adult peritubular cells consisting mainly of Leydig cells, or by neonatal germinal epithelial cells containing pre-Sertoli cells, which are adapted to promoting spermatogenesis. mESCs without exposure of these cells served as a control.

MATERIALS AND METHODS: Over a 6-month period, mESCs were differentiated into epithelial-like cells (EpILCs) and PGCLCs. Peritubular cells derived from adult mouse testes were isolated by differential plating; germ-line cells from neonatal mouse cells were isolated by trypsinization of testes and placed on the mesh. After 7 passages, 1.2 x 10^6 mESCs were plated on each well with MEFs and cultured in the mesh interphase system. Continued expression of Oct4 (>90%) was detected in the cells at day 3, suggesting the retention of stemness. Cytoplasmic DAZL positivity at day 5 demonstrated early meiotic differentiation into spermatocyte lineage. On day 8, approximately 30% expressed VASA positivity, indicating further progression into meiosis. Cells cultured in media conditioned by adult interstitial cells had greater expression of DAZL and VASA than those cultured with neonatal interstitial cells. The optimal condition was determined to be a 1:5 ratio of adult cells to mESCs. DAZL and VASA expression were negative in the control group; suggesting the important role of the medium conditioned by testicular cells.

CONCLUSIONS: These results indicate that our novel culture system can promote differentiation of mESCs into PGCLCs and further meiotic differentiation. Initiation of neospermatogenesis using mESCs can be optimized in the presence of factors secreted from Leydig cells derived from adult mouse testes. Reproducing spermatogenesis in vitro may provide valuable information on overcoming male infertility due to spermatogenic arrest or germ cell aplasia.

**REPRODUCTIVE ENDOCRINOLOGY**

O-247 Wednesday, October 16, 2019 10:45 AM

**VARYING LEVELS OF SERUM ESTRADIOL DO NOT ALTER THE TIMING OF THE EARLY ENDOMETRIAL SECRETORY TRANSFORMATION.** Emily K. Osman, MD,a Tianren Wang, M.D., Ph.D.,a Min Yang, Ph.D.,b Yiping Zhan, Ph.D.,b Caroline R. Juncaud, MD,ab Scott J. Morin, MD,b Emre Seli, M.D.,ab Richard Thomas Scott, Jr., MD,ab Jason M. Fransasiak, MD.a IVI-RMA New Jersey, Basking Ridge, NJ, aFoundation for Embryonic Competence, Basking Ridge, NJ, bAudubon Fertility, New Orleans, LA, aIVI-RMA Northern California, San Francisco, CA.

OBJECTIVE: Endometrial receptivity is induced by the systematic exposure of estradiol (E2) followed by progesterone (P4). There has been concern that the exaggerated E2 levels seen in stimulated cycles may attenuate the impact of P4 rise and initiation of secretory transformation, ultimately altering the window of receptivity. This study aimed to determine if supra-physiologic E2 levels in the ranges attained during normal and high response superovulation cycles can modify the onset of secretory transformation.

DESIGN: Prospective, randomized, paired.

MATERIALS AND METHODS: A total of 30 biopsies were collected from 10 volunteers that were enrolled and randomized to the order in which they completed 3 different uterine stimulation cycles: physiologic (approximately 180 pg/mL), moderately supraphysiologic (600-800 pg/mL) or supra-physiologic (2000 pg/mL) levels of E2. Follicle development was assessed by staining serial ovarian sections with hematoxylin and eosin. Ability to generate oocytes (germinal vesicle [GV] and metaphase II [MII]) was assessed after injection with PMSG (5IU) or PMSG and hCG (5IU). RNA sequencing analysis was performed using pooled Mfn1−/− and WT secondary follicle-enclosed oocytes (n=3 mice per group). Protein and mRNA expression were assessed using immunofluorescence (IIF)-qRT-PCR, respectively.

RESULTS: Mfn1−/− female mice were infertile and did not produce any pups. Mfn1−/− mice (8-weeks-old) ovaries had similar number of primordial, primary, and secondary follicles compared to WT, but no antral follicles. They also did not produce mature (MII) oocytes (p <0.001), and generated a significantly lower number of immature oocytes (17±3.6 vs 40±3.0, p <0.01). When changes in follicular pool was assessed across mouse reproductive lifespan, Mfn1−/− mice were found to have significantly lower number of primordial and primary follicles compared to WT at 6 months, and depletion of follicles of all stages at 12 months (p<0.01 for all comparisons). RNA-seq analysis revealed a total of 982 genes that were differentially regulated in Mfn1−/− oocytes with a number of affected pathways including cell death (apoptosis) signaling and ceramide biosynthesis (p<0.01). As suggested by RNAseq analysis, caspase 6 (mediator of apoptosis) and ceramide levels were elevated in Mfn1−/− secondary follicle-enclosed oocytes compared to WT (p<0.01). Because elevated intracellular ceramide may induce apoptosis, we tested whether decreasing ceramide levels in Mfn1−/− mice would rescue reproductive phenotype. Indeed, treatment with ceramide synthesis inhibitor myriocin (1.5 mg/kg daily injection for 21 consecutive days) rescued follicular defects in Mfn1−/− mice and resulted in development of antral follicles.

CONCLUSIONS: Absence of MFN1 in oocytes results in infertility and diminished ovarian reserve and may be exploited to improve human reproductive efficiency will need to be further investigated.
CHRONIC EXPOSURE TO AMH MAY ACCELERATE GROWTH OF FOLLICLES VIA DOWNREGULATION OF AMHRII
Limor Man, M.D. M.Med.Sc., Eleni Kallinos, B.S., Daylon James, Ph.D., Zev Rosenwaks, M.D. Assistant Professor of research, NYC, NY, NYC; The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Anti-Müllerian hormone (AMH) has been suggested to exert a repressive input on activation and growth during folliculogenesis. We have previously shown that direct paracrine delivery of AMH via engineered endothelial cells (ECs) reduces premature follicle mobilization and growth in short-term human ovarian tissue xenografts (Man et al., 2017). Others, using continuous administration of AMH via an osmotic pump or intraperitoneal injection of lentivirally encoded AMH in a murine model, have shown similar results (Kano et al., 2017). Here, we investigated the influence of AMH-producing ECs on follicle growth in long-term grafts.

DESIGN: Xenograft of human ovarian tissue into NOD scid/gamma (NSG) mice with co-transplantation of control ECs or ECs that constitutively secrete AMHRII.

RESULTS: In contrast to short-term grafts (2 weeks), in which AMH-ECs promoted quiescence (primordial: growing follicles ratio: CTRL 0.32 vs. AMH-ECs 1.39, P < 0.01), the AMH group in long-term grafts revealed a shift in the follicular pool toward accelerated growth (primordial: growing follicle ratio: 8 weeks - CTRL 0.55 vs. AMH ECs 0.19, P < 0.06; and 14 weeks - CTRL 0.29 vs. AMH 0.12, P = 0.05). Notably, at 14 weeks, antral follicles from the AMH group exhibited 3-fold larger diameter than antral follicles in the control group (CTRL median diameter 0.5 mm vs. AMH-ECs 1.5 mm, P < 0.01). Lastly, measurement of AMHRII protein level revealed a median ratio of 22.4 in the CTRL compared to 1.15 in the AMH group (P = 0.001).

CONCLUSIONS: As autotransplantation of ovarian tissue becomes more widely practiced, resolving the mechanisms mediating follicular activation and growth is increasingly relevant. Our unexpected finding, given previous results indicating a suppressive input of AMH, suggests that a chronic AMH stimulus of theca may initially suppress activation but ultimately induces a reductive effect, in part, via negative feedback and downregulation of AMHRII.


CONCLUSIONS: Lack of change in serum creatinine showed there was no overexpression due to variable infusion volumes. FT4 and total T3 were unchanged, suggesting that the increase in TSH was a thyrotropic cell response to lipid/insulin and not a result of altered thyroid hormone. Cortisol, an inhibitor of TSH production, was unaffected by infusion condition. Levels of the lactotroph hormone PRL were not impacted by lipid/insulin, confirming that effects on the pituitary are both complex and cell type specific. Our results imply that the impact of obesity on the hypothalamic-pituitary-gonadal axis is not simply suppressive, and extends beyond reproductive functions. Further research is needed to elucidate mechanisms underlying the selective modulatory pituitary trophic hormones in response to changes in diet and metabolism.

SUPPORT: Internal funding, CRMI.
ETHNIC DISCORDANCE IN SERUM MULLERIAN HORMONE (AMH) IN HEALTHY WOMEN; POPULATION STUDY FROM CHINA AND EUROPE. Scott M. Nelson, MD, PhD; Gemma L. Clayton, PhD; Abigail Fraser, PhD; Sun Ajun, PhD; University of Glasgow, Glasgow, United Kingdom; University of Bristol, Bristol; University of Bristol, Bristol, United Kingdom; Peking Union Medical College Hospital, Beijing, China.

OBJECTIVE: Chinese women are known to have an earlier age at natural menopause than their European counterparts, whether they also have a lower functional ovarian reserve is unknown. This study was designed to assess whether there are ethnic differences in Anti-Mullerian Hormone (AMH) in women of reproductive age.

MATERIALS AND METHODS: Women with regular menstrual cycles, not on hormonal contraception or with any medical history of note, were recruited to provide a day 2-5 early follicular sample in China and Europe. AMH was determined using the Roche Elecsys assay. AMH decline was modelled with a linear, quadratic and quadratic with interaction on age equation to assess the impact of ethnicity.

RESULTS: 1348 subjects met the inclusion criteria and participated in the study; 887 European and 461 Chinese women. Despite the Chinese population being slightly younger 34.07±8.38 years than their European counterparts 34.75±8.87 years, their median AMH was lower 1.87 (IQR 0.73, 3.64) as compared to 2.11 (IQR 0.73, 3.96), with evidence of increasing discordance from age 25 years. In all regression models of the AMH age-related decline, there was evidence of a difference between Chinese and European women. On average AMH was 16% geometric mean ratio:0.49 (95% CI 0.44 to 0.55) lower in the Chinese population compared to the European population.

CONCLUSIONS: There were independent effects of age and ethnicity on serum AMH concentrations, with Chinese women having a substantially lower AMH in adult life than their European counterparts from age 25 onwards.

SUPPORT: None.

REPRODUCTIVE IMMUNOLOGY

INTERFERON GAMMA-INDUCED PROTEIN 10 (IP-10) IS SIGNIFICANTLY LOWER AT EARLY IMPLANTATION IN TWIN VERSUS SINGLETON PREGNANCIES. Samantha Simpson, MD; Janina Kaislasuo, MD, PhD; Gang Peng, PhD; Paulomi Aldo, MS; Michael Paudas, MD; Seth Guller, PhD; Gil Mor, MD, PhD; Lubna Pal, MBBS; Yale University, New Haven, CT; Affiliation not provided.

OBJECTIVE: To determine if pro-inflammatory cytokines in maternal serum differ between twin and singleton gestations in the implantation phase.

MATERIALS AND METHODS: Women with an initial positive β-hCG serum draw after a double or single embryo transfer following in vitro fertilization (IVF) were eligible to participate. Patients were selected for analysis based on healthy term singleton (n=21) or healthy term dichorionic diamniotic (di/di) twin (n=6) delivery. Cytokines tumor necrosis factor alpha (TNFα) and interferon gamma-induced protein 10 (IP-10) were analyzed in day 9-15 serum samples (n=94) from day 9-15 after blastocyst/di/di embryo transfer using the SimplePlex immunoassay platform. Samples were compared throughout the sample period using t-tests and Cohen’s D.

RESULTS: TNFα and IP-10 were detected in all sera samples. From day 9-15, IP-10 was significantly lower in di/di twin gestations than in singleton gestations (day 9-11, 84.5 ± 28.5 v 129.1 ± 67 pg/mL; p=0.01; day 12-13, 93.8 ± 29.2 v 120.8 ± 40.7 pg/mL; p=0.05; day 14-15, 102.7 ± 19.9 v 145.6 ± 63.7 pg/mL; p=0.01). Looking at the overall trend, Cohen’s D was -0.59, indicating that IP-10 was significantly lower in days 9-15 in twin pregnancies (95% confidence interval -1.15 to -0.04). During this same time frame, TNFα showed no significant difference (day 9-11, 5.3 ± 1.7 v 6.2 ± 1.5 pg/mL; day 12-13, 5.2 ± 1.4 v 5.8 ± 1.4 pg/mL; day 14-15, 5.4 ± 1.2 v 6.4 ± 2.2 pg/mL). Cohen’s D for TNFα also was not significantly different (-0.29, 95% confidence interval -0.83 to 0.26).

CONCLUSIONS: This is the first report describing IP-10 in serum in the early implantation phase, and the first report comparing pro-inflammatory cytokines between patients with singletons and di/di twins. We demonstrate that serial IP-10 concentrations are significantly lower throughout the early implantation phase in di/di twin pregnancies when compared to normal singleton pregnancies, while TNFα concentrations are not. This strengthens the inhibitory roles ascribed to IP-10 regarding angiogenesis in pregnancy, as increased angiogenesis was expected in a healthy di/di twin pregnancy.

SUPPORT: Prelude Fertility - Scientific Advisory Board Grant.

SUPEROVULATION ALTERS THE HUMAN UTERINE NATURAL KILLER CELL REPERTOIRE DURING THE WINDOW OF IMPLANTATION. Anna Sokalska, MD, PhD; Scott Gordon, MD, PhD; Snehja Mani, PhD; Charikleia Kalliouri, MD; Monica Mainigi, MD; University of Pennsylvania, Philadelphia, PA; Children’s Hospital of Philadelphia, Division of Neonatology, Philadelphia, PA.

OBJECTIVE: Adverse perinatal outcomes associated with fresh IVF, including pre-eclampsia and growth restriction, have been at least partially attributed to abnormal placentaion secondary to the maternal hormonal environment following superovulation. Trophoblast invasion and uterine vascular remodeling is regulated in part by maternal immune cells, with multiple adverse pregnancy outcomes associated with disturbances in the immune cell populations. A recent study defined three subtypes of natural killer (NK) cells (NK1, NK2, NK3) in the endometrium that may play a role in humoral immune system. The aim of this study was to evaluate the immune cells in superovulation on human endometrial immune cell distribution during the window of implantation.

MATERIALS AND METHODS: Endometrial biopsies and peripheral blood samples were collected from 25 subjects: 16 samples obtained in natural cycle, 3 following a positive pregnancy test and 9 samples obtained 7 days after egg retrieval in gonadotropin stimulated IVF cycles. All participants had regular menstrual cycles, no known history of endometriosis or autoimmune disorders and were free of hormonal and chronic anti-inflammatory treatment prior to their biopsies. Immune cell populations were analyzed using flow cytometry. Serum estradiol (E2) and progesterone (P4) levels were measured by chemiluminescent competitive immunoassay. Student t-test or Mann-Whitney U-test was used to evaluate between-group differences.

RESULTS: Baseline characteristics were comparable for both groups. As expected, serum E2 levels on the day of biopsy were significantly higher in patients following gonadotropin stimulation. No differences in serum P4 levels were noted. Characterization of the total leukocyte population (CD45+ cells) revealed a statistically significant reduction in CD56bright endometrial NK cells in stimulated cycles compared to natural cycles (24.54 ± 3.62 vs. 37.23 ± 2.63 % of total CD45+ cells, p=0.009). When NK cell subtypes were analyzed, there was a significant increase in endometrial NK1 subpopulation as a proportion of all NK cells (19.14 ± 5.4 vs. 9.49 ± 2.53 % of total CD56bright cells, p=0.008) and a decrease of endometrial NK3 subpopulation (28.8 ± 3.3 vs. 49.29 ± 3.86 % of total CD56bright cells, p=0.043) in the stimulated cycles compared to natural cycles. The fraction of NK2 cells as a proportion of all NK cells was unchanged. Changes were seen in the percentage of endometrial CD16+CD56− monocytes/macrophages. There were no differences in the immune cell populations in peripheral blood on the day of biopsy.
CONCLUSIONS: These findings demonstrate that superovulation affects the distribution of NK cells in the endometrium during the window of implantation. Uterine NK cell, specifically NK3 cells, based on marker expression and cytokine production, appear to function in regulating trophoblast invasion during early implantation. These data provide a potential mechanism by which alterations in the maternal hormonal environment may lead to an increased risk of disorders of placentaation and adverse perinatal outcomes.

O-255 Wednesday, October 16, 2019 11:15 AM

UNRAVELLING THE IMMUNOGENETICS OF PREGNANCY: PARENTAL HLA-C ALLOTYPES ARE PREDICTIVE OF PREGNANCY LOSS AFTER SINGLE EUPLOID EMBRYO TRANSFERS. Diego Marin, M.S.,a Xin Tao, Ph.D.,b Li Sun, Ph.D.,b Richard Thomas Scott, Jr., MD. b IVI-RMA New Jersey, Basking Ridge, NJ; bFoundation for Embryonic Competence, Basking Ridge, NJ.

OBJECTIVE: Uterine natural killer cells (uNK) orchestrate successful implantation through cellular responses mediated by their killer cell immunglobulin-like receptors (KIR) and the HLA-C ligands (C1 or C2) presented by trophoblast cells. It has been reported that when patients have KIR AA genotypes (inhibitory) and their embryos are homoz vigorous for the HLA-C2 allele, the risk of miscarriage increases significantly compared to other combinations. Since it is not always feasible to know the embryonic HLA-C ligands before a transfer, this study aimed to evaluate if parental HLA-C genotypes are predictive of clinical outcomes in a context of euploid single embryo transfer (SET).

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Patients undergoing a euploid SET with own eggs were included in the study. Only the first SET per couple and SETs that resulted in a positive B-hCG were included in the analysis since the effect of KIR-HLA interactions occurs after implantation. Maternal KIR and parental HLA-C genotyping was performed using quantitative PCR. The variable “nC2” was created to score each couple based on the number of their C2 alleles. Next, the number of maternal C2s was subtracted from the paternal ones (PC2-MC2) so as to assess if a higher HLA-C2 load from either parent is associated with outcomes. Primary endpoints were ongoing pregnancy and clinical loss rates. Logistic regressions and the Fisher’s exact test were computed when appropriate.

RESULTS: 790 euploid SETs were included in the analysis. Mean maternal age was 35.96 ± 3.74 years. The overall frequency of maternal KIR AA and Bx genotypes was 28.7% and 71.3% respectively. For parental HLA-C alleles, the frequencies were: C1C1 37.4%, C1C2 46.6% and C2C2 16%. Overall ongoing pregnancy rate was 77.59 % (95% CI 74.52-80.45) and remained statistically unchanged irrespective of parental HLA-C or maternal KIR. However, clinical pregnancy loss was positively dependent of parental nC2 in KIR AA patients only (β = 0.73, p = 0.0027), reaching 33.33% when both parents were homoz vigorous C2C2. Regarding each parent’s C2 load, a higher paternal C2 load was significantly associated with lower risk of pregnancy loss in patients only (β = -0.4, p = -0.0074), which also shows that a higher paternal C1 load is associated with a higher risk of clinical loss in this group. In fact, when there were more C1 alleles from father than mother per couple (PC1 > MC1) the risk of clinical loss was significantly increased in the Bx population (OR: 2.37, 95% CI: 1.33 – 4.18).

CONCLUSIONS: The risk of miscarriage increased significantly in relation to parental C2 allotypes in KIR AA patients. Notably, when the parental origin of HLA-C allotypes was investigated, a higher paternal C1 load increased the risk of clinical loss in patients activating KIR (Bx), a finding in alignment with the theory of immunological memory of uNK cells with maternal HLA-C allotypes. This data also suggests that parental KIR-HLA-C genotyping could be useful for counselling patients undergoing euploid SET in cases where HLA-C-based embryo selection is not feasible.

O-256 Wednesday, October 16, 2019 11:30 AM

EFFICIENCY OF IMMUNOMODULATION OF ENDOMETRIUM WITH MIXED PARENTAL AND MATERNAL PERIPHERAL MONONUCLEAR CELLS IN REPEATED INTRACYTOPLASMIC Sperm INJECTION (ICSI) FAILURES. Haneen Eloumi, Dr. Khaleed Mahmoud, Dr. Sonia Maalllah, Dr. Mariem ben Khelifa, Phd. Fathi Zhioua, Dr. Khaleed Terras, Dr. Mohamed Khrouf, Dr clinique la rose, centre FERTILLIA, Tunis, Tunisia.

OBJECTIVE: To date, implantation is the rate-limiting step for the success of IVF. The process of implantation is a complicated process that requires the orchestration of a series of events involving both the embryo and the endometrium. Recently, accumulating evidence has suggested that local immune cells at the implantation site have actively contributed to embryo implantation. Some studies suggested the role of endometrium immunomodulation with maternal activated peripheral mononuclear cells (PBMCs) in implantation success. However, the effect of intra uterine insemination of mixed paternal and maternal activated PBMCs before embryo transfer in RIF cases has not been studied enough. In this direction, the aim of our work is to examine the influence of the type and the number of intrauterine peripheral blood mononuclear cells application on embryo implantation rates for infertile patients.

DESIGN: Prospective study conducted between February 2018 and February 2019. Forty one couples with RIF were included. The patients were categorized into two groups with regard to their treatment type, autologous PBMC: group A (n=18) and co-cultured maternal and paternal PBMC; group B (n=26). Subgroups were defined according to the number of PBMC inseminated: < 2 millions (Group A1 (n=8) and group B1 (n=10); and ≥ 2 millions (Group A2 (n=11) and group B2 (n=13)).

MATERIALS AND METHODS: Mononuclear cells were isolated from patient’s peripheral blood by density gradient centrifugation using commercially available lymphocyte preparation and then cultured for 3 days and transferred into the endometrial cavity prior to embryo transfer. All patients were selected on the following inclusion criteria: failure to achieve a pregnancy following a minimum of three IVF/ICSI cycles in which more than 5 high-grade embryos were transferred, age ≥ 40 years old, primary infertility and absence of uterine pathology.

RESULTS: Baseline clinical parameters and number of embryos transferred were found to be comparable in all groups. Our study demonstrates that activated PBMC promote clinical pregnancy rates (CPR) (39 %). The CPR were significantly higher when at least 2 millions of co-cultured maternal and paternal PBMC were inseminated, group B2, (62%) in comparison respectively to group A1, A2 and B1 (38%; 37%; 10%); (p<0.05). The implantation rate was also significantly higher in group B2 (35.5%) in comparison respectively to group A1, A2 and B1 ((19%; 22%; 8.3%); (p<0.05).

CONCLUSIONS: In conclusion, we provide for the first time the effect of the adjunction of paternal activates PBMC to immune modulate endome trium. Intra Uterine insemination of paternal cultured-activated PBMC 48th prior embryo transfer can provide biological signals specifically paternal antigen and cytokines that can exerts a considerable influence on female reproductive tract physiology by inducing pro inflammatory cytokines, chemokines and interleukines profiles changes to mediate maternal immuno tolerance of the embryo at implantation. The precise mechanism of PBMCs action still unclear and both in vitro and in vivo experiments are needed in order to clarify the mechanism.

O-257 Wednesday, October 16, 2019 11:45 AM

UTERINE NK CELL ACTIVITY IN RECURRENT IMPLANTATION FAILURE- ROLE OF INTRALIPIDS. Krishna Deepika, MS, FRM,a Arveen Vohra, MS, FRM,a bConsultant in Rep Med, Bangalore, India; aSenior Consultant , Milann Fertility Centre, Bangalore, India.

OBJECTIVE: To evaluate Uterine NK cell activity among women with Recurrent Implantation Failure (RIF) and to derive a range of uterine NK cell activity so as to identify the subset of RIF population who would benefit from intralipid infusion therapy.

DESIGN: Prospective study cohort consisted of RIF patients who underwent uterine NK cell activity analysis and depending on RIF NK cell activity, intralipid therapy was administered (n=120). The retrospective control group comprised of RIF patients who did not undergo uterine NK cell analysis for intralipid therapy (n=80).

MATERIALS AND METHODS: Inclusion criteria : Woman who had RIF (defined as failure to achieve a clinical pregnancy after transfer of at least four good-quality embryos in a minimum of three fresh or frozen cycles in a woman under the age of 40 years) who had undergone antagonist protocol IVF cycles with frozen embryos.

Exclusion criteria : Fresh embryo transfer, Thrombophilius, uterine cavity abnormalities, fibroid uterus, adenomyosis and those with contraindications to intralipids such as lipid nephropathy, impaired renal function, pathological hyperlipidemia and acute pancreatitis. Prospective cohort (n=120) underwent endometrial biopsy for uterine NK cell activity on Day 21 of previous cycle after obtaining informed written consent. The Navios-CYTO-STAT tetraCHROME CD45-FITC/CD56-RD1/CD19-EC/CD3-PC5 is a standardised instrument reagent system from Beckman Coulter for evaluation of peripheral T cells, B cells and NK cells from whole blood / tissue samples. Absolute counts were calculated from the total
lymphocyte counts obtained from a Beckman Coulter LH500 analyzer. A level greater than 30% of total endometrial lymphocyte population was adjudged the criteria for administering intravascular intralipid infusion of 20% as bolus dose, when optimal endometrium (thickness ≥ 8 mm and Applebaum Zone 3–4) was observed in transvaginal ultrasound. Sample size calculation was based on to achieve 80% power to detect a difference of proportion of 0.2 of clinical pregnancy rate between the groups. The test statistic used was the two-sided Z test with pooled variance. The significance level of the test was targeted at 0.05.

RESULTS: Receiver operator curve analysis shows that at an elevated uterine NK cell level of 30–38% (at a sensitivity of 60.7% and specificity of 52.2%), minimal benefit was discernible with Intralipid in achieving a positive clinical pregnancy (positive predictive value 49.2%, negative predictive value 63%). The area under the curve depicting predictive value of uterine NK cell level among patients receiving intralipid for predicting clinical pregnancy is only 53%, which is very low — hence the benefit was deemed to be minimal. Above 38% uterine NK cell activity, no benefit was observed with intralipid therapy. Clinical pregnancy rate among those who received intralipid was comparable to those who did not (43.2% vs 42.2%).

CONCLUSIONS: Uterine NK cell activity of 30–38% in RIF patients, minimal benefit of intralipid therapy was discernible. However, there seems to be no significant increase in the pregnancy outcome with Intralipid.

SUPPORT: NIL.

O-258 Wednesday, October 16, 2019 12:00 PM

EXPRESSION AND FUNCTION OF THE PD-1 IMMUNE CHECKPOINT IN THE HUMAN OVARY AND FALLOPIAN TUBE. Joshua Johnson, PhD, Evelyn Mercades Llerena Cari, M.S., Peter Ka Sam, B.S., Elise S. Bales, B.S., Susan Ryu, Ph.D., Liesl Nel-Themaat, PhD, HCCLD, Amanda Nicole Kallen, MD, Alex J. Polotsky, M.S., M.S., Miriam D. Post, M.D., David J. Orlicky, Ph.D., Kimberly Jordan, Ph.D., Benjamin G. Bletter, Ph.D. aUniversity of Colorado Anschutz Medical Campus, Aurora, CO; bYale University, New Haven, CT; cUniversity of Colorado Anschutz Medical Campus, Department of Pathology, Aurora, CO; dUniversity of Colorado Anschutz Medical Campus, Department of Immunology and Microbiology, Aurora, CO.

OBJECTIVE: The Programmed Cell Death Protein-1 (PD-1)/PD-L1 signaling pathway has powerful immunomodulatory action in the context of disease, including cancer. PD-1 receptor activation by its ligands suppresses immune responses, and cancer cells avoid surveillance via PD-1 and/or ligand expression. Conversely, blocking PD-1 signaling can improve cancer immune surveillance and in some cases, treatment outcomes and patient survival. A soluble variant of PD-1 (sPD-1) has been shown to modulate immune response(s), including T cell activation. Because immune and inflammatory pathways impact ovarian function, we asked whether the PD-1 immune checkpoint functions in the human ovary or fallopian tube.

MATERIALS AND METHODS: Deidentified normal patient ovary and oviduct tissue (n=10 per group), and, follicular fluid (FF) collected during clinical oocyte retrievals (n=60 unique samples) were screened for PD-1 pathway expression using immunohistochemical (IHC) staining and ELISA for FF soluble proteins, respectively. Bioactivity of soluble pathway factors was assessed by adding FF to activated human T cells, with and without blocking antibody controls, and interferon gamma (IFNg) was measured as an indicator of T cell activation.

RESULTS: PD-1, PD-L1 and PD-L2 are expressed by ovary and fallopian tube resident immune cells (T cells and macrophages), and also by non-immune cells, including granulosa cells and oocytes. PD-L1 is expressed by normal and transformed (e.g., p53 mutant) cells of the tubal epithelium. Most FF samples contained sPD-1 (30/36 assayed), and all contained soluble ligands (sPD-L1 and sPD-L2) (50/50). Soluble receptor and ligands were present in FF at bioactive levels that can control the degree of T cell activation. Compared to PBS negative control samples, FF addition was found most often to significantly enhance T cell IFNg production. In samples that contained the highest levels of sPD-1, T cell IFNg production was instead lower than control levels. IFNg was negligible in the media of non-activated T cells. Additional controls included alternative first antibodies and no-first antibody controls for IFNg, and blocking antibody controls for T cell activation assays; all of these minimize but do not eliminate the role of chance.

CONCLUSIONS: We herein present data on novel PD-1 signaling in non-immune cells of the ovary that suggest that the pathway may be involved in physiological ovarian functions including the enforcement of follicle, oocyte and embryo immune privilege. These data are immediately relevant to the ontogeny of ovarian cancer and the tubal origins of the disease.


SUPPORT: CU-Anschutz Department of Obstetrics and Gynecology Research Funds and award NIHRO0CA194318 to B.G.B were used to support this study.

PARENTAL AGING

O-259 Wednesday, October 16, 2019 10:45 AM

INFLUENCE OF MATERNAL AGE AND OVARIAN RESERVE ON THE DECISION TO CONTINUE OR TO CANCEL IVF CYCLES IN PATIENTS WITH ONE OR TWO LARGE FOLLICLES. Guy Sharem, M.D., Alina Mariana Maftoudh, M.A., Jacques Balayla, M.D., Nauma Steiner, M.D., Alexander Volodarsky-Perel, M.D., Sara Henderson, M.Sc., Atif Zeadna, M.D., Weon-Young Son, Ph.D., Mali Salman-Divon, Ph.D., Michael H. Dahan, MD aMcGill University, Montreal, QC, Canada; bMontreal, QC, Canada; cAffiliation not provided; dMcGill University Health Centre, Montreal, QC, Canada; eDivision of Reproductive Endocrinology and Infertility, McGill University Health Care Centre, Montreal, QC, Canada; fSenior Lecturer, Ariel, Israel.

OBJECTIVE: To determine factors that influence IVF stimulation that result in one or two mature follicles.


MATERIALS AND METHODS: 465 patients that developed 1-2 follicles ≥14mm on hCG administration day were included. We divided the cycles into three groups based on the female age: ≤34 years old, 35-39 years old, ≥40 years old. Sub-analysis based on antral follicle count and female age was conducted. Statistical analysis was performed with multivariate logistic regression. Power analysis demonstrated a two-sided alpha level of 5% power to detect a difference of 25% with alpha 5% in a sample of 365.

RESULTS: Of the 465 cycles included in the study, 365 cycles (78.8%) ended in embryo transfer. The live birth rate was 5.2% per cycle. The pregnancy rates and LBR per cycle respectively were: 35.5% and 15.6%, for the ≤34-year-olds; 14.7% and 6.4%, for the 35-39-year-olds and 8.4% and 2.7%, for the ≥40-year-olds (P value <0.0001 and 0.001, respectively). Evaluating odds of pregnancy and live birth (LB) as a function of age and antral follicle count (AFC) with multivariate logistic regression controlling for confounding effects, revealed that a one-year increase in age reduces the likelihood of pregnancy and LB by 11% (p=0.002 and 0.026 respectively), and one unit increase in AFC count lead to a 9% increase in the odds of both outcomes (p=0.005 for pregnancy and 0.017 for LB). Evaluating odds of pregnancy and live birth (LB) as a function of age and antral follicle count (AFC) with multivariate logistic regression controlling for confounding effects, revealed that a one-year increase in age reduces the likelihood of pregnancy and LB by 11% (p=0.002 and 0.026 respectively), and one unit increase in AFC count lead to a 9% increase in the odds of both outcomes (p=0.005 for pregnancy and 0.017 for LB). Evaluating odds of pregnancy and live birth (LB) as a function of age and antral follicle count (AFC) with multivariate logistic regression controlling for confounding effects, revealed that a one-year increase in age reduces the likelihood of pregnancy and LB by 11% (p=0.002 and 0.026 respectively), and one unit increase in AFC count lead to a 9% increase in the odds of both outcomes (p=0.005 for pregnancy and 0.017 for LB). Evaluating odds of pregnancy and live birth (LB) as a function of age and antral follicle count (AFC) with multivariate logistic regression controlling for confounding effects, revealed that a one-year increase in age reduces the likelihood of pregnancy and LB by 11% (p=0.002 and 0.026 respectively), and one unit increase in AFC count lead to a 9% increase in the odds of both outcomes (p=0.005 for pregnancy and 0.017 for LB).

CONCLUSIONS: Our data suggests a paradigm shift in reasoning from age being the predictor of outcomes in women with a low response at IVF being the predictor of outcomes in women with a low response at IVF with AFC. The evaluation of both AFC and 2011-2014.


Wednesday, October 16, 2019 10:45 AM
follicles have developed with IVF. This result while controlling for the effect of age and ovarian reserve elucidates that ovarian reserve plays a role in both quality and quantity.

SUPPORT: None.

O-260 Wednesday, October 16, 2019 11:00 AM

SUBDERMAL HORMONE IMPLANT AS TREATMENT FOR THE IMPROVEMENT OF MENOPAUSAL SYMPTOMS IN A PRIVATE FERTILITY CENTER. Arnoldo Gonzalez, M.D., Pasquale Patrizio, M.D., Julio C. Rosales, M.D., Guillermo Russell, M.D., Salomon Alvarado, M.D., Roberto Santos, M.D. *IECH, Monterrey, NL, Mexico; †Yale Fertility Center, New Haven, CT.

OBJECTIVE: To evaluate the effect of testosterone subdermal implants on improvement of menopausal symptoms.

DESIGN: A prospective, observational, inferential analytical study.

MATERIALS AND METHODS: A total of 96 consecutive patients who attended the menopause clinic from August 2017 to December 2018 were prospectively enrolled. Symptoms evaluation was performed with the Menopause Rating Scale (MRS), a specific scoring scale of menopausal symptoms. It is composed of 11 points or items of symptoms that are grouped into three subscales or dimensions: 1) Somatic-vegetative. 2) Psychological. 3) Urogenital. Higher MRS scores are associated with increased deterioration in the quality of life.

Subcutaneous testosterone (2 mg/kg) implants were applied for symptoms relief in all patients and MRS scores assessed before and after. The application of testosterone was carried out in the office under local anesthesia, in the subcutaneous tissue of the gluteal or abdominal regions. The time of effect of the implant was 6 months and no patients required implant removal. The follow-up questionnaire was performed 12 weeks after initial placement. Paired Student t tests were performed to compare variables.

RESULTS: The mean age of the 96 patients was 51 years ± 6.51 and the onset of menopausal symptoms was less than 5 years in all. The mean MRS score (31.93 ± 4.76) had a significant decline (12.37 ± 7.4, P < 0.001) once the implant was applied. Patients experienced the most improvements in Hot flashes (P < 0.001), Cardiac palpitations (P < 0.001), Sleep disorders (P < 0.001), Mood (P < 0.001), Irritability (P < 0.001), Tiredness (P < 0.001), Vaginal Dryness (P < 0.001).

CONCLUSIONS: Testosterone hormone subdermal implants represent a valid alternative to hormone replacement therapy, effectively improving major menopausal symptoms. Further studies and follow-ups are required to evaluate continuous efficacy, tolerability and safety of testosterone implants.

O-261 Wednesday, October 16, 2019 11:15 AM

CIRCULATING ESTRADIOL (E2) LEVELS IN POST-MENOPAUSAL USERS AND NON-USERS OF VAGINAL ESTROGEN. Molly B Moravek, MPH, Sybil L. Crawford, PhD, Daniel McConnell, PhD, John F. Randolph, MD, Elaine Waetjen, MD, Fangbai Sun, MPH, Henry Zhang, PhD, Nanette Santoro, M.D. *University of Michigan, Ann Arbor, MI; †University of Massachusetts Medical School, Worcester, MA; ‡University of California Davis School of Medicine, Sacramento, CA; §Yale University School of Public Health, New Haven, CT; ‡University of Colorado Denver, Aurora, CO.

OBJECTIVE: The U.S. Food and Drug Administration (FDA) applies the same “black box” warning to vaginal estrogens as for systemic estrogens, implying they carry similar cardiovascular, thromboembolic, and breast cancer risks, yet the systemic impact of topical vaginal estrogen use is largely unknown. Using data from the Study of Women Across the Nation (SWAN), we examined serum E2 levels in postmenopausal women using vaginal estrogen products (V-E2) compared to non-estrogen users (NoE2), with the hypothesis that serum E2 levels would be equivalent among the two groups.

DESIGN: Prospective, observational study of 3302 women at baseline who were followed through the menopausal transition and beyond (SWAN) and queried annually about hormone use.

MATERIALS AND METHODS: Serum E2 was measured using a direct, ultrasensitive chemiluminescent immunoassay (England, Clin Chem 2002, 48:1584; detection limit 6pg/mL). We compared postmenopausal V-E2 and NoE2 users before and after adjusting for smoking, body mass index (BMI), race/ethnicity, and study site. We also compared serum E2 levels between recent (<2-4 weeks), remote (≥4 weeks), and never users. Serum E2 values were calculated for all menopause stages for reference. Observations with concurrent systemic estrogen or androgens were excluded from analysis. Data were analyzed using linear mixed models following log transformation of E2 levels; results were backtransformed for presentation.

RESULTS: There were 215 postmenopausal observations (from 131 women) containing V-E2 use and 10232 postmenopausal observations (from 2409 women) with NoE2 use. White women and women with a normal BMI were more prevalent among V-E2 than NoE2 users (68 vs 45% and 57 vs 32%, respectively). Prior to covariate adjustment, serum E2 did not differ between V-E2 and NoE2 users (18.5 ± 8.5 vs 19.1 ± 10.9 ng/mL, P = 0.53). Serum E2 was not related to smoking (p = 0.26), but higher E2 was associated with higher BMI (P < 0.001) and African American race (p = 0.001). After covariate adjustment, mean serum E2 was slightly higher in V-E2 users compared to NoE2 users (20.1 ± 10.6 vs 19.3 ± 10.9 ng/mL, P = 0.01). Adjusted mean serum E2 levels were 20.62 pg/mL in recent V-E2 users, 17.23 pg/mL in remote users, and 17.93 pg/mL in never users; the difference between never users and recent users was statistically significant (P = 0.007). Mean (95% CI) serum E2 (pg/mL) was 50.72 (48.69, 52.83) in premenopause, 48.69 (47.73, 49.67) in early perimenopause, 28.13 (27.10, 29.21) in late perimenopause, 17.87 (17.55, 18.21) in natural postmenopause, and 17.81 (16.46, 19.28) in surgical postmenopause.

CONCLUSIONS: Serum E2 levels are greater in V-E2 users compared to NoE2 users, and in recent V-E2 users compared to never users, but are overall lower than pre- and early perimenopause levels. Women with higher BMI appear less likely to use V-E2, and have slightly higher circulating E2, which may indicate they are less symptomatic. The clinical significance of these small differences in E2 is not known, and may be further clarified by the use of mass spectrometry-based methods.

SUPPORT: Supported by R25HD075737 to NFS and SWAN. The Study of Women’s Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHH, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women’s Health (ORWH) (Grants U01NR004061; U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495). The content of this abstract is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH.

O-262 Wednesday, October 16, 2019 11:30 AM

DO ORAL OVULATION INDUCTION AGENTS OFFER BENEFITS IN WOMEN 38 YEARS AND OLDER? Naama Steiner, M.D.; Jacob Rutter-Ligeti, M.D.; Guy Shrem, M.D.; Alexander Volodarsky-Perel, M.D.; William Buckett, M.D.; Michael H. Dahan, MD. *McGill University Health Centre, Montreal, QC, Canada; †Division of Reproductive Endocrinology and Infertility, McGill University Health Care Centre, Montreal, QC, Canada; ‡Division of REI, McGill University and OriginElle Fertility Clinic and Women’s Health Centre, Montreal, QC, Canada.

OBJECTIVE: Gonadotropins generally have higher pregnancy and multiple rates when compared to oral ovulation inducing medications. This study was performed to compare outcomes in women with age factor infertility, who traditionally were felt not to be good candidates for oral medications with intrauterine insemination (IUI).

DESIGN: This retrospective cohort study was performed to compare the success of ovulation induction using oral agents versus gonadotropins in women ≥38 years old, compared to a control group of younger women.

MATERIALS AND METHODS: First to third stimulated IUI cycles in a single academic fertility center between January 2011 and March 2018. Primary outcome was pregnancy rate (defined by a Beta HCG > 10 mIU/mL) per cycle. A total of 5405 IUI cycles were included. Of these, 3816 IUIs were for women < 38 years at the time of insemination, 1537 (40.3%) cycles with oral agents (Le-trazole or Clomiphene citrate), and 2279 (59.7%) cycles were Gonadotropin stimulation. 747 IUIs were for women 38-39 years old, 254 (34%) cycles with oral agents and 493 (65%) cycles with Gonadotropins. The last group included 842 IUIs for women 40-43 years old, 202 (24%) cycles with agents and 640 (76%) cycles with Gonadotropins. Fisher exact test was performed. Power analysis demonstrated a 98% power to detect a 10% difference with alpha error 5% and 1589 cycles in subjects at least 38 years of age.

RESULTS: Among women older than 38 years, the pregnancy rate did not differ between IUIs using oral agents (N = 166/1537, 10.8%) compared to IUIs with Gonadotropins (N = 267/2279, 11.7%) (p = 0.40). Among women
38-39 years old, the pregnancy rate also did not differ between IUIs using oral agents (N=28/254, 11.02%) compared to IUIs with Gonadotropins (N=52/493, 10.55%) (p=0.90). Surprisingly, in women 40-43 years, the pregnancy rate was significantly higher in the oral agents (N=26/202, 12.87%) compared to IUIs with Gonadotropins (N=39/640, 6.09%) (p=0.0006).

CONCLUSIONS: Likely an undetected bias resulted in lower gonado-tropin pregnancy rates among women 40-43 years of age. However, the use of oral agents for ovarian stimulation with IUI in women older than 40 years of age is an effective treatment strategy given pregnancy rates above 10% per cycle.

O-263 Wednesday, October 16, 2019 11:45 AM

A 5-YEAR ANALYSIS OF DEMOGRAPHICS, CYCLE CHARACTERISTICS AND REPRODUCTIVE OUTCOMES OF 907 EGG FREEZING CYCLES IN PATIENTS WITH DIMINISHED OVARIAN RESERVE AND AGE-RELATED FERTILITY DECLINE. Aylin P. Cil, M.D., Remzi Abali, M.D., Aysen Boza, M.D., Lale S. Karakis, M.D., Mehmet Ceyhan, M.D., Ece Aksakal, M.D., Ipek Keles, Ms, Ozgur Oktem, M.D., Mustafa Barsi Ata, M.D., Mustafa Bahceci, M.D. Ph.D., Bulent Urman, M.D. American Hospital, Istanbul, Turkey; Bahceci Health Group-Fulya IVF Centre, Istanbul, Turkey; Koc University School of Medicine, Istanbul, Turkey.

OBJECTIVE: Since the adoption of new regulations on ART procedures in 2014, non-medical oocyte cryopreservation has been legalized in Turkey for childless women with diminished ovarian reserve (DOR). As older women face age related fertility decline regardless of their ovarian reserve, they also benefit from egg freezing under this regulation. Since there are no studies to date addressing the cycle characteristics and reproductive outcomes of egg freezing cycles in patients with DOR, we aim to evaluate cycle characteristics and reproductive outcomes of women with DOR with those of women with age related fertility decline.

DESIGN: Retrospective data analysis.

MATERIALS AND METHODS: Electronic databases or charts of patients who underwent egg freezing in 3 IVF centers in Istanbul between 2014 and 2019 were retrospectively reviewed. Egg freezing cycles of patients with DOR (DOR group) or patients who were ≥ 38 years with normal/high ovarian reserve according to their age (NR-Aged group) were included into the study. This study reviewed 907 egg freezing cycles of 586 patients. Sixteen percent of women were <35 years old, whereas 66% were over the age of 38. 517 patients with DOR underwent 825 egg freezing cycles and 69 NR-Aged patients underwent 82 egg freezing cycles. In the DOR group, 76 cycles (9%) were cancelled due to inadequate follicular development, premature ovulation, no oocyte or no mature oocytes collected. The mean age and AMH of the DOR group at the time of freezing were 37.4/0.4ng/dl, respectively. Mean number of frozen MII oo-ocytes per cycle was 3.4/2.3. The average number of egg freezing cycles per patient was 1.6±1.1 resulting in a total frozen MII oocyte number of 5.3±3.7 per patient. In the NR-Aged group the mean AMH level was 2.2±1.4 and the mean number of frozen MII oocytes was 11.8±4.1.

A total of 20 patients returned to use their frozen oocytes. None of the three patients returned in the NR-Aged group who had more than 12 frozen oocytes got pregnant. Of the 17 patients in the DOR group, 6 patients did not have embryo transfers and only 5 patients had live births (17.6%), of the two from thawed oocytes (11.7%). However, the third patient got pregnant in the following fresh cycle after thawed oocytes could not be fertilized. In order to increase the number of oocytes, 7 thawing cycles were combined with fresh cycles.

CONCLUSIONS: To our knowledge, this is the first reported analysis of egg freezing cycles of patients with DOR. Young women with DOR is the most important group who will benefit from preventive egg freezing. Since the cycle cancellation rate is high and reproductive outcomes of these pa-tients are very low, these patients should be counseled accordingly about the risks and expectations, and advised to have higher number of oocytes frozen. In accordance with previously published reports, despite high number of frozen oocytes, the chances of getting pregnant for older patients are extremely low. Follow-up and future reproductive outcomes of patients with DOR who undergo egg freezing is very important as these results will be helpful in counseling this patient population.

SUPPORT: None.
POSTER SESSION

ACCESS TO CARE

P-1 Tuesday, October 15, 2019 6:30 AM

DOES AN INSURANCE MANDATE COVER INFERTILITY TREATMENT INCREASE ACCESS TO IN VITRO FERTILIZATION? Kelly Payne, B.A., a Nannan Thirumavalavan, M.D., a Jabez Gondokusumo, B.S., a Adithya Balasubramanian, B.A., a Michael Lehner, B.S., b Jason Scovell, Ph.D., a J. Scott Gabrielsen, M.D., Ph.D., a Dolores J. Lamb, Ph.D., a Larry I. Lipshultz, M.D., a Baylor College of Medicine, Houston, TX; University Hospitals Urology Institute/Case Western Reserve University, Cleveland, OH; University of Texas McGovern Medical School, Houston, TX; Weill Cornell Medical College, New York, NY.

OBJECTIVE: Financial constraints limit many patients from being able to access infertility care, especially assisted reproductive technologies (ART) such as in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI). We sought to determine the impact of state insurance mandates for infertility mandates on the utilization of IVF within each state.

DESIGN: Retrospective analysis of publicly available data.

MATERIALS AND METHODS: All IVF centers in the United States in 2017, their zip code, and number of cycles performed were extracted from CDC data. Using US census data, the median salaries for zip code and state were extracted. The number of IVF centers and number of IVF cycles between states with and without infertility coverage insurance mandates were compared for states where the association between geographic region, income and the number of IVF cycles was evaluated. IVF centers in mandate and non-mandate states were sequentially sorted by the median household income of the zip code they are located in and grouped into successive increments of $10,000 of median household income. Total number of cycles per successful $10,000 income bracket were compared in mandate and non-mandate states. Paired and unpaired Student’s T-tests were performed for continuous variables.

RESULTS: Fifteen states mandate some degree of infertility coverage. States with insurance mandates for infertility coverage had a greater number of yearly IVF cycles per 100,000 residents compared to states without infertility coverage mandates (104 cycles vs 57 cycles per 100,000 residents p = 0.029). However, there was no difference between the number of IVF centers per person between states with and without infertility coverage mandates (0.16 vs 0.13 per 100,000 residents, p = 0.58). On average, IVF centers were located in zip codes with greater median incomes than their respective states ($73,325.17 vs $62,607.53, p < 0.001). This relationship held true for both states with infertility insurance mandates ($79,894.00 vs $66,820.87, p < 0.001) and without infertility insurance mandates ($65,813.11 vs $57,759.77, p < 0.001). There was no significant difference between number of cycles in mandate and non-mandate states at IVF centers located in median household income brackets below $80,000. In centers located in median household income brackets greater than $80,000, the total number of cycles performed was significantly greater in mandate states vs. non-mandate states (p = 0.0461).

CONCLUSIONS: States with insurance mandates for infertility coverage have a greater number of IVF cycles per 100,000 residents, but surprisingly do not have a greater number of IVF centers carrying out these cycles. On the whole, IVF centers are located in relatively wealthier zip codes in both mandate and non-mandate states. Only at IVF centers in zip codes with median household income greater than $80,000 do mandate states have a greater number of IVF cycles than non-mandate states. This suggests that state insurance mandates for infertility coverage may not be making IVF more accessible for all but may be selectively benefitting wealthier geographic regions.

P-2 Tuesday, October 15, 2019 6:30 AM

DEFINING INFERTILITY: HOW THE LANGUAGE USED TO DESCRIBE INFERTILITY SHAPES PUBLIC PERCEPTION AND POLICY. Abigail C. Mancuso, MD, Karen M. Summers, MPH CHES, Rebecca K. Chung, MD, Aaron Scherer, PhD, Ginny L. Ryan, MD, MA, University of Iowa Carver College of Medicine, Iowa City, IA.

OBJECTIVE: To investigate if the label associated with infertility has a causal impact on public perceptions of infertility and infertility treatment.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: Participants aged 18 or older were recruited using an online survey platform. Quotas were set so gender, age, and race/ethnicity reflected national rates.

Participants read a description of infertility that randomly included the label of infertility as a 1) condition, 2) disease, or 3) disability. Participants were then asked about their thoughts on different policies related to infertility including insurance coverage and public assistance programs for treatment, sex education, and public awareness campaigns. At the end of the survey, participants were asked which label they thought best defined infertility. Demographic data collected included age, gender, marital status, political party, religiosity, schooling, income, and history of infertility.

Comparisons were made between both the assigned label and the preferred participant label with the policy outcomes using ANOVA for continuous and chi-square for categorical variables.

RESULTS: Of the 1221 participants, a majority (78%) preferred labeling infertility as a “condition” compared to “disability” (12%) or “disease” (10%). Participants who preferred the label condition were older and less likely to have a previous infertility diagnosis (p < .001) and those reporting higher religiosity were more likely to prefer disease (p = .028). There were no other demographic differences. Participants who preferred labeling infertility as a disability or disease were more likely to support infertility policies such as insurance coverage for treatments and fertility preservation, public awareness campaigns, coverage during sex education, and public assistance programs for treatment (Table).

<table>
<thead>
<tr>
<th>Policy</th>
<th>Condition</th>
<th>Disability</th>
<th>Disease</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insurance Coverage</td>
<td>58*</td>
<td>56</td>
<td>63</td>
<td>.001</td>
</tr>
<tr>
<td>Fertility Preservation</td>
<td>60</td>
<td>59</td>
<td>66</td>
<td>.001</td>
</tr>
<tr>
<td>Coverage</td>
<td>71</td>
<td>70</td>
<td>76</td>
<td>.023</td>
</tr>
<tr>
<td>Public Awareness Campaigns</td>
<td>68</td>
<td>67</td>
<td>73</td>
<td>.010</td>
</tr>
<tr>
<td>Ice Education</td>
<td>71</td>
<td>69</td>
<td>74</td>
<td>.001</td>
</tr>
</tbody>
</table>

*Scale 0-100 with 100 indicating complete support.

The assigned infertility label had little effect on the public perception measures, however, participants were more likely to prefer labeling infertility as a disease or disability if they had been exposed to those labels (p < .001).

CONCLUSIONS: Although there was an overall preference for labeling infertility as a condition, participants who thought of infertility as a disability or disease were more likely to support public policies supporting infertility treatment coverage and increasing infertility awareness.

P-3 Tuesday, October 15, 2019 6:30 AM

PATIENT ACCESS AND UNTAPPED POTENTIAL: CAN NEW DATA DRIVE PROGRESS? Howard Task, BA, b Patty Stull, BS, a Andrew F. Khair, PhD. M.B.A, b Gaurang S. Daftary, MD, M.B.A, bFertility Dynamics, Washington, DC; bFerring Pharmaceuticals, Inc, Parsippany, NJ.

OBJECTIVE: Determine gaps and factors that cause a discrepancy between the potential for, and utilization of, infertility care in the U.S.

DESIGN: Multivariate models to determine potential number of patients for, and actual numbers receiving, treatment in all Nielsen determined U.S. Designated Market Areas (DMAs).

MATERIALS AND METHODS: The number of women receiving treatment by a reproductive endocrinologist was calculated using fresh cycle data reported by the CDC, combined with an estimate of IU1-only patients based on state insurance mandate. A multivariate prediction model was created using ≥20 variables including insurance mandate, age, gender and psycho-demographics in 115 DMAs to predict numbers of patients receiving treatment. Variable coefficients related to treatment potential (defined as need and predisposed) were separated from those impacting
OBJECTIVE: Across the US, the number of patients being cared for in fertility centers has grown considerably over the last years. However, the differential access to infertility care in the regions of the country remains to be understood. Taking into consideration population growth, this study describes and quantifies the evolution and regional variation of the utilization of assisted reproduction (AR) treatment in the US over five years.

DESIGN: Retrospective study.

MATERIALS AND METHODS: We used the publicly available Society for Assisted Reproductive Technology (SART) dataset to measure utilization of AR services in the US between 2011 and 2015. Clinics were grouped into states and into the 4 US census regions. The number of clinics per million (Clinics/1M) and cycles per thousand (Cycles/1k) per region was standardized using the US Census data on the number of females of reproductive age (20-44 years). Trends were assessed using Mann-Kendall test and statistical significance set at P<0.05.

RESULTS: There were 958,231 cycles performed in the US during the study period. On average, there were 8.7 fertility clinics per million females, ranging from an average of 7.6 per million in the South to 10.5 per million in the Northeast. Contrary to the absolute number of cycles, which increased in all regions, the number of cycles per thousand females only increased significantly in the West and Midwest, remaining stable in the Northeast and South (Table). The results for states can be visualized at http://bit.ly/asrm19var.

CONCLUSIONS: The number of cycles in the US increased significantly over the last five years, but the population-standardized rate remained stable in two of the US regions. In association with the unchanging number of clinics, this suggests that in some regions the expansion of fertility services is driven by the female population growth and not by an increasing fraction of this population seeking infertility care. Further research is needed to evaluate the reasons for these variations and their impact on outcomes. These results should be considered when evaluating policies aimed at...

P-5 Tuesday, October 15, 2019 6:30 AM

VARIATION IN AVAILABILITY OF FERTILITY CARE TREATMENTS ACROSS US REGIONS. Leslie B. Ramirez, PhD,1 Alexis Adler, BS,2 Bat-Sheva L. Maslow, MD, MSCTR,3 Joshua U. Klein, MD,4 Urbano L. Franca, PhD.5 Extend Fertility, New York, NY; "Boston Children’s Hospital / Harvard Medical School, Boston, MA.

OBJECTIVE: Across the US, the number of patients being cared for in infertility centers has grown considerably over the last years. However, the differential access to infertility care in the regions of the country remains to be understood. Taking into consideration population growth, this study describes and quantifies the evolution and regional variation of the utilization of assisted reproduction (AR) treatment in the US over five years.

DESIGN: Retrospective study.

MATERIALS AND METHODS: We used the publicly available Society for Assisted Reproductive Technology (SART) dataset to measure utilization of AR services in the US between 2011 and 2015. Clinics were grouped into states and into the 4 US census regions. The number of clinics per million (Clinics/1M) and cycles per thousand (Cycles/1k) per region was standardized using the US Census data on the number of females of reproductive age (20-44 years). Trends were assessed using Mann-Kendall test and statistical significance set at P<0.05.

RESULTS: There were 958,231 cycles performed in the US during the study period. On average, there were 8.7 fertility clinics per million females, ranging from an average of 7.6 per million in the South to 10.5 per million in the Northeast. Contrary to the absolute number of cycles, which increased in all regions, the number of cycles per thousand females only increased significantly in the West and Midwest, remaining stable in the Northeast and South (Table). The results for states can be visualized at http://bit.ly/asrm19var.

CONCLUSIONS: The number of cycles in the US increased significantly over the last five years, but the population-standardized rate remained stable in two of the US regions. In association with the unchanging number of clinics, this suggests that in some regions the expansion of fertility services is driven by the female population growth and not by an increasing fraction of this population seeking infertility care. Further research is needed to evaluate the reasons for these variations and their impact on outcomes. These results should be considered when evaluating policies aimed at...
expanding access to fertility care and the allocation of resources by new fertility centers.

SUPPORT: None.

**P-6 Tuesday, October 15, 2019 6:30 AM**

**NATIONWIDE SURVEY OF ACCESS TO CARE INITIATIVES IN REI PRACTICES ASSOCIATED WITH OB/GYN RESIDENCY PROGRAMS.** Tia Jackson-Bey, MD MPH; Holly Mehr, MD MS; Jacqueline Ho, MD MS; Lasine Aghajanova, MD PhD; Molly M. Quinn, MD; Jacquelyn Rose Hoffman, BA; Christopher N. Herndon, MD; University of Illinois at Chicago, College of Medicine, Chicago, IL; University of California, Los Angeles, Los Angeles, CA; University of Southern California, Los Angeles, CA; Stanford University School of Medicine, Stanford, CA; University of Arizona College of Medicine - Tucson, Tucson, AZ; University of Washington, Seattle, WA.

OBJECTIVE: To survey practice patterns designed to increase access to infertility care among REI practices associated OB/GYN residency programs in the United States.

DESIGN: Cross-sectional survey.

MATERIALS AND METHODS: A total of 281 ACGME certified OB/GYN residency programs were identified. Contact information was found for 270 programs, which were contacted via email and asked to have their REI division director or REI resident rotation director complete an anonymous online survey. The survey included 28 questions on demographics of the residency program, associated REI practice, and presence of initiatives at the institution to expand access to infertility care. Responses were analyzed with logistic regression analysis using STATA software, with significance set at alpha=0.05.

RESULTS: A total of 80 responses were received for a 30% response rate. Of these, 41% (n=33) of REI practices associated with OB/GYN residency programs identified as academic, 24% (n=19) private practice, 26% (n=21) hybrid academic/private, 4% (n=3) military practices and 5% (n=4) other. Responses were received in all US geographic regions with 22% (n=17) located in the Northeast, 33% (n=26) South, 29% (n=23) Midwest, and 16% (n=13) West. In regards to practice size, 20% (n=16) of practices had 1-2 REI providers, 40% (n=32) had 3-5 providers, and 31% (n=25) had 6 or more providers. Eighty eight percent (n=70) of practices offered IVF and of those 78% (n=55) reported utilizing an onsite embryology lab. Thirty eight percent (n=30) of practices reported having an REI fellowship. Of clinical initiatives to expand access to infertility care to lower income patients, respondents reported having an REI fellowship. Of clinical initiatives to expand access to infertility care (39%, n=31), institutional based discounts or write-offs (41%, n=9), and pharmaceutical company based medication discount programs (36%, n=8). Of practices with a low-cost IVF program, 40.9% (n=9) were developed within the past five years.

CONCLUSIONS: To our knowledge, this study of REI practices associated with OB/GYN residency programs is among the first to broadly survey clinical access to infertility care initiatives across the United States. Our findings demonstrate utilization of diverse approaches to expand access to care. Larger practices and academic REI programs were more likely to have clinical initiatives to increase access to care.
cryopreservation performed for medical indications was associated with higher gonadotropin dose (aRR 1.22, 95% CI 1.12-1.33) and higher likelihood of cancellation (aRR 1.68, 95% CI 1.46-1.92) to compare to elective OC.

CONCLUSIONS: The number of OC cycles among women with a cancer diagnosis has increased over the past 5 years; however the percentage OC cycles for cancer has remained stable. While patient demographic characteristics were different among those freezing eggs for fertility preservation due to cancer, the cycle outcomes were comparable to elective OC after controlling for potential confounding. Women freezing eggs for oncologic reasons can be reassured that their cycle outcomes are comparable to those freezing eggs electively. The outcomes of the subsequent egg thaw, fertilization, and transfer cycles remain unknown.

SUPPORT: N/A.

P-8 Tuesday, October 15, 2019 6:30 AM

RISK FACTORS FOR ATYPICAL HYPERPLASIA AND ENDOMETRIAL CANCER IN THE INFERTILITY POPULATION: A CASE-CONTROL STUDY. Jenna Lipson Kahn, M.D.,a 1 2 3 Lindsey Buckingham, M.D., 1 a University of California San Diego School of Medicine, La Jolla, CA; 1 University of Pennsylvania Health System, Philadelphia, PA; 1 Affiliation not provided; 2University of Pennsylvania Health System, Philadelphia, PA; 3 University of Pennsylvania Health System, Philadelphia, CA; 4 University of Pennsylvania, Philadelphia, PA GA.

OBJECTIVE: The reported incidence of atypical endometrial hyperplasia (AH) and endometrial cancer (EC) in American women under the age of 50 years old is <0.01%. The incidence of AH and EC diagnosed on routine infertility evaluation in a diverse American population is unknown. The study objectives were to estimate the incidence and identify independent risk factors for AH/EC in infertile women.

DESIGN: Case-control study.

MATERIALS AND METHODS: Data were abstracted from the electronic medical record on all female patients ages 18-50 years seeking initial evaluation at an academic infertility center from 11/1/2009 to 12/31/2018. Patients with prior diagnosis of breast, ovarian, or colon cancer, or known genetic pre-disposition to cancer were excluded, leaving 11,569 infertile women contributing information. For the case-control study, cases were defined as patients who were diagnosed with AH or EC as part of an infertility workup (n=22). Controls without AH or EC were randomly selected from other women whose infertility was attributed to any female or unexplained factor and underwent an infertility evaluation during the same year in a 10:1 ratio (n=220). A logistic regression was used to estimate odds of AH or EC accounting for covariates such as age, race, BMI, and presence of ovulatory dysfunction. A forward variable selection method was used to arrive at a multivariable model of independent risk factors and to examine potential confounders.

RESULTS: We identified a total of 13,634 women with breast cancer who underwent treatment with chemotherapy. The median age was 39 years with 755 women <30 (5.5%) years of age and 12,879 >30 (94.5%) years old. AH/EC was identified in 111 of these women (0.83%). The incidence of AH/EC identified during an infertility workup is approximately 10 times higher than that reported in a general population. The rate of AH/EC was higher in women age 15-30 years compared to women age 30-45 (2.8% vs 0.7%) (P<0.001). During the study period, the utilization of GnRH agonist increased from 0.3% in 2008 to 1.3% in 2017 (P<0.001). Use of GnRH agonist was higher in the Northeast (2.0%) compared to the northern central (0.7%), southern (0.6%) and western (0.5%) U.S. (P<0.001).

CONCLUSIONS: The utilization of GnRH agonists among reproductive age women with breast cancer undergoing chemotherapy is extremely low.

P-9 Tuesday, October 15, 2019 6:30 AM

UTILIZATION OF GONADOTROPIN-RELEASING HORMONE AGONISTS FOR PRESERVATION OF OVARIAN FUNCTION IN WOMEN WITH BREAST CANCER RECEIVING CHEMOTHERAPY. Sally F. Vitez, MD, Ling Chen, MD MPH, Paula C. Brady, MD, Jason D. Wright, MD, Columbia University Medical Center, New York, NY.

OBJECTIVE: To determine the use and predictors of GnRH (gonadotropin-releasing hormone) agonists for ovarian conservation in young, reproductive age women with newly diagnosed breast cancer undergoing chemotherapy.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The MarketScan database was used to identify women 15-45 years of age with newly diagnosed breast cancer from 2008-2017. All patients underwent cancer-directed surgery (lumpectomy, mastectomy, biopsy or lymph node evaluation) and received cytotoxic chemotherapy within three months before or after surgery. Patients were considered to have received GnRH agonist therapy if they had one claim for a GnRH agonist in the same period. All women with history of oophorectomy before or during the study period were excluded from the study. Trends and predictors of GnRH agonist use were described and compared using Cochran-Armitage trend test and Chi-square tests.

RESULTS: We identified a total of 13,634 women with breast cancer who underwent treatment with chemotherapy. The median age was 39 years with 755 women <30 (5.5%) years of age and 12,879 >30 (94.5%) years old. AH/EC was identified in 111 of these women (0.83%). The incidence of AH/EC identified during an infertility workup is approximately 10 times higher than that reported in a general population. The rate of AH/EC was higher in women age 15-30 years compared to women age 30-45 (2.8% vs 0.7%) (P<0.001). During the study period, the utilization of GnRH agonist increased from 0.3% in 2008 to 1.3% in 2017 (P<0.001). Use of GnRH agonist was higher in the Northeast (2.0%) compared to the northern central (0.7%), southern (0.6%) and western (0.5%) U.S. (P<0.001).

CONCLUSIONS: The utilization of GnRH agonists among reproductive age women with breast cancer undergoing chemotherapy is extremely low.
P-11 Tuesday, October 15, 2019 6:30 AM

REPRODUCTIVE POTENTIAL OF VITRIFIED OO CYTES AND EMBRYOS PRODUCED FROM IN VITRO MATURATION CYCLES OF CANCER PATIENTS FOR FERTILITY PRESERVATION. Weon-Young Son, Ph.D, Helene Creux, M.D., Sara Henderson, M.Sc, Shaoguang Jin, Ph.D., Jhin-Ta Chung, M.Sc., William Buckett, M.D. Division of Reproductive Endocrinology and Infertility, McGill University Health Care Centre, Montreal, QC, Canada.

OBJECTIVE: Few clinical options for fertility preservation (PF) are available to women with cancer. Although vitrification of oocytes/embryos obtained from IVF cycles has been used successfully in the PF program, controlled ovarian stimulation (COH) is contraindicated for patients with certain forms of cancer. In addition, many cancer patients have limited time to do COH before therapy. In these cases, immature oocyte collection followed by in vitro maturation (IVM) can be an alternative. This vitrification technique has also been applied to cryopreserve oocytes/embryos obtained from IVM program, but data about embryological and clinical outcomes is limited. The aim of this study was to evaluate post-thawing outcomes of immature oocytes collected by transvaginal aspiration in a fertility preservation program for women with cancer.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: IVM treatment for cancer patients was performed after withdrawal of the menstrual cycle. IVM oocyte retrieval was performed 38 h after an administration of 10,000 IU hCG. Immature oocytes obtained were cultured in vitro until 48 hours. The matured oocytes were cryopreserved using vitrification method either mature stage or cleavage stage after fertilization with partner sperm. We conducted study of cancer patients treated in a university based IVF center for 16 years (2003-2018). We reviewed the records of 213 cancer patients who underwent IVM cycles (n=237) for PF for cancer. All embryos and oocytes that were vitrified and warmed were included in the study. Post-warming embryological and clinical outcomes were evaluated.

RESULTS: Most frequent cancer for PF in our IVM program was breast cancer (67.6%) followed by hematological cancer (17.8%). The median time lapse between returning to normal ovarian function after chemotherapy was 6.0 (4–13) years for IVM oocyte and 5.5 (4–13] years for IVM embryo cryopreservation. Thirty-four cycles (14.8%) were cryopreserved from eight IVM cycles (mean = 2.7 (range 1–4)). Survival rate per embryo was 92.4 % and 24 embryos (mean =2.0) were transferred. Three patients became clinically pregnant (25.0% per cycle), resulting in the normal delivery of a healthy baby, one ongoing for 34 weeks and one miscarriage. Live birth/ongoing pregnancy rate per patient was 25.0% (2/8). In the IVM oocyte cryopreservation, 77 oocytes were warmed from 8 patients (9 cycles), survival rate per oocyte was 71.6 %, 56.8 % normal fertilization and cleavage rate per embryo was 68.1%. Two cycles of embryo transfers were canceled due to no cleavage. Out of 7 ET cycles, there were 2 biochemical pregnancies, but no clinical pregnancy. While these agents are known to decrease ovarian reserve, our novel time point to pregnancy was between age at pregnancy attempt and CED was also not significant (p=0.71). No associations were found between race, BMI, age at cancer diagnosis, or age at pregnancy attempt and risk of infertility.

CONCLUSIONS: Abdominopelvic radiation was associated with a 3-fold higher rate of infertility. Exposure to alkylating chemotherapy, cyclophosphamide, and CED were not associated with infertility in AYA survivors. However, cryopreservation of oocytes collected from IVM pregnancy. Out of 7 ET cycles, there were 2 biochemical pregnancies, but no clinical pregnancy. While these agents are known to decrease ovarian reserve, our novel time point to pregnancy was between age at pregnancy attempt and CED was also not significant (p=0.71). No associations were found between race, BMI, age at cancer diagnosis, or age at pregnancy attempt and risk of infertility.

CONCLUSIONS: Abdominopelvic radiation was associated with a 3-fold higher rate of infertility. Exposure to alkylating chemotherapy, cyclophosphamide, and CED were not associated with infertility in AYA survivors. However, cryopreservation of oocytes collected from IVM pregnancy. Out of 7 ET cycles, there were 2 biochemical pregnancies, but no clinical pregnancy. While these agents are known to decrease ovarian reserve, our novel time point to pregnancy was between age at pregnancy attempt and CED was also not significant (p=0.71). No associations were found between race, BMI, age at cancer diagnosis, or age at pregnancy attempt and risk of infertility.

CONCLUSIONS: Abdominopelvic radiation was associated with a 3-fold higher rate of infertility. Exposure to alkylating chemotherapy, cyclophosphamide, and CED were not associated with infertility in AYA survivors. However, cryopreservation of oocytes collected from IVM pregnancy. Out of 7 ET cycles, there were 2 biochemical pregnancies, but no clinical pregnancy. While these agents are known to decrease ovarian reserve, our novel time point to pregnancy was between age at pregnancy attempt and CED was also not significant (p=0.71). No associations were found between race, BMI, age at cancer diagnosis, or age at pregnancy attempt and risk of infertility.

CONCLUSIONS: Abdominopelvic radiation was associated with a 3-fold higher rate of infertility. Exposure to alkylating chemotherapy, cyclophosphamide, and CED were not associated with infertility in AYA survivors. However, cryopreservation of oocytes collected from IVM pregnancy. Out of 7 ET cycles, there were 2 biochemical pregnancies, but no clinical pregnancy. While these agents are known to decrease ovarian reserve, our novel time point to pregnancy was between age at pregnancy attempt and CED was also not significant (p=0.71). No associations were found between race, BMI, age at cancer diagnosis, or age at pregnancy attempt and risk of infertility.
likely to be offered cryopreservation (p<0.001 and p=0.005, respectively). Patients aged 30-39, 40-49, and 50-60 were significantly less likely to receive counseling when compared to patients aged 18-29 while controlling for other variables (OR 0.41, 0.12 and 0.05 respectively, p<0.001 for all 3 groups).

CONCLUSIONS: Reproductive side effects are not as commonly discussed as other systemic side effects when a patient receives a cancer diagnosis or when they start treatment. Our study indicates that cryopreservation is vastly underdiscussed. Younger patients, those undergoing chemotherapy during their treatment period, and a diagnosis of testicular and prostate cancer were more likely to receive cryopreservation counseling. As assisted reproductive techniques have become more successful and readily available, it is important to include options and counseling for all patients.

P-14 Tuesday, October 15, 2019 6:30 AM
FERTILITY-SAVING TREATMENT (FST) AND ASSISTED REPRODUCTIVE TECHNOLOGY (ART) IN PATIENTS WITH ENDOMETRIAL CARCINOMA (EMCA) AND ENDOMETRIAL INTRAEPITHELIAL NEOPLASIA (EIN): PREGNANCY OUTCOMES AFTER EMBRYO TRANSFER (ET), Hilary Friedlander, MD, Jennifer K. Blakemore, MD, David H. McCulloh, Ph.D., Mary Elizabeth Fino, MD, NYU School of Medicine, New York, NY; NYU Langone School of Medicine, New York, NY; NYU Langone Health, New York, NY.

OBJECTIVE: Non-surgical management for patients desiring future fertility with EMCA and its' precursor, EIN, has the goal of clearance of affected tissue and reversion to normal endometrial function (1). Only approximately 15% of these patients will have a livebirth (LB) without the need for ART (2). Despite this low number, little information exists on the pregnancy outcomes for patients who will go on to utilize ART. We investigated the pregnancy outcomes for patients who underwent ET after FST.

DESIGN: Retrospective cohort study of all patients who underwent ET after FST for EMCA or EIN at a single center between 1/2003 and 12/2018.

MATERIALS AND METHODS: An analysis of all patients and ET outcomes after FST was performed. Patients who utilized ART but did not yet return for ET were excluded. Descriptive data are presented as mean ± SD. Observed ET outcomes were sub-grouped into 1) LB + ongoing pregnancy (OP) and 2) spontaneous abortion (SAB) + not pregnant (NP). Observed outcomes were compared to expected outcomes matched for age and type of transfer [fresh or frozen, number of embryos transferred, and with or without pre-implantation genetic testing (PGT) at our center] with a Wilcoxon Signed-Rank Test, p < 0.05 considered significant.

RESULTS: 14 patients, 3 with EMCA and 11 with EIN, met criteria for inclusion for a combined total of 40 ETs. The mean age at initiation for ART following FST was 35.14 ± 4.77 (range 28 to 44) and includes two patients, aged 40 and 44, who ultimately used donor eggs. The average BMI at diagnosis was 26.51 ± 6.17. FSTs prior to ET included megestrol acetate (n=7), oral progesterone (n=5), levonorgestrel intrauterine device (n=1), and polypectomy (n=1). The average time from diagnosis to first ET was 1.62 years ± 2.70 years. The average number of ETs per patient was 2.86 ± 2.03, with a range of 1 to 9. Of 40 ETs, 10 transfers were fresh ETs with an average of 2.70 ± 1.06 embryos transferred per cycle. Three ETs were untested donor eggs, each with a single embryo transferred per cycle. Thirteen were frozen untested ETs, with an average of 1.77 ± 0.81 embryos transferred per cycle. Six patients elected to use PGT [Array Comparative Genomic Hybridization (aCGH) and Next Generation Sequencing (NGS)] for FST of 14 ETs and 24 ETs, with an average of 1.69 ± 0.87 embryos transferred per cycle. Outcomes for all ETs included 7 LB, 1 OP, 8 SAB, and 24 NP. An analysis of observed outcomes by sub-group, compared to the expected from matched controls (age, ET type and number, and PGT as described above) showed that patients with EMCA/EIN after FST had a significantly lower LB/OP rate than expected, Z = -5.04, df = 39, p < 0.01. A sub-group analysis of the 14 euploid ETs (7 single by NGS, 4 single by aCGH, 3 double by aCGH) resulted in a LB/OP rate of 21.4% compared to an expected rate of 62.8% (Z = -3.32, df = 13, p < 0.001).

CONCLUSIONS: Patients who have undergone FST for EMCA/EIN have significantly poorer outcomes than expected after ET. Further evaluation of the impact of the diagnosis, treatment and repeated cavity instrumentation for EMCA/EIN is necessary to create an individualized and optimized approach for this unique patient population.


P-15 Tuesday, October 15, 2019 6:30 AM
OVARIAN STIMULATION IN CANCER PATIENTS: RANDOM VERSUS CONVENTIONAL START. Andrea Natalia Coscia, MD, Mariana Miguens, M.D., Mariana Cecilia Calvo, MD, Rocio Belen Anria, M.D., Milfra Espinal, MD, Elayne Margarita Vasquez, MD, Sergio D. Papier, Sr., M.D. CEGYR, Ciudad Autonoma de Buenos Aires, Argentina; Cegyr, Buenos Aires, Argentina.

OBJECTIVE: To determine if random start ovarian stimulation in cancer patients provides similar results compared to conventional stimulation starting in follicular phase.

DESIGN: Retrospective data analysis at a single center (CEGYR).

MATERIALS AND METHODS: All patients undergoing oocyte cryopreservation for fertility preservation due to recent cancer diagnosis were reevald from 2012 to 2018.

Patients were grouped according to random start or conventional start of the ovarian stimulation. Conventional start was defined as scheduled in early follicular phase initiation of gonadotrophins; random start was initiated at any other moment of the menstrual cycle.

The analyzed variables were: number of oocytes, number of matured oocytes (metaphase II), and cycle length.

RESULTS: 71 cycles met inclusion criteria. Oocytes were collected of 23 (33%) patients on the random start group and 48 (67%) from the conventional one.

Mean age was 33.8 years old in the conventional and 33.25 years old in the random start groups. (p=0.65 IC95%, 2.04-3.23).

The mean number of oocytes collected were similar 11.9 (conventional) versus 10.4 (random) (p=0.47 IC95%, 2.65-5.66) and mean number of mature oocytes vitrified was also similar (metaphase II): 9.30 (conventional) vs 7.6 (random) (p=0.34 IC95%, 1.81-5.13).

The cycle duration was different, being the conventional shorter (9.7 days) than the random group (11.3 days) (p=0.0019 IC95%, 0.61-2.58).

CONCLUSIONS: Random start stimulation cycles for cancer patients has comparable results and allows patients to start gonadotrophin stimulation irrespective of menstrual cycle phase, with no impairment of oocyte yield and only a small increase of cycle duration.

Random start is a good opportunity for patients who are run out of time and face a fertility threatening medical condition.

P-16 Tuesday, October 15, 2019 6:30 AM
ADDED BENEFIT OF IMMATURE OOCCYTE MATURATION FOR FERTILITY PRESERVATION IN WOMEN WITH MALIGNANCY. Samer Tammou, M.D., Alexander Volodarsky-Perel, M.D., Weon-Young Son, Ph.D, Togas Tulandi, M.D., William Buckett, M.D. Reproductive center- IVF unit. Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; Division of Reproductive Endocrinology and Infertility, McGill University Health Care Centre, Montreal, QC, Canada.

OBJECTIVE: To assess the added value of maturing immature oocytes collected during fertility preservation treatments in women with malignancy.

DESIGN: A retrospective case control study conducted at a tertiary academic IVF unit.

MATERIALS AND METHODS: Patients: 327 cancer patients undergoing fertility preservation treatment from 2009 to 2017. We compared oocyte maturation rates and cycle parameters from 3 types of fertility preservation treatments: 1. Stimulated IVF cycle (n=143), 2. Non-stimulated IVM cycle (n=158), 3. Follicle aspiration and oocyte collection from ovarian tissue prepared for ovarian tissue cryopreservation followed by in vitro maturation of the immature oocytes (n=48). The primary outcome measure was the maturation rate and the number of mature oocytes. The secondary outcomes were oocyte fertilization and embryo development rates.

RESULTS: The mean maturation rate in IVF cycles was 38% and in the non-stimulated IVM cycles was 55%. In women who chose to cryopreserve their oocytes, similar fertilization and embryo cleavage rates were found in oocytes that matured after stimulated IVF cycles compared to non-stimulated
OBJECTIVE: Endometrial intraepithelial neoplasia (EIN) is the precursor to type 1 endometrioid adenocarcinoma, which is caused by unopposed estrogenic proliferation of the endometrium. Hysterectomy is curative in up to 98% of cases, but women desiring fertility preservation now have access to hormonal therapy as a treatment option. Our objective was to characterize patient satisfaction and subsequent reproductive outcomes among patients with EIN or grade 1 endometrial adenocarcinoma who elected fertility-sparing treatment.

DESIGN: retrospective cohort, survey.

MATERIALS AND METHODS: We performed a retrospective medical record review for all patients seen in consultation for EIN or grade 1 endometrial adenocarcinoma from a single gynecologic oncology practice at a tertiary care hospital from 2007 through 2016. The abstracted data included patient characteristics, fertility treatment, and reproductive outcomes. We also invited patients to complete a survey, either online or via telephone, to understand patient experiences with fertility-sparing management of EIN and type 1 endometrioid adenocarcinoma. Reported data are from a combination of the medical record review and the survey.

RESULTS: There were 64 eligible patients, and 41 (64%) completed the survey. Among the 64 patients, the majority (77%) had EIN. Initial treatment included a progestin-containing intrauterine device for 61%, an oral progestin for 33%, and both for 1%; initial treatment was unknown for 5%. Complete regression was documented in 69% of patients, and 26% underwent hysterectomy. Roughly half of patients (56%) had a documented infertility consultation, and 36% pursued treatment with ova

OBJECTIVE: Ovarian stimulation with exogenous gonadotropins leads to a significant rise in circulating estrogen levels which could aggravate the spread of breast cancer. The use of anti-aromatase agents such as letrozole could prevent this elevation. But is it safe and effective in fertility preservation?

DESIGN: We conducted a prospective comparative study.

MATERIALS AND METHODS: A total of 171 patients were referred to our FP consult. Only 143 patients underwent fertility preservation (oocyte/embryo vitrification) and 75 amongst them had breast cancer.

A FP consultation is provided by both a gynecologist and a biologist of the department. A complete physical examination is performed. An informed consent is signed before starting the procedure. The evaluation of the ovarian reserve is done by Antral Follicle Count (AFC) ultrasound and AMH dosage.

The stimulation is conducted according to a random-start antagonist protocol using GnRH agonist triggering. For patients with breast cancer, the adjunction of letrozole 5mg/day was started the first day of ovarian stimulation and continued 7 days after oocyte pick up, while closely monitoring estrogen levels during COH.

We compared the number of mature oocytes obtained between patients with breast cancer (Group 1) and patients diagnosed with other types of cancer (group 2).

RESULTS: The average age of our patients (years) in group 1 was 30.3 +/- 3.7 and 26.9 +/- 6.7 in group 2; with no significant statistical difference (p = 0.73). The evaluation of ovarian reserve using AFC (12.3 +/- 6.2 vs 13.9 +/- 6.4; p = 0.7) and serum AMH levels (2.43 +/- 2.3 ng/ml vs 2.8 +/- 2.45 ng/ml; p = 0.3) showed similar results in both groups.

The duration of the ovarian stimulation was not significantly different between both two groups: 10.2 +/- 2.3 days vs 11.8 +/- 3.1 days; (p = 0.5).

Estradiol level on the day of ova
tirritation was 479 +/- 323 pg/ml in the breast cancer group versus 1701 +/- 682 pg/ml in the other group (p = 0.02).

The number of CCOs obtained in the breast cancer group was 10.76 +/- 8.39 compared with 9.11 +/- 6.81 in the group 2 and the difference was not significant (p = 1.83).

The mean number of mature metaphase II oocytes collected in the breast cancer group was 7.38 +/- 6.11 oocytes versus 6.09 +/- 4.72 oocytes in group 2. The difference was not statistically significant either (p = 1.33).

CONCLUSIONS: Breast cancer is one of the most frequent malignancies in women worldwide and the demand for fertility preservation is on the rise. Letrozole would provide much ease and safety during emergency controlled ovarian stimulation, without negatively impacting its outcome.
Objective: To validate an automated and robotic liquid nitrogen vapor-based storage tank for cryopreserved embryos and gametes.

DESIGN: Experimental study.

MATERIALS AND METHODS: Cryopreserved mouse embryos (2PN-stage) in straws (Embryotech, Haverhill, MA) were distributed into platform-specific containers and either robotically uploaded into the automated tank (Group A) or transferred to a liquid nitrogen-filled dewar (Group B). Five days of storage ensued after which the embryos were robotically or manually retrieved from the tank or dewar, respectively, for warming. In each group, post-warming survival was evaluated and embryos were randomly allocated to culture in groups of 10 for incubation at 37°C in an atmosphere of 5% CO2/5%O2 for 96 hours. At the end of the incubation period, blastocyst formation rate (%blastocysts/2PN) was assessed. One-way ANOVA was applied for statistical analysis.

RESULTS: In both Groups A and B, post-warming survival of 2PN was 100%. Blastocyst formation rates were 93.2 ± 100% (p = 0.57) in Group A and 91.3 ± 0.57% (95% CI 1.02 - 1.45) in Group B. In the multimodal regression model, shorter interval was significantly associated with having more favorable outcome, even when controlling for age and AMH (p = 0.03).

CONCLUSIONS: Our data suggest that there is no evidence to support waiting 1 MC before undergoing a subsequent retrieval in women undergoing OC. Furthermore, intervals of ≥ 3 MC may be associated with decreased yield. While this study may be limited by its sample size, it represents the largest to date evaluating oocyte yield in subsequent cycles in either IVF or OC cycles.

P-20 Tuesday, October 15, 2019 6:30 AM


OBJECTIVE: To validate an automated and robotic liquid nitrogen vapor-based storage tank for cryopreserved embryos and gametes.

DESIGN: Experimental study.

MATERIALS AND METHODS: Cryopreserved mouse embryos (2PN-stage) in straws (Embryotech, Haverhill, MA) were distributed into platform-specific containers and either robotically uploaded into the automated tank (Group A) or transferred to a liquid nitrogen-filled dewar (Group B). Five days of storage ensued after which the embryos were robotically or manually retrieved from the tank or dewar, respectively, for warming. In each group, post-warming survival was evaluated and embryos were randomly allocated to culture in groups of 10 for incubation at 37°C in an atmosphere of 5% CO2/5%O2 for 96 hours. At the end of the incubation period, blastocyst formation rate (%blastocysts/2PN) was assessed. One-way ANOVA was applied for statistical analysis.

RESULTS: In both Groups A and B, post-warming survival of 2PN was 100%. Blastocyst formation rates were 93.2 ± 100% (p = 0.57) in Group A and 91.3 ± 0.57% (95% CI 1.02 - 1.45) in Group B. In the multimodal regression model, shorter interval was significantly associated with having more favorable outcome, even when controlling for age and AMH (p = 0.03).

CONCLUSIONS: Our data suggest that there is no evidence to support waiting 1 MC before undergoing a subsequent retrieval in women undergoing OC. Furthermore, intervals of ≥ 3 MC may be associated with decreased yield. While this study may be limited by its sample size, it represents the largest to date evaluating oocyte yield in subsequent cycles in either IVF or OC cycles.

P-20 Tuesday, October 15, 2019 6:30 AM

AUTOMATED VITRIFICATION FOR EMBRYO CRYOPRESERVATION: PRELIMINARY COMPARATIVE RESULTS AND FIRST LIVE BIRTH IN EUROPE. Mariabeatrice Dal Canto, BSci, PhD, Clarissa Moutier, BSci, Fausta Brambillasca, BSci, PHD, Maria Cristina Guglielmo, BSci, PHD, Alessandro Bartolacci, BSci, Mario Mignini Renzini, MD, Rubens Fadini, MD, Jose Buratini, DVM, PHD, Biogenesi Reproductive Medicine Centre, Monza, Italy; Biogenesi Reproductive medicine Center, Monza, Italy.

OBJECTIVE: Automated vitrification has been made available recently, but its clinical efficiency has not been properly addressed in relation to manual vitrification. Therefore, the objective of this ongoing study is to compare clinical outcomes following automated embryo vitrification with those achieved after manual vitrification.

DESIGN: In June 2018 we began a study in which, so far, we have vitrified 9 mature cleavage stage embryos and 161 blastocysts using the automated vitrification system (Gavi®-Genea Biomedx), and 203 cleavage stage embryos and 255 blastocysts using the universally accepted/gold-standard system for manual vitrification (Kitazato Vitrification - Cryotop® Kit). This study is still in progress.

MATERIALS AND METHODS: Participants are couples undergoing embryo transfer following vitrification from June 2018 in our fertility centre. Embryos were cryopreserved using Gavi® according to manufacturer’s
instructions or with Cryotop®. Embryo quality, number of transferred embryos and patient age have been balanced in both groups. Embryos were thawed according to the manufacturer's instructions and transferred in double (cleavage stage embryos) or single transfers (blastocysts). The clinical end-point for the comparative analysis is clinical pregnancy rate. Clinical pregnancy has been diagnosed by ultrasound examination 7 weeks after transfer, following a positive β-hCG test.

RESULTS: So far, we thawed 30 cleavage stage embryos vitrified with Gavi®, which were utilised in 15 double embryo transfers. During the same period, 66 cleavage stage embryos vitrified with Cryotop® were also double transferred (33 DET). So far, clinical pregnancy rates after automated and manual vitrification of cleavage stage embryos are 26.7% (4/15) and 33.3% (11/33), respectively. In parallel, we thawed 36 blastocysts after automated vitrification and 77 blastocysts after manual vitrification, all of them utilised in single transfers, except for 1 blastocyst from the manual vitrification group which was classified as degenerated after thawing. So far, clinical pregnancy rates after automated and manual vitrification of blastocysts are 44.4% (16/36) and 32.9% (25/76), respectively. No miscarriages have been observed so far after automated vitrification of cleavage stage embryos (0/4), whereas the abortion rate following manual vitrification of cleavage stage embryos is 27.3% (3/11) so far. For cryopreserved blastocysts, abortion rates are 12.0% (3/25) and 12.5% (2/16) with manual and automated vitrification, respectively, so far. Theses results transferred in the first twenty pregnancies following automated embryo vitrification in Europe. At the time this abstract was written, one live birth, the first in Europe, had already occurred.

CONCLUSIONS: These data suggest that automated vitrification is technically efficient and may benefit the consistency of clinical outcomes following vitrification, as well as the logistics of the fertility centres.

P-23 Tuesday, October 15, 2019 6:30 AM
PROLONGED SEMEN CRYOPRESERVATION DECREASES MOTILE CONCENTRATION
Rhodel Simbulan, MS, Emanii Harris, BS, Feurdeliza Rabara, BS, CLS, Sean Pae, BS, MS, Fang Xie, PhD, Liza Jalalian, BS, CLS, Mitchell P. Rosen, MD, HCLD, University of California San Francisco, San Francisco, CA.

OBJECTIVE: There is a paucity of data regarding the viability of cryopreserved sperm. Good laboratory practice involving cryopreservation include QA/QC, equipment maintenance and stable temperatures of ~196°C. These ensure tissues remain viable for later use. However, cryopreservation has been shown to alter the structure and function of stored spermatozoa. This study aims to determine if sperm viability is affected by long-term storage.

DESIGN: Before-After Study.

MATERIALS AND METHODS: Patients sperm samples that were abandoned over the years of 1995-2014 (average 14.5 years) were thawed and analyzed before discard. Samples were considered abandoned if patients couldn’t be contacted within the last 5 years to continue storage. Prior to initial freeze, semen analyses were performed. Semen samples were stored in a 1:1 mixture of test yolk buffer, aliquoted into a 1.5 ml cryovial and suspended in nitrogen vapor for 30 minutes prior to being plunged into liquid nitrogen. Vials were thawed by placing cryovials into 37°C heat blocks for 20 minutes. Post-thaw survival of sperm was determined by calculating sperm concentration, motility and progression. Pre and post analyses were analyzed using regression analyses with a cluster analysis to account for pair differences between groups. Overall there is a significant decline in sperm motility with years of storage as vials stored for 20 years and longer show a 70% decrease compared to 10 years and less (p<0.0012). The patient age or initial sperm concentration at the time of freeze has no impact on sperm survival.

CONCLUSIONS: Despite appropriate measures to maintain specimen in storage, it appears that prolonged storage in liquid nitrogen may impact sperm survival. This result warrants further study as viability of tissues may be affected over time and reduce the success of fertility outcomes.

P-24 Tuesday, October 15, 2019 6:30 AM
EMBRYOS FROZEN WITHIN A SHORT TIME OF REACHING THE EXPANDED BLASTOCYSTS FROM THE EARLY BLASTOCYSTS HAVE HIGH VIABILITY: TIME-LAPSE INVESTIGATION OF 5177 BLASTOCYSTS.

OBJECTIVE: Morphological grading of blastocysts is in widespread use; however, morphokinetic grading by time-lapse monitoring is much less commonly applied. As PGS is not permitted in Japan, a method for estimating the potential viability of embryos using morphokinetic evaluation is required. It is known that Day5 blastocysts have higher viability than Day6 blastocysts. However, it is less understood whether an interval between early blastocysts and expanded blastocysts affects the embryo fertility.

DESIGN: The data was obtained in a retrospective study of 4097 cycles (mean patient age 38.2 years old) in the period 2013–2017.

MATERIALS AND METHODS: In total, 7283 embryos derived from IVF or ICSI were monitored using a time-lapse system (EmbryoScope, Vitrolife, Denmark) and the time from reaching the blastocysts to freezing the expanded blastocysts was recorded. The blastocysts selected for freezing had an ICM and inner diameter of more than 160 μm. 5177 blastocysts were subsequently thawed for transfer. The survival rate at thawing, the pregnancy rate after single embryo transfer, and the live birth rate were determined. These three metrics were compared among embryos classified by the time between reaching the blastocysts and freezing the expanded blastocysts.

RESULTS: Three groups of thawed embryos were compared: 0–20 hours (3083), 21–40 hours (1117), and 41 hours or more (83) from last contact to formation to expanded blastocysts frozen-thawed. Survival rates at thawing were 97.6% (3010/3083), 95.0% (1091/1117), and 92.8% (77/83), respectively, in these groups; the rate was significantly higher in the 0–20 hour group compared to the other 2 groups. Pregnancy rates of 58.8% (1767/3004), 42.9% (819/1907), and 14.3% (11/77) were obtained; the rate in the 0–20 hour group was significantly higher than the other 2 groups. Live birth rates were 68.6% (1212/1767), 62.6% (513/819), and 54.5% (25/47); the 0–20 hour group was significantly higher than the other 2 groups.

CONCLUSIONS: As the viability of the thawed embryos with a short interval between reaching blastocysts and freezing expanded blastocysts was higher than in embryos with longer intervals, we suggest that patients with multiple blastocysts should be preferentially transplanted with those frozen a short time of developing expanded blastocysts.

Reference: None.

SUPPORT: None.

---

**TABLE 1. Summary of difference between initial and post-thaw motile concentrations**

<table>
<thead>
<tr>
<th>Years Stored</th>
<th>n</th>
<th>Pt Age</th>
<th>Initial Motile Concentration (M/ml)</th>
<th>Post-Thaw Motile Concentration (M/ml)</th>
<th>Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>30</td>
<td>38.8±4.9</td>
<td>37.6±33.5</td>
<td>19.6±29.8</td>
<td>0.26±0.26</td>
</tr>
<tr>
<td>10-14</td>
<td>36</td>
<td>37.7±7.5</td>
<td>28.2±29.3</td>
<td>16.6±22</td>
<td>0.28±0.18</td>
</tr>
<tr>
<td>15-19</td>
<td>36</td>
<td>38.7±8.7</td>
<td>68.8±36</td>
<td>10.1±21.9</td>
<td>0.18±0.21</td>
</tr>
<tr>
<td>&gt;20</td>
<td>29</td>
<td>34.7±8.7</td>
<td>45±58.2</td>
<td>11.7±24.1</td>
<td>0.29±0.13*</td>
</tr>
</tbody>
</table>

*p<0.05
THE TWO-STEP ASYNCHRONOUS VITRIFIED-THAWED BLASTOCYST EMBRYO TRANSFER STRATEGY: THE IMPACT ON MULTIPLE PREGNANCY RATE. Viktor Veselovsky, MD Nadiya Clinic, Kyiv, Ukraine.

OBJECTIVE: To compare clinical and multiple pregnancy rate among women who underwent two-step asynchronous blastocyst embryo transfer (TSABET) versus DET in the frozen embryo transfer (FET) cycle with patients who had at least two vitrified blastocysts.

DESIGN: Retrospective single-center cohort study.

MATERIALS AND METHODS: All patients (534 consecutive IVF/ICSI cycles) at NADIYA Clinic from 6/30/2015-12/31/2018 who met such criteria as age <38, good quality day 5-6 blastocysts, and at least 2 remaining cryopreserved blastocysts and subsequently underwent FET, were included in this study. Exclusion criteria were preimplantation genetic testing (PGT) cycles and donor oocyte cycles.

Primary outcomes were clinical pregnancy rate per transfer and multiple pregnancy rate. Secondary outcomes were miscarriage rate, ectopic pregnancy rate. All women received estradiol for the preparation of the endometrium. The administration of progesterone (50 mg in oil, daily) was initiated when endometrium thickness exceeded 8 mm. In the DET group (433 cycles), on day 6 (P+6) or 7 (P+7) after the initiation (P+1) of progesterone treatment, two blastocysts were transferred. In the TSABET (101 cycles), on day P+6 and day P+9 the blastocysts were transferred twice.

The results between the DET and the TSABET cycles were compared (see Table below). Chi-squared tests and t-tests were used to compare demographic, cycle characteristics and outcome data between groups.

RESULTS: Demographic characteristics were similar between DET and TSABET patients. TSABET patients had a significantly higher clinical pregnancy rate than DET patients (70.3% vs 57.0%). However, DET patients had a significantly higher multiple pregnancy rate (44.1% vs 9.9%). There was no difference in ectopic pregnancy and abortion rate seen between groups.

CONCLUSIONS: To our knowledge, this is the first study of using two-step vitrified-thawed blastocyst transfer strategy with 72h interval between transfers.

In the group of good prognosis patients TSABET strategy resulted in a higher clinical pregnancy rate than DET, but also was associated with a much lower multiple pregnancy rate. When deciding on the two embryos to transfer in this group, TSABET strategy should be preferable.

P-26 Tuesday, October 15, 2019 6:30 AM

IMPACT OF EQUILIBRATION DURATION DURING OOCYTE VITRIFICATION PROTOCOL: PRELIMINARY RESULTS OF A PROSPECTIVE OBSERVATIONAL STUDY. Charlene Herbemont, Pharm.D,1 Isabelle Cedrin-Durnerin, M.D,2 Michael Gryenberg, M.D., Ph.D.,3 Christophe Sifer, M.D.,*Jean Verdier Hospital, Bondy, France; Jean Verdier Hospital, Bondy, France.

OBJECTIVE: Oocyte cryopreservation is a valuable technique in the field of fertility preservation (FP) as well as oocyte donation programs. Numerous studies have already analyzed outcomes following oocyte vitrification. Regarding technical aspects, open versus (vs) closed carriers have mainly been investigated. However, vitrification protocols commercially available do describe various durations of the equilibration step (from 6 to 10 minutes (min)). To date, a potential impact of this variability on the outcomes after warming has never been investigated.

DESIGN: This prospective observational study has been in progress since 2014, including all oocyte cryopreservation cycles. Vitrification/warming (n=64) were performed using commercialized media (Kitazato, Japan). During equilibration, according to the manufacturer’s procedure, 9 oocytes maximum were deposited by 3 in 3 drops of equilibration solution (ES). After 6min, the vitrification step was initiated for the first 3 oocytes (duration 1min), and the following oocytes straw-by-straw were vitrified immediately thereafter, respectively after 7 and 8min of equilibration.

MATERIALS AND METHODS: Oocyte vitrification/warming required patients’ written consent. To date, 64 couples underwent the whole procedure of warming and ICSI. The allocation of oocytes per straw depended on the total number of mature oocytes, explaining the variable number of oocytes in groups 6/78min. Survival, fertilization, embryo quality and suitability for transfer/freezing were assessed per oocyte and compared according to the duration of equilibration.

RESULTS: Indications for cryopreservation were: oocyte accumulation (46%); oocyte donation (33%); FP prior to cancer treatment (3%), for endometriosis (10%) poor ovarian reserve (1%); absence of sperm on the day of ICSI (7%). Overall, 388 oocytes were warmed, and 329 of them survived (survival rate (SR)=84.8%). The analysis according to the equilibration duration showed a slight difference in terms of SR: 82.5% (188/228) in group 6min vs 85.6% (101/118) in group 7min vs 95.2% (40/42) in group 8min (global p value=0.06). Interestingly, SR after 8min of equilibration was significantly or close to significantly higher than after respectively 6min (p=0.02) and 7min (p=0.07). After ICSI, fertilization rate (68.1 vs 74.5 vs 60.6%, p=0.29), Day 2 top (28.9 vs 37.1 vs 19.0%, p=0.23) and good quality embryo rates (43.0 vs 47.1 vs 33.3%, p=0.52) and rates of embryos suitable for transfer/freezing (70.3 vs 67.1 vs 52.4%, p=0.28) were statistically similar whatever the duration of the equilibration phase.

CONCLUSIONS: The equilibration duration during oocyte vitrification protocol might influence SR after warming but might not impact further embryo development of the surviving oocytes. If these data were confirmed, larger investigations should be performed on the different vitrification media commercially available. Then, manufacturers’ recommendations on vitrification protocol should be amended accordingly. Furthermore, clinical outcomes should be analyzed.

P-27 Tuesday, October 15, 2019 6:30 AM

COMPARATIVE STUDY OF FERTILITY PARAMETERS IN VITRIFIED HUMAN SPERM IN THE PRESENCE AND ABSENCE OF EMBRYORP®: A NOVEL ANTI-OXIDANT. César Rodrigo Coria, College degree, a Paulina Torres, Master Degree, a Latina Villar, Sr., MD, a Israel Maldonado, MD, a Israel Jiménez, Sr., MD, a Claudia Lydia Trevino, PhD, a Instituto de Biotecnología, Cuernavaca, MR, Mexico; Clínica de Reproducción Asistida in the Ciudad de Mexico, Ciudad de Mexico, DF, Mexico.

OBJECTIVE: Find out if presence of the antioxidant EmbryORP® in vitrification medium is a critical element that may reduce cryodamage in native sperm samples.

DESIGN: This study included 20 normozoospermic sperm samples from healthy donors between 23 and 40 years old, that were used to evaluate a novel antioxidant: EmbryORP® on functional and structural sperm quality parameters in a standard vitrification protocol.

MATERIALS AND METHODS: All samples were vitrified with the Easy-Sperm kit Sperm and divided into two aliquots: vitrified (V) and vitrified + EmbryORP® (V-E). Concentration, motility and pH were assessed with a novel instrument LensHooke®. Oxidation-reduction potential (ORP) were evaluated with the MIOXSYS® system. Acrosomal reaction, mitochondrial membrane potential (MMP) and vitality were also assessed by flow cytometry and compared between both groups.

RESULTS: Previously we measured the ORP in the seminal fluid of 50 infertile patients with an average of 30.3±17.88mV which is significantly lower to the estimate of 280mV in the vitrification medium. 10al of EmbryORPα per milliliter diminished the ORP to 94.9mV in the vitrification medium and to 92.7mV in devitrification medium, values that are closely to physiological parameters of the cell. We found out no statistical difference in the progressive motility (p =0.2068), non-progressive (p = 0.3225) vitality (p=0.1610), morphology (p=0.8881), preservation of the acrosome (p=0.3031) and MMP (0.2743) post cryopreservation in both groups. The presence of the antioxidant lowers the pH of the medium to near 7 while the vitrification medium remains if physiological values (p < 0.0001). The concentration of the V-E group was lower after the freezing protocol compared to the V group (p = 0.0145). The ORP was lower in vitrified cells supplemented with the antioxidant (p < 0.0001).

CONCLUSIONS: We concluded from these results that the use of Embryo-ORP® is not the best option from sperm cryopreservation.
**P-28** Tuesday, October 15, 2019 6:30 AM

**IS THE INCREASE IN EGG FREEZING CYCLES RELATED TO INCREASED NUMBERS OF SINGLE WOMEN IN THE UNITED STATES?**  
Alexandra Peyser, M.D., Avner Hershlag, M.D., Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

**OBJECTIVE:** In 2017, the United States Census reported 110.6 million unmarried persons over the age of 18, 53.2% of which were women. At the same time, the number of women choosing to freeze their eggs has increased over the last decade. The objective of this study was to determine whether there is an association between the rise in egg freezing and the number of single women in the United States.

**DESIGN:** Retrospective Cohort.

**MATERIALS AND METHODS:** Data on oocyte banking for fertility preservation from the SART database from 2014-2017 was analyzed. In addition, data from the United States Census Bureau on marital status of single women was obtained for the same years. The total number of single women reported was compared with the number of oocyte banking cycles. The Pearson correlation test was used to investigate associations between the number of egg freezing cycles and single women. Significance was defined as p<.05.

**RESULTS:** Between 2014-2017, a total of 33,324 egg freezing cycles were recorded from the SART database. Over this time frame, the number of cycles has increased by 79% while the total number of single women reported has increased 5% (Table 1). We found a high correlation between the increasing number of egg freezing cycles in the USA and the increasing numbers of single women nationwide. However, it did not reach statistical significance (coeff=.87, p=.13).

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of egg freezing cycles (n)</th>
<th>Single (n)</th>
<th>Married (n)</th>
<th>Total(n)</th>
<th>Percentage single (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>6090</td>
<td>37,311,000</td>
<td>66,732,000</td>
<td>129,871,000</td>
<td>28.73</td>
</tr>
<tr>
<td>2015</td>
<td>7591</td>
<td>37,394,000</td>
<td>67,217,000</td>
<td>131,355,000</td>
<td>28.46</td>
</tr>
<tr>
<td>2016</td>
<td>8707</td>
<td>38,995,000</td>
<td>67,450,000</td>
<td>132,862,000</td>
<td>29.39</td>
</tr>
<tr>
<td>2017</td>
<td>10,936</td>
<td>39,087,000</td>
<td>68,082,000</td>
<td>133,405,000</td>
<td>29.30</td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** 1. In just 4 years, egg freezing has seen an exponential rise of 79%.
2. During the same period, the number of single women in the USA increased by 5%.
3. These two observations are highly correlated, yet did not reach statistical significance. We suggest that an increase in the numbers of years of egg freezing cycles reported could reach significance.
4. Likely, the sharp rise in egg freezing is also related to improvements in egg freezing technique and results, increased awareness of reproductive ageing, the impact of social media and advertising and more. These factors cannot be enumerated and, might have diluted impact of the increase rate of single women over the same time period.
5. Last but not least: the relationship between egg freezing statistics and the number of single women may have already shifted from uni-directional to bi-directional. How many women delay marriage because egg freezing is readily available and increasingly more reliable?.

**P-29** Tuesday, October 15, 2019 6:30 AM

**THE IMPACT OF THE SHORT-TERM HUMAN SPERM STORAGE IN THE CRYOPROTECTANT-FREE MEDIUM ON SPERM MOTILITY AND VITALITY.**  
Nabil Sayme, Dr. med.,  
Marija Kljajic, Master of Biology Science,  
Thomas Krebs, Biology,  
Dieter Maas, Prof. Dr. med.  
Team Kinderwunsch Hannover, Hannover, Germany;  
Saarland University Medical Center, Homburg, Germany.

**OBJECTIVE:** Slow freezing is currently the most commonly used technique for sperm cryopreservation since the vitrification of spermatozoa is still a rather unexplored methodology. Storage sperm at +4 C is a relatively new technique and in the aim of reach better recovery rates, many studies confirmed that freezing/store sperm without cryoprotectants gives better results. The purpose of the study was to investigate does it the sperm storage in the cryoprotectant-free medium a good alternative for short-time preservation (up to 4 weeks) compared to the conventional slow freezing, as well as the impact of the short-term human sperm storage on sperm motility and vitality.

**DESIGN:** The study included 20 sperm samples collected between February 2018- April 2018. Out of 20 samples, 10 were normozoospermic, 5 were teratozoospermic and 5 were asthenozoospermic. Native samples with volume higher than 3 ml before preparation was divided equally in the aim to reach the same sperm concentration. After gradient preparation, the volume of 200 µl sample was treated with the same volume of cryoprotectant (GM501 Sperm store, Gynemed, Germany) or sperm preserve medium (Sperm Preserve, Gynemed, Germany).

**MATERIALS AND METHODS:** After slow freezing two straws of each sample were preserved into liquid nitrogen for a period of one and four weeks. Samples treated with Sperm Preserve were divided as well into two straws and stored in fridge on 4 C degrees for the same period. After this period samples were thawed with Sperm Active (GM501 Sperm Active, Gynemed, Germany) and motility and vitality after these two freezing procedures were compared. For statistical analysis, a One-Way ANOVA was used.

**RESULTS:** After one week of slow freezing and storage in liquid nitrogen, 24.9±11.22% of spermatozoa regained their motility compare to samples which were stored on 4 C where recovery rate was 32.75±11.02%. One-Way ANOVA confirmed that there is a significant difference between these two groups (p=0.31). The sperm motility rate after four weeks was slightly lower 20.4±6.87% in the slow freezing sample group, compare to 28.05±9.81% after storage at 4 C but still, further statistical analysis confirmed a significant difference between these two groups (p=0.005). Asthenozoospermic samples stored at 4 C had better motility recovery rate after one week 28.8±11.6% vs 13.6±2.96% (p=0.02) than after four weeks 24.2±14% vs 12.8±4.7% where the difference between these two groups was not statistically significant as well as neither between teratozoospermic samples. Vitality was one of the characteristics which we analyzed as well and the difference was significant especially after one week (p=0.0001) where survival rate after slow freezing was 40.5±11.80% compared to the storage sample where that number was 54.25±13.20 %. After four weeks as well, a higher percentage of sperm survive in the storage group 39.75±7.88% compare to the 30.7±6.78% of slow frozen samples (p=0.011).

**CONCLUSIONS:** The cryoprotectant-free sperm storage protocol tested in this study renders considerably better recovery rates (motility and vitality) of the sperm compared to slow freezing.

**SUPPORT:** Gynemed.

**FERTILITY & STERILITY®**
P-30 Tuesday, October 15, 2019 6:30 AM


OBJECTIVE: To investigate as part of a larger study of changing U.S. practice patterns in IVF, how the utilization of third-party donor eggs has changed between 2005-2016.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: IVF outcome data are generated annually under Congressional mandate by the Center for Disease Control and Prevention (CDC), including almost all (in 2016, 463/502) of the nation’s IVF centers, and are publicly reported with approximately two-and-a-half years delay. Most recent available data are, therefore, in the 2016 Annual Assisted Reproduction Summary Report from the CDC. We here report on CDC outcome reports longitudinally between years 2005-2016, with years 2005, 2010, 2015 and 2016 serving as index years.

RESULTS: With advancing female age, third-party donor egg cycles universally increased in all years as a subgroup of all IVF cycles until around 2010, when they peaked, representing 37% of all cycles. By 2015 they were only 34% and by 2016 only 33% of all cycles at ages 43-44; at ages above 44 years, they in 2010 represented as much as 73% of all cycles but by 2015 only 71% and by 2016 only 65%. We also observed a dramatic switch from use of fresh to frozen donor eggs, also starting in 2010, gaining ground much quicker especially above age 42. Above age 42 in 2005, 36% of donor cycles utilized frozen eggs, by 2010 38% of 43-44 year-olds and 45% of women above age 44 utilized frozen oocytes; by 2015 those numbers had further risen to 65% of 43-44 year-olds and 70% of women above age 44 years.

CONCLUSIONS: These data reveal a welcome decline in third party donor egg cycles after 2010, suggesting that more IVF centers are offering older patients the chance of pregnancy and delivery with use of own eggs. They, however, also raise concern about the rapid switch from use of fresh to frozen donor eggs. Since 2010, likely caused by growth in commercial frozen egg banks, since frozen donor eggs produce ca.10% lower birth rates than fresh eggs. These developments, therefore, may adversely affect live birth rates with third-party donors.

References: 1. Zimmerman et al., Noninvasive prenatal aneuploidy testing of populations and be useful during genetic counseling. Women choosing NIPT after donor oocyte/IVF cycles should be informed of risks for lower FF and higher test failure rates which are associated with increased risks of adverse perinatal outcomes and obstetric complications.

Future analysis should determine the effect on FF of donor oocyte versus non-donor IVF cases, of various IVF techniques (ICSI, fresh vs. frozen embryos) used to achieve pregnancy and of different etiologies of infertility.


5. van der Hoorn ML et al., Clinical and immunologic aspects of egg donation pregnancies: a systematic review. Hum Reprod Update.Ä 2010;16(6):704-12


Support: Natera, Inc.

P-31 Tuesday, October 15, 2019 6:30 AM

DONOR OOCYTE PREGNANCIES AND FETAL FRACTION: MANAGING PATIENT EXPECTATIONS AND PROVIDING ACCURATE INFORMATION. Melissa K. Maisenbacher, MS, Georgina Goldring, MS, Wendy DiNonno, MS, Allison Ryan, PhD Natera, San Carlos, CA.

OBJECTIVE: Determine if differences in fetal fraction (FF) are observed in donor oocyte pregnancies compared to the general population.

DESIGN: Retrospective analysis

MATERIALS AND METHODS: Noninvasive prenatal testing (NIPT) samples from singleton pregnancies were analyzed at a single reference lab. NIPT was performed using a SNP-based method with FF measured as previously described.1 FF from 1611 donor oocytes was analyzed and compared to a large set of reference cases matched for maternal weight (MW) and gestational age (GA). A z-score was calculated for each donor oocyte compared to its reference data. If no impact to FF from the use of donor or IVF, the average z-score is expected to be zero.

Statistical analysis was performed using a z-test to establish if this was the case.

RESULTS: For donor cases the average z-score was -0.4. A z-test determined this deviation from normal to be significant (p < 0.00001), showing that donor cases have lower FF than their corresponding reference data. The average MW was 154.3 lbs. (range 79.2-370.4 lbs.), average GA was 12.9 weeks (range 9-33 weeks) and average FF was 8.4%.

CONCLUSIONS: The adoption of NIPT over other screening and diagnostic methods continues to grow, especially among women using donor oocyte/IVF. This population’s preference for NIPT may stem from increased anxiety, higher false positive rates with traditional serum screening and avoidance of diagnostic procedures carrying miscarriage risk. Therefore, understanding the differences in FF in this population is critical. 2,3

Previous studies have reported lower FF in patients undergoing IVF and in donor oocyte populations.4,5 Lower FF has also been associated with increased MW, early GA, certain maternal health conditions, and abnormal fetal results (T18/T13/triploidy).6,8,9 Our results reveal statistically significant lower FF in donor oocyte pregnancies compared to matched reference data.

It is unknown why FF is lower in donor oocyte/IVF pregnancies. Hormone treatment and higher rates of abnormal cord insertion among IVF pregnancies and a high degree of antigenic dissimilarity among donor oocyte pregnancies suggest that the IVF process may impair implantation.3,5,7,10,11 However, lower fetal fractions are also associated with increased risk for chromosome abnormalities. Thus, choosing a NIPT lab with high FF accuracy will the reduce risk of false negatives for this vulnerable population.

Identifying factors that affect FF can optimize NIPT algorithms for various populations and be useful during genetic counseling. Women choosing NIPT after donor oocyte/IVF cycles should be informed of risks for lower FF and higher test failure rates which are associated with increased risks of adverse perinatal outcomes and obstetric complications.

Support: Natera, Inc.
OBJECTIVE: An egg-sharing programme provides a good opportunity for recipients and donors to achieve motherhood. At present, there are no evidences to ensure that the cryopreservation of shared eggs is not detrimental to recipients' treatment outcomes. The objective of this study was to investigate the influence of cryopreservation on donated eggs in terms of laboratory and clinical outcomes of intracytoplasmic sperm injection (ICSI) cycles.

DESIGN: Historical cohort study.

MATERIALS AND METHODS: Data analyzed in this study were obtained via chart review of 267 oocyte donor ICSI cycles (age range 19-34 years), and 320 oocyte recipients (age range 26-48) undergoing 307 vitrified and 119 fresh oocyte recipient ICSI cycles, participating in an egg-sharing donation program, from 2015 to 2018, in a private university-affiliated IVF center. The sample size calculation suggested that 199 cycles would be enough to demonstrate a 20% effect with 80% power and 5% significance level considering as primary outcome blastocyst development rate. The impact of oocyte cryopreservation on recipients' ICSI outcomes was investigated using General Mixed Models fit by restricted maximum likelihood, followed by Bonferroni post hoc test for the comparison of means between fresh and warm oocyte donation groups. The model was generated using co-variates as fixed effects and egg-donors and egg-recipients as random effects, with unstructured covariance structure, adjusted for oocyte dysmorphisms and other potential confounders.

RESULTS: The fertilization rate (80.7% vs. 75.8%, p = 0.034), high quality embryos rate on days 2 (70.3% vs. 57.8%, p = 0.047) and 3 (50.2% vs. 34.6%, p = 0.003), normal cleavage speed rate on days 2 (90.6% vs. 77.2%, p = 0.027) and 3 (97.5% vs. 99.0%, p < 0.001), and blastocyst rate (47.1% vs. 19.8%, p < 0.001) were significantly higher on fresh oocyte donation cycles compared to warmed oocyte donation cycles. There were no statistically significant differences between fresh and warmed oocyte donation cycles in terms of high-quality blastocyst rate (71.2% vs. 62.0%, p = 0.328), implantation rate (35.7% vs. 25.7%, p = 0.182), clinical pregnancy rate (51.4% vs. 42.9%, p = 0.313), and miscarriage rate (12% vs. 15.9%, p = 0.745). The surplus embryos cryopreservation rate was significantly higher on fresh cycles compared to warmed cycles (65.4% vs. 24.1%, p = 0.015).

CONCLUSIONS: In an egg-sharing donation program, fertilization and embryo developmental competence are reduced when vitrified oocytes are used for ICSI compared to fresh oocytes. Despite no statistical significant differences were observed in terms of pregnancy outcomes, cycles using fresh oocytes had higher rates of surplus embryo cryopreservation, which is interesting for those patients with a negative pregnancy outcome, allowing them to resort to warmed embryo transfer instead of a new cycle of oocyte donation. Efforts must be made to provide open donor-recipient matching making it possible to receive fresh eggs.

References: NA.

SUPPORT: None.

P-33 Tuesday, October 15, 2019 6:30 AM

DONOR DIALOGUE: A CROSS-SECTIONAL ASSESSMENT OF LONG-TERM MEDICAL AND PSYCHOLOGICAL HEALTH STATUS AFTER ELECTIVE OOCYTE DONATION. Jennifer K. Blakemore, MD,a Paxton E. Voigt, BA,b Mindy R. Schiffman, PhD,c Shelley Lee, PhD,d Mary Elizabeth Fino, MD,* “NYU Langone School of Medicine, New York, NY; "NYU School of Medicine, New York, NY; "NYU Langone Fertility Center, New York, NY.

OBJECTIVE: There is an inverse relationship between the use of elective oocyte donation and the understanding of long-term potential impact. We sought to assess the long-term medical and psychological health status of all elective oocyte donators (anonymous, directed, agency) at a single institution.

DESIGN: Anonymous quantitative and qualitative survey.

MATERIALS AND METHODS: An anonymous survey was emailed to all elective oocyte donators (anonymous, directed, agency) at a single institution. The sample size calculation suggested that 199 cycles would be enough to demonstrate a 20% effect with 80% power and 5% significance level considering as primary outcome blastocyst development rate. The impact of oocyte cryopreservation on recipients' ICSI outcomes was investigated using General Mixed Models fit by restricted maximum likelihood, followed by Bonferroni post hoc test for the comparison of means between fresh and warm oocyte donation groups. The model was generated using co-variates as fixed effects and egg-donors and egg-recipients as random effects, with unstructured covariance structure, adjusted for oocyte dysmorphisms and other potential confounders.

RESULTS: The fertilization rate (80.7% vs. 75.8%, p = 0.034), high quality embryos rate on days 2 (70.3% vs. 57.8%, p = 0.047) and 3 (50.2% vs. 34.6%, p = 0.003), normal cleavage speed rate on days 2 (90.6% vs. 77.2%, p = 0.027) and 3 (97.5% vs. 99.0%, p < 0.001), and blastocyst rate (47.1% vs. 19.8%, p < 0.001) were significantly higher on fresh oocyte donation cycles compared to warmed oocyte donation cycles. There were no statistically significant differences between fresh and warmed oocyte donation cycles in terms of high-quality blastocyst rate (71.2% vs. 62.0%, p = 0.328), implantation rate (35.7% vs. 25.7%, p = 0.182), clinical pregnancy rate (51.4% vs. 42.9%, p = 0.313), and miscarriage rate (12% vs. 15.9%, p = 0.745). The surplus embryos cryopreservation rate was significantly higher on fresh cycles compared to warmed cycles (65.4% vs. 24.1%, p = 0.015).

CONCLUSIONS: In an egg-sharing donation program, fertilization and embryo developmental competence are reduced when vitrified oocytes are used for ICSI compared to fresh oocytes. Despite no statistical significant differences were observed in terms of pregnancy outcomes, cycles using fresh oocytes had higher rates of surplus embryo cryopreservation, which is interesting for those patients with a negative pregnancy outcome, allowing them to resort to warmed embryo transfer instead of a new cycle of oocyte donation. Efforts must be made so donor-recipient matching makes it possible to receive fresh eggs.

References: NA.

SUPPORT: None.

P-34 Tuesday, October 15, 2019 6:30 AM

IS PATERNAL AGE PLAYING A MAJOR ROLE IN OOCYTE DONATION PROGRAM? Pamela E. Villanueva, MD, PhD,a Luis Noriega-Hoces, MD,b Fabrizio Vizcarra, MD,c Jazmin Meza, BSc,b Luis Noriega-Portella, MD,a Luis Guzman, PhD,b aDoctor, Lima, Peru; bEmbryologist, Lima, Peru.

OBJECTIVE: To determine the impact of paternal age on clinical pregnancy in oocyte donation program.

DESIGN: Retrospective study.

MATERIALS AND METHODS: The present study evaluated our oocyte donation program from January 2015 to December 2018. In total, 152 donors donated their oocytes to perform 475 IVF cycles. The paternal age was classified in group 1: younger than 40 years (N=229); group 2: 40 to 50 years (N=183) and group 3: older than 50 years (N=63). The main result was clinical pregnancy. A linear Poisson log regression models was used.

<table>
<thead>
<tr>
<th>Paternal Age</th>
<th>Clinical Pregnancy n = 290 (%)</th>
<th>No pregnancy n = 185 (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40</td>
<td>150 (65.5)</td>
<td>79 (34.5)</td>
<td>0.082</td>
</tr>
<tr>
<td>40 - 50</td>
<td>108 (50.0)</td>
<td>75 (41.0)</td>
<td></td>
</tr>
<tr>
<td>&gt; 50</td>
<td>32 (50.8)</td>
<td>31 (49.2)</td>
<td></td>
</tr>
<tr>
<td>Mean of oocytes</td>
<td>11.0 ± 2.6</td>
<td>10.9 ± 3.1</td>
<td>0.616**</td>
</tr>
<tr>
<td>assigned per cycle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fertilization rate</td>
<td>0.7 ± 0.2</td>
<td>0.7 ± 0.2</td>
<td>0.246***</td>
</tr>
<tr>
<td>Blastulation rate</td>
<td>0.6 [0.4 - 0.8]</td>
<td>0.6 [0.3 - 0.7]</td>
<td>0.005**</td>
</tr>
<tr>
<td>Embryo quality (SART criteria)</td>
<td>Good 0.5 [0.3 - 0.6]</td>
<td>0.4 [0.1 - 0.6]</td>
<td>0.056***</td>
</tr>
<tr>
<td></td>
<td>Fair 0.4 [0.3 - 0.6]</td>
<td>0.4 [0.2 - 0.6]</td>
<td>0.529</td>
</tr>
<tr>
<td>Poor 0.0 [0 - 0.3]</td>
<td>0.0 [0 - 0.3]</td>
<td>0.220</td>
<td></td>
</tr>
<tr>
<td>Direct oocyte recipient age</td>
<td>41.6 ± 4.6</td>
<td>42.2 ± 5.2</td>
<td>0.204</td>
</tr>
<tr>
<td>Insemination technique</td>
<td>FIV 71 (63.4)</td>
<td>41 (36.6)</td>
<td>0.561</td>
</tr>
<tr>
<td></td>
<td>ICSI 219 (60.3)</td>
<td>144 (39.7)</td>
<td></td>
</tr>
</tbody>
</table>

References: None.
RESULTS: Young women who donated oocyte to our program give oocytes to 3 partners as an average. Pregnancy was not associated to paternal age (see table 1). Additionally, number of oocytes, fertilization rate, donor oocyte recipient age and insemination technique (ICSI or FIV) were not related to clinical pregnancy. Interestingly, blastulation rate and the embryo quality were the only parameters associated to pregnancy.

CONCLUSIONS: The strength of the present study was that the same donors give oocytes to different partners. Our results suggest that paternal age does not influence the clinical pregnancy. Although, prospective studies are need by using sibling oocytes.

SUPPORT: None

EMBRYO CULTURE

P-35 Tuesday, October 15, 2019 6:30 AM

PROSPECTIVE RANDOMIZED MULTICENTER STUDY ON CULTURE OF SIBLING HUMAN OOCYTES IN A SEQUENTIAL MEDIA SYSTEM WITH AND WITHOUT ANTIOXIDANTS: THE EFFECT OF FEMALE AGE

Shigetoshi Mizumoto, Ph.D.; Atsumi Yoshida, M.D., Ph.D., MBA; Takeshi Kuramoto, M.D., Ph.D.; Miho Tanaka, M.Sc.; Markus HM. Montag, Ph.D.; David Gardner, Ph.D.; Kumamoto Women’s Clinic, Fukuoka, Japan; bKiba Park Clinic, Tokyo, Japan; cCalifornia Infertility Associates, Orange, CA; dUniversity of California, Davis, CA; eShiga University of Medical Science, Otsu, Shiga, Japan; fThe University of Melbourne, Melbourne, VIC, Australia.

OBJECTIVE: To investigate the combined effect of three antioxidants Acetyl-L-Carnitine (ALC), N-Acetyl-L-Cysteine (NAC) and α-Lipoic Acid (ALA) in a sequential culture media system on human embryo development and clinical outcome in relation to maternal age

DESIGN: Prospective randomized sibling oocyte multicenter study

MATERIALS AND METHODS: This study included couples intending to undergo IVF or ICSI, with female age ≤ 40 years old and at least eight cumulus-oocyte-complexes after retrieval. Cycles involving PGT, split IVF/ICSI and surgically retrieved sperm were excluded. Human oocytes were randomly distributed to Vitrolife G-Series with or without a combination of three antioxidants (10 μM ALC /10 μM NAC /5 μM ALA (A3)). IVF/ICSI and embryo culture were conducted in 5% oxygen. Embryo quality on day 3 and day 5/6 and clinical outcome were assessed in relation to maternal age (< 35 versus >35). Good embryo quality on day 3 was defined as 8 to 10-cells with even cells and low fragmentation; good quality blastocysts as equal or greater than 3BB. Clinical outcome was assessed in either fresh or vitrified-warmed embryo transfer cycles. The study was registered with clinicaltrials.gov (NCT02999958).

RESULTS: A total of 133 patients participated in the study. The mean female age was 33.8 ± 3.1 years. 1783 oocytes were collected of which 890 were allocated to G-Series media with A3 and 893 to standard G-Series media. When analyzing for age groups in G-Series with A3 compared to standard G-Series, the following results were obtained:

- Good quality Day 3 embryo development was significantly higher in the younger age group in G-Series with A3 (<35: 50.2% vs 38.2%, P < 0.05; ≥ 35: 48.6% vs 41.1%, n.s.)
- The overall blastocyst rate on Day 5 + 6 was higher in both age groups in G-Series with A3 (<35: 61.3% vs 56.6%; ≥ 35: 66.2% vs 60.7%) but not significant.
- The good quality blastocyst rate on Day 5 + 6 was higher in both age groups in G-Series with A3 (<35: 32.8% vs 28.2%; ≥ 35: 27.8% vs 25.9%).

More blastocyst were used for cryopreservation and transfer on Day 5 +6 in G-Series with A3 in both age groups (<35: 41.2% vs 37.2%; ≥ 35: 43.5% vs 38.8%).

We noted no difference between G-Series with A3 vs G-Series in the younger age group for implantation per fetal sac, per fetal heart and for the ongoing pregnancy rate (< 35: 50.6% vs 55.3%, 48.2% vs 52.6% and 48.1% vs 52.6%, respectively). A significant difference (P < 0.05) was found for the same parameters in the older age group for G-Series with A3 (< 35: 57.5% vs 23.5%, 50.0% vs 26.5% and 50.0% vs 25.8%, respectively).

CONCLUSIONS: In general the presence of antioxidants during IVF and embryo culture imparts significant benefits on day 3 embryo quality and a trend to better day 5 embryo quality and utilization rate. Implantation rates and ongoing pregnancy rates are significantly higher in media with A3 in patients with advanced maternal age but not in younger patients, but cumulative pregnancies could increase as more embryos were cryopreserved. Supplementation of antioxidants to culture media may improve the viability of human embryos in ART; plausibly through the reduction of oxidative stress, and improve clinical outcomes in certain age groups.

SUPPORT: Vitrolife sponsored part of the media for the study.

P-36 Tuesday, October 15, 2019 6:30 AM

MODELING OF AIRBORNE EMBRYOTOXIC VOLATILE ORGANIC COMPOUNDS (VOCs) IN THE IVF CULTURE ENVIRONMENT – THEIR CONCOMITANT CYTOTOXIC CONCENTRATION WITHIN THE GROWTH MEDIA AND EMBRYO

Kathryn Colonna Worrilow, Ph.D.; aAlicia R. Urrutia, B.S.; bHuey T. Huynh, M.S.; cJohn T. Fox, Ph.D.; cLifeAire Systems, Allentown, PA; dLehigh University, Bethlehem, PA.

OBJECTIVE: VOCs are a common component of laboratory ambient air. VOCs are unique in their polarity, molecular weight and structure and play a critical role in preimplantation toxicology and epigenetic processes. This study sought to define the mechanisms of cytotoxicity associated with VOCs found in the IVF culture environment. The concomitant concentrations of VOCs common to IVF laboratories were modeled with Henry’s Law (HL) from the gaseous to aequous phase, and the final resulting concentration within the embryo was modeled with octanol water partitioning coefficients (OWPC).

DESIGN: HL was used to model VOC mass transfer from the air to the water/media phase. This model uses the air-water partitioning coefficient and the definition that the ratio between the liquid and air phase concentration is defined and unique for each organic compound. The OWPC was used for each compound to correlate the mass transfer from the water/media phase to the embryo using the ratio between the organic phase and water phase concentration.

MATERIALS AND METHODS: Evaluation of over 40 IVF laboratories identified the mean total VOC (TVOC) levels and 6 most common VOCs. HL and OWPC calculations determined the concomitant VOC concentrations in the culture media, embryo in culture, and time required to reach equilibrium for each compound. Research has shown that TVOC concentrations greater than or equal to 500 ppb in the media is embryotoxic and exerts a statistically significant impact on blastocyst conversion rates. Air phase VOC concentrations were compared to known embryotoxic VOC levels in cell culture media to determine if typical VOC levels in IVF laboratories are embryotoxic.

RESULTS: The concentration of each VOC within the embryo (Cembryo) was modeled based on airborne VOC levels measured. This modeled Cembryo

<table>
<thead>
<tr>
<th>Compound</th>
<th>Time for Airborne VOC to Reach Equilibrium in Media (min)</th>
<th>Embryotoxic Cembryo (mg VOC/kg of embryos)</th>
<th>Modeled Cembryo (mg VOC/kg of embryos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetone</td>
<td>241</td>
<td>285</td>
<td>421.8 (toxic)</td>
</tr>
<tr>
<td>Acrolein</td>
<td>0.2</td>
<td>489</td>
<td>47.1</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>216.0</td>
<td>1,132</td>
<td>48,992 (toxic)</td>
</tr>
<tr>
<td>Isopropanol</td>
<td>90.7</td>
<td>15</td>
<td>119.2 (toxic)</td>
</tr>
<tr>
<td>Styrene</td>
<td>4.1</td>
<td>445,715</td>
<td>5,989.9</td>
</tr>
<tr>
<td>Toluene</td>
<td>4.2</td>
<td>244,963</td>
<td>1,521.4</td>
</tr>
</tbody>
</table>
was compared to the embryotopic level when embryos were cultured in an aqueous environment of 500 ppb VOCs. Levels of acetone, formaldehyde and isopropanol measured in IVF laboratories resulted in cytotoxic cellular levels.

CONCLUSIONS: Airborne VOCs are driven to reach equilibrium and can be magnified in concentration as they partition from the air to the cell culture media, and ultimately, into the embryo. Once cultured, the VOCs exert a negative influence on blastocyst conversion, implantation, and clinical pregnancy rates. This study related the measured concentration of airborne VOCs to the modeled concentration within the embryo. This novel study further defines the mechanisms of cytotoxicity of VOCs by defining their partition from the gaseous to aqueous phase, and most importantly, to the cellular phase. This data furthers our understanding of the role of VOCs in epigenetic variation and cytotoxicity.

P-37 Tuesday, October 15, 2019 6:30 AM

RANDOMIZED STUDY OF EMBRYO COMPETENCE AND DEVELOPMENTAL POTENTIAL IN GLOBAL BLASTOCYST MEDIUM AND G-TL MEDIUM, DESIGNED FOR TIME LAPSE. Nina Desai, Ph.D., HCLD., a Jeffrey M. Goldberg, M.D., b Rebecca Flyckt, MD, a Marjan Attaran, M.D., c Julie Tanthibhedhyangkul, M.D., c Cynthia M. Austin, M.D. c Cleve- land Clinic, Beachwood, OH; bCleveland Clinic, Cleveland, OH.

OBJECTIVE: Continuous uninterrupted culture of embryos to the blastocyst stage requires that the medium be exchangeable on day 6 without refreshment. Global Blastocyst (GB) medium initially formulated for conventional culture with medium exchange on day 3 has been used successfully in time-lapse (TL) chambers. Our study objective was to compare zygote performance in G-TL medium, designed for continuous culture to Global Blastocyst medium.

DESIGN: Randomization of sibling zygotes between culture media and retrospective analysis of embryo morphokinetic and outcome data

MATERIALS AND METHODS: A total of 7331 zygotes from consecutive non-PCOS patients undergoing IVF from 2016 thru December 2018 were cultured in the Embryoscope TL chamber, G-TL (with human serum albumen-HSA) and GB medium with 10% added HSA protein supplement with globulins (SPS) were placed in the Embryoscope slide (6 wells per medium). Sibling zygotes were randomly distributed amongst wells and cultured at 37 °C with 5% CO2/5% O2. Time lapse videos were annotated daily for cell divisions and dysmorphisms. The following kinetic markers were assessed: tSYN (synonymy), t2 (time to 2c), t13, t14, t15, t18, tM (fully compacted morula), tSB (start of blastulation), tBL (time of blastulation), tEBL (time of expanded blastocyst). Blastocyst grade (BG) based on maturity (4=hatched, 3=expanded, 2=full blastocyst, 1=early) and ICMT/TE quality (3=good, 2=fair and 1=poor) were scored using ESHRE criteria. Overall embryo utilization (transferred or frozen) and percent good quality embryos (GQE) for cryopreservation was calculated for each medium. Embryonic competence based on implantation (sac, fetal heart-FHT) in fresh and frozen single embryo transfer (SET) cycles was assessed. Differences between treatment groups were analyzed using ANOVA and the chi-square test. P values were calculated by t-test with Graphpad Prism.

RESULTS: With G-TL, 80% of blastocysts were BG3/4 as compared to 77% of GB blastocysts (p=0.03) but ICMT/TE scores did not differ. Multinucleation was higher in GB vs G-TL (44% vs 40%, respectively; p=0.009).

CONCLUSIONS: This large study with randomization of sibling zygotes allowed a more robust comparison between culture media. Both media performed well. No difference was detected in clinical outcomes in either fresh or frozen SET cycles.

GB GT-L p Value
Cultured zygotes (n) 3859 3472
Blastoscyts (%) 2592 (67%) 2218 (64%) 0.002
Expanded blastocysts (%) 1990 (52%) 1722 (50%) NS
Embryo utilization (%) 2273 (59%) 1889 (54%) 0.001
GQE-Frozen(%) 1851 (48%) 1599 (46%) NS
Transfers
Fresh SET IR-Sac (%) 82/142 (58%) 51/82 (62%) NS
Fresh SET IR-FHT (%) 80/142 (56%) 49/82 (60%) NS
Frozen SET IR-Sac (%) 81/124 (65%) 76/126 (60%) NS
Frozen SET IR-FHT (%) 77/124 (62%) 69/126 (54%) NS


Desai N, Goldberg J, Austin C, and Falcone T. Are cleavage anomalies, multinucleation, or specific cell cycle kinetics observed with time-lapse imaging predictive of embryo developmental capacity or ploidy? Fertil Steril 2018 109 (4)A 665-674

SUPPORT: None

P-38 Tuesday, October 15, 2019 6:30 AM

3D GYRATORY ROCKER MAY ACCELERATE EMBRYONIC ZO1 EXPRESSION AND FURTHER EMBRYONIC DEVELOPMENT IN MOUSE EMBRYOS. Sook Young Yoon, Ph D , a Miseon Park, M.Des, a Jin Hee Eum, Ph.D. a Jin Young Kim, M.D. Ph.D. a Woo Sik Lee, M.D. Ph.D a Fertility Center of CHA Gangnam Medical Center, Seoul, Korea, Republic of (South); bAffiliation not provided; cCHA Fertility Center Gangnam Medical Center, Seoul, Korea, Republic of (South).

OBJECTIVE: Before implantation, zygote travels the oviduct and uterus along fluid flow by beating of the cilium and muscle contraction. This condition makes fluid flow, shear stress, rolling effect of embryo and external stimuli to support embryo movement and development. Oviductal condition lead to movement of embryos with punctuate fluid velocity. To mimic these physical/mechanical environment, new static culture system is developed includes a well of the well system, GPS culture dish, sub-micro drop culture. And dynamic micro-vibration culture system.

DESIGN: MII eggs from inbred and outbred mouse were fertilized and cultured in vitro with or without the 3D gyroratory rocker in the traditional incubator.

MATERIALS AND METHODS: At 14hr post hCG injection, MII-cumulus mass were collected from both oviducts. Pooling the MII eggs from several mouse with 0.1% hyaluronidase and fertilized with epididymis sperm from fertile male mouse. 8hr post IVF, zygote with 2PN were collected and cultured in KSOM on the 3D gyroratory rocker or regular shelves. 3D gyroratory rocker is controlled 70 rpm in speed, and 12 degree in angle of tilt continually. We investigated three different medium size to make shear stress. After 3 day culture, morula from both culture condition were subjected real time-PCR with embryonic ZO-1 alpha form. After 5 day culture, blastocyst and hatching rate were observed and counted ICMT/TE cells. ICMT/TE counts were performed by immunostaining with anti-Oct 4 and DAPI staining. P value were calculated by t-test with Graphpad Prism.

RESULTS: In both imbred or out bred mouse, blastocyst formation and hatching rate are higher percentage in 3D gyroratory rocker than regular platform. Pooling the MII eggs from several mouse with 0.1% hyaluronidase and fertilized with epididymis sperm from fertile male mouse. 8hr post IVF, zygote with 2PN were collected and cultured in KSOM on the 3D gyroratory rocker or regular shelves. 3D gyroratory rocker is controlled 70 rpm in speed, and 12 degree in angle of tilt continually. We investigated three different medium size to make shear stress. After 3 day culture, morula from both culture condition were subjected real time-PCR with embryonic ZO-1 alpha form. After 5 day culture, blastocyst and hatching rate were observed and counted ICMT/TE cells. ICMT/TE counts were performed by immunostaining with anti-Oct 4 and DAPI staining. P value were calculated by t-test with Graphpad Prism.

SUPPORT: This research was supported by NRF-2017R1A1B10328155.

P-39 Tuesday, October 15, 2019 6:30 AM

GROUP EMBRYO CULTURE STRATEGIES AFFECT THE OXIDATIVE STATUS OF THE SPENT CULTURE MEDIA AND EMBRYO DEVELOPMENT. Lorenza Bori, PhD, a Raquel Del Gallego, PhD, b Lucia Alegre, PhD, b Silvia Azagra, MSc, c Tamara Vitoria, PhD, a Marcos Meseguer, PhD, b IVIRMA Global, Valencia, Spain; b IVIRMA Global, Valencia, Spain, Tel Aviv, Israel.

OBJECTIVE: To describe the impact of the group embryo culture over the oxidative profile of the medium and over the fertilization and the blastocyst rates in two types of culture dishes from two time-lapse incubators.

DESIGN: A retrospective analysis, including 299 IVF cycles from May 2017 to December 2018, was conducted. Culture media from 413 groups

SUPPORT: None
of embryos (15 μl/group) monitored with EmbryoScope Plus® (ES+) and Geri Plus® were analysed by the Thermochemistry luminescence (TCA) Analyzer® (Carmel Diagnostics, Israel).

MATERIALS AND METHODS: A total of 299 spent embryo culture media from 94 patients were analyzed. Sequential medium was used in 227 embryo groups and single-step medium in 186. The TCA Analyzer® consists on the heat-induced oxidation of biological fluids, leading to the production of light energy counted as photons emitted per second (cps). The oxidative parameters were obtained after 55 sec. (H1), 155 sec. (H2) and 255 sec. (H3). A smoothing algorithm (sm) was used to normalize data. Data were analyzed with ANOVA and Chi-squared tests (SPSS software).

RESULTS: Higher fertilization rates were found as the number of oocytes increased in the same group. However, blastocyst rate and the number of good quality blastocysts decreased when the number of embryos per group increased: 73.6±30.3% for ≤ 6 embryos, 69.0±23.7% for 7-8 embryos, 67.4±23.1% for 9-12 embryos and 64.9±23.2% for ≥ 13 embryos. The comparison between two time-lapse incubators with this kind of embryo culture showed significantly (p < 0.05) higher fertilization rates for Geri (78.9±17.3% for Geri vs. 73.7±20.6% for ES+) and higher blastocyst rates for ES+ (70.6±26.7% for ES+ vs. 65.7±22.6% for Geri). According to our data, sequential culture medium worked significantly better (p < 0.05) than single-step medium in terms of blastocyst rate (72.13±24.5% for sequential medium vs. 65.57±26.6% for single-step medium). In addition, oxidative stress level of the medium the fifth day post ICSI was significantly higher as more oocytes were successfully fertilized (Table). Table: Mean and standard deviation of the TCA parameters according to the number of successfully fertilized oocytes.

<table>
<thead>
<tr>
<th>Oocytes fertilized</th>
<th>N (Groups)</th>
<th>H1 (ms)</th>
<th>H2 (ms)</th>
<th>H3 (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 4</td>
<td>117</td>
<td>88.7 ± 32.8</td>
<td>91.5 ± 34.9</td>
<td>98.3 ± 39.4</td>
</tr>
<tr>
<td>5-6</td>
<td>108</td>
<td>83.6 ± 35.9</td>
<td>85.8 ± 37.5</td>
<td>92.9 ± 41.5</td>
</tr>
<tr>
<td>7-8</td>
<td>93</td>
<td>103.3 ± 49.2</td>
<td>108.0 ± 54.5</td>
<td>117.14 ± 63.8</td>
</tr>
<tr>
<td>≥ 9</td>
<td>95</td>
<td>105.1 ± 32.3</td>
<td>109.9 ± 32.6</td>
<td>121.3 ± 37.1</td>
</tr>
<tr>
<td>P Values</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Group embryo culture strategies affect embryo development results: as the number of oocytes cultured per group increased fertilization rates were improved, but not blastocyst rates, which were higher when medium was replaced. Moreover, media’s oxidative stress level was higher when more fertilized oocytes were cultured per group.

P-40 Tuesday, October 15, 2019 6:30 AM

THE EFFICACY OF THE NEW EMBRYO CULTURE MEDIUM WHICH DESIGNED FROM THE COMPONENTS OF HUMAN TUBAL FLUID; PROSPECTIVE RANDOMIZED TRIAL. Takafumi Utsunomiya, M.D., Ph.D., Yoko Shimura, B.S., Minako Sugishima, B.S., Yasuyuki Mio, M.D., PHD “Mio Fertility Clinic, Yokonaka, Japan; 3Japan.

OBJECTIVE: A study in 2017 observed perivitelline threads in more than 50% of cleavage-stage human embryos using time-lapse imaging, and the rate of cytoplasmic fragmentation (at the first cleavage) was significantly decreased in embryos without perivitelline threads (P < 0.001). While it is proposed that perivitelline threads play an important role in crosslinking the cumulus cells and oocyte during maturation, the mechanism underlying such a role remains unclear. It is also unknown whether the threads still function in mature MII oocytes. Therefore, in this study, zona pellucida of abnormally-fertilized oocytes which were donated by patients was removed at pronuclear stage. Those zona-free oocytes were observed in time-lapse culturing system in order to examine developmental morphology.

DESIGN: Prospective study.

MATERIALS AND METHODS: This study used 57 abnormally fertilized (3PN) embryos (n=57) donated by assisted reproduction technology patients in our clinic with informed consent since 2017. After confirming the three pronuclei, we removed the ZP from each 3PN embryo using a laser, and the resultant zona-free embryos were cultured and observed in an incubator equipped with a time-lapse imaging system. For ZP removal, 3PN embryos were placed in drops of 0.125M sucrose-containing HEPES media that had been covered with mineral oil and warmed to 37°C. Despite a small reduction in ooplasm size, half of the ZP was removed by laser (Saturn 5; Origo, Lykos; Hamilton Thorne). Subsequently, the ooplasm were completely separated from their ZPs by pipetting, and those zona-free 3PN embryos were cultured continuously for 5 days with time-lapse imaging.

RESULTS: Of 58 zona-free embryos in total, 54 (94.7%) were cleaved, and there was no significant decrease in cleavage rate compared to 2PN embryos (98%) used routinely in our clinic. Furthermore, 28 of the 54 embryos (51.9%) developed to the morula stage after third cleavage, and 18 embryos (33.3%) formed a blastocoele and became blastocysts. Thus, removing the ZP before cleavage did not adversely affect the embryo development. In terms of the amount of fragmentation, based on the modified Veeck’s criteria, 36 of 54 zona-free 3PN embryos (66.7%) showed less than 20% of the volume in fragments, compared to the total volume of cytoplasm at the first cleavage (Grade 1 and 2), 14 (25.9%) showed 20-40% fragments (Grade 3), and only 4 (7.4%) showed > 40% fragments (Grade 4). These results suggested that the rate of fragmentation was decreased by ZP removal before the first cleavage.

CONCLUSIONS: This study revealed that the ZP is not always necessary for normal development after the pronuclear stage because the zona-free
embryos studied herein developed normally, maintained their cell adhesion well, and showed a decreased rate of fragmentation. This innovative culture system might provide the major breakthrough needed for patients who have difficulty obtaining good-quality embryos.

**SUPPORT:** None

**P-42** Tuesday, October 15, 2019 6:30 AM

**TYPE OF CULTURE MEDIUM IS ASSOCIATED WITH PREIMPLANTATION EMBRYO DEVELOPMENT.** Linette van Duijn, MD, M:\textsuperscript{a} M:\textsuperscript{a} Malek Roussian, MD, PhD, M:\textsuperscript{a} Eva S. van Marion, MD, M:\textsuperscript{a} Joop S. E. Laven, MD, PhD, M:\textsuperscript{a} Régine P. M. Steegers-Theunissen, MD, PhD, M:\textsuperscript{a} Esther B. Baart, PhD. M:\textsuperscript{a} Erasmus University Medical Centre, Rotterdam, Netherlands; M:\textsuperscript{b} Erasmus University Medical Center, Rotterdam; M:\textsuperscript{c} Erasmus MC University Medical Center, Rotterdam, Netherlands.

**OBJECTIVE:** Previous research has demonstrated several influences of the periconception maternal environment on health later in life. The culture medium used in IVF/ICSI treatment, however, can be considered as an artificial environment that affects the preimplantation embryo. Since the introduction of the EmbryoScope\textsuperscript{TM} time-lapse incubator preimplantation embryo development can be closely observed. The aim of this study is to investigate the influence of two commercially available culture media on the developmental kinetics of the pre-implantation embryo, and IVF/ICSI treatment outcome.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** Data were obtained between 2012-2017 of 545 women undergoing their first IVF/ICSI treatment at the Erasmus MC. In this study, women were assigned to the Vitrolife G1 (n = 255) and Sage 1-Step (n = 290) culture media were subsequently. Embryos were cultured until day 3 of development in the EmbryoScope\textsuperscript{TM} time-lapse incubator and morphokinetic parameters of all transferred and frozen embryos were retrospectively annotated and not used for embryo selection. Treatment and patient characteristics were retrieved from medical records. Crude and adjusted associations between culture media and morphokinetic parameters were investigated using linear mixed models. Differences in treatment outcome were assessed by logistic regression.

**RESULTS:** Embryos cultured in Sage 1-Step medium show faster development over all developmental stages (from fusing of pronuclei to 8-cell stage) compared to Vitrolife G1. For example, embryos cultured in Sage 1-Step reach the 2-cell stage 2.08 (95\% CI 1.57-2.60) and 8-cell stage 3.61 (95\% CI 1.78-5.44) hours faster, respectively. After adjustment for female age, fertilisation method, type of ovarian stimulation, lowered oxygen culture and overall embryonic improvement over time, embryos cultured in Sage 1-Step reach the 2-cell stage 3.07 (95\% CI 1.18-5.62) and 8-cell stage 9.89 (95\% CI 2.80-16.99) hours faster. After adjustment for female age, fertilisation method and type of ovarian stimulation, embryos cultured in Vitrolife G1 demonstrated similar odds for positive β-hCG-test, fetal heartbeat and liveborn, when compared with embryos cultured in Sage 1-Step medium.

**CONCLUSIONS:** When compared to embryos cultured in Vitrolife G1, embryos cultured in Sage 1-Step culture medium are associated with faster development, however ongoing pregnancy rate is not significantly different. Our statistical approach enables analysis of the whole cohort of usable embryos per patient for an association between the type of culture medium and developmental kinetics. As embryo kinetics are likely to reflect embryo metabolism, the type of culture medium may impact embryo metabolism but not implantation potential. Further prospectively collected data is needed to unravel the relation between pre-implantation embryo kinetics and post-implantation development.

**P-44** Tuesday, October 15, 2019 6:30 AM

**EMBRYO CULTURE IN TIME-LAPSE SYSTEM PROVIDES BETTER RATES OF BLASTOCYST FORMATION, DECREASES EMBRYO DEVELOPMENT ARREST RATE COMPARED TO TRADITIONAL TRIPLE-GAS CULTURE SYSTEM.** Mariana Niccolini, BSc,\textsuperscript{a} Catherine Jacobs, BSc,\textsuperscript{a} Andrea Belo, BSc,\textsuperscript{a} Ana Paula Reis, BSc,\textsuperscript{a} Renata Erberelli, BSc,\textsuperscript{a} Fabiana Mendez, BSc,\textsuperscript{a} Marina Fanelli, BSc,\textsuperscript{a} Livia Cremonesi, BSc,\textsuperscript{a} Paulo Cesar Serafini, MD, PhD,\textsuperscript{b} Eduardo LA. Motta, MD, PhD,\textsuperscript{b} Aline R. Lorenzo, PhD,\textsuperscript{b} Jose Roberto Alegretti, M:\textsuperscript{a} Huntington Medicina Reprodutiva, Sao Paulo, Brazil; Huntington Medicina Reprodutiva, Clinical Department, Sao Paulo, Brazil; Scientific Coordinator, Huntington Medicina Reprodutiva, Sao Paulo, Brazil.

**OBJECTIVE:** Evaluate rates of blastocyst formation and embryo development arrest between uninterrupted (time-lapse) and triple-gas (90\% N\textsubscript{2}, 5\% CO\textsubscript{2}, 5\% O\textsubscript{2}) systems.
DESIGN: This is a cohort study analyzing laboratory data between January 2018 and March 2019 at Huntington Medicina Reprodutiva Clinic in São Paulo, SP, Brazil.

MATERIALS AND METHODS: A total of 1,276 cycles of IVF were evaluated. A total of 9,482 mature oocytes followed in vitro fertilization, 4,936 in the triple-gas system group (90% N₂ / 5% CO₂ / 5% O₂), mean age 37.56±3.59 years old and embryos were externally evaluated on days 1, 3, 5, and 7, if applicable. In the time-lapse group (EmbryoScope®), 595 cycles, mean age 37.54±3.47 years old, were cultured uninterrupted. Blastocyst formation rate (no. blastocysts/no. 2PN), blastocyst mean number formed per cycle, and cycle cancellation rate due to embryo development arrest were compared.

RESULTS: A total of 9,482 mature oocytes followed in vitro fertilization, 4,936 in the triple-gas system group and 4,546 in the time-lapse group, being fertilized 3,565 (72.23%) and 3,746 (73.06%) oocytes, respectively. From those, 1,791 blastocysts were formed in the traditional incubator group and 1,942 in the time-lapse group (50.2% versus 56.7%, p=0.001, chi-square test). Blastocyst mean number formed in the time-lapse group were generally higher than the control group (3.4±2.8 versus 2.7±2.8 p<0.0001, t-test). When maternal age was considered in analysis, ages between 35 and 42 years old showed gains in blastocysts mean number formed in time-lapse group: a) 34 years or less, no difference (4.1±3.1 versus 3.9±3.3, p=0.34); b) 35 to 37 years, higher in time-lapse group (3.8±3.2 versus 3.0±2.7, p=0.02); c) 38 to 40 years, higher in time-lapse group (3.2±2.6 versus 2.4±2.5; p=0.0003); d) 41 to 42 years, higher in time-lapse group (2.6±2.2 versus 1.8±2.5; p=0.001) and e) 43 years or older, no difference (1.7±1.4 versus 1.4±1.4, p>0.05). Embryo developmental arrest rate was also lower in the time-lapse group (11% versus 15%, respectively; p=0.05, chi-square test).

CONCLUSIONS: The uninterrupted culture available at the time-lapse system produced better blastocyst formation rates, especially between 35 and 42 years old showed gains in blastocysts mean number formed in time-lapse group. No benefits were shown from time-lapse to traditional culture media samples. When comparing culture media samples from male embryos compared to female ones (Levene’s Test for Equality of Variances, p<0.05) was considered statistically significant. All embryos were tested by next-generation sequencing (NGS) technique and only the balanced ones were used for analysis. hCG-H levels in the culture media were evaluated by ELISA kit (Cusabio Biotech, CBS-EL1803h) according to the manufacturer’s instructions. The absorption was measured on a microplate reader (Beckman Coulter DTX 880 Multimode detector) at 450 nm, absorbance analysis was performed using SPSS v21 (IBM Corp., Armonk, NY, USA). Descriptive parameters and patients’ characteristics were reported as mean ± SD. P<0.05 was considered statistically significant.

RESULTS: The NGS analysis revealed that 37% of the embryos (n=29) were balanced, 48% (n=14) of them were female (XX) and 52% (n=15) were male (XY). The presence of hCG-H was confirmed in all embryo culture media samples. When comparing culture media samples from male versus female embryos hCG-H levels were not significantly different (0.09±0.01 mIU/ml vs. 0.10±0.03 mIU/ml; p=0.37, respectively). However, the variety in hCG-H concentration was significantly lower in the samples from male embryos compared to female ones (Levene’s Test for Equality of Variances, p=0.004).

CONCLUSIONS: Our results suggest that the chromosomal sex of human embryos could have an effect on the secretion of hCG-H. The female embryos produce more variable quantities of hCG-H compared to the male ones.
OBJECTIVE: It has recently been reported that two separate bipolar spindles aligned their poles before anaphase keeping the parental genomes apart during the first cleavage in mammalian zygote including mouse and human. In mouse, the failure of spindle alignment by increasing the distance between the two pronuclei, which led to a larger gap between the spindles, gives rise to multinucleated two-cell embryos phenocopying frequently observed errors in IVF clinics. The purpose of our study is to examine the relationship between pronuclear (PN) proximity in zygote and multinucleation (MN) of early cleavage embryos in human using time-lapse system (TLS).

DESIGN: Data were retrospectively collected from TLS performed from May 2018 to February 2019 in the Fertility center of CHA Gangnam Medical Center. We analyzed 220 zygotes from 64 patients.

MATERIALS AND METHODS: We assessed the PN proximity, distance, MN, and development of early cleavage embryos using EmbryoScope™ (Vi- troLife, Gothenburg, Sweden). Drawing tool was used to measure the distance from a PN center to another PN center in the same focal plane before PN fade. Zygotes were divided into two groups according to the proximity (group Gap [G; n=17] and group Juxtaposition [J; n=203]). The number of MN in 2-cell and 4-cell embryo was checked then the embryos were divided into three groups (No MN, MN, and N/A; not available due to abnormal division). Embryo development was checked up to day 3. The quantitative variables were expressed as mean ± SD and statistically analyzed with Student t test. p <0.05 was considered to be statistically significant.

RESULTS: The incidence of gap between PN was considerably low (G; 7.7% vs. J; 92.3%). The average of PN distance was significantly different between the two groups (G; 31.2 ± 5.1 μm vs. J; 21 ± 4.9 μm, * p < 0.05). The rate of No MN (23.5%/2C and 52.9%/4C) was highly decreased but the rate of MN (41.2%/2C and 5.9%/4C) and N/A (35.3%/2C and 41.2%/4C) was increased in the Gap group compared with Juxtaposition group (49.8%/72.9%/2C/4C, 38.4%/5.4%/2C/4C, and 11.8%/21.7%/2C/4C). Also the rate of 3D good quality embryo is slightly decreased in Gap group (G; 82.4%/ J; 89.7%).

CONCLUSIONS: This study suggests that the PN proximity is also one of the applicable explanations for the MN in early cleavage embryos of human due to the failure of zygotic spindle alignment as other mammalian embryos such as mouse. As the presence of MN in human embryos, especially during the first and second mitotic divisions, is generally considered to be abnormal, our study on the relationship between PN proximity and MN combined with TLS could be used as a noninvasive technique to enhance selection of competent embryos likely to have the greatest potential of development. This may be of particular benefit to patients desiring elective single embryo transfer without PGS screening.

P-48 Tuesday, October 15, 2019 6:30 AM

OXIDATIVE STRESS IN HUMAN TESTICULAR TISSUE BEFORE AND AFTER CRYOPRESERVATION: A COMPARATIVE STUDY. Alaa Moubasher, MD, a Hanan Morsy, MD, b Aya Hassan Younis, MD, b Mikel Effat, MD, c Emad Taha, MD d Assiut University, Assiut, Egypt; Affiliation not provided; e Assiut University, Biochemistry department, Assiut, Egypt.

OBJECTIVE: To compare oxidative stress in human testicular tissue in both cases of obstructive (OA) and non-obstructive or functional azoospermia (NOA) before and after cryopreservation.

DESIGN: Comparative study.

MATERIALS AND METHODS: Azoospermic patients with OA and NOA were subject to surgical sperm retrieval with needle aspiration using a 14G needle. Cryopreservation was done in cryovials immersed in liquid nitrogen (−196°C). Assay of Catalase activity (CAT) and Malondialdehyde level (MDA) using colorimetric methods in fresh testicular samples and after cryopreservation of samples with positive sperm retrieval. In addition, assessing the number of retrieved sperms and Johnson spermatic score were done in fresh testicular samples.

RESULTS: The study included 21 OA (group A), 16 positive NOA (group B) and 21 negative NOA (group C) with negative sperm retrieval. Mean CAT activity in positive and negative NOA groups (151.90 ± 122.32 U/gm protein) (146.00 ± 121.7Illustration of the results of the study., P = 0.017, P = 0.018 respectively). MDA level was also significantly higher in positive and negative NOA (31.50 ± 15.81 nmol/ml) (40.38 ± 14.42 nmol/ml) groups than OA group (21.33 ± 9.61 nmol/ml) (P = 0.043, P = 0.000 respectively).CAT activity and MDA level correlated negatively with mean number of retrieved sperms (in groups with positive sperm retrieval A&B) (r = -0.261, P = 0.048, r = -0.402, P = 0.002 respectively). After thaw there was significant increase in CAT activity in OA only (213.67 ± 160.36 v 65.67 ± 72.99 U/gm protein) (P = 0.000), while there was no significant difference in MDA level in both OA and positive NOA. However, after thawing mean MDA level was still significantly higher in NOA than OA (26.94 ± 11.21 v 24.19 ± 15.97 nmol/ml) (P = 0.049).

CONCLUSIONS: Men with NOA seem to have increased basal testicular oxidative stress compared to those with OA as indicated by increased CAT activity and MDA level in fresh testicular samples. These markers of oxidative stress correlated negatively with spermatogenic activity. Furthermore, OA seem to resist oxidative injury induced by cryopreservation by enhancing CAT activity more efficiently than NOA.

P-49 Tuesday, October 15, 2019 6:30 AM

SELF-CORRECTION OF ANEUPLOIDY IN HUMAN BLASTOCYSTS AND SELF-ORGANIZING GASTRULIDUS. Tiago Rito, PhD, a Jeff Nafitaly, BA, b Norbert Gleicher, MD, a Ali H. Brivanlou, PhD, d Rockefeller University, New York, NY; Center for Human Reproduction, New York, NY.

OBJECTIVE: Finding of aneuploid cells in trophoderm biopsies at blastocyst stage is currently considered cause for disposal of embryos. Degree of tolerated aneuploidy and whether embryos self-correct downstream have, however, become one of the most controversial issues in reproductive medicine. Objective of this study was, therefore, investigation of degree of self-correction of aneuploidy in human blastocyst-stage embryos and in an in vitro model of early human gastrulation, - gastruloids.

DESIGN: We tracked aneuploidy in pre-implantation human embryos using single-cell RNA-seq data and conducted prospective in vitro studies on the impact of aneuploidy on human gastrulation.

MATERIALS AND METHODS: We induced aneuploidy in human embryonic stem cells by treatment with reversine, an inhibitor of MPS1, crucial for the spindle assembly checkpoint and the error correction pathway during cell division. Aneuploid and euploid cells were mixed to generate chimeric human gastruloids and their developmental outcomes were measured using a highly quantitative micropatter platform. To provide in vivo relevance, we used a computational approach to track aneuploidy in pre-implantation human embryos using single-cell RNA-seq data.

RESULTS: Aneuploid colonies did not affect maintenance of pluripotency, albeit displaying increased TP53. Chimeric euploid-aneuploid differ-entiated gastruloids showed differential cell death. This was particularly acute in the ectodermal (SOX2+) and mesendodermal (BRα+, SOX17+) lineages, without affecting extra-embryonic (GATA3+CDX2+) tissue. Using bioinformatics, we showed the presence of wide-spread but selective chromosomal instability in human blastocysts. The gene expression signature of aneuploid cells was closely associated to that of euploid cells and, consistent with the above noted gastruloid studies. Originally high levels of aneu- ploidy (up to 50%) gradually corrected themselves with time.

CONCLUSIONS: Similarly to the mouse, aneuploidy is tolerated in humans in extra-embryonic tissue but not in cells contributing to the embryo proper. Altogether, these results strongly suggest that presence of aneuploidy in human trophoderm is not an indicator of embryo quality to be used for embryo selection in human IVF.


P-50 Tuesday, October 15, 2019 6:30 AM

EMBRYO RESPIRATION TO EVALUATE THE EMBRYO QUALITY AND VIABILITY, AND ITS CLINICAL OUTCOME. Atsushi Fukui, MD, PhD, Yuji Ukita, MD, Hyogo College of Medicine, Nishinomiya, Hyogo, IL, Japan; Norbert Gleicher, MD, b Ali H. Brivanlou, PhD. a Rockefeller University, New York, NY; b Center for Human Reproduction, New York, NY.

OBJECTIVE: Earlier prediction of the quality and viability of in vitro developing embryo is very important. The measurement of embryo oxygen consumption, that is embryo respiration may be one of the objective methods to know the embryo quality and viability. Oxygen consumption is an ideal indicator of overall metabolic activity because ATP is generated
RESULTS: Human preimplantation embryos show endogenous DNA damage, demonstrated by γH2AX, RPA and abnormal nucleation. Cleavage embryos had significantly greater foci and micronucleation vs blastocysts (γH2AX cleavage mean 2.3 vs blastocyst 1.0, p < 0.0001; RPA cleavage mean 1.7 vs 0.3, p<0.0001; abnormal nucleation cleavage mean 15.9% vs blastocyst 4.2%, p<0.0001). DNA damage foci coincided with RPA33, indicating RPA phosphorylation by G2 checkpoint kinase ATR, Rad51, indicating repair by homologous recombination, and 53BP1, indicating unpaired DNA is passed to daughter cells.

Apahdicolin-induced replication delay resulted in DNA damage (γH2AX and RPA), and RPA33, indicating an ATR-dependent G2 checkpoint. Additional DNA repair mechanisms included Rad51 and 53BP1, similar to human embryos. Though some unreplicated DNA is tolerated in mitosis and compatible with euploidy, apahdicolin-induced under replication in the first cell cycle precipitated instability in later cell cycles, leading to decreased blastulation (45% after 8h apahdicolin vs 91.8% control, p<0.0001), and poor quality embryos as evidenced by significantly fewer total cells and inner cell mass with significantly greater DNA damage and micronucleation with increasing duration of apahdicolin exposure compared to controls.

CONCLUSIONS: DNA damage responses to incomplete replication in G2 (ATR and Rad51), and the G1 response to unreplicated DNA (53BP1) mirror endogenous repair activity in human preimplantation embryos. Developmental consequences of replication stress likely persist beyond the preimplantation stage and may contribute to failed implantation or miscarriage. The murine model of genomic instability enables further study of these processes and identified targeted drugs.


SUPPORT: New York Stem Cell Foundation (NYSCF), New York State Stem Cell Science Program (NYSTEM).

P-52 Tuesday, October 15, 2019 6:30 AM
THE EFFECT OF ZONA PELLUCIDA THICKNESS VARIATION ON FERTILIZATION AND SUBSEQUENT EMBRYONIC DEVELOPMENT: A LARGE SINGLE CENTER COHORT STUDY.

OBJECTIVE: During in vitro fertilization (IVF), variations in zona pellucida (ZP) thickness are frequently observed in retrieved oocytes. It is possible that these variations in ZP appearance are caused by the alteration of patterning glycoprotein matrix, which may be associated with oocyte cytoplasmic competence for embryonic development. In the present study, a large cohort of 1,664 oocytes was evaluated to understand the relationship between ZP thickness and embryonic outcomes.

DESIGN: This was a retrospective, single-center, cohort study.

MATERIALS AND METHODS: A retrospective study on 1,664 oocytes from 978 cycles (827 patients, mean age: 40.7 ± 0.1 years) was conducted from August 2018 to January 2019 in a single center. All patients underwent clomiphene citrate-only minimal stimulation IVF cycles. Maturation status of oocytes was confirmed by the appearance of meiotic spindles and oocytes were inseminated by intracytoplasmic sperm injection (ICSI). The ZP thickness was measured relative to a line drawn along the major axis of the oocyte, two ZP thickness measurements were taken at opposite sides of the line and values were averaged. Spearman’s correlation coefficient was used to evaluate the relationship between the female and ZP thickness. Multivariable logistic regression analysis, which included all significant confounding factors, yielding adjusted odds ratios (ORs) and 95% confidence intervals (CIs), was used to evaluate the correlation of ZP thickness to embryonic outcomes. Values were considered statistically significant when p-values were <0.05.

RESULTS: The mean ZP thickness was 19.0±0.1 μm. A significant negative correlation was observed between ZP thickness and age of the female (Spearman’s correlation coefficient, r = −0.0656, p = 0.0078). Fertilization, cleavage, blastocyst formation, and blastocyst utilization rates in this cohort were 64%, 90% (4,139/4,610) and 34%, respectively (3,061/8,830), and 42.7% (70/1,664), respectively. Multivariable logistic regression analysis revealed that there were no statistically significant associations between ZP thickness and fertilization (adjusted OR: 1.011, 95% CI: 0.960-1.065, p = 0.6725), cleavage (adjusted OR: 0.991, 95% CI: 0.942-1.042, p = 0.7303), blastocyst formation (adjusted OR: 0.974, 95% CI: 0.940-0.997).
OBJECTIVE: NCSs are histological markers of the window of implantation in natural and controlled ovarian hyperstimulation cycles. Thus far, NCSs have not been detected in frozen embryo transfer artificial (FET-A) cycles. This study aims to detect NCSs in endometrial aspirations obtained immediately prior to embryo transfer during FET-A cycles without affecting implantation.

DESIGN: Prospective study at a single university-affiliated site

 MATERIALS AND METHODS: Patients undergoing FET-A using estradiol and progesterone for endometrial preparation are consented for an inner uterine segment aspiration using an open tip embryo transfer catheter during a mock embryo transfer performed immediately prior to the actual embryo transfer. The aspirated endometrial secretions containing endometrial cells are then analyzed for the presence of NCSs using indirect immunofluorescence. Based on a prior study, positive NCS status was defined as the presence of NCS in at least 3 endometrial epithelial cells (EECs). Pregnancy outcomes are monitored to ensure that there is no effect of the aspiration on implantation rates.

RESULTS: Uterine secretions were obtained from 5 patients immediately prior to embryo transfer. The average age of women was 37.2 ± 4.2 years. NCSs were detected in exfoliated EECs of uterine secretions in 4 of 5 (80%) samples and could not be unequivocally identified in 1 of 5 (20%), which was designated as indeterminate. Implantation as evidenced by a positive BHCG was seen in 5 of 5 (100%) of the patients who underwent aspiration with a clinical pregnancy rate of 40% and an ongoing pregnancy rate of 20%.

CONCLUSIONS: This is the first report of NCS detection in FET-A cycles in the absence of follicular development and ovulation. NCS status can be determined in exfoliated EECs of uterine secretions obtained at the time of embryo transfer while maintaining implantation. Our study provides proof of principle to determine endometrial receptivity through individualized point of care testing of NCS status during frozen embryo transfer in artificial cycles.

SUPPRT: This study was supported by a grant from the NIH (HD094293 to U.T.M.).
of whole genome (28.7 million CpG sites). The average DNAme level was 15%. Aneuploid embryos showed significantly lower DNAme levels compared to euploid embryos (p<0.0001). Increased patient age was correlated with elevated DNAme levels in blastocysts (p=0.04). Blastocysts cryopreserved on day 6 had significantly lower DNAme compared to those that were cryopreserved on day 5 (p=0.001). Whole chromosomal aneuploidy predicted by calculating the fraction of read count from each chromosome showed 100% consensus with previous diagnosis. The chromosomes involved in monosomy embryos (-4,-13,-16, and -18) showed reduced methylation rates compared to the other chromosomes.

CONCLUSIONS: DNAme levels detected by RRBS in trophectoderm biopsies from human blastocysts is associated with ploidy status, maternal age, and embryo growth characteristics. This novel tool could provide a foundation for the development of epigenetic biomarkers of reproductive competence.

P-56 Tuesday, October 15, 2019 6:30 AM

MATERNAL AGE AND BLASTOCYST QUALITY DO NOT INFLUENCE THE EMBRYO PRODUCTION OF HYPERGLYCOXYLATED HUMAN CHORIONIC GONADOTROPIN. Dimitar Parvanov, PhD, a Dragomira Nikolova, PhD, a Rumiana Guneva, MSc, a Kristina Nikolova, MSc, a Magdalena Vasileva, MSc, a Ivaylo Rangelov, MSc, a Fabio Scarpellini, MD, b Giorgi Stamenov Stamenov, MD/PhD, b Nadezda Women’s Health Hospital, Sofia, Bulgaria; b Department of Medical Genetics, Medical Faculty, Medical University – Sofia, Sofia, Bulgaria; c Centre for Endocrinology and Reproductive Medicine, Rome, Italy.

OBJECTIVE: The purpose of the study was to evaluate the associations between the human embryo quality, maternal age and the amount of human chorionic gonadotropin (hCG-H) in the secretome of in-vitro cultured embryos.

DESIGN: Observational study.

MATERIALS AND METHODS: Individual embryos from 49 women were cultured to the blastocyst stage in 25 μL of single-step culture medium in the EmbryoScope. Media samples (n=54) were collected on day 5 from wells containing good, fair or poor quality blastocysts, respectively. Media from wells without an embryo were also collected as controls. The quality of the embryos was assessed morphologically. Measurement of hCG-H concentration in culture media is performed with ELISA kit (Cusabio Biotech, C14 Büro E1503b) according to the manufacturer’s instructions. The absorption is measured on a microplate reader (Beckman Coulter DTX 880 Multimode detector) at 450 nm. SPSS v.21 is used for the statistical analysis (IBM Corp., Armonk, NY, USA). P<0.05 indicates the statistical significance between the compared groups.

RESULTS: The median age of the patients included in the study was 38.08 ± 4.28 years. The number of observed Day 5 good, fair and poor quality blastocysts was 26, 22 and 6, respectively. The presence of hCG-H was confirmed in each culture media sample but was absent in the controls. Comparison between good, poor and excellent quality embryos was made by Mann-Whitney U test as parameters were not normally distributed. The measured mean hCG-H levels were not significantly different between poor, fair and good quality embryos (0.095 mIU/mL vs. 0.095 mIU/mL vs. 0.08 mIU/mL; p=0.91, respectively). In addition, there was a lack of significant correlation between women’s age and the level of hCG-H, produced by embryos (R=-0.17, p=0.23).

CONCLUSIONS: Our results suggest that the embryo’s secretion of hCG-H is not influenced by maternal age and morphological quality of human blastocysts.

P-57 Tuesday, October 15, 2019 6:30 AM

EVALUATING THE ABILITY OF AN OOCYTE TO REPAIR FRAGMENTED SPERM CHROMATIN. Derek Keating, B.A., a Alessandra Parrella, M.Sc., a Zev Rosenwaks, M.D., b Gianpietro D. Palermo, M.D., b Ph.D. a The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To evaluate the ability of oocyte DNA repair mechanisms to detect and fix deficiencies in sperm chromatin integrity and support embryo implantation.

DESIGN: From 2006-2017, ejaculates from 127 men were assessed for sperm chromatin fragmentation (SCF). Intracytoplasmic sperm injection (ICSI) clinical outcomes were divided into groups according to the SCF level of the male partner and the proportion of mature oocytes obtained at retrieval. Proportional oocyte nuclear maturity was considered an indirect marker for presumed cytoplasmic readiness of the oocyte, suggesting its ability to repair the damaged genome during prophase I orientation.

MATERIALS AND METHODS: Samples from consenting couples were screened for SCF levels by terminal deoxynucleotidyl dUTP nick-end labeling (TUNEL) utilizing a commercially available kit. A minimum of 500 spermatozoa were assessed per patient, and an SCF of 15% or below was considered normal. From the retrieved cohort, the proportion of metaphase-II oocytes at the time of ICSI was recorded and used for this assessment. ICSI was performed in the standard fashion. Female partners were limited to ≤35 years of age to control for eventual confounding female factors.

RESULTS: A total of 127 couples underwent 191 ICSI cycles. Of them, 84 couples in which the male partner had a normal SCF level (9.8±3.1%) underwent 125 ICSI cycles; conversely, 43 couples in which the male partner had an abnormal SCF level (24.1±11.1%; P<0.0001) underwent 67 ICSI cycles.

When the proportion of mature oocytes was over 80% at the time of retrieval, there was no difference in the ICSI clinical outcome between couples with normal and abnormal SCF levels, indicating that a mature ooplasm overcomes compromised genomic integrity. However, when the proportional oocyte maturity dropped below 80%, ICSI cycles carried out with spermatozoa with a normal SCF level (n=62) retained an implantation rate of 25.0%, whereas the embryos generated from spermatozoa with an abnormal level of SCF (n=27) showed an impaired implantation ability (8.3%) to implant (P<0.05). The latter implies that the ooplasm of the MII oocyte was unable to properly repair male genomic deficiencies.

CONCLUSIONS: These findings support the notion that an appropriate nuclear and cytoplasmic maturity is needed to unravel the male genome and repair eventual nicks and breaks within the chromatin. The implied ooplasmic dysfunction, occurring with a suboptimal MII cohort, may not efficiently overcome compromised sperm chromatin integrity.
mass index was 22.3±1.5. A positive correlation of the relative level of mtDNA in the CCs with the patients’ age (p = 0.008) and AMH levels (p = 0.003) was revealed. There was no statistically significant correlation between mtDNA copy number and embryo morphology on day 5 (p>0.7). There was a tendency to increase mtDNA copy number in group 1 vs. group 2, 390 and 299, respectively (p>0.05). In this study we didn’t find relationship between median mtDNA content of CCs and embryos ploidy (356 vs. 325, in euploid (n=74) and aneuploid (n=56) blastocyst, respectively, p>0.05).

CONCLUSIONS: mtDNA content in CCs correlated with female age and AMH level. However, the determination of mtDNA copy number in CCs don’t predict embryos implantation potential.

P-59 Tuesday, October 15, 2019 6:30 AM

**DYNAMIC AND VIABILITY OF HUMAN DAY-6 TROPOPHODERM CELLS DURING 141 DAYS OF CELL CULTURE.** Oscar Perez, Ph.D.,1 Hannalie Adriana, BS,2 Breana Tilley, MSc,2 Gabriella Navarrete, BS,2 Ravi Gada, MD,2 Laura Lawrence, MD,2 Mika R. Thomas, MD,2 Karen Lee, MD,2 Samuel Chantilis, MD2 Dallas Fertility Center, Dallas, TX; 3Dallas Fort Worth Fertility Associates, Dallas, TX.

**OBJECTIVE:** To determine the dynamic and viability of derived human trophectoderm cells (TE) in vitro cultured for 141 days.

**DESIGN:** Research ongoing study.

**MATERIALS AND METHODS:** Study trophectoderm cells were obtained from day-6 blastocysts determined to be non-viable after undergoing in vitro fertilization. This study was conducted in accordance with an IRB. Trophectoderm cells (TE) in vitro cultured for 141 days. TE cells were settled at the bottom of three wells in a central depression with a diameter of 200 μm. The media was changed every 24 hours. TE cells were video monitoring in the 10-minute cycle time with seven focal planes for 141 days. TE cells from the same well were counted (using a cell counter) three times to obtain the average number. A sample of 5 μl aliquot of cells was taken for each well and analyzed by Veriseq (real-time PCR) to confirm the viability and the chromosomal analysis of the TE cells. Genetic testing was performed by Reprogenetics Recombine Genesis Genetics (Cooper Genomics). The remaining cells were discarded.

**RESULTS:** Dynamic reproduction of TE cells was observed in all biopsied samples. TE cells responded with aggressive expansion and growth during the first 30 days of culture and then remained in a plateau growth pattern during the rest of the cell culture time. The number of cells was an estimated average, but it could be inaccurate due to the size of the cells and the focal plane of the video picture. The viability of the cells was determined by the genetic information outcome, color, and integrity of the cells.

### Number of TE Cells at 141 Days of Cell Culture (Average of 3 Counts)

<table>
<thead>
<tr>
<th>Biopsied Specimen of TE Cells (Average)</th>
<th>Number of TE Cells at 30 Days of Cell Culture (Average of 3 Counts)</th>
<th>Number of TE Cells at 141 Days of Cell Culture (Average of 3 Counts)</th>
<th>Genetic Screening at 141 days of Cell Culture (Next Generation Sequencing)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25</td>
<td>1200</td>
<td>5000 Aneuploid</td>
</tr>
<tr>
<td>2</td>
<td>25</td>
<td>2300</td>
<td>6000 Euploid</td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td>3500</td>
<td>8000 Euploid</td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** Deriving TE cells from human day-6 blastocysts is possible. This outcome opens the opportunity to explore new trophectoderm cell culture conditions. Increment in trophectoderm cells might offer new alternatives to improve our knowledge of this type of cells on IVF patients with a poor number of trophectoderm cells on day-6 embryos.

P-60 Tuesday, October 15, 2019 6:30 AM

**IS LOW MITOCHONDRIAL DNA (mtDNA) CONTENT AFTER FERTILIZATION FAILURE DUE TO OOCYTE AGING IN CULTURE?** Marta Perez, PhD, student,1 Amapro Mercader, PhD,2 Diana Beltrán, Master,3 Arantza Delgado, PhD,2 Laura Escrich, PhD,2 Antonio Pellicer, MD, PhD,3 Carmen Vidal, M.D., Ph.D.,3 Ma José de los Santos, PhD,3 IVI foundation, Instituto de Investigación Sanitaria La Fe, Valencia, Spain; 2IVIRMA Valencia, Valencia, Spain; 3IVIRMA ROMA, Roma, Italy.

**OBJECTIVE:** Low mitochondrial DNA (mtDNA) content in oocytes has been correlated with oocyte fertilization failures. However, all the studies with failed-fertilized oocytes have been performed in in-vitro aged oocytes. As the results have relevant clinical implications on understanding oocyte competence, the aim of the study was to evaluate the effect of in vitro aging in mtDNA content in failed-fertilized oocytes.

**DESIGN:** A prospective cohort study was performed with 101 samples consisting on 36 “fresh” non-inseminated MII donated oocytes, 31 in-vitro aged failed-fertilized oocytes, 17 “fresh” failed-fertilized oocytes from patients and another 17 from donors.

**MATERIALS AND METHODS:** Samples were collected in PCR tubes the same day of follicle aspiration in the case of donated MII oocytes, after 19-22 hours post-IVF for “fresh” failed-fertilized oocytes and after 5-6 days of culture in the case of in vitro aged failed-fertilized oocytes. Q-PCR was performed with SurePlex DNA Amplification System (Illumina) using specific primers for the ATP8 gene to assess the total mtDNA copy number. Data was analyzed by ANOVA test with Scheffé multiple comparison.

**RESULTS:** Significant higher mtDNA content was found in “fresh” non-inseminated MII oocytes comparing with “fresh” and failed-fertilized ones (P<.05) in both patients and donors. Besides, there were no significant differences in terms of mtDNA content between “fresh” and in-vitro aged failed-fertilized oocytes (P=0.5).

**CONCLUSIONS:** As it appears in literature, we have observed a significant decrease in mtDNA content associated with failed-fertilized oocytes compared to “fresh” non-inseminated MII oocytes. Such decrease occurs regardless of the in vitro aging. In addition, we observed that the decrease of mtDNA content in failed-fertilized oocytes is independent of the maternal age. Furthermore, it seems that the decrease of mtDNA content observed in failed-fertilized oocytes compared to non-fertilized oocytes is due to the fail of fertilization itself and not because of the mtDNA degradation in culture, since when we compare fresh failed-fertilized oocytes and failed-fertilized oocytes that were sampled after 5 or 6 days after ICSI, we do not observe significant differences. Therefore, we can conclude that the fail of fertilization is related to oocytes with an unusually low mtDNA content and this finding supports the importance of the mtDNA content in oocytes as a biomarker for embryo viability.

**Support:** This work was funded by a grant from the Generalitat Valenciana (Spain).
suggested that male embryos grow faster than female embryos and as a result embryologists are more likely to select a male embryo for transfer. The objective of this study is to assess whether an embryo’s sex and/or chromosomal normalcy may be related to their rate of development.

DESIGN: A retrospective study of PGT-A results obtained between 2016 and 2018.

MATERIALS AND METHODS: Information was derived from PGT-A results of 151 patients (691 embryos; 21 uncounted due to being beyond parameters or missing information). We determined the ratios of day-5 XY to XX, labeling this as group A, day-6 XY to XX as group B, day-5 euploid (N) to aneuploid (AN) as group C, and day-6 N to AN as group D. These ratios were then tested to determine whether embryo growth exhibited any significant patterns.

RESULTS:

Table: Chi-Square Test

<table>
<thead>
<tr>
<th>Group</th>
<th>Total Day 5 XY</th>
<th>Total Day 5 XX</th>
<th>Expected Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>242</td>
<td>208</td>
<td>225</td>
<td>0.11</td>
</tr>
<tr>
<td>B</td>
<td>108</td>
<td>112</td>
<td>110</td>
<td>0.79</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Our results do not support the notion that male embryos grow faster than female embryos. The was a significant difference in the rate of aneuploidy seen when comparing day 6 blastocysts to those that reached the blastocyst stage on day 5.

References: n/a

SUPPORT: n/a

P-62 Tuesday, October 15, 2019 6:30 AM

TROPHECTODERM CELL DEVELOPMENT FROM DAY-6 HUMAN BLASTOCYSTS. IS IT POSSIBLE TO REPRODUCE THEM IN VITRO?" Oscar Perez, Ph.D., a
Hannalie Adriaanse, BS, a Breanna Tilley, MSC, a
Gabriella Navarrete, BS, a Linda Lay, BS, a Lucille M. Little, BS, a
Ravi Gada, MD, a Laura Lawrence, MD, b Karen Lee, MD, b
Mika R. Thomas, MD, c Samuel Chantilis, MD c Dallas Fertility Center, Dallas, TX; dDallas Fort Worth Fertility Associates, Dallas, TX.

OBJECTIVE: To create trophectoderm (TE) cells in vitro from discarded day-6 blastocysts.

DESIGN: Research ongoing study

MATERIALS AND METHODS: Trophectoderm cells from non-viable, discarded, day-6 blastocysts were selected for this study. Specimens were derived from unused cells obtained from in vitro fertilization patients who had consented to have these discarded cells used for this IRB-approved research study. Three biopsied cell masses were cultured in RPMI 1640 medium supplemented with 20% HSA. TE cells were cultured with human fibroblast growth factor-4 in a time-lapse incubator (Embryoscope®). TE cells were video monitored every ten minutes with seven different focal planes for 500 hours of cell culture.Derived TE cells from the same specimen were divided into two groups according the size of the cell in μm. TE cells were counted (using a cell counter) three times to obtain the group number.

RESULTS: Trophectoderm cell derivation started after initial cell culture. Proliferated TE cells resulted in smaller cells of approximately 2-5 μm. Some of these smaller cells grew and reached the same size as the original TE cell source. The number of cells was an estimate number, but it could be inaccurate due to the size of the cells and the focal plane of the video picture.

CONCLUSIONS: Developing trophectoderm cells in vitro is possible. Although some of the derived cells resembled the same origin, the growth pattern of most cells was prolonged. Moreover, most of the resulted TE cells were smaller than 5 μm. These smaller TE cells might need different culture protocols and growth factors to express similar characteristics as the original TE cells from day-6 blastocysts.

ENDOMETRIAL PHYSIOLOGY

P-64 Tuesday, October 15, 2019 6:30 AM

THE INFLUENCE OF HYPOXIA ON ANGIOGENESIS AND METABOLISM IN HUMAN ENDOMETRIAL STROMAL CELLS. Hidetaka Okada, MD, a Takeharu Kido, MD, b Kansai Medical University, Hirakata, Japan.

OBJECTIVE: Hypoxia is a physiological event that occurs in the endometrial tissues during the premenstrual period and implantation. Hypoxia-inducible factor-1 (HIF-1) is the master regulator of the cellular response to hypoxia. HIF-1α activation by the hypoxic microenvironment is involved in angiogenesis and metabolism. The aim of this study is to investigate the effects of hypoxic stress on the regulation of HIF-1α and vascular endothelial growth factor (VEGF), and on the changes in the metabolic pathway in the endometrium.

DESIGN: Prospective in vitro studies using human primary endometrial stromal cell cultures.

Development of trophectoderm cells in vitro

<table>
<thead>
<tr>
<th>Specimen 1</th>
<th>Specimen 1</th>
<th>Specimen 2</th>
<th>Specimen 2</th>
<th>Specimen 3</th>
<th>Specimen 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>TE Cells ≥ 10</td>
<td>TE Cells ≤ 10</td>
<td>TE Cells ≥ 10</td>
<td>TE Cells ≤ 10</td>
<td>TE Cells ≥ 10</td>
<td>TE Cells ≤ 10</td>
</tr>
<tr>
<td>0 hours</td>
<td>25</td>
<td>0</td>
<td>25</td>
<td>0</td>
<td>25</td>
</tr>
<tr>
<td>500 hours</td>
<td>200</td>
<td>1000</td>
<td>300</td>
<td>2000</td>
<td>250</td>
</tr>
</tbody>
</table>

Vol. 112, No. 3, Supplement, September 2019
MATERIALS AND METHODS: Human endometrial tissues were obtained from 21 patients aged 32–46 years undergoing hysterectomy for benign reasons with regular menstrual cycles. The human endometrial stromal cells (ESCs) were purified by the standard enzyme digestion method. ESCs were cultured under hypoxic (2% O2) or normoxic (20% O2) conditions with echinomycin, a small-molecule inhibitor of HIF-1α activity. The mRNA levels and production of VEGF were assessed by real-time PCR and ELISA, respectively. The HIF-1α protein levels were measured using western blot analysis. Metabolome analysis was measured by capillary electrophoresis electrospray ionization time-of-flight mass spectrometry and capillary electrophoresis-triple quadrupole mass spectrometry. Differences in the measured parameters across the different groups were statistically assessed using ANOVA followed by Dunnett’s test and a level of P < 0.05 was considered statistically significant.

RESULTS: Real-time PCR analysis demonstrated that hypoxia caused a significant increase in the levels of VEGF mRNA expression (P < 0.01). Hypoxia caused a significant increase of VEGF production after 6 h of culture compared with normoxia (P < 0.01), and this effect continued until the end of the study (48 h). Hypoxic stress significantly induced the expression of HIF-1α protein (P < 0.05), and its highest expression was observed at 6 h. Echinomycin inhibited hypoxia-induced VEGF production without affecting the HIF-1α protein level. These results suggest that hypoxia acts to increase VEGF via HIF-1α-dependent manner. A total of 116 metabolites were analyzed. Hypoxia significantly increased glucose 6-phosphate and fructose 6-phosphate in the glycolytic pathway (P < 0.05). However, while hypoxia suppressed cis-aconitic acid, isocitric acid, and citric acid in the tricarboxylic acid cycle, the decrease only reached the borderline of significance (P = 0.08).

CONCLUSIONS: These results indicate a mechanism for the action of hypoxic conditions that could influence angiogenesis and metabolism in the human endometrium.

P-65 Tuesday, October 15, 2019 6:30 AM
DOES THE ENDOMETRIUM HAVE A ROLE IN SELECTING EMBRYO GENDER?: Javier Herreros, Sr., MSc, Hector Huete Ferriz, MSc, Mireia Florena, MSc, Marga Esbert, PhD IVI RMA Barcelona, Barcelona, Spain.

OBJECTIVE: It is still unknown if the endometrium can select the embryo depending on the gender. To date, it has been thought that the gender of the newborn children depends on the spermatozoa which fertilized the oocyte was carrier of Y or X chromosome. Nevertheless it is possible that the endometrium could have an important role on this event. The aim of our study is to prove if the endometrial receptivity could change depending on the gender of the transferred embryo.

DESIGN: Retrospective study.

MATERIALS AND METHODS: This retrospective study includes 2237 IVF cycles performed in our center between January 2004 and May 2018. Patients were divided into 2 different branches:

Branch 1: study the gender percentage of the newborn children in couples who have undergone DET (double embryo transfer) in one cycle, obtaining all the possible combinations: male-male, female-female and male-female.

Branch 2: compare if there is any tendency towards the embryo’s implantation depending on whether the replaced embryo has the same sex as the previous children or not in couples with two or more newborn children resulting from cycles at IVI Barcelona.

We have analyzed our data with a Chi-squared test.

RESULTS: Depending on the embryo gender of the newborn children, we have classified the different combinations in 10 groups. In the first branch (n = 1763) there are no difference among the frequency of the three groups: 46.5% (1), 25.7% (2) and 27.6% (3). Analyzing the combinations 2 and 3 (n = 979) the probability of having two females is slightly higher than having two males, 52.19% vs 47.8%, but without statistical significant difference.

As for the second branch (n = 474), we have divided the cycles into three different groups depending on the number of newborn children. Group A (n = 384) with two newborn children, group B (n = 84) with three newborn children and the group C (n = 6) with four newborn children. We have observed that the results agrees with the natural proportion in all three groups. As an example, in the group A the combinations 1 are 54%, combination 2 is 25% and combination 3 is 21%.

CONCLUSIONS: Our findings suggest that having a first newborn child has no influence on the gender of the following newborn children irrespective of the number of embryos replaced or the number of cycles performed. Therefore, according to our results, the endometrium does not play a role in selecting the embryo gender.

EUPLOID EMBRYO PREDICTORS

P-66 Tuesday, October 15, 2019 6:30 AM
THE ASSOCIATION OF AGING MARKERS IN LUTEINIZED GRANULOSA CELLS AND EMBRYO ANEUPLOIDY RATE IN PREIMPLANTATION GENETIC TEST FOR ANEUPLOIDY CYCLES. Tsung-Hsien Lee, MD, PhD, 1 En-Hui Cheng, PhD, 1 Maw-Sheng Lee, MD, PhD. 1 2 Chung Shan Medical University Hospital, Taichung, Taiwan; 1Lee Women’s Hospital, Taichung, Taiwan; 3Chung Shan Medical University, Taichung, Taiwan.

OBJECTIVE: The ovarian aging is associated with poor quality oocytes, especially increasing aneuploidy rate. In addition to chronological age, several biomarkers could represent the aging status of individual person, such as telomere length and mitochondrial copy number in somatic cells. Nonetheless, the correlation between these aging biomarkers and embryo aneuploidy rate in ART cycles is not clear.

DESIGN: This prospective cohort study was performed for the patients for preimplantation genetic test for aneuploidy (PGT-A) programs in a single reproductive center in Taiwan.

MATERIALS AND METHODS: The telomere length and mitochondria copy number in leukocytes and luteinized granulosa cells were measured as aging biomarkers. The association among these aging biomarkers was explored. The correlation between these aging biomarkers and embryo aneuploidy rate was investigated with Spearman correlation test and linear regression model.

RESULTS: A total of 110 PGT-A cycles was recruited for this study. The telomere length and the mitochondria copy number are intimately correlated.

### Table 1. Correlation between biomarkers of aging (Spearman correlation test)

<table>
<thead>
<tr>
<th>Spearman correlation coefficient</th>
<th>Leukocyte telomere length</th>
<th>Granulosa cell telomere length</th>
<th>Leukocyte mitochondrial copy number</th>
<th>Granulosa cell mitochondrial copy number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.093</td>
<td>-0.186</td>
<td>-0.069</td>
<td>-0.019</td>
</tr>
<tr>
<td>P</td>
<td>0.334</td>
<td>P=0.051</td>
<td>P=0.472</td>
<td>P=0.846</td>
</tr>
<tr>
<td>AMH</td>
<td>-0.015</td>
<td>0.385</td>
<td>0.006</td>
<td>0.261</td>
</tr>
<tr>
<td>P</td>
<td>0.875</td>
<td>P&lt;0.001</td>
<td>P=0.954</td>
<td>P=0.006</td>
</tr>
<tr>
<td>Leukocyte telomere length</td>
<td>1.000</td>
<td>0.008</td>
<td>0.477</td>
<td>0.095</td>
</tr>
<tr>
<td>P</td>
<td>0.931</td>
<td>P=0.001</td>
<td>P=0.321</td>
<td></td>
</tr>
<tr>
<td>Granulosa cell telomere length</td>
<td>0.008</td>
<td>1.000</td>
<td>-0.075</td>
<td>0.361</td>
</tr>
<tr>
<td>P</td>
<td>0.931</td>
<td>P=0.001</td>
<td>P=0.437</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Leukocyte mitochondrial copy number</td>
<td>0.477</td>
<td>-0.075</td>
<td>1.000</td>
<td>-0.020</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.001</td>
<td>P=0.437</td>
<td>P=0.839</td>
<td></td>
</tr>
<tr>
<td>Granulosa cell mitochondrial copy number</td>
<td>0.095</td>
<td>0.361</td>
<td>-0.020</td>
<td>1.000</td>
</tr>
<tr>
<td>P</td>
<td>-0.321</td>
<td>P=0.001</td>
<td>P=0.839</td>
<td></td>
</tr>
</tbody>
</table>
with each other within leukocytes or granulosa cells, but not correlated between leukocytes and granulosa cells. In addition, serum anti-Mullerian hormone (AMH) is closely correlated with telomere length and mitochondrial copy number in granulosa cells, but not those in leukocytes. Linear regression model revealed that chronological age is the sole aging biomarker associated with aneuploidy rate of embryos in ART cycles.

CONCLUSIONS: Although the serum AMH, telomere length of granulosa cells, mitochondrial copy number in granulosa cells are closely correlated with each other, the chronological age is the main factor to affect aneuploidy rate of embryos in PGT-A cycles. The results suggest that the main source of aneuploidy is oocyte meiosis, especially if the oocyte stayed at proterone stage for a long period of time.

SUPPORT: The study was supported by a grant from Ministry of Science and Technology for Maw-Sheng Lee (MOST 106-3114-B-040-001).

P-68 Tuesday, October 15, 2019 6:30 AM
THE IMPACT OF LEAD FOLLICLE SIZE AND DURATION OF STIMULATION ON THE PROBABILITY OF EUPLOID EMBRYOS. Denis Schapira Wajman, MD.a David L. Keeffe, M.D., b David H. McCulloh, Ph.D.a James A. Grifo, MD, PhD.b Cheogneon Oh, PhD.d "NYU Langone, New York, NY; dNew York University School of Medicine, Department of Obstetrics and Gynecology, New York, NY; eNYU Langone Fertility Center, New York, NY.

OBJECTIVE: Clinical guidelines on the optimal duration of controlled ovarian stimulation and ideal follicle size were developed for fresh embryo transfer cycles. Whether these apply to freeze all cycles remain unclear. We evaluated the impact of lead follicle size and duration of stimulation on the probability of euploid embryos in women undergoing IVF/PGT-A.

DESIGN: Cross-sectional study

MATERIALS AND METHODS: Data from 721 patients undergoing at least two cycles of COS for IVF with preimplantation genetic testing for aneuploidy (PGT-A) via Next Generation Sequencing (NGS) (1859 cycles). Mixed-effect logistic regression, which can account for correlations among repeated outcomes within sample patients, was used to evaluate the association between independent variables and probability of achieving euploid embryos. We first conducted a mixed-effect logistic regression in a univariate manner. All variables then were evaluated in a multivariable model to control for confounding effects. Significant variables to p<0.05 were retained in the final model. p-values <0.05 were considered significant. Statistical analyses were performed using "nlme" and "lme4" package from R project. Results are reported as odds ratios (OR) with 95% confidence intervals (CI).

RESULTS: Increasing sum (1.034 [1.022 1.046]/p<0.001) and mean diameter (1.129 [1.046 1.219]/p=0.002) of the 5 largest follicles increased the probability of forming euploid embryos. Increasing days of stimulation showed a non-significant trend toward lower chance of forming euploid embryos (0.976 [0.923 1.031]/p=0.382) (Table 1).

CONCLUSIONS: Allowing the lead follicles to exceed 18mm increases the total number of euploid embryos formed per cycle, presumably by enabling retrieval of additional mature oocytes. Evidence of a detrimental effect of excessive follicle size was not evident in our study, though the number of cycles with follicles exceeding 24 mm was limited. The non-significant trend toward decreased euploid embryos following prolonged stimulation may reflect the effects of poor responders.

TABLE 1.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Unadjusted OR [95% CI]/p-value</th>
<th>Adjusted OR [95% CI]/p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;35</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>35-38</td>
<td>0.586 [0.399 0.861]/0.007</td>
<td>0.665 [0.447 0.989]/0.044</td>
</tr>
<tr>
<td>38-41</td>
<td>0.382 [0.265 0.550]/&lt;0.001</td>
<td>0.371 [0.254 0.541]/&lt;0.001</td>
</tr>
<tr>
<td>41-43</td>
<td>0.158 [0.107 0.233]/&lt;0.001</td>
<td>0.172 [0.114 0.258]/&lt;0.001</td>
</tr>
<tr>
<td>43+</td>
<td>0.051 [0.030 0.087]/&lt;0.001</td>
<td>0.067 [0.039 0.117]/&lt;0.001</td>
</tr>
<tr>
<td>Folicle size</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
<td>1.003 [0.991 1.015]/0.609</td>
<td></td>
</tr>
<tr>
<td>Top 5 average</td>
<td>1.002 [0.996 1.007]/0.584</td>
<td></td>
</tr>
<tr>
<td>Top 5 sd</td>
<td>1.129 [1.046 1.219]/0.002</td>
<td></td>
</tr>
<tr>
<td>Top 5 sum</td>
<td>1.034 [1.022 1.046]/&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Simulation days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>10-12</td>
<td>1.050 [0.785 1.405]/0.741</td>
<td></td>
</tr>
<tr>
<td>12+</td>
<td>0.876 [0.635 1.207]/0.417</td>
<td></td>
</tr>
<tr>
<td>Mature Eggs Retrieved</td>
<td>1.150 [1.124 1.178]/0.001</td>
<td>0.976 [0.907 1.051]/0.526</td>
</tr>
</tbody>
</table>
OBJECTIVE: To determine the effect of adjuvant human growth hormone (hGH) during IVF/PGT-A cycles on euploid embryo rate in women with and without poor ovarian response (POR).

DESIGN: Retrospective non-randomized cross over study

MATERIALS AND METHODS: The study was carried out at a single clinic site from 2014-2018. Inclusion criteria: women who underwent one cycle of IVF/PGT-A and at least one consecutive IVF/PGT-A cycle with hGH within a 1-year period. hGH (1.45 mg) was started on the first day of ovarian stimulation and continued until trigger. Patients were stratified as POR by Bologna criteria. Women without POR were offered hGH if prior cycles had a suboptimal response or suboptimal blastocyst development as predicted by age/antral follicle count/AMH. Using a two-tailed paired t-test, sample size of 34 was sufficient to detect a significant difference of 0.5 or greater at 0.05 power. Paired t-test analysis was performed with GraphPad Prism 8.0 to detect statistical significance of p < 0.05.

RESULTS: 51 patients underwent 79 cycles during the study period and met inclusion criteria. Table 1 shows cycle outcomes for POR women compared to non-POR. Interestingly, in POR patients there was a small but statistical increase in number of biopsied blastocysts but no difference in number of euploid embryos/euploid rate. In women classified as non-POR, there were significant improvements in all cycle parameters. When the data was stratified according to age, euploid rate was increased in hGH cycles in both <37 years (8.75% vs. 53.9%, p = 0.001) and >38 years (12.7% vs. 26.7%, p = 0.03). However, when stratified by AMH, women with AMH <1 did not show a significant increase in euplaid rate (5.26% vs. 11.8%, p = 0.4), whereas women AMH >1 did show a significant benefit (14.5% vs. 40.0%, p = 0.0003).

CONCLUSIONS: Prior studies have focused on use of hGH in poor responder women during IVF, but little is known about the utility in non-POR. This study shows that hGH significantly increases the number of euploid embryos/euploid rate in women who are not poor responders but had suboptimal response or poor embryo development. Interestingly, this study shows that in POR patients, all cycle outcomes are significantly improved by hGH except euploid rate. In conclusion, our study shows the use of hGH should be considered in non-POR women to improve IVF cycle outcomes.

Table 1: IVF-PGT-A cycle outcomes in women with and without adjunct use of hGH: Mean (SD)

<table>
<thead>
<tr>
<th></th>
<th>Non-POR (n=60)</th>
<th>POR (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No hGH</td>
<td>hGH</td>
</tr>
<tr>
<td>Mature oocytes (MII)</td>
<td>7.7 (4.85)</td>
<td>10 (6.6)</td>
</tr>
<tr>
<td>Biopsied Blastocysts</td>
<td>1.28 (1.29)</td>
<td>2.83 (2.56)</td>
</tr>
<tr>
<td>Euploid Blastocysts</td>
<td>0.23 (0.5)</td>
<td>1.51 (2.4)</td>
</tr>
<tr>
<td>% Euploid</td>
<td>14.5 (31.8)</td>
<td>40.0 (42.0)</td>
</tr>
</tbody>
</table>

the blastocysts for this analysis resulting in a euploid rate of 53% (49/92), 47% (43/92) euploid, and 4 no determinations. In 8.2% (11/134) of the cycles, the hCG level was present 13 days after IUI. The hCG levels in all cycles resolved spontaneously, or after curettage with or without methotrexate. A logistical regression was performed to determine whether there was any correlation between covariates (days of stimulation, mean total gonadotropins, mean total hMG, mean maximum estradiol and follicles 16mm at trigger) and euploid status. No significant associations were found between any of the variables and euploid status.

CONCLUSIONS: This study reinforces existing IVF data that imply gonadotropin stimulation is not associated with higher rates of aneuploidy but now performed in an in vivo data set. These findings support the continued use of stimulation in the process of uterine lavage. However, the sample size is small, and the lavage system is not fully optimized to recover all embryos.

SUPPORT: Previvo Genetics, Inc.
same incubator for embryogenesis. Fertilization was assessed on Day 1 and resulting embryos were cultured until Days 5, 6 and 7 for blastocyst tropho-
toderm biopsy. Biopsied samples were PGT-A analyzed by Next Generation Sequencing. The total number of euploid embryos were compared between the two males in each couple. The male partner with the higher number of euploid embryos was denoted as Male A; and the other male with an equal or fewer number of euploid embryos was denoted Male B. The data was analyzed using Chi-square analysis with a significance set at p<0.05.

RESULTS: The data from eight same-sex male couples was analyzed, with a total of 187 mature oocytes inseminated; 94 and 93 oocytes for Males A and B, respectively. There was a total of 35 euploid embryos (57.4% of those biop-
sied). 22 for Male A and 13 for Male B, demonstrating a statistically signif-
ificant difference (p<0.05) in euploidy rates among the groups analyzed.

CONCLUSIONS: This study demonstrates that same-sex male couples desiring to generate embryos equally using the same oocyte donor at the
time of a single IVF cycle, do not yield an equivalent number of euploid em-
byos even when both males are normospermic and under the same exact cul-
ture conditions. This study indicates that there is likely an underlying sperm
factor that impacts euploidy rates even in fertile normospermic males. More
research is needed to elucidate the cause of this observation in order to help clinicians in counseling same-sex male couples.

P-72 Tuesday, October 15, 2019 6:30 AM

ANEUPLOIDY RATE IN BRCA CARRIERS IS SIMILAR TO AGE-MATCHED INFERTILE WOMEN. Maria Facadito Antero, MD, a
Mindy S. Christianson, MD, a William G. Kearns, MD, PhD. a b
John Hopkins University School of Medicine, Lutherville, MD; bJohns
Hopkins University School of Medicine, Lutherville, OR; cJohns
Hopkins University School of Medicine, Ad vagenix, 9430
Key West Hwy, Suite 130, MD.

OBJECTIVE: BRCA 1 and BRCA 2 are tumor suppressor genes involved in
DNA mismatch repair. Studies have shown that ovarian aging is acceler-
ated in women with BRCA mutations secondary to diminished ovarian reserve and accumulation of DNA damage in the oocytes of primordial fol-
icles.[i] It is unclear whether this DNA damage seen in primordial follicles
translates to a higher aneuploidy rate. This study sought out to compare aneu-
plody rates between BRCA1 and BRCA2 mutation carriers undergoing in vi-
tro fertilization (IVF) and preimplantation genetic testing for monogenic condition (PGT-M) and for aneuploidy (PGT-A) with age-matched control
women with infertility undergoing IVF/PGT-A.

DESIGN: Retrospective analysis of an anonymous database at a commer-
cial genetics laboratory.

MATERIALS AND METHODS: This study included BRCA 1/2 mutation
carriers undergoing IVF with PGT-M for BRCA 1/2 and PGT-A from 2018-2019. Infertile, non-carriers undergoing IVF with PGT-A during the
same period were included as controls. All embryos were biopsied at the blastocyst stage. PGT-A for both groups was performed by Next Generation Sequencing (NGS). The primary outcome of this study was to compare the aneuploidy rates between BRCA carriers and non-carriers and women with infertility undergoing IVF/PGT-A.

RESULTS: The data from eight same-sex male couples was analyzed, with a total of 187 mature oocytes inseminated; 94 and 93 oocytes for Males A and B, respectively. There was a total of 35 euploid embryos (57.4% of those biop-
sied). 22 for Male A and 13 for Male B, demonstrating a statistically signif-
ificant difference (p<0.05) in euploidy rates among the groups analyzed.

CONCLUSIONS: This study demonstrates that same-sex male couples desiring to generate embryos equally using the same oocyte donor at the
time of a single IVF cycle, do not yield an equivalent number of euploid em-
byos even when both males are normospermic and under the same exact cul-
ture conditions. This study indicates that there is likely an underlying sperm
factor that impacts euploidy rates even in fertile normospermic males. More
research is needed to elucidate the cause of this observation in order to help clinicians in counseling same-sex male couples.

FERTILITY PRESERVATION

P-74 Tuesday, October 15, 2019 6:30 AM

ESTIMATES OF INFERTILITY IN AN ERA OF INCREASING STI RATES, 2002-2015. Morgan Snow, BA,a Tyler McClung, BS, MS,b Maria Trent, MD, MPH,c Jamie Perin, PhD dJohns Hopkins School of Medicine, Balti-
more, MD; dJohns Hopkins University, Baltimore, MD.

OBJECTIVE: Has the decline in infertility remained uniform across sub-
groups? How do factors like PID and status of STI care affect infertility?

DESIGN: Pelvic inflammatory disease (PID) has declined in an era of increasing sexually transmitted infection (STI) rates. Meanwhile, access to
sexual and reproductive health (SRH) services remains tenuous for young and low-income women. This study aims to estimate the changes in infertility from 2002 to 2015 and explain the impact of PID and receipt of SRH services on fertility in the United States.

MATERIALS AND METHODS: Periodic data from the 2002, 2010, 2013, and 2015 cycles of the National Survey for Family Growth (NSFG) were
and the average storage time was 2.8

Raymond Joseph Os

RESULTS: The decline in infertility among married and cohabiting women from 7.0% in 2002 to 5.8% in 2010 is significant; the increases to 6.3% and 7.0% in 2013 and 2015 respectively, however, are not. This trend was present across nearly all subgroups. The multivariate model showed that women who were nulliparous, had fewer years of education, or were not receiving SRH services were more likely to be infertile.

CONCLUSIONS: This study confirms that parity and education level continue to impact infertility. Further, the results demonstrate that access to SRH services plays an important role in infertility. In contrast to previous studies, infertility in the United States is no longer on the decline, and age, race, and ethnicity did not have significant impacts on infertility. Given the rise of STIs and the persistent lack of access to SRH services, particularly among already vulnerable groups, the connection between access to care and infertility is rife for further investigation.

P-75 Tuesday, October 15, 2019 6:30 AM

FERTILITY PRESERVATION FOR SOCIAL REASONS IN A POPULATION OF OLDER WOMEN: MYTH OR REALITY? Raymond Joseph Oecs, MD, Alberto Valcarcel, PhD, Marisa Tiveron, MS, Mercedes Leticia Guildobono, MS, Macarena Felici, MS, Soledad Bouzas, MS, Alberto Kenny, MD, IFER Ciudad Autónoma de Buenos Aires, Argentina.

OBJECTIVE: Oocyte cryopreservation for social reasons in older women is increasingly being performed in Argentina. Reproductive results derived from such approach remains controversial. The aim of this study was to evaluate the reproductive performance of our oocyte vitrification program in this older population that chose fertility preservation for social reasons.

DESIGN: Retrospective descriptive study.

MATERIALS AND METHODS: The results of our Anticipated Gamete Exhaustion (AGE) banking program during the 2008-2017 year-period are presented. A total of 490 women were included in our study. Of these, 80.8% were ≥ 36 years old (396/490): 265 were between 36-39 and 131 ≥ 40 years old at the time of vitrification.

RESULTS: The average age of the patients at the time of oocyte vitrification was 37.6 ± 3.5 years old, and the number of vitrified MII oocytes was 6.2 ± 4.9. Only 32 women (6.5%) used their oocytes stored to date. In the group, the average age at cryopreservation was 39.1 ± 2.9 years and the average storage time was 2.8 ± 1.8 years. The average age at the time of thawing was 41.9 ± 3.4 years old. The average number of vitrified oocytes was 5.2 ± 3.1 with a survival rate of 96.5 ± 9.0%. The average number of injected oocytes was 5.0 ± 3.0 and 3.5 ± 2.2 achieved fertilization. Fertilization rate was 70.7 ± 27.8%. The average number of cleaved embryos was 3.2 ± 2.0 and the average number of day-3 embryos that were transferred was 2.2 ± 1.0. Seventy-five percent of women who harvested their vitrified oocytes used sperm samples belonging to their male partners (24/32) while 25% (8/32) used donor sperm at the time of the procedure. A total of 36 IVF procedures were performed in 32 women and 34 embryo transfers were done; two of the patients had no embryos for transfer. A total of 79 embryos were transferred. Clinical pregnancy rate was 29.4% (10/34), and implantation rate was 12.6% (10/79), abortion rate 20% (2/10) and live birth rate was 23.5% (8/34). The live birth/cryopreserved oocyte rate was 5.1% (8/158). Of the 8 births recorded, 3 corresponded to women who vitrified their oocytes at 40 years of age, 2 at 41 years, 1 at 37 years, 1 at 38 years and 1 at 42 years.

CONCLUSIONS: According to our results, it is a myth that cryopreservation of any number of oocytes at any age in patients who choose to postpone their motherhood for social reasons ensures future biological motherhood. For that matter, it is a reality that a clear advice, based on the number of oocytes retrieved and the age of the patient at the time of cryopreservation, should be given regarding the real possibilities of becoming a biological mother when later using the cryopreserved material. Nonetheless, the ready availability of this reproductive strategy in this older age group offers, perhaps, the only chance of having their own genetic children in the future.

P-76 Tuesday, October 15, 2019 6:30 AM

THE QUANTIFICATION OF RESIDUAL CRYOPROTECTANT CONCENTRATION AFTER THAWING OF OVARIAN TISSUE FOR OVARIAN TISSUE TRANSPLANTATION. Yodo Sugishita, M.D., Ph.D., a Yuki Suzuki, M.D., Ph.D., a Sandy Nishimura, M.S., b Meng Lingbo, M.D., b Atsushi Uekawa, Ph.D., b Akiko Tozawa, M.D., Ph.D., a Nao Suzuki, M.D., Ph.D., a St.Marianna University, School of Medicine, Kawasaki, Kanagawa, Japan; St. Marianna University, Kanagawa, Japan.

OBJECTIVE: Ovarian tissue cryopreservation for cancer patients has been gradually increasing in numbers. Though the standard method for ovarian tissue cryopreservation is slow freezing, the simple and feasible vitrification method has been gaining popularity, especially after the reports of live births using vitrification. Since vitrification uses high concentration of cryoprotectant, the safety concerning the residual cryoprotectant in thawed tissues should be verified.

DESIGN: This study quantified the residual cryoprotectant in thawed ovarian tissue and demonstrated the minimal culturing time needed before transplantation.

MATERIALS AND METHODS: Bovine ovaries were used to make ovarian tissue pieces (10×10×1mm) for slow freezing (DMSO 1.5M and PrOH 1.5M) and vitrification (EG 35%). One week later, the frozen ovarian tissue were thawed/warmed in media for either 60 minutes or 120 minutes. Then the amount of residual cryoprotectant in the thawed ovarian tissue were measured by gas chromatography.

RESULTS: Before thawing, DMSO and PrOH concentration were 8.77±1.19% and 7.77±0.75% in slow frozen ovarian tissues, respectively, and EG concentration was 27.9±1.63% in vitrified ovarian tissues. Immediately after thawing, DMSO and PrOH concentration dropped to 0.71±0.18% and 0.66±0.08%, respectively; however, EG concentration remained relatively high (3.17±0.13%). After 60 minutes media culturing, DMSO, PrOH and EG concentrations were measured at 0.0072±0.0027%, 0.025±0.012% and 0.038±0.011%, respectively. When doubling the media culturing time to 120 minutes DMSO, PrOH and EG concentration to minimal respectively.

CONCLUSIONS: The ovarian tissues, cryopreserved either by slow freezing or vitrification, needs to be thawed/warmed for at least 120 minutes in media to completely remove the cryoprotectants from the thawed ovaries. The concentration of cryoprotectants is removed by free diffusion. This research demonstrated the safety of thawed ovarian tissue for transplantation.


SUPPORT: Grant-in-Aid for Scientific Research(B), Nao Suzuki.

P-77 Tuesday, October 15, 2019 6:30 AM

EMPLOYER-BASED INSURANCE COVERAGE DRAMATICALLY INCREASES UTILIZATION OF PLANNED OOCYTE CRYOPRESERVATION. Arielle S. Yeshua, MD, Christine Mullin, M.D., Avner Hershlag, M.D., Tomer Singer, MD, Randi H. Goldman, M.D. Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: Planned oocyte cryopreservation (OC) is gaining recognition in the public and medical communities as a viable option for fertility preservation. However, cost is a significant barrier to planned OC utilization for many women, and most insurance plans do not include this benefit. Beginning in 2018, our tertiary care academic medical center initiated coverage for planned OC. The purpose of this study is to determine the impact on planned OC utilization at our center in the year immediately prior to and the year of insurance coverage commencement for employees.

DESIGN: Retrospective Cohort Study

MATERIALS AND METHODS: Planned OC cycles from 2017 and 2018 were analyzed. Patient demographics and cycle outcomes were compared
between cycles occurring in 2017 vs. 2018 according to insurance coverage. The number of oocyte banking cycles increased linearly in 2017 vs. 2018 (p = 0.001). In contrast, the number of self-pay patients significantly decreased from 2017 to 2018 (p = 0.001). No significant differences were found regarding cycle outcomes, including number of oocytes cryopreserved.

<table>
<thead>
<tr>
<th>Variable</th>
<th>2017</th>
<th>2018</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% with any insurance coverage</td>
<td>71.9</td>
<td>40.4</td>
<td>0.001</td>
</tr>
<tr>
<td>% employees</td>
<td>5</td>
<td>41.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (y)</td>
<td>35.0</td>
<td>35.2</td>
<td>NS</td>
</tr>
<tr>
<td>AMH (ng/mL)</td>
<td>2.94</td>
<td>3.13</td>
<td>NS</td>
</tr>
<tr>
<td>Number oocytes retrieved</td>
<td>14.6</td>
<td>16.2</td>
<td>NS</td>
</tr>
<tr>
<td>Number oocytes cryopreserved</td>
<td>11.6</td>
<td>12.5</td>
<td>NS</td>
</tr>
</tbody>
</table>

CONCLUSIONS: A greater proportion of women seeking planned OC at our facility had insurance coverage for treatment in 2018 vs. 2017. Employer-based insurance coverage for planned OC yielded a significant increase in planned OC utilization rates by hospital employees. This data underscores the impact insurance coverage has on planned OC utilization rates in just one year. As awareness of coverage increases and other employers begin to expand benefits, we expect planned OC utilization rates to continue to rise.

P-78 Tuesday, October 15, 2019 6:30 AM

OCYTE VITRIFICATION FOR ANTICIPATED GAMETE EXHAUSTION (AGE-BANKING) - A SYSTEMATIC REVIEW AND META-ANALYSIS OF SOCIAL TRENDS AND EFFICACY

Shira Baram, MD, a Randi H. Goldman, M.D., b Tomer Singer, M.D., c Christine Mullin, M.D., d Lenox Hill Hospital - Northwell Health, New York, NY; eNorthwell Health Fertility, Manhasset, NY; fNorthwell Health Fertility, Zucker School of Medicine at HofstraNorthwell, Manhasset, NY.

OBJECTIVE: To explore current trends in attitudes and knowledge of oocyte vitrification freezing (VF) for fertility preservation, as well as to provide an update on the efficacy of the process.

DESIGN: A systematic review and meta-analysis.

MATERIALS AND METHODS: We conducted a systematic search using PubMed/MEDLINE, EMBASE, the Cochrane Database and PsychINFO, using appropriate controlled vocabulary, to identify all relevant studies published from Jan 2007 to Nov 2018. The review protocol followed PRISMA guidelines in PECO format, and was registered with PROSPERO (#CRD42019128268). The protocol was comprised of two parts; the first addressed attitudes and knowledge regarding AGE-banking, the second focused on evaluating AGE-banking efficacy and outcomes while comparing these metrics with efficacy and outcomes in vitrified donor oocytes and in cases of superovulation oocytes vitrified following infertility treatments. Only original articles published in peer-reviewed journals written in English were included.

RESULTS: The literature search yielded 8038 articles of which 58 were included in the meta-analysis: 20 in the section exploring attitudes towards AGE-banking, and 38 in the section exploring its efficacy. Most respondents were aware of AGE-banking, mainly from online sources, and believed the ideal timing for AGE-banking is before women turn 35y/o. Only 40% of respondents answered correctly, when asked about the procedure and its associated risks and anticipated success rates. While two-thirds endorse AGE-banking for others, only a third would consider it for themselves. The main factors affecting the decision whether or not to perform AGE-banking in declining order were: 1. being wary of potential health implications, 2. perceived low success rate of the procedure, 3. financial considerations, and 4. time commitment. The results of AGE-banked vitrified oocytes, were favorable and approached those obtained utilizing donor oocytes, with a post-thaw survival of 84%, fertilization rate of 74%, cleavage rate of 89%, implantation rate of 41%, clinical pregnancy rate of 50%, and live birth rate of 32%. Results obtained by utilizing superovulatory vitrified oocytes lagged behind. Currently there is no available data regarding blastulation rate and embryo quality for embryos derived from AGE-banked oocytes.

CONCLUSIONS: AGE-banking provides a reasonable and adequate method for preserving fertility, yet gaps in attitudes and knowledge, as well as affordability, result in under-utilization. This review points to a general lack of awareness regarding the process, its efficacy, and the ideal time to pursue AGE banking. Future research should include large scale cohort studies to further evaluate changes in attitudes and knowledge. There is also a need for establishing international registries for AGE-banking that would provide information on the efficacy of the process as well as on related health implications.

SUPPORT: Create Fertility Centre

P-79 Tuesday, October 15, 2019 6:30 AM

FERTILITY PRESERVATION: FROZEN IN TIME?

Stephanie R. Baum, MD, a Randi H. Goldman, M.D., b Tomer Singer, M.D., c Christine Mullin, M.D., d Northwell Health Fertility, Zucker School of Medicine at HofstraNorthwell, Manhasset, NY.

OBJECTIVE: There has been an increase in the number of patients opting to undergo oocyte and embryo banking since removal of the “experimental” egg freezing label. However, to date, relatively few women have returned to use frozen gametes. The purpose of this study is to examine the relationship between number of oocyte and embryo banking cycles and use of previously frozen oocytes and embryos.

DESIGN: Retrospective study of select SART-affiliated clinics

MATERIALS AND METHODS: A total of 179,982 cycles from 69 SART-affiliated clinics from four states (Georgia, Illinois, Massachusetts, and New York) were identified; 10 clinics were excluded due to missing SART data. Information on number of oocyte and embryo banking cycles as well as number of cycles from previously frozen oocytes and embryos was collected from the years 2015-2017. The ratio between number of new oocyte and embryo banking cycles to cycles utilizing previously banked oocytes and embryos was calculated.

RESULTS: From 2015 to 2017, there was an increase in the total number of cycles from 54,540 to 65,138, representing an increase of approximately 19%. The number of embryo banking cycles was largely unchanged in this time frame, ranging from 918 to 1,007, approximately 1.5-1.7% of the total number of cycles. The number of oocyte banking cycles increased linearly from 2,563 to 3,185, representing an increase of 19.5%. In 2015, 2016, and 2017, the number of embryo banking cycles converted from fertility preservation was 25%, 18%, and 20% of the total number of embryo banking cycles, respectively. The number of oocyte banking cycles converted from fertility preservation was only about 1-1.5% of the number of oocyte banking cycles.

CONCLUSIONS: Fertility preservation continues to be a major focus of reproductive health and utilization of planned oocyte cryopreservation is increasing. In this select population, the number of embryo banking cycles converted from fertility preservation cycles is approximately 20-25% of the number of embryo banking cycles, but the number of oocyte banking cycles converted from fertility preservation remains a small percentage of the number of oocyte banking cycles. To date, relatively few women have returned to use their frozen gametes. We expect this percentage to rise.

References: None

SUPPORT: None

P-80 Tuesday, October 15, 2019 6:30 AM

PROVIDING PATIENTS WITH SUBSIDIZED FERTILITY PRESERVATION SERVICES IMPROVES ACCESS TO CARE

Lauren T. Bouchard, MD, a Kristin Van Heerum, MD, a Amelia Baffa, MSN, RN, a PMINP-BC, c Kathryn D. Coyne, MD, d Daniel L. Kuhn, MD, e James Goldfarb, MD, MBA, e Rachel S. Weinerman, MD, e University of Vermont Medical Center.

OBJECTIVE: Fertility preservation continues to be a major focus of reproductive health and utilization of planned oocyte cryopreservation is increasing. In this select population, the number of embryo banking cycles converted from fertility preservation cycles is approximately 20-25% of the number of embryo banking cycles, but the number of oocyte banking cycles converted from fertility preservation remains a small percentage of the number of oocyte banking cycles. To date, relatively few women have returned to use their frozen gametes. We expect this percentage to rise.

References: None

SUPPORT: None

P-81 Tuesday, October 15, 2019 6:30 AM

PROVIDING PATIENTS WITH SUBSIDIZED FERTILITY PRESERVATION SERVICES IMPROVES ACCESS TO CARE

Lauren T. Bouchard, MD, a Kristin Van Heerum, MD, a Amelia Baffa, MSN, RN, a PMINP-BC, c Kathryn D. Coyne, MD, d Daniel L. Kuhn, MD, e James Goldfarb, MD, MBA, e Rachel S. Weinerman, MD, e University of Vermont Medical Center.

OBJECTIVE: Fertility preservation continues to be a major focus of reproductive health and utilization of planned oocyte cryopreservation is increasing. In this select population, the number of embryo banking cycles converted from fertility preservation cycles is approximately 20-25% of the number of embryo banking cycles, but the number of oocyte banking cycles converted from fertility preservation remains a small percentage of the number of oocyte banking cycles. To date, relatively few women have returned to use their frozen gametes. We expect this percentage to rise.

References: None

SUPPORT: None
OBJECTIVE: Fertility preservation counseling is recommended for all patients undergoing fertility impacting cancer treatments. Although multiple options exist, patients face significant barriers to fertility preservation including knowledge deficits, access issues, possible treatment delays, psychological stress and high cost. Our fertility division has partnered with a non-profit foundation to provide fully funded fertility preservation to patients undergoing cancer treatment. The goal of this project is to explore referral patterns and follow up for fertility preservation when all options are provided with access to the patients. 

DESIGN: Retrospective chart review

MATERIALS AND METHODS: All female patients ages 15-39, with cancer or pre-cancerous diagnoses, who were referred for outpatient fertility preservation between 2010-2018. All procedure and monitoring costs were covered by the foundation for patients who did not have insurance coverage for fertility preservation and the met the income criteria. Data on demographics, cancer treatment and fertility preservation were collected from medical records. Outcomes included age, insurance status, fertility preservation treatment offered, and acceptance and follow-through of fertility preservation services.

RESULTS: 122 women met the inclusion criteria with a mean age of 28 at the initial visit. 90.2% (n=110) of patients presented for the scheduled appointment. Of those scheduled, 26.7% had public insurance, 66.7% had private insurance, 5.0% were uninsured and 1.6% had no insurance data available for review. 95.5% (n=110) of patients were offered oocyte or embryo cryopreservation. 66% (n=69) of those patients who were offered fertility preservation followed through with cryopreservation. 40% of uninsured patients and 56% of those with public insurance underwent oocyte/embryo cryopreservation.

CONCLUSIONS: Fertility preservation counseling is essential in the care of adolescent and reproductive-aged patients with cancer. However, fertility preservation can be expensive and is often not covered by insurance, which limits many patients’ abilities to proceed with oocyte or embryo cryopreservation. The majority of patients in this study not only presented for their appointments but also followed through with treatment when offered in the setting of a cost-covering grant. This type of non-profit foundation could serve as a model for others practicing in states without broad insurance coverage for fertility preservation.

P-81 Tuesday, October 15, 2019 6:30 AM

SPERM CRYOPreservation FOR FERTILITY PRESERVATION IN MEN WITH NON-MALIGNANT DISEASES. Tspei Takeshima, M.D. Shinnosuke Kuroda, M.D. Yasushi Yumura, Ph.D. Yokohama City University, Medical Center, Yokohama, Japan.

OBJECTIVE: Advanced cancer treatments have improved the prognosis of cancer survivors. Simultaneously cancer treatments such as chemotherapy have been known to cause harmful effect on fertile capacity. Therefore, the peri-treatment fertility preservation in AYA patients is of crucial importance and recommended in the guideline of ASCO. However, for non-malignant disease, there have been few reports on peri-treatment fertility preservation ever. Gonadotoxic agents such as alkylating agents are often used for non-malignant diseases. Of course, pretreatment fertility preservation for such cases is thought to be essential.

DESIGN: In this study, we retrospectively investigated the cases sperm cryopreservation was attempted for non-malignant diseases.

MATERIALS AND METHODS: This study retrospectively assessed the medical records of patients with non-malignant diseases who attempted sperm cryopreservation at the Reproduction Center of Yokohama City University Medical Center between January 2012 and September 2017. The following are thought to be essential: the status prior to or immediately after treatment, treatment to be performed or ongoing treatment, pre-freeze semen parameters, success or failure of cryopreservation, and maintenance status of cryopreservation. Moreover, we compared semen characteristics and feasibility of cryopreservation with cases of malignancies observed during same period in our facility.

All patients provided written informed consent prior to their participation. The study design was approved by the institutional review board of our facility.

RESULTS: A total of 217 patients were referred and attempted sperm cryopreservation in Yokohama City University Medical Center from January 2012 to September 2017. Of those, 12 patients (5.5%) were in status peri-treatment of non-malignant diseases at the time of consultation. The median age was 29.5 years (range: 18–51 years). Breakdown of original diseases was aplastic anemia (3), interstitial pneumonia (2), eosinophilic granulomatosis with polyangitis (2), and others (5: collagen disease etc.). Breakdown of therapeutic regimen was cyclophosphamide with hematopoietic cell transplantation (9), cyclophosphamide and methotrexate (2), and others (5: glucocorticoid etc.).

Mean sperm concentration was significantly higher than that of patients with malignancies (58.2±42.53 vs. 27.13±29.08 million/ml, P<0.001).

And in all cases, sperm cryopreservation was successfully carried out. Of the 5 cases referred from our own institution, 3 were still in maintenance, and in 2 cases, samples were discarded on their request. On the other hand, of 7 cases referred from other institutions, 5 patients have not visited our hospital.

CONCLUSIONS: For patients with non-malignant diseases, pretreatment sperm cryopreservation should be carried out before gonadotoxic treatment. In addition, establishing a network that encourages patients to visit us for maintenance of cryopreservation is thought to be essential because patients from other facilities did not visit for maintenance at a higher rate.

P-82 Tuesday, October 15, 2019 6:30 AM

EQUAL OPPORTUNITY FOR ALL? AN ANALYSIS OF RACE AND ETHNICITY IN FERTILITY PRESERVATION (FP) IN A MAJOR AMERICAN CITY. Paxton E. Voigt, BA,a Jennifer K. Blakemore, MD, b David H. McCulloh, Ph.D.,c Mary Elizabeth Fino, MD, d aNYU School of Medicine, New York, NY; bNYU Langone School of Medicine, New York, NY; cNYU Langone Health, New York, NY; dNYU Langone Fertility Center, New York, NY.

OBJECTIVE: It has been suggested that socio-demographic factors may affect access to FP opportunities. In one of America’s most racially diverse cities, we sought to compare the racial make-up of patients with cancer (Ca) who completed FP against the overall racial diversity (including Hispanic origin) identified in the incidence of Ca in women of reproductive age in our city.

DESIGN: A retrospective cohort study and cross-sectional comparison of all medical embryo banking (Em) and egg freezing (Eg) cycles from 1/2017-12/2018 at our center.

MATERIALS AND METHODS: All patients who completed at least one medical Em or Eg cycle were reviewed. Race was self-reported at time of consultation. A calculation of the expected incidence of Ca by race in women of reproductive age in our city was determined using the most recent Ca incidence data by race and available city census data by race, age and gender. Statistical analysis included chi square goodness of fit test and test for independence where appropriate, with p<0.05 considered statistically significant.

RESULTS: 107 patients who completed medical FP were included. Overall, 55 (51.4%) identified as White, 3 (2.8%) as Black, 13 (12.2%) as Asian, 6 (5.6%) as Hispanic, 3 (2.8%) as other and 27 (25.2%) did not report. 40.2% of patients were diagnosed with Breast Ca, 15.0% Gynecologic Ca, 15.0% Hematologic Ca, 5.6% Neurologic Ca, 4.7% GI Ca, 4.7% Sarcoma, 3.7% Endocrine Ca, 2.8% other Ca and 7.5% tested BRCA+ with scheduled BSO. There was no significant difference in racial distribution by Ca type (p=0.255). A subgroup analysis excluding the BRCA+ patients and those races not reported by the census (n=69) was then performed to compare the racial distribution of patients who completed medical FP at our center with the racial distribution of women of reproductive age who were diagnosed with Ca in our city. Based on the calculated frequency of race within the incidence of Ca in women of reproductive age (42% White, 21% Black, 8.9% Asian, 2.8% Hispanic), an expected number of FP cases for each race was calculated and compared. Results show that there is a statistically significant difference between observed (O) and expected (E) cases of FP by race at our center; White 470/29E, Black 30/15E, Asian 60/0E, Hispanic 60/19E (X2 36.9, df 3, p <0.001). This FP subgroup was further analyzed by FP type [Em (n=31, 44.9%) vs Eg (n=38, 55.1%)]. A statistically significant difference in racial distribution by FP type was observed; White 66.0% Eg vs 34.0% Em, Black 33.3% Eg vs 66.7% Em, Asian 46.2% Eg vs 53.8% Em and Hispanic 0% Eg vs 100% Em (X2 10.60, df 3, p <0.014).

FERTILITY & STERILITY®
CONCLUSIONS: There is a difference in the observed versus expected racial distribution of patients completing medical FP at our clinic, as well as a difference in the racial distribution between procedure types (Eg vs Em). Black and Hispanic patients were underrepresented in FP and White patients had a higher incidence of Eg, while non-White patients had a higher incidence of Em. Further studies are needed to determine if these differences generalize beyond our clinic and to identify modifiable factors that can improve equal opportunity to all patients.


SUPPORT: None

P-83 Tuesday, October 15, 2019 6:30 AM

WHAT IS IMPORTANT TO WOMEN CONSIDERING FERTILITY PRESERVATION BEFORE CANCER TREATMENT? COMPARING DECISION-MAKING VALUES WITH AND WITHOUT USING THE PATHWAYS PATIENT DECISION AID WEBSITE. Sukhamal Campbell, MD,¹ Aubri Hoffman, PhD,³ June Weston, Sr Research Coordinator,² Laura Covarrubias Crocker, MSPH,² Deborah Holman, CRNP,³ Ashley Houston, MSCI, OTD,³ Robert Volk, PhD,³ Terri Woodard, MD,³ Baylor College of Medicine, Houston, TX; ⁴The University of Texas MD Anderson Cancer Center, Houston, TX.

OBJECTIVE: Deciding whether to undergo fertility preservation treatment prior to initiating cancer treatment is a complex personal decision. Patient decision aids have been proposed to help women navigate these decisions by providing up-to-date, balanced information and helping women clarify how they value key factors in their decision. The objective of this study was to compare female cancer patients’ decision-making values (i.e., the importance of 10 key factors) and treatment preferences with and without the use of the Pathways patient decision aid website.

DESIGN: Randomized Controlled Trial

MATERIALS AND METHODS: Pathways – a fertility preservation patient decision aid website for women with cancer explains the risk of cancer-related infertility and describes fertility preservation treatments (tailored by cancer type) and other family-building options. It also provides structured decision-making activities to help women personalize the information and prepare to discuss the options with their providers. Thirty newly-diagnosed reproductive-age women were randomized to view Pathways or standard educational brochures, then rate how important 10 patient-identified key factors were in their decision (“Not Sure”, or from 0 = Not Important to 10 = Very Important) and to indicate their treatment preferences. At 2 months, women indicated whether they had completed a fertility preservation treatment.

RESULTS: Among the 10 factors, women rated Avoiding regret about my decision, Starting my cancer treatment as soon as possible, and Being able to genetically screen my future child for cancer as most important in their decision-making (9.4, 9.2, and 7.5 out of 10). As expected, decision-making values were highly individual and no systematic differences were observed between groups. Women who viewed the patient decision aid were more confident in their treatment preferences (9.3 versus 8.2 out of 10). All of the women in the control group indicated they were Not Sure or would Wait and See, while half of the women who viewed Pathways chose egg or embryo freezing. However, only 11 women were able to complete the study and only one woman had chosen fertility preservation at 2 months.

CONCLUSIONS: Interacting with an interactive patient decision aid may help women become more clear and confident in their fertility preservation decisions. It may also help providers assess patients’ values and preferences. However, addressing dissemination challenges may be key in providing timely care for all women.

P-84 Tuesday, October 15, 2019 6:30 AM

ELECTIVE OOCYTE CRYOPRESERVATION COUNSELING TOOL BASED ON NEXT GENERATION SEQUENCING RESULTS. Mariana Miguens, M.D.,¹ Andrea Natalia Coscia, MD,² Daniela Lorenzi, B.Sc,³ Melina Elena Bilinski, B.Sc,³ Mariana Cecilia Calvo, MD,² Rocio Belén Anria, M.D.⁴ Milfra Espinal, MD,² Sergio D. Papier, Sr., M.D,² CEGYR, Ciudad Autonoma de Buenos Aires, Argentina; ³NOVA-GEN, Ciudad Autonoma de Buenos Aires, Argentina.

OBJECTIVE: The aim of this study was to determine the appropriate age for counseling and referral in fertility preservation, based on the number of mature oocytes (MII) needed to achieve an euploid embryo. We consider that age is the main variable that determines the quantity and quality of oocytes as well as the average and euploidy of embryos obtained.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: 150 patients who performed preimplantation genetic testing of aneuploidies (PGT-A) cycles from 2016 to 2018 at a private IVF practice were included for this study. The molecular analysis was performed by Next-generation sequencing (Veriseq- PGS, Illumina).

The age range was between 27 and 46 years. Patients were arbitrarily divided into four groups: <35, 35-37, 38-40 and >40 years.

The variables analyzed per cycle were: the number of metaphase II oocytes (MII), the number of euploid blastocyst, the number of MII required to obtain an euploid blastocyst. Statistical analysis was performed by ANOVA

RESULTS: Oocyte cryopreservation by social reasons represents a legitimate exercise of women reproductive autonomy. One of its main advantages is that oocytes can be stored for a long time without this implying a quality detriment. There is a worldwide tendency to postpone motherhood. As a woman ages, the chance of having an aneuploid embryo increases.

PGT-A is an alternative to perform in advanced maternal age.

Based on our results, we can infer that oocyte recovery is lower after the age of 35, affecting mainly patients older than 37 years old. Aneuploidy increases after 38 years old. The most relevant data for counseling is the number of MII oocytes required to obtain an euploid embryo. Also, we can conclude that up to 35 years old, patients would have enough oocytes to have at least two euploid embryos in a single cycle. Between 35-37 years old patients would only achieve one euploid embryo per cycle. After 38 years, between two to four cycles would be needed to have an euploid embryo.

Women age has a great impact on her reproductive capacity. We recommend assessment on fertility preservation between 30-34 years as the first approach and a second assessment between 35-37 years old.

Our conclusions emerge from an indirect analysis of the embryonic euploidy and there is still a need for comprehensive studies to develop an accurate clinical counseling tool.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Number of cycles</th>
<th>MII average / cycle</th>
<th>Euploid blastocysts average / cycle</th>
<th>MII required to achieve at least one euploid blastocyst</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>18</td>
<td>13.28 (Min:5 Max: 24)</td>
<td>1.89 7.02 (CI95%: 4.08-9.03)*</td>
<td></td>
</tr>
<tr>
<td>35-37</td>
<td>33</td>
<td>9.42 (Min:2 Max: 26)</td>
<td>1.15 8.19 (CI95%: 6.59-10.07)*</td>
<td></td>
</tr>
<tr>
<td>38-40</td>
<td>55</td>
<td>8.15 (Min:3 Max: 22)</td>
<td>0.53 15.38 (CI95%: 14.16-16.75)*</td>
<td></td>
</tr>
<tr>
<td>&gt;40</td>
<td>44</td>
<td>8.18 (Min:1 Max: 24)</td>
<td>0.29 28.2 (CI95%: 26.83-29.6)*</td>
<td></td>
</tr>
</tbody>
</table>

(*p<0.05, min: minimum, max: maximum)
ENHANCING REPRODUCTIVE OPPORTUNITIES: THE BIOLOGIC POTENTIAL OF VITRIFIED INVIVO MATURED OOCYTES. Carlos Hernandez-Nieto, MD; Christine Briton-Jones, PhD, HCLD; Daniel E. Stein, MD; Tanmoy Mukherjee, MD; Benjamin Sandler, M.D.; Alan B. Copperman, MD.

OBJECTIVE: Oocyte In-vitro maturation (IVM) is a technique aimed to maximize reproductive potential for patients undergoing fertility preservation. Patients who suffer from compromised ovarian reserve, poor egg quality, or low number of MII oocytes at retrieval may benefit from employing IVM prior to cryopreservation. Over the past decade, optimization of oocyte maturation and cryopreservation techniques has enhanced cellular survival rates. More recent studies have suggested clinical utility of vitrified/thawed IVM oocytes (1), but data remains limited within the literature regarding reproductive potential. This study aims to assess the reproductive potential and genomic composition of blastocysts derived from vitrified/thawed IVM oocytes. DESIGN: Retropective cohort analysis.

MATERIALS AND METHODS: The study included all patients who underwent an elective oocyte vitrification cycle(s) with subsequent thawing and fertilization from 2010 and 2019. After oocyte retrieval, immature oocytes (Metaphase I and Germinal Vesicle stages) were cultured and were first assessed for maturity after 6 hours: Early-IVM (E-IVM). A second assessment was performed after 24 hours in culture: Late-IVM (L-IVM) as described by Escrich L et al. Matured oocytes were vitrified/thawed, underwent ICSI, and cultured sequentially to blastocyst stage. Cohorts were segregated into 2 groups: E-IVM and L-IVM oocytes. Fertilization, blastulation, and euploidy rates were compared among cohorts. X2, T-test, and logistic regression analyses were performed, significance was considered at (p<0.05).

RESULTS: 292 IVM oocytes obtained from 105 patients were thawed over the course of the study. 203 oocytes were E-IVM, while 89 oocytes were L-IVM. No differences were found in survival rates (81.2%, 80.8%, p=0.94), fertilization rate (53.9%, 56.9%, p=0.67), percentage of zygotes reaching cleavage stage (87.6%, 90.2%, p=0.93), and blastulation rate (49.4%, 40.2%, p=0.24). Utilizable blast cells was similar among groups (E-IVM: 38.6%, L-IVM: 37.9%, p=0.95), though a difference was found in the percentage of good quality blastocyst stage among groups: (70.5%, 9%, p=0.0004). Biopsied blast cells per group (34%, 27.5%, p=0.56) and euploidy rates (25%, 37.5%, p=0.53) were similar among cohorts. After adjusting for age, BMI, AMH, and total number of eggs retrieved per cycle, no association was found between the time to maturation and the odds of aneuploidy (OR 0.6, CI95% 0.05-7.85, p=0.74) or the odds of developing a good quality embryo (OR 0.18, CI95% 0.02-1.4, p=0.11).

CONCLUSIONS: 292 IVM oocytes obtained from 105 patients were thawed over the study course. 203 oocytes were E-IVM, while 89 oocytes were L-IVM. No differences were found in survival rates, fertilization rate, and blastulation rate. Utilizable blast cells was similar among groups, though a difference was found in the percentage of good quality blastocyst stage among groups. After adjusting for age, BMI, AMH, and total number of eggs retrieved per cycle, no association was found between the time to maturation and the odds of aneuploidy or the odds of developing a good quality embryo. Supported by the Reproductive Medicine Associates of New York.

SUPPORT: None.
RESULTS: To date (January-April, 2019), 8 patients have participated in the clinical study. Four patients were diagnosed with PCOS, two patients with PCO and recurrent pregnancy loss, one patient with fibroids and unexplained infertility, and one patient with DOR and poor embryo quality. Average patient characteristics included: Age, 31.5 ± 3.5; BMI, 24.5 ± 3.8; Days 3 FSH, 6.3 ± 3.1 mIU/mL; AFC, 45.1; and BMI 28.5. On the day of retrieval, average E2 was 248 pg/mL and the average size of the largest follicle was 9.1 mm. In total, 234 immature oocytes were retrieved (average 29.3 oocytes per patient, range 5-55), of which 27 were atretic (11.5%). After pre-IVM and IVM, 114 (55.1%) oocytes matured; an additional 41 oocytes matured the following day for a total maturation percentage of 74.9% (155/207). After ICSI, 81/155 (52.3%) of eggs fertilized normally. Following culture, 6 good quality blastocysts (7.4%) were produced on D5, and 16 (19.8%) overall. Five of the eight patients (62.5%) produced at least 1 good quality blastocyst; all of these 5 were POC/PAC patients. Ten of the 16 blastocysts produced were euploid (62.5%). To date, 2 patients have undergone FET; one has an ongoing pregnancy.

CONCLUSIONS: IVM is successful in a clinical setting, and is logistically feasible in the typical IVF laboratory work flow. This finding alleviates concerns of hyper-stimulation, and drastically reduces medication costs and injections. Thus, IVM is a realistic alternative ART approach for PCOS patients.

SUPPORT: None.

EMBRYOLOGIST FRIENDLY PROGRAMMED IVM WITH DELAYED BLASTOCYST TRANSFER. Bruce I. Rose, MD, PhD, Kevin Nguyen, MS, Samuel Brown, MD. Brown Fertility LLC, Jacksonville, FL.

OBJECTIVE: To design an approach to IVM (in vitro maturation) which can be easily integrated into a busy IVF laboratory and which results in oocytes with a high maturation rate, a good blastocyst production rate, and a reasonable pregnancy rate.

DESIGN: Our IVM protocol uses a programmed approach to enable scheduling cases and requires only laboratory techniques already used by the embryologist. Retrieval is designed to improve environmental conditions for oocytes. Embryos are transferred back in a subsequent FET cycle.

MATERIALS AND METHODS: Patients with a PCO pattern in their ovaries were recruited. Oral contraceptives were used to plan prospectively for a day for retrieval. Letrozole was started on day 5 after stopping oral contraceptives (SOC). FSH (25 to 75U/day) was started on the 7 after SOC. Ovulation was cultured on day 11 or 12 after SOC. Oocyte retrieval was performed on day 13 or 14 after SOC. Cycles were adjusted if all follicles were less than 8 mm or if one follicle was greater than 13 mm.

RESULTS: IVM protocol used a 5 cm 19g needle to enable flushing and limit dead space in the oocyte collection system to 0.000004 ml. This needle is constructed from a 5 cm 19g needle attached to a 17g needle with fluid entering the space in the oocyte collection system to 0.000004 ml. This needle is constructed from a 5 cm 19g needle attached to a 17g needle with fluid entering the space in the oocyte collection system to 0.000004 ml. This needle is constructed from a 5 cm 19g needle attached to a 17g needle with fluid entering the space in the oocyte collection system to 0.000004 ml.

EMBRYOLOGIST FRIENDLY PROGRAMMED IVM WITH DELAYED BLASTOCYST TRANSFER. Bruce I. Rose, MD, PhD, Kevin Nguyen, MS, Samuel Brown, MD. Brown Fertility LLC, Jacksonville, FL.

OBJECTIVE: To design an approach to IVM (in vitro maturation) which can be easily integrated into a busy IVF laboratory and which results in oocytes with a high maturation rate, a good blastocyst production rate, and a reasonable pregnancy rate.

DESIGN: Our IVM protocol uses a programmed approach to enable scheduling cases and requires only laboratory techniques already used by the embryologist. Retrieval is designed to improve environmental conditions for oocytes. Embryos are transferred back in a subsequent FET cycle.

MATERIALS AND METHODS: Patients with a PCO pattern in their ovaries were recruited. Oral contraceptives were used to plan prospectively for a day for retrieval. Letrozole was started on day 5 after stopping oral contraceptives (SOC). FSH (25 to 75U/day) was started on the 7 after SOC. Ovulation was cultured on day 11 or 12 after SOC. Oocyte retrieval was performed on day 13 or 14 after SOC. Cycles were adjusted if all follicles were less than 8 mm or if one follicle was greater than 13 mm.

RESULT: Twenty patients were recruited. Two cycles were canceled for follicles that were too large. The average number of oocytes retrieved was 11. The average maturation rate was 85%. The average fertilization rate per mature oocyte was 86%. Two patients had an oocyte aspiration, which did not produce blastocysts. Thus 89% of retrievals resulted in blastocysts with an average of 3 blastocysts per patient and with 36% of fertilized oocytes becoming blastocysts. After one FET cycle, 50% of patients had a clinical pregnancy, and 38% had an ongoing or delivered pregnancy.

CONCLUSIONS: IVM can be adapted to not disrupt a clinical IVF lab. Better treatment of oocytes during retrieval resulted in better maturity and blastocyst production.
preimplantation genetic testing for aneuploidy (PGT-A). To date, the role of parental age on ART outcomes remains controversial. This study sought to determine whether increasing paternal age is associated with adverse outcomes in the setting of a single embryo transfer (SET) of a euploid embryo.

**MATERIALS AND METHODS:** This study was performed at a large fertility practice. Included couples underwent a first cycle of in vitro fertilization (IVF) using ejaculated sperm and then underwent intracytoplasmic sperm injection (ICSI) and PGT-A followed by SET of a euploid embryo. Kruskal-Wallis testing, Chi-square analysis, and linear regression models were utilized to assess the relationship between paternal age and rates of implantation, delivery, biochemical loss, and clinical loss. The relationships between paternal age and fertilization rate, blastulation rate, and euploid rate was also analyzed.

**RESULTS:** 4367 couples met inclusion criteria. Mean male partner age was 37.1 ± 5.5 years, with 87 male patients over age 50. Mean female partner age was 34.9 ± 4.0 years. Among couples undergoing SET of a PGT-A tested embryo, implantation rate was 82.1% (3566/4367 embryos transferred), delivery rate was 56.8% (2480/4367 embryos transferred), biochemical loss rate was 8.8% (385/4367 embryos transferred), and clinical loss rate was 7.2% (313/4367 embryos transferred). Adjusting for female age, there was no statistically significant association between male partner age and implantation rate (p = 0.40), delivery rate (p = 0.48), biochemical loss rate (p = 0.18), or clinical loss rate (p = 0.19). A sub-group analysis evaluating men over age 50 (n = 87) also failed to demonstrate a relationship between paternal age and implantation rate (p = 0.32), delivery rate (p = 0.19), biochemical loss rate (p = 0.08), or clinical loss rate (p = 0.42).

For men over age 50, there was a significant association observed between paternal age and blastulation rate (p = 0.01) as well as euploid rate (p = 0.03) but no significant association between age and fertilization rate (p = 0.92). When using 40 years as a cutoff point, the relationship between paternal age and blastulation rate remained significant (p = 0.0006) but there was no association between age and euploid rate (p = 0.86) or fertilization rate (p = 0.70).

**CONCLUSIONS:** When couples undergo SET of a euploid embryo, increasing paternal age does not appear to detrimentally impact pregnancy outcomes, including implantation rate, delivery rate, biochemical loss rate, and clinical loss rate. However, paternal age greater than 50 negatively affects blastulation and euploid rates. Poorer blastulation was also seen in men over age 40. If a single euploid embryo is transferred, the role of paternal age is unlikely to be significant, but increasing paternal age may negatively impact a couple's ability to create a euploid embryo and thus cumulative pregnancy rate.

**SUPPORT:** None.

**P-92 Tuesday, October 15, 2019 6:30 AM**

**CLINICAL PREGNANCY OUTCOME ACCORDING TO AGE OF PATIENTS WITH HIGH PROPORTION OF FAILED OOCYTE MATURATION IN ICSI**

**CASES:** Yeon Sook Park, MS, Su Hyeon Kim, MS, Han Su Kim, MS, Jae Won Kim, MD, Hee Sun Lee, MD, Myung Hee Kim, M.D, Hyeon Jeong Jeong, M.D, Mi Kyung Chung, Ph.D, Seoul Rachel Fertility Center, Seoul, Korea, Republic of (South).

**OBJECTIVE:** The purpose of this study was to compare the clinical pregnancy outcomes according to age of patients with high proportion of maturational arrest oocytes in ICSI cases.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** From June 2011 to December 2018, a total of 2495 cycles were analyzed in this study. The patients underwent ICSI cycle followed by fresh embryo transfer. Inclusion criteria: female age between 23 and 48yrs, use of fresh or cryopreserved sperm. Exclusion criteria: surgically retrieved sperm.

These patients were divided into group A (maturational arrest rate <40%, Age <38yrs), group B (maturational arrest rate ≥40%, Age <38yrs), group C (maturational arrest rate <40%, Age ≥38yrs) and group D (maturational arrest rate ≥40%, Age ≥38yrs). The pregnancy outcomes were compared among these 4 groups.

**RESULTS:** A total of 2495 cycles were included (group A (n = 1353, group B (n = 90, group C (n) =960 and group D (n) = 54). There was no significant differences in fertilization rate between groups (group A vs. B: 80.7% ± 20.0 vs 81.0% ± 24.1, P = 0.958 and group C vs. D: 83.2% ± 20.1 vs 83.4% ± 19.6, P = 0.737). But there was a significant difference in implantation rate, pregnancy rate and miscarriage rate. More than 40% of oocyte maturation failure group had lower levels of embryo quality. There was significant difference in at least one good quality embryo transfer cycle rate (group A vs. B: 69.4% vs 46.7%, P<0.001 and group C vs. D: 63.1% vs 55.6%, P<0.001).

**CONCLUSIONS:** According to our study, high rate of oocyte maturation failure group had lower embryo quality, pregnancy rate and higher miscarriage rate. However, there was no effect on in fertilization rate. There was a similar
tendency in analysis according to age. High clinical results can be maintained only by lowering the proportion of mature failed oocyte as much as possible.


IVF OUTCOME PREDICTORS - EMBRYO CULTURE

P-93 Tuesday, October 15, 2019 6:30 AM
IS THE NUMBER OF BLASTOCYST MORPHOLOGIC EVALUATIONS (BMA) ON DAY 6 CORRELATED WITH DAY 7 EMBRYONIC COMPETENCE?* Jenna Fricenthal, MD,b Dmitry Gounko, MA,b Joseph A. Lee, BA,b Christine Briton-Jones, PhD, HCLD,b Alan B. Copperman, MD,a Lawrence Grunfeld, MD.b aIcahn School of Medicine at Mount Sinai, New York, NY; bReproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Blastocyst morphologic assessments (BMAs) are used to determine the optimal time to perform trophectoderm (TE) biopsy for preimplantation genetic testing for aneuploidy (PGT-A). Embryos that have not hatched by the morning of day 6 may be cultured to Day 7 to await TE herniation. There is concern that repeated exposure of embryos outside of incubation may induce environmental stressors that can impact embryonic metabolic activity [1]. Thus, our study sought to assess the relationship between the number of BMAs on Day 6 and development of Day 7 embryos.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The study included patients who had embryos cultured and biopsied to Day 7 for PGT-A from 2015 to 2019. Cases were separated into 2 groups: (Study Group: 2 BMAs - morning and afternoon of Day 6; Control Group: 1 BMA - morning of Day 6). The primary outcome was the rate of blastocysts that adequately expanded for TE biopsy (BBR) and top quality blastocyst rate (TQBR) (≥8BB Modified Gardner). Secondary outcomes included euploid rate (ER), clinical pregnancy rate (CPR), ongoing pregnancy/live birth rate (OP/LBR), and spontaneous abortion rate (SABR). Student’s t-test and chi-square tests were used for statistical analysis, with p<0.05 considered significant. Multivariate logistic regression analysis was performed to control for confounding variables.

RESULTS: A total of 5,034 embryos were cultured to Day 7. Within the 2 BMAs group (n=1,412), 478 were biopsied on Day 7. Within the 1 BMA group (n=3,622), 1,407 were biopsied on Day 7. TQBR, BBR, and ER were significantly higher in the 1 BMA group. When controlling for confounders, having 1 BMA was significantly associated with the number of TQBR (β = 0.73, p<0.0001). However, our model demonstrated no correlation between the count of BMAs on Day 6 and the probability of a Day 7 blastocyst having adequately expanded for TE biopsy (β = 0.02, p=0.02) or rate of euploid embryos (β = 0.10, p=0.42). There were no significant differences in CPR, OP/LBR, or SABR.

CONCLUSIONS: Our results demonstrated that the number of BMAs on Day 6 of development for embryos cultured Day 7 did not correlate with clinical outcomes. Our data shows that a single check on Day 6 may optimally minimize environmental exposures and allow for the subsequent acquisition of critical embryonic genomic data via PGT-A without comprising outcomes of Day 7 embryos. These results may be used as a guide for other reproductive centers. These results suggest that increasing the culture time of embryos in one day to improve selection before transfer does not increase pregnancy rate. More studies are necessary to confirm our results.

REFERENCE: None.

SUPPORT: Grant form CNPq (Brazilian research council) to Selmo Geber.

P-95 Tuesday, October 15, 2019 6:30 AM
USABLE BLASTOCYST DEVELOPMENT RATE IS INFLUENCED BY MATURE AGE AND ULTRA-LOW OXYGEN TENSION IN EXTENDED CULTURE. Alice Fournier, MD,a Aneta Andreaea, RESIDENT,a Anna Gala, MD,a Sophie Brouillet, PharmD, PhD,b Cecile Brunet, MD,c Claire Vincens, MD,c Samir Hamamah, MD, PhD,c Arnaud de Ville-uneuve Hospital, CHU Montpellier, Montpellier, France; cART-PGD department, Arnaud de Villeuneuve Hospital, CHU Montpellier, Montpellier, France.

OBJECTIVE: To determine if maternal age affects usable blastocyst development rate according to extended embryo culture conditions (low or ultra-low oxygen tension).

DESIGN: This is a single-center retrospective cohort study performed from November 2014 to October 2018. The endpoint was to evaluate the rate of blastocyst formation as well as usable blastocyst rates as a function of maternal age and extended embryo culture conditions. All embryos were cultured in 6% CO2/5% O2 from day 0 to day 3. From day 3 until day 5/6, either 5% O2 tension was used (control group; n=4000 embryos, n=653 patients) or there was a switch to 2% O2 (study group; n=3771 embryos, n=482 patients). The two groups were similar for age, attempt rank, mean number of retrieved oocytes.

MATERIALS AND METHODS: Patients were classified according to the maternal age as following: <30, 30-34, 35-37, 38-39, 40-42, and ≥43 years of age. All blastocysts were morphologically evaluated according to the standard Gardner grading system. Blastocyst and usable blastocyst formation rates were based on the number of embryos in extended culture. Usable blastocysts were considered as expanding (grade 3), fully expanded (grade 4), partially hatching (grade 5) or fully hatched (grade 6) with at least a grade A or B trophoderm quality. In order to evaluate blastocyst yield according to embryo quality, we divided embryos as following on day 3: <6, 6-7, 8 and >8 blastomers.

RESULTS: Maternal age significantly affects blastocyst formation rate (58.3% for <30, 60% for 30-34, 57.4% for 35-37, 48.9% for 38-39, 43.5% for 40-42 and 36.2% for ≥43, p<0.0001); as well as usable blastocyst rate (35.7% for <30, 38.2% for 30-34, 34.4% for 35-37, 25.9% for 38-39, 23.1% for 40-42 and 14.5% for ≥43, p<0.0001). Multivariate analysis...
showed that both maternal age and oxygen tension in extended embryo culture affect blastocyst formation rate, and that both maternal age and embryo quality on day 3 also affect usable blastocyst rate (p<0.0001). Blastocyst formation rate was significantly higher in the 2% O2 group (58.3%) than in the 5% O2 group (55%), p<0.0005. The extended culture under ultra-low O2 tension improved for 35-37 year of age group both blastocyst formation rate: 61.1% vs 53.4% in the 2% O2 and 5% O2 groups respectively, p<0.002; and usable blastocyst rate: 38.7% vs 31.8% in the 2% O2 and 5% O2 groups respectively, p<0.005. Maternal age impacts negatively on blastocyst formation rate as well as usable blastocyst rate in each group of day 3 embryo quality.

CONCLUSIONS: Blastocyst and usable blastocyst formation rates on day 5/6 both significantly decrease with maternal age. Beyond the age of 37, blastocyst rate is reduced by 28%. Therefore, this study leads us to question the relevance of extended culture beyond that age. Nevertheless, 2% O2 tension in extended culture is associated with better blastocyst yield. In 35-37 years of age group, it also improves usable blastocyst rate. This data supports the idea that maternal age and embryo quality on day 3 are crucial criteria to be considered for the choice of extended culture strategy.

P-96 Tuesday, October 15, 2019 6:30 AM
THE EFFECTS OF CO-CULTURE WITH AUTOLOGOUS CUMULUS CELL ON PREGNANCY OUTCOMES BY MATERNAL AGE. Daehan Kim, Master, Jeong-Ho Cha, Ph.D., Sun-Hee Shin, Master, Yun-Jung Kim, Master, Seul-Ki Lee, Master, Ji-Hae Kim, Master, Hwa-yeong Kim, Master, Seung-Hyun Back, Master, Ji-Hyun Ahn, M.D., Hye-Young Kim, M.D., Kyung-Ah Pak, M.D., Ji-Sung Yoon, M.D., Soo-Young Park, M.D. Agaon fertility clinic, seoul, Korea, Republic of (South).

OBJECTIVE: It is known that the incidence of apoptosis in cumulus cells is associated with women age. In this study, we aimed to evaluate the influence of autologous cumulus cell co-culture on pregnancy outcomes by maternal age.

DESIGN: A retrospective study was performed from January 2014 to December 2018.

MATERIALS AND METHODS: A total of 588 cycles which underwent GnRH long or antagonist protocol with fresh embryo transfer were analyzed. The cycles with severe male factor and single embryo transfer were excluded. The cycles were divided into two groups according to maternal age: 32-36 years (Group 1), ≥37 years (Group 2). Each group had embryos cultured in defined medium with autologous cumulus cell (ACC) or without autologous cumulus cell (No ACC). The ACC was dissected from the patient’s oocyte-cumulus complexes using two 29-gauge needles and washed twice. The collected ACC was directly put into the culture medium without hyaluronidase treatment. We compared the rates of clinical pregnancy, ongoing pregnancy, and implantation between ACC and No ACC by maternal age.

RESULTS: The woman age, man age, and Day 3 good quality embryo rate were similar in the two groups. In the Group 1 cultured with ACC, the pregnancy rates were significantly increased than No ACC (Clinical Pregnancy: 49.4% vs. 37.2%, P < 0.05; Ongoing Pregnancy: 45.6% vs. 30.1%, P < 0.05; Implantation: 32.1% vs. 22.1%, P < 0.05). The clinical pregnancy and ongoing pregnancy rates were not statistically different between ACC and No ACC in Group 2 (Clinical Pregnancy: 16.5% vs. 26.3%, P = 0.06; Ongoing Pregnancy: 13.4% vs. 19.4%, P = 0.21). However, implantation rate was significantly decreased in ACC (9.0% vs. 15.8%, P < 0.05).

CONCLUSIONS: The age of women might influence the pregnancy outcomes. These results suggested that co-culture with autologous cumulus cell, for patients under 37 years old, could improve the rates of clinical pregnancy, ongoing pregnancy, and implantation. However, it is considered that co-culture with autologous cumulus cell is not recommended to patients over 37 years old for the improvement of pregnancy rate. Further studies are needed to measure the incidence of apoptosis in autologous cumulus cells to compare the correlation between woman age and the incidence of apoptosis.

IVF OUTCOME PREDICTORS - EMBRYO TRANSFER
P-97 Tuesday, October 15, 2019 6:30 AM
LIVE BIRTH RATES AFTER BLASTOCYST TRANSFERS PERFORMED BY FELLOWS. Dana B. McQueen, M.D., M.A.S., Jared C. Robins, MD, John Zhang, PhD, Eve C. Feinberg, M.D. Northwestern University, Chicago, IL.

OBJECTIVE: To evaluate live birth rates following embryo transfer performed Reproductive Endocrinology and Infertility fellows compared to attending physicians.

DESIGN: Retrospective Cohort Study.

MATERIALS AND METHODS: Institutional Review Board approval was obtained. Women undergoing blastocyst transfer between 1/2015 and 1/2018 were reviewed. Cycle characteristics and outcomes were compared between embryo transfers performed by fellows and attending physicians. A sample size of 750 embryo transfers was required to detect a 10% difference between groups, with 80% power and alpha of 0.05.

RESULTS: A total of 940 blastocyst transfers were included; 254 performed by five fellows and 686 performed by ten attending physicians. There were no differences in the mean age, anti-mullerian hormone (AMH) levels or rate of preimplantation genetic testing for aneuploidy (PGT-A) testing between groups (Table). The afterload technique was utilized more frequently by fellows, 95.2% (242/254) vs. 87.6% (602/686), P=0.0004. A stylet was used less frequently by fellows, 0.4% (1/254) vs. 4.5% (31/686), P=0.0008. The pregnancy rate in the fellow group was not significantly different from the pregnancy rate in the attending group; 72.8% (182/254) among fellows versus 76.7% (461/686) among attending physicians, p=0.27. There were also no significant differences in the live birth rate between groups, 51.6% (131/254) versus 49.4% (339/686) respectively, P=0.61. After controlling for embryo transfer technique and stylet use, there remained no difference in pregnancy outcomes. The average pregnancy rate among fellows performing their first 20 embryo transfers was 67.4% (58/86), and was no different from the average pregnancy rate among attending physicians, 67.6% (461/686) P=1.0.

TABLE 1 Group Characteristics (N=940 transfers)

<table>
<thead>
<tr>
<th>Age (SD), yr</th>
<th>Fellow ET (N=254)</th>
<th>Attending ET (N=686)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>34.1 (3.4)</td>
<td>34.1 (3.6)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>AMH (SD), ng/mL</td>
<td>3.9 (3.1)</td>
<td>3.8 (3.3)</td>
<td>0.68</td>
</tr>
<tr>
<td>% PGS testing</td>
<td>22.0% (56/254)</td>
<td>22.6% (152/686)</td>
<td>0.93</td>
</tr>
<tr>
<td>% Fresh Transfer</td>
<td>41.3% (105/254)</td>
<td>34.4% (236/686)</td>
<td>0.06</td>
</tr>
<tr>
<td>Afterload technique</td>
<td>95.2% (242/254)</td>
<td>87.8% (602/686)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Stylet</td>
<td>0.4% (1/254)</td>
<td>4.5% (31/686)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Blood on catheter tip</td>
<td>4.3% (11/254)</td>
<td>6.8% (47/686)</td>
<td>0.17</td>
</tr>
<tr>
<td>Embryo Retained</td>
<td>0% (0/254)</td>
<td>0.3% (2686)</td>
<td>1.0</td>
</tr>
<tr>
<td># Embryos</td>
<td>1.2 (0.5)</td>
<td>1.3 (0.5)</td>
<td>0.1</td>
</tr>
<tr>
<td>Transferred (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy Rate</td>
<td>72.8% (182/254)</td>
<td>67.6% (464/686)</td>
<td>0.27</td>
</tr>
<tr>
<td>Miscarriage Rate</td>
<td>18.9% (48/254)</td>
<td>16.8% (115/686)</td>
<td>0.44</td>
</tr>
<tr>
<td>Live Birth Rate</td>
<td>51.6% (131/254)</td>
<td>49.4% (339/686)</td>
<td>0.61</td>
</tr>
</tbody>
</table>

TABLE 1. Comparison of pregnancy outcomes between ACC and No ACC according to the age of patient. | ACC | No ACC |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (Age)</td>
<td>Cycle (n)</td>
</tr>
<tr>
<td>Group 1 (32-36)</td>
<td>79</td>
</tr>
<tr>
<td>Group 2 (≥37)</td>
<td>97</td>
</tr>
</tbody>
</table>

* P < 0.05
CONCLUSIONS: Embryo transfer success rates were not different between fellows and attending physicians. Barriers to fellowship training in embryo transfer should be evaluated and addressed, as there was no compromise in pregnancy rates, even in the first twenty embryo transfers performed.

MATERIALS AND METHODS: Prior to April 2017, ASRM guidelines allowed for the transfer of 2 embryos in women under the age of 38 after the failure of an initial single embryo transfer. The new guidelines altered that recommendation to limit the transfer of 2 embryos only after the failure of multiple embryo transfer cycles in good prognosis patients. Our clinic, by policy, will not transfer more embryos than the ASRM guidelines, making it an ideal data set to analyze the impact of these guideline changes. We analyzed women under 38 years old in the two years before and after the national guideline change. The primary outcome was twin live birth. Only women on their second embryo transfer cycle were included. PGT and donor oocyte cycles were excluded. Published SART data was also compared between 2016 and 2017, to assess for national changes in the twin birth rate in patients under 38 years old. Differences in twin clinical pregnancy and live birth rates were compared by chi square test. Logistic regression controlled for embryo quality. Statistical significance was assumed at P<0.05.

RESULTS: 367 live births in women under 38 years old with one prior embryo transfer were analyzed. The number of embryos in these patients was significantly reduced from 1.38 per patient to 1.0 after implementation of the new guidelines (P<0.001). This resulted in a significant reduction in the clinical twin pregnancy rate (14.2% vs 2.5%, P<0.001) and twin live birth rate (12.5% vs 2.5%, P<0.001). There were no higher order multiple gestations. Despite the reduction in the number of embryos transferred, there was no change in the overall live birth rate per transfer in this patient group at 46.9% before and 50.3% after the policy change (P=0.31). The percentage of transfers with a good quality embryo increased from 61% to 67% over this time frame. Live birth remained similar before and after the 2017 guidelines even after adjustment for embryo quality (P=0.52). National SART data also showed a reduction in twin live births when comparing 2016 to 2017. In over 90,000 cumulative retrieval cycles in patients under 35 years old, the twin rate decreased from 16.5% to 13.3% (P<0.001). In over 50,000 cumulative retrieval cycles in patients 35-37 years old, the twin rate decreased from 15.6% to 12% (P<0.001). The SART data was less dramatic in the twin reduction, likely because it was not limited to patients with a prior cycle.

CONCLUSIONS: Implementation of the 2017 ASRM guidelines decreased the twin rate in good prognosis women in our clinic and at a national level. Good prognosis women under 38 years old benefit from single embryo transfer, even if it is not their first embryo transfer.

THE CONTINUED PUSH TOWARDS ELIMINATING TWIN PREGNANCY: THE CLINICAL IMPACT OF THE 2017 ASRM EMBRYO TRANSFER GUIDELINES. Allison A. Eubanks, MD, Anthony DeAngels, MD, PhD,1,2,3,5,6,7,8,9,10,11,12,13,14,15 Mae W. Healy, DO,1,2,3,5,6,7,8,9,10,11,12,13,14,15 Rhiana D. Saunders, MD,1,2,3,5,6,7,8,9,10,11,12,13,14,15 Saisa Torrealday, MD,4,5,6,7,8,9,10,11,12,13,14,15 Alan H. Decherney, MD,1,2,3,5,6,7,8,9,10,11,12,13,14,15 Nanette Rollene, MD,4,5,6,7,8,9,10,11,12,13,14,15 John M. Csokmay, MD,4,5,6,7,8,9,10,11,12,13,14,15 Jason A. Barritt, PhD,3,5,6,7,8,9,10,11,12,13,14,15

OBJECTIVE: To evaluate the differences in twin birth rates and after implementation of the 2017 ASRM guidelines which limits the number of embryos transferred.

DESIGN: Retrospective cohort study.

TUDINAL ANALYSIS AND NUMBER OF EMBRYOS TRANSFERRED IN DECREASING RATES OF MULTIPLE GESTATION

P-101 Tuesday, October 15, 2019 6:30 AM

DECREASING RATES OF MULTIPLE GESTATION AND NUMBER OF EMBRYOS TRANSFERRED IN GESTATIONAL CARRIER PREGNANCIES: A LONGITUDINAL ANALYSIS. Rachel S. Mandelbaum, MD, Meghan B. Smith, MD, Jacqueline Ho, MD MS, Richard J. Paulson, MD, MS, Kristin Bendikson, M.D. University of Southern California, Los Angeles, CA.

OBJECTIVE: The recent national push towards elective single embryo transfer (eSET) has decreased rates of multiple gestations. However, this translates to gestational carrier (GC) pregnancies has not been well established.1 We sought to evaluate the number of embryos transferred (ET) and this translates to gestational carrier (GC) pregnancies has not been well established.1 We sought to evaluate the number of embryos transferred (ET) and the incidence of multiple gestations in GC pregnancies as well as if these metrics have changed over time.

DESIGN: A retrospective analysis of all GC deliveries from a single agency between 2008-2019.

MATERIALS AND METHODS: Data from a large agency that consisted of matched GCs and intended parent (IP) couples for an index GC pregnancy were reviewed. GCs were excluded if the number ET or number delivered were not reported. Data collected for analysis included number ET, number delivered for the index GC pregnancy as well as a history of surrogacy or multiple gestations for each GC. All variables were analyzed using unpaired student’s t-test and Pearson’s correlation for continuous variables where appropriate and chi-squared for dichotomous variables.

RESULTS: Of 836 GC pregnancies, 187 (22.4%) were multiple gestations, consisting of 183 (21.9% of all pregnancies) twins, 3 (0.4%) triplets, and 1 (0.1%) quadruplet pregnancy; 116 (13.9%) GCs overall had a history of a multiple gestation prior to the current GC pregnancy, of which 53.6% were due to another prior GC pregnancy. There was a similar rate of multiple gestation in the index GC pregnancy when comparing GCs with a history of prior singleton vs multiple gestations (P = 0.882). There was also no difference between first-time or repeat surrogates in likelihood of having a multiple gestation (P = 0.435). In terms of number of ET, 422 GCs (61.7%) had 2 or more ET, and 14 (1.7%) had four or more. Number of ET was positively correlated with number of infants delivered in the GC pregnancy (r = 0.207, P < 0.001).

CONCLUSIONS: There is a significant impact on implantation success between catheter types. There is also a significant impact on implantation success based on which sonographer is assisting with imaging during the embryo transfer. The catheter choice demonstrated a bigger impact than the sonographer. There are limitations to this study. The physician performing the embryo transfer was not analyzed in this study. Individual physicians could have an impact on this analysis, thus potentially skewing the results. Reference: NONE.

SUPPORT: NONE.

P-102 Tuesday, October 15, 2019 6:30 AM

DOES CATHETER TYPE AND/OR SONOGRAPHER IMPACT SUCCESS RATES FOR EMBRYO TRANSFER? Emily Sarah Lin, BA pending, Angela claire Thyer, MD, Paul Chungyu Lin, MD, Northe Western University, Evanston, IL; Seattle Reproductive Medicine, Seattle, WA.

OBJECTIVE: To evaluate whether catheter type or individual sonographer differences affect the success of embryo implantation.

DESIGN: Retrospective chart analysis from 1/1/2016 to 4/18/2018 for all patients under age 38 that underwent an embryo transfer at a large, private in-vitro fertilization clinic.

MATERIALS AND METHODS: 2,537 transfers were performed over a two-and-a-half-year period by 11 physicians. Nine different catheters' and 11 sonographers' results were analyzed against implantation success. Biochemical pregnancy and clinical intrauterine gestation were both considered a positive implantation result, and not pregnant was considered a negative implantation result. In order to decipher whether implantation success was significantly affected by catheter or sonographer, a chi-squared test was performed for each factor. Given an alpha of 0.05 and 20 degrees of freedom, the value indicating significance was 10.851 for sonographers. Given alpha of 0.05 and 16 degrees of freedom, the value indicating significance was 7.962 for catheters. Once significance was found, the degree to which positive outcomes observed was more than expected (Observed-Expected/Expected) was combined with the degree to which negative outcomes observed was less than expected ((Expected-Observed/Expected), giving an overall degree to which positive outcomes were seen for each factor.

RESULTS: Both catheters and sonographers had a significant effect on success of implantation. The chi-squared test for sonographers resulted in a total value of 13.024. A value of 10.851 was needed for significance. The chi-squared test for catheters resulted in a total value of 40.735. A value of 7.962 was needed for significance. It was found that the Wallace 18cm and the Sureview 18cm both had overall positive results with an overall positive score of 0.07 and 0.09, respectively, whereas the others did not. It was found All sonographers B, C, D, G, and H had overall positive results, with an overall positive score of 0.15, 0.18, 0.53, 0.02, and 0.17 respectively, whereas the others did not.

CONCLUSIONS: There is a significant impact on implantation success between catheter types. There is also a significant impact on implantation success based on which sonographer is assisting with imaging during the embryo transfer. The catheter choice demonstrated a bigger impact than the sonographer. There are limitations to this study. The physician performing the embryo transfer was not analyzed in this study. Individual physicians could have an impact on this analysis, thus potentially skewing the results. Reference: NONE.

SUPPORT: NONE.

P-103 Tuesday, October 15, 2019 6:30 AM

EVIDENCE BASED QUANTITATIVE PREDICTION OF RISK OF MULTIPLE GESTATION RESULTING FROM THE TRANSFER OF MULTIPLE EMBRYOS. Michael Awadalla, MD, Kristin Bendikson, M.D., Jacqueline Ho, MD MS, Ali Ahmady, PhD, Richard J. Paulson, MD, MS. University of Southern California, Los Angeles, CA.

OBJECTIVE: To develop and evaluate a quantitative model for prediction of risk of multiple gestation after transfer of multiple embryos that can be used with a mobile device application.

DESIGN: Cross sectional analysis of clinic based data.

MATERIALS AND METHODS: We developed a three-step model to quantitatively predict the outcomes of multiple embryo transfers. We used data from three years of autologous cleavage stage and blastocyst embryo transfers at a single academic fertility center. The data set consisted of 760 embryo transfers of a total of 1928 embryos.

First, a training set of data was used to develop a best fit model. The data consists of the number of live births that resulted from an embryo transfer, maternal age at oocyte retrieval (<35 years, 35-37 years, 38-40 years, or 41+ years), number of embryos, embryo stage (cleavage or blastocyst), and embryo quality determined by the embryologist (good or fair/poor). Based on the training data a rate of live birth was calculated for each of 16 embryo categories through the use of a specifically designed computer program.
Second, the same computer program was utilized to make a quantitative assessment about the likelihood that two embryos transferred concurrently will both implant more often than would be expected by chance alone. This accounts for universal factors that affect all embryos transferred concurrently.

Third, means and standard deviations of outcomes for a test sample of embryo transfers were predicted using the best fit model and random number generation. We tested the model with six groups of multiple embryo transfers (Table 1). The differences between predicted and actual rates of multiple birth were not statistically significant and the standard errors were normally distributed on a quantile-quantile plot.

**RESULTS:** The predicted and actual rates of multiple birth for each of six embryo transfer groups is shown in Table 1. The differences between predicted and actual rates of multiple birth were not statistically significant and the standard errors were normally distributed on a quantile-quantile plot.

**TABLE 1. Predicted and actual rates of multiple birth (multiple deliveries / total deliveries)**

<table>
<thead>
<tr>
<th>embryos transferred</th>
<th>less than 38 years</th>
<th>38 years &amp; greater</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 blastocysts</td>
<td>predicted (95% CI)</td>
<td>actual</td>
</tr>
<tr>
<td>predicted (95% CI)</td>
<td>36% (23-50%)</td>
<td>30% (p = 0.37)</td>
</tr>
<tr>
<td>actual</td>
<td>7% (0-30%)</td>
<td>17% (p = 0.30)</td>
</tr>
<tr>
<td>2 cleavage stage</td>
<td>predicted (95% CI)</td>
<td>actual</td>
</tr>
<tr>
<td>predicted (95% CI)</td>
<td>9% (0-25%)</td>
<td>16% (5-29%) *</td>
</tr>
<tr>
<td>actual</td>
<td>16% (p = 0.31)</td>
<td></td>
</tr>
<tr>
<td>3 cleavage stage</td>
<td>predicted (95% CI)</td>
<td>actual</td>
</tr>
<tr>
<td>predicted (95% CI)</td>
<td>34% (18-52%)</td>
<td>19% (p = 0.59)</td>
</tr>
<tr>
<td>actual</td>
<td>29% (p = 0.51)</td>
<td></td>
</tr>
<tr>
<td>4 or 5 cleavage stage</td>
<td>predicted (95% CI)</td>
<td>actual</td>
</tr>
<tr>
<td>predicted (95% CI)</td>
<td>21% (8-36%)</td>
<td>17% (p = 0.59)</td>
</tr>
<tr>
<td>actual</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* this group included transfer of 2 or 3 cleavage stage embryos

**CONCLUSIONS:** Current recommendations for number of embryos to transfer are based on expert opinion. This model can be used with a mobile device application at the point of care for evidence based quantitative prediction of risk of multiple gestation after transfer of multiple embryos.

**P-105 Tuesday, October 15, 2019 6:30 AM**

**REDDUCING SIZE OF TRANSFER SYRINGE IS BENEFICIAL FOR IVF PREGNANCY OUTCOMES**

Van Pham, B.S., Randall Dunn, M.D., Subodh Chauhan, M.D.,† Leah Schenk, M.D.,† Rakesh Mangal, M.D.,‡ Ertug Kovanci, M.D.,§ George M. Granert, M.D.,¶ Wan-Song A Wun, PhD,∥ Aspire Fertility, Houston, TX; Harvest Fertility, Arcadia, TX.

**OBJECTIVE:** Embryo transfer has been emphasized as one of significant factors relates to IVF pregnancy. In addition to non-traumatic technique, fluid dynamic actions during embryo transfer has studied (Ding et al., 2018). In the transfer catheter, embryos encounter sudden increase of pressure (due to push down syringe plunger) then fast decompression when out of catheter. In the mouse model, sudden pressure alteration causes blastomer apoptosis (Grygoruk et al, 2011,2012). How the consequence of sudden pressure alteration impacts human IVF success is waiting for clarification. This study compared two types of transfer syringe (1ml or 0.2 ml) to examine potential beneficial effect by reducing the size of transfer syringe.

**DESIGN:** A retrospective study.

**MATERIALS AND METHODS:** By ethical concern, it is improper to perform embryo transfer in a Pair t design. The study retrospectively compared data in 2 periods of time with different size of transfer syringes. All frozen embryo transfers during 2016-2018 included in the study. Frozen embryos were PGTa tested euploidy. During 2016, 1 ml of air tight syringe was used for embryo transfer. During 2017-2018, 0.2 ml of microsyringe (Embryon, Rocket) was utilized for embryo transfer. Embryo transfer catheter was Wallace Sure-Pro (PE623) or PEB623 for difficult transfer. Implantation, fetal heart beat (FHB), and spontaneous abortion (SAB) rates were compared between two examined periods.

**RESULTS:** The results summarized in the following table

**CONCLUSIONS:** It is a fact that fluid moving from high pressure to low pressure. In the human IVF, the pressure differential generates by pushing down plunger during embryo transfer. With the same speed to push down the plunger, the higher the volume of syringe the higher the differential pressure generated. The higher pressure alteration gives higher stress to embryos/blastomeres. The consequence of higher stress reflects by the significantly lower implantation and fetal heart beat rates. The results from this study correspond to mouse embryo observations (Grygoruk et al, 2011,2012). Reducing the size of transfer syringe is beneficial for IVF success.


**SUPPORT:** None.

**IVF OUTCOME PREDICTORS - EMBRYOS**

**P-105 Tuesday, October 15, 2019 6:30 AM**

**ONGOING PREGNANCY RATE OF VITRIFIED-WARMED BLASTOCYST TRANSFERS IN AUTOLOGOUS PATIENTS: SINGLE VS DOUBLE TRANSFER ACCORDING TO THE DAY OF DEVELOPMENT**

Juergen Liebermann, PhD, HCLD, Sara Sanchez-Julias, BS, Rebecca Brohammer, BS, Janna Schwab, MS, Meike L. Uhler, M.D., Jennifer E. Hirshfeld-Cytron, MD, Christopher Sipe, MD. Fertility Centers of Illinois, Chicago, IL.

**OBJECTIVE:** Improvement in cryopreservation techniques has led to increasing implantation rates transferring vitrified-warmed embryos. This development has supported the move to recommend single embryo transfers to a greater proportion of patients. Considering the high frequency of day 6 blastocyst formation, the associated lower implantation potential of day 6 blastocyst becomes clinically important. Therefore, in an effort to optimize the pregnancy of transferring growth-delayed day 6 blastocysts, we compared their outcome to normally-developing day 5 blastocysts, and evaluated their efficiency in regards to ongoing (oPR), implantation rate (IR), and Twin pregnancies.

**DESIGN:** Retrospective analysis.

**MATERIALS AND METHODS:** The study included a total of 3,559 day 5, and 1,740 day 6 vitrified-warmed blastocyst transfers (VBT) in autologous women of 37 years of age and younger recorded between 2004 and 2018. The day 5 group contained 1,857 single (D5sVBT), and 1,702 double (D5dVBT) transfers, whereas the day 6 group contained 680 single (D6sVBT), and 1,060 double (D6dVBT) transfers. The vitrified blastocysts were warmed about 2hrs prior to transfer. Both natural and hormone replacement cycles were used to increase receptivity of the endometrium. Progesterone was supplemented on day 15 of the cycle and blastocysts were warmed on day 5 of progesterone supplementation. Chi-square test was used for statistical analysis of oPR between single and double-vitrified-warmed embryo transfers and according to the day of development (day 5 vs. day 6).

**RESULTS:** The total oPR was significant lower in the day 6 group compared with those in the day 5 group (35.4% vs 51.1%). The oPR was not significantly different between the D5sVBT group and D5dVBT group (49.5 vs 52.8%). However, the oPR was significantly higher in the...
Denotes statistical significance \( ^{a,b}P<0.01; ^{a,a,b}P<0.001 \)

D6dVBT group compared with the D6sVBT group (39.4 vs 29.1). The Twin PR was statistically significantly lower in both sVBT groups (1.7% vs. 2.1%) compared to both dVBT groups (42.1% vs 33.1%) regardless of the day of development.

CONCLUSIONS: This study showed that D5sVBT resulted in comparable oPR compared to D5dVBT, while D6sVBT resulted in significantly lower oPR compared to D6dVBT. However, in any oVBT the number of embryos transferred should always carefully considered, because transferring 2 blastocysts regardless of day of development always yielded a significantly higher twin rate.

SUPPORT: None.

P-106 Tuesday, October 15, 2019 6:30 AM

RELATIONSHIP OF EMBRYO SEX TO EMBRYO QUALITY, DAY OF BLASTOCYST TRANSFORMATION, AND IVF OUTCOMES. Christopher P. Moutos, MD,1 William G. Kearns, MD, PhD,2 Sarah E. Farmer, MS,3 Jon P. Richards, MD,4 Antonio F. Saad, MD,a John R. Crochet, Jr., MD.c
1University of Texas Medical Branch, Galveston, TX; 2Johns Hopkins University School of Medicine, Baltimore, MD; 3Advagenix, 9430 Key West Hwy, Suite 130, Houston, TX; 4Center of Reproductive Medicine, Houston, TX.

OBJECTIVE: While it has been theorized that the energy required for X chromosome inactivation in female embryos may have an impact on embryo development, conflicting data exists regarding the impact of embryo sex on blastocyst development and quality and subsequent IVF outcomes. The primary objective of this study is to determine if there is a relationship between embryo sex as determined by preimplantation genetic testing for aneuploidy (PGT-A) and blastocyst transformation and quality and the IVF outcomes.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: A retrospective chart review was conducted of patients age 21-47 who underwent PGT-A (n=3708) and subsequent autologous elective single embryo transfer (eSET) (n=539) from June 2007 to December 2018. Primary analyses focused on the relationship of embryo sex to day of blastocyst transformation (day of trophectoderm biopsy) and embryo quality. Secondary analyses examined the relationship of embryo sex to morphological grade, genetic diagnosis, and rates of implantation, clinical pregnancy (CP), ongoing pregnancy (OP), chemical pregnancy, spontaneous abortion, and ectopic pregnancy. Pearson’s chi-squared test was used with \( P<0.05 \) being considered significant.

RESULTS: There was no difference in embryo sex and day of blastocyst transformation \((P=0.566)\), embryo grade \((P=0.057)\), or maternal age \((P=0.837)\). Similar results were observed when the analysis was repeated stratified by maternal age and being euploid. Female embryos were more likely than male embryos to be aneuploid (54.6% vs 47.2%, \( P<0.001 \)). When embryos with sex chromosome aneuploidy were excluded, there was also no correlation between embryo sex and grade \((P=0.363)\) or day of blastocyst transformation \((P=0.094)\). Embryos undergoing blastocyst transformation on day 5 vs day 6 were more likely to result in implantation (71.8% vs 52.6%, \( P<0.001)\), CP (69.4% vs 50.9%, \( P<0.001)\) and OP (59.1% vs 44.7%, \( P=0.018)\). High-grade embryos were also more likely then mid/low-grade embryos to result in implantation (70.8% vs 60.3%, \( P=0.018)\), CP (69.2% vs 56.4%, \( P=0.005)\) and OP (59.3% vs 48.1%, \( P=0.018)\). Day 6 embryos were more likely to result in a chemical pregnancy (5.1% vs 1.0%, \( P=0.004)\). Implantation, CP, and OP rates were not different among sex embryo groups. Unlike male embryos, female embryos undergoing blastocyst transformation on day 5 vs day 6 were more likely to result in a CP (68.8% vs 52.0%, \( P=0.012)\) and tended towards being more likely to result in an OP (58.2% vs 45.3%, \( P=0.062)\).

CONCLUSIONS: To our knowledge, this is the largest and most comprehensive study to evaluate the potential relationship between embryo sex and quality or development and first to also look at the subsequent IVF outcomes. Despite not finding a difference between embryo sex and embryo blastocyst development or IVF outcomes, female embryos were more likely to be aneuploid, which is likely due to an increased frequency of X chromosome aneuploidy. In addition, faster developing and higher-grade embryos were more likely to have favorable IVF outcomes.

P-107 Tuesday, October 15, 2019 6:30 AM

IMPACT OF FRESH-EMBRYO PARAMETERS ON SURVIVAL AND IMPLANTATION IN VITRIFIED BLASTOCYST CYCLES: ANALYSIS OF 11936 WARMED BLASTOCYSTS. Aila Coelho, PhD,a Ma José de los Santos, PhD,a Mar Nahales, PhD,b Marcos Meseguer, PhD,b Jose Alejandro Remohi, MD, PhD,3 Ana Cobo, PhD,b 1IVIRMA VALENCIA, VALENCIA, Spain; 2IVIRMA VALENCIA, VALENCIA, Spain; 3IVIRMA Global, Valencia, Spain, Tel Aviv, Israel; 4IVIRMA Valencia, Valencia, Spain.

OBJECTIVE: To correlate blastocyst features with the predictive potential of survival and successful implantation in vitrified/warmed blastocyst cycles.

DESIGN: Retrospective study.

MATERIALS AND METHODS: The study included 11936 vitrified-warmed blastocysts transferred from January 2017 to December 2018. No PGT-A cycles were included. Pre-vitrification morphological parameters analyzed for all blastocysts were as follows: i) day of vitrification (5 vs 6); ii) blastocyst expansion degree: cavitated (BC), fully expanded (BE) and hatching out of the zona (BH); iii) trophectoderm (TE) quality (A, B and C); iv) inner cell mass (ICM) quality (A, B and C); and (v) oocyte origin (donor vs. autologous). Survival and implantation rates were analyzed using a logistic regression model. Odds ratios and 95% confident intervals (CI) were calculated. \( P<0.05 \) was considered statistically significant.

RESULTS: Logistic regression model estimated that the day of vitrification (5 vs. 6) was the strongest predictor of embryo survival (1.71; 95% CI: 1.42 – 2.04; \( P<0.001)\). Additionally, the odds of survival increased in blastocysts catalogued as BC with respect to those catalogued as BH (2.05; 95% CI: 1.48 – 2.83; \( P<0.001)\), and decreased in blastocysts with TE C compared to those with TE A (1.31; 95% CI: 1.07 – 1.59; \( P<0.0001)\). However, survival was not affected by the oocyte origin. Regarding implantation, the model showed that TE quality followed by the day of vitrification were the most significant morphological predictors of success. The odds of implantation were doubled for blastocysts with TE graded as A compared to those with TE graded as C (2.03; 95%CI: 1.75 – 2.36; \( P<0.001)\), and were cut by half for blastocysts vitrified on day 6 compared to those vitrified on day 5 (0.51; 95% CI: 0.45 – 0.57; \( P=0.001)\). The odds of implantation were also increased when transferring hatching blastocysts (1.63; 95%CI: 1.41 – 1.87; \( P<0.001)\) and ICM was graded as A (1.35; 95%CI: 1.13 – 1.60; \( P<0.005)\).

CONCLUSIONS: Blastocysts vitrified on day 5 with top quality TE should be given priority when warming. The degree of blastocoele expansion when vitrifying is closely related to success: BC embryos showed higher survival but lower implantation rates and should be cultured after warming to allow them to expand prior to the embryo transfer. The possibility of double embryo transfer should be considered in vitrified cycles with blastocysts graded as day 6 and TE C.

P-108 Tuesday, October 15, 2019 6:30 AM

DEVELOPMENT AND PRELIMINARY VALIDATION OF AN AUTOMATED STATIC DIGITAL IMAGE ANALYSIS SYSTEM UTILIZING MACHINE LEARNING FOR BLASTOCYST SELECTION. Alejandro Chavez-Badiola, MD,a Adolfo Flores-Saiffe Farias, MSc, PhD, b Gerardo Mendizabal-Ruiz, PhD,a Rodolfo Garcia-Sanchez, MSc,a Andrew J. Drakeley, MD FRCOG,a b New Hope Fertility Center Mexico, Mexico City, EM, Mexico;
OBJECTIVE: To assess an automated static digital image analysis system’s capabilities to predict a blastocyst’s potential to achieve a pregnancy by analyzing morphometric features extracted from single images and computing these utilizing artificial intelligence.

DESIGN: Retrospective morphometric study to evaluate an automated static digital image-processing algorithm’s predictive capabilities.

MATERIALS AND METHODS: Two balanced and high-quality embryo micrograph databases with pregnancy outcomes from single blastocyst transfers (Database A: 134 images; Database B: 87 images), were used to create a pipeline that extracts relevant morphometric features which, along with metadata, allowed us to predict pregnancy defined as beta hCG >20iu, 7 days following blastocyst transfer. Several classifiers were tested within the pipeline using cross-validation techniques to assess the generalization capabilities of the models: Support Vector Machines, Neural Networks, and Ada Boost. Using artificial intelligence, the probability of achieving pregnancy was then estimated.

RESULTS: A total of 221 images of blastocysts selected for single embryo transfers were included. The developed algorithm was successful at extracting relevant morphological features from every micrograph. Furthermore, it was successfully able to predict a positive pregnancy test in both datasets. With the use of the computed morphological features in combination, it was possible to achieve an F1 score of 0.76: accuracy of 0.75; and sensitivity of 0.77 for database A. For database B we created a predictive model with 0.74 of F1 score; accuracy of 0.67; and sensitivity of 0.78.

CONCLUSIONS: The proposed computational tool based on machine-learning has the capacity to link variables, extracted from single static digital images of blastocysts, to pregnancy. By doing so, it allows for a new approach to embryo classification while supporting embryologists towards a more objective and accurate embryo selection process. Different from other approaches, this machine-learning tool doesn’t rely on time-lapse incubators, making it a low cost candidate for easy integration into routine clinical practice. A prospective study on a larger scale is underway to replicate our initial results while, at the same time, aiming to improve predictability capabilities through automated machine-learning.


P-109 Tuesday, October 15, 2019 6:30 AM

ODDS OF EUPOLOYD ARE SIGNIFICANTLY ASSOCIATED WITH NOT ONLY AGE BUT BLASTOCYST MORPHOKINETIC PARAMETERS AND ICM/TROPHOCTODERM CHARACTERISTICS. Nina Desai, Ph.D., HCLD.; Jeffrey M. Goldberg, M.D.; Rebecca Feyckt, M.D.; Marjan Attaran, M.D.; Julie Tantibhedhyangkul, M.D.; Cynthia M. Austin, M.D.; Cleveland Clinic, Beachwood, OH; Cleveland Clinic, Cleveland, OH.

OBJECTIVE: Morphokinetic data from time-lapse (TL) imaging cannot diagnose euploidy with the specificity of preimplantation genetic screening but may provide valuable insight into parameters associated with a euploid diagnosis. This study analyzes the kinetics of blastocyst formation, early cleavage dysmorphisms, ICM/trophectoderm quality and the odds of the blastocyst having a normal chromosome complement.


MATERIALS AND METHODS: A total of 2493 zygotes were cultured in the EmbryoScope TL chamber. Embryo videos were annotated daily for the following: t2 (time to 2c), t3, t4, t5, t8, tM morula), tSB (start of blastulation), tFBL (full blastocyst), tEBL (expanded blastocyst), tHB (hatching blastocyst). Presence of dysmorphisms were also recorded. Assisted hatching was performed on day3. Blastocyst maturity stage was scored: 1=early, 2=full, 3=expanded, 4=hatching. ICM and trophectoderm morphology was graded as: 1-good,2-fair or 3-poor, based on cell organization and number. An overall blastocyst quality score (BQS) from 1 to 6, with 6 being the best was then assigned. Trophectoderm biopsy was performed on day 5/6 and cells were sent for analysis. Euploid embryos were transferred either in the fresh cycle or subsequent frozen cycles.

RESULTS: Of the 1258 biopsied blastocysts, 37% (95% CI 34-40%) were diagnosed as euploid. After adjusting for age, seven variables were independently associated with odds of euploidy: For each hours increase in interval between tSB and tEB, the odds of euploidy decreased by 4.5% (OR 0.96; 95% CI 0.93-0.98; p=0.002). If tSB was <96.2, the likelihood of euploidy was 1.5 times higher (95% CI 1.21-1.9; p=0.006). The presence of more than a single dysmorphism during early cleavage lowered the odds of the blastocyst being euploid by 49% (OR 0.51, 95% CI 0.33-0.80; p=0.003). Development was also associated with blastocyst maturity stage (p<0.001), ICM grade (p=0.002 and trophectoderm grade (p<0.001). Percent euploidy correlated significantly to BQS score: 1=22%, 2=13.2%, 3=21.7%, 4=25.5%, 5=39.9% and 6= 47.7% (p<0.001)). A logistic regression model to enhance the probability of selecting a euploid blastocyst was then constructed. ROC analysis to determine the predictive ability of a
model using a combination of these parameters to predict euploidy gave an AUC value of 0.70. In FET cycles, a model combining cryopreservation and TE grade is not significantly correlated with implantation rate (p = 0.11). Odd of implantation for TE 1 vs TE 3 were 6-fold higher (OR 6.61; 95% CI 2.20-22.89; p = 0.0006) and almost 2.5 fold higher with TE 1 vs TE 2 (OR 2.45; 95% CI 1.24-4.92; p = 0.0097).

CONCLUSIONS: The predictive model described here increases the probability of selecting a chromosomally normal blastocyst. Further study is needed to determine if such a model can increase odds of successful implantation in non-PGS patients.


SUPPORT: None.

P-110 Tuesday, October 15, 2019 6:30 AM

BLASTOCYST GRADE PREDICTS OUTCOME AFTER FROZEN EUPLOID TRANSFER IN PATIENTS WITH RECURRENT PREGNANCY LOSS. Gayathree Murugappan, MD,¹ Julia G. Kim, MD, MPH,² Jonathan D. Kort, MD,² Brent M. Hanson, MD,³ Shelby A. Neal, MD,³ Ashley W. Tieg, MD,³ Emily K. Osman, MD,³ Richard Thomas Scott Jr, MD,³ Ruth B. Lathi, MD,⁴ Stanford University Medical Center, Sunnyvale, CA;⁵IVI-RMA New Jersey, Basking Ridge, NJ; ⁶IVI/Reproductive Medicine Associates of Northern California, San Francisco, CA; ⁷Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA.

OBJECTIVE: Trophectoderm (TE) grade has been shown to be the most significant predictor of implantation and live birth after fresh untested blastocyst transfer in infertile cohorts. The goal of this study was to determine if TE grade or inner cell mass (ICM) grade are predictive of clinical outcomes in a cohort of RPL patients pursuing PGT-A.

DESIGN: Retrospective cohort study from a single fertility center between 2002 and 2018.

MATERIALS AND METHODS: Patients with 2 or more prior pregnancy losses performing PGT-A with at least one euploid embryo for transfer were included. All patients underwent ICSI and single euploid frozen blastocyst transfer (eFET). Outcome of the first eFET was recorded. Implantation was defined as beta hCG > 5 mIU/mL. Clinical pregnancy was defined as a visualized gestational sac. Pregnancy loss was defined as loss of pregnancy from implantation to twenty weeks gestation. Multivariable logistic regression analysis was used to evaluate the effect of age, TE grade and ICM grade on clinical outcomes.

RESULTS: 660 eFET were included, with clinical outcomes stratified by ICM and TE grade (Table 1). After adjusting for age, ICM grade is not significantly correlated with implantation rate (p = 0.12, CI 0.93-1.92), miscarriage rate (p = 0.18, CI 0.47-1.16), or pregnancy loss rate (p = 0.21, CI 0.56-1.13) but is significantly correlated with live birth rate (p = 0.03, CI 1.02-1.81). TE grade is not significantly correlated with implantation rate (p = 0.32, CI 0.86-1.56) or miscarriage rate (p = 0.11, CI 0.52-1.07) but is significantly correlated with live birth rate (p = 0.02, CI 1.06-1.71) and pregnancy loss rate (p = 0.04, CI 0.55-0.98). 16 blastocysts were grade CC, with implantation rate 69% (n = 11), clinical pregnancy rate 50% (n = 8), live birth rate 31% (n = 5), clinical miscarriage rate 38% (n = 3) and pregnancy loss rate 55% (n = 6).

CONCLUSIONS: Compared to embryos with grades A or B, TE and ICM grade C is correlated with lower likelihood of live birth and TE grade C is correlated with higher likelihood of pregnancy loss among RPL patients performing eFET. These results suggest that euploid pregnancy loss in the setting of RPL is still likely of embryonic origin.


SUPPORT: None.

P-111 Tuesday, October 15, 2019 6:30 AM

SURVIVAL BEHAVIOR OF EMBRYO COHORT IN CULTURE IS ASSOCIATED WITH PREGNANCY PERFORMANCE OF A SURVIVING EUPLOID BLASTOCYST AFTER SINGLE EMBRYO TRANSFER (SET): THE CANARIES IN THE COAL MINE? Eleni A. Greenwood, MD, MSc,¹ Rhodel Simbulan, MS,¹ Charles E. McCalloch, PhD,¹ Marcellie I. Cedars, MD,¹ Mitchell P. Rosen, MD, HCLD² University of California San Francisco, San Francisco, CA;¹UCSF, San Francisco, CA;¹University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: Improving metrics for embryo selection is of great interest in the field of assisted reproductive technology. Preimplantation genetic testing for aneuploidy (PGT-A) is one powerful selection tool available today. Our objective was to investigate whether the survival behavior of an embryo cohort in culture associated with 1) euploid rates of biopsied blastocysts produced from that cohort, or 2) pregnancy outcomes after subsequent single euploid embryo transfer.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Blastocyst biopsies for PGT-A at a single academic center between 2010-2019 were reviewed. At our institution, grade BB (Gardner criteria) or better blastocysts are biopsied on day 5 or 6 and subsequently frozen. A “Poor Embryo Survival” (PES) subset of women was defined as those women for whom >70% of normally fertilized embryos (2PNs) did not progress to biopsiable blastocysts (i.e. dropout, corresponding to the ≥75%ile for embryo dropout). Euploid rates (euploid blastocysts / biopsied blastocysts per ovarian stimulation cycle) were compared between the PES women and the remaining 75% (“Controls”), using generalized linear models to control for age of the oocyte and account for the clustered nature of the data. Pregnancy outcomes following single euploid embryo transfer in a subsequent frozen cycle were similarly compared between PES and Control groups.

RESULTS: 1,400 women underwent 2,087 ovarian stimulation cycles yielding 10,087 trophectoderm biopsies for review. Average age in PES women was 38.2y vs 37.1y in Controls. Although increasing age was associated with higher embryo dropout, euploid rates from surviving, biopsied blastocysts were no different between PES women (Table) vs Controls after adjusting for age in the model (p = 0.23). On the other hand, pregnancy outcomes after euploid SET differed based on embryo cohort survival (Table). A euploid blastocyst from a PES cycle had 37% reduced odds of generating an ongoing pregnancy or live birth vs a euploid blastocyst from a Control cycle (OR 0.63, 95% CI 0.41, 0.95, p = 0.03).

SUPPORT: None.

TABLE 1.

<table>
<thead>
<tr>
<th>ICM grade</th>
<th>Clinical pregnancy, n (%)</th>
<th>Live birth/ongoing pregnancy, n (%)</th>
<th>Clinical miscarriage, n (%)</th>
<th>Pregnancy loss, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>217 (33%)</td>
<td>185 (85%)</td>
<td>164 (76%)</td>
<td>145 (67%)</td>
</tr>
<tr>
<td>B</td>
<td>405 (61%)</td>
<td>327 (81%)</td>
<td>293 (72%)</td>
<td>244 (60%)</td>
</tr>
<tr>
<td>C</td>
<td>38 (6%)</td>
<td>29 (81%)</td>
<td>24 (63%)</td>
<td>19 (50%)*</td>
</tr>
<tr>
<td>TE grade</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>312 (47%)</td>
<td>259 (83%)</td>
<td>232 (74%)</td>
<td>203 (65%)</td>
</tr>
<tr>
<td>B</td>
<td>277 (42%)</td>
<td>228 (82%)</td>
<td>205 (75%)</td>
<td>172 (62%)</td>
</tr>
<tr>
<td>C</td>
<td>71 (11%)</td>
<td>54 (76%)</td>
<td>44 (62%)</td>
<td>33 (46%)*</td>
</tr>
</tbody>
</table>

*p<0.05, multivariate regression analysis adjusting for age

FERTILITY & STERILITY® e151
CONCLUSIONS: Survival rates of embryo cohorts in culture do not appear to correlate with the likelihood of identifying a euploid blastocyst among blastocysts surviving to biopsy, after accounting for age of oocyte. On the other hand, high rates of embryo dropout between fertilization and blastocyst biopsy are associated with reduced odds of live birth or ongoing pregnancy following euploid SET. Embryo cohort behavior in culture may reflect non-genomic pregnancy potential of embryos emerging from these cohorts.


SUPPORT: None.

P-113 Tuesday, October 15, 2019 6:30 AM

**BLASTOCYST MORPHOLOGY CORRELATES WITH PREIMPLANTATION GENETIC TESTING FOR NEUPOIDY (PGT-A) RESULTS AND MAY FURTHER PRE Dictate PREDICT PREGNANCY POTENTIAL AFTER EUPOID SETS (PGT-A**

**OBJECTIVE:** To 1) evaluate the relationship between blastocyst morphology and ploidy via PGT-A, and 2) determine whether morphology might further differentiate pregnancy potential among euploid blastocysts following single embryo transfer (SET)  

**MATERIALS AND METHODS:** PGT-A results from trophectoderm biopsies of 615 transfers utilizing euploid SET were analyzed. Fully hatched blastocysts (n=73) showed a significantly lower PR (4%) when compared to blastocysts with a blastocoel of more than or equal to half the volume of the embryo (n=168) (58%) (p<0.001), expanded blastocysts (n=260) with a full blastocoel (60%) (p<0.001) and hatching blastocysts (n=150) (65%) (p=0.001). SETs with fully hatched blastocysts showed the lowest IR% (29%) when compared to full blastocysts (51%) (p=0.002), expanded blastocysts (53%) (p=0.0002) and hatching blastocysts (56%) (p=0.0004). Moreover, CPR% was significantly impacted after the transfer of fully hatched blastocysts (27%) when compared to full blastocysts (47%) (p=0.004), expanded blastocysts (53%) (p=0.002) and hatching blastocysts (56%) (p=0.006). Day of development did not influence the clinical outcomes between the different stages of blastocysts (p=0.18). Also the analysis showed no significant difference among the stages of development within the same category for neither the performing physician nor the transferring embryologist (p=0.94, p=0.65 respectively).

**CONCLUSIONS:** It has been recently reported that the transfer of fully hatched blastocysts results in significantly lower success rates when compared to other stages of blastocyst development (James, R. M et al., 2018). It has also been suggested that the complete removal of the zona pel lucida increases the implantation potential. However, these studies lack evidence to support the hypothesis (Alteri, A et al, 2018). Despite the striking differences in the outcomes, other factors such as age and day of development did not influence the final result. These findings suggest that the zona pel lucida confers some level of protection during transfer, and its absence may contribute to lower clinical outcomes.


SUPPORT: None.

**EUPLOID NOT PREGNANT**

<table>
<thead>
<tr>
<th>PGT-A result</th>
<th>Poor Embryo Survival (PES)</th>
<th>Biochemical pregnancy</th>
<th>Clinical miscarriage</th>
<th>Ectopic pregnancy</th>
<th>Ongoing pregnancy/ Live birth*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euploid</td>
<td>42.4%</td>
<td>3.9%</td>
<td>7.9%</td>
<td>0.5%</td>
<td>48.3%</td>
</tr>
<tr>
<td>Control</td>
<td>45.5%</td>
<td>3.8%</td>
<td>6.2%</td>
<td>0.3%</td>
<td>56.2%</td>
</tr>
</tbody>
</table>

*<0.05

**P-112 Tuesday, October 15, 2019 6:30 AM**

**FULLY HATCHED EUPOID BLASTOCYSTS EXHIBIT LOWER PREGNANCY OUTCOMES WHEN COMPARED TO OTHER BLASTOCYST STAGES IN FROZEN SET CYCLES.** Ahmad Mori Aba Maizar, M.Sc.  

**OBJECTIVE:** To determine and compare the clinical outcomes of transferring a trophectoderm biopsied fully hatched blastocyst to other blastocyst stages in Single Embryo Transfer (SET) cycles.

**DESIGN:** Retrospective analysis of private clinic data outcomes.

**MATERIALS AND METHODS:** Pregnancy Rate (PR), Implantation Rate (IR) and Clinical Pregnancy Rate (CPR) of PGT-tested blastocyst SETs during 2017-2018 were analyzed. All fertilized oocytes underwent uninterrupted extended culture until the day of biopsy. Trophodectom biopsy was performed on culture day 5, 6, or 7 using a single pulse laser breach of the zona pellucida, followed by the insertion of a beveled needle with excision of 3-5 cells. PGT testing was performed utilizing NextGen sequencing. All transfers were performed with vitrified/warmed blastocysts. PR was determined by hCG level of >5mIU/mL. IR was determined by the number of sacs present at 3 weeks after positive pregnancy, and CPR by the presence of a positive fetal heart beat (FHB) at 7 weeks gestation. Statistical analysis was performed using Chi-square (P<0.05).

**RESULTS:** Outcomes from 651 transfers utilizing euploid SET were analyzed. Fully hatched blastocysts showed a significantly lower IR% (29%) when compared to blastocysts with a blastocoel of more than or equal to half the volume of the embryo (58%) (p<0.001), expanded blastocysts (53%) (p=0.0002) and hatching blastocysts (56%) (p=0.0004). SETs with fully hatched blastocysts showed the lowest IR% (29%) when compared to full blastocysts (51%) (p=0.002), expanded blastocysts (53%) (p=0.0002) and hatching blastocysts (56%) (p=0.0004). Moreover, CPR% was significantly impacted after the transfer of fully hatched blastocysts (27%) when compared to full blastocysts (47%) (p=0.004), expanded blastocysts (53%) (p=0.002) and hatching blastocysts (56%) (p=0.006). Day of development did not influence the clinical outcomes between the different stages of blastocysts (p=0.18). Also the analysis showed no significant difference among the stages of development within the same category for neither the performing physician nor the transferring embryologist (p=0.94, p=0.65 respectively).

**CONCLUSIONS:** Survival rates of embryo cohorts in culture do not appear to correlate with the likelihood of identifying a euploid blastocyst among blastocysts surviving to biopsy, after accounting for age of oocyte. On the other hand, high rates of embryo dropout between fertilization and blastocyst biopsy are associated with reduced odds of live birth or ongoing pregnancy following euploid SET. Embryo cohort behavior in culture may reflect non-genomic pregnancy potential of embryos emerging from these cohorts.

**REFERENCES:**


SUPPORT: None.
The object of this study was to investigate whether there is a difference in live-birth gender proportion between mean area ratio of ICM to blastocyst among embryos that gave clinical pregnancy was 0.33 +/- 0.05 as against 0.30 +/- 0.09 among embryos that did not give clinical pregnancy (p value – 0.015). Mean area ratio of ICM to blastocyst among embryos that gave clinical pregnancy was 0.14 +/- 0.04 as against 0.13 +/- 0.07 (p value – 0.26). Morphological scoring was calculated from grading as per Istanbul consensus and quantified as 1/ICM score x 1/ Trophoderm score x Expansion score. Mean morphological scoring of embryos that gave clinical pregnancy was 2.45 +/- 1.27 as against 2.04 +/- 1.08 among embryos that did not give clinical pregnancy (p value – 0.03).

Correlation coefficient between morphological scoring and mean diameter ratio of ICM to blastocyst was 0.23 (p = 0.003), showing mean diameter ratio is positively correlated with morphological scoring. Correlation coefficient between mean area ratio of ICM to blastocyst to morphological scoring was 0.14 (p = 0.06).

Area under curve (AUC) for ICM to blastocyst diameter ratio to predict clinical pregnancy was 0.586 (p=0.04), for area ratio was 0.576 (p=0.04) and for morphological scoring was 0.595 (p=0.04). The predictive ability for clinical pregnancy was highest for existing morphological scoring followed by ICM to blastocyst diameter ratio and least for area ratio.

CONCLUSIONS: Ratio between ICM to blastocyst dimensions would serve as a simple, cost-effective tool for selecting embryos prior to transfer in developing countries.

SUPPORT: NIL.

P-115 Tuesday, October 15, 2019 6:30 AM

EMBRYO SELECTION IN DEVELOPING COUNTRIES- INNER CELL MASS TO BLASTOCYST DIMENSION RATIO AS A PREDICTOR OF PREGNANCY OUTCOME. Deepika Krish, MS, FRM. Consultant in Rep Med, BANGALORE, India.

OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) is typically performed on a trophectoderm (TE) biopsy prior to vitrification. When no PGT-A result is returned, patients can request a second biopsy and re-vitrification. Additionally, patients do request PGT-A of prior untested cryopreserved embryos which requires a single biopsy and re-vitrification. The aim of this study was to evaluate the impact of double biopsy and double vitrification on reproductive outcomes following a euploid frozen embryo transfer (FET).

OBJECTIVE: Is there a correlation between inner cell mass (ICM) to blastocyst dimensions (diameter and area) ratio and pregnancy outcome, which can be used to select embryo for transfer in developing countries?

DESIGN: A prospective observational study was performed for a duration of 18 months at a tertiary level IVF centre. 185 subjects who had autologous or donor egg derived blastocyst transfers were included in the study.

MATERIALS AND METHODS: 385 Blastocysts were photographed at 116 hours post ICSI. ICM to blastocyst dimensions ratio was calculated using Image J software. Morphological scoring of embryos was performed according to Istanbul consensus. Predictive value of ICM to blastocyst diameter and area ratios to implantation and clinical pregnancy rate were studied by ROC curve analysis. Correlation coefficients were drawn between dimensions ratio and morphological scoring.

RESULTS: Mean diameter ratio of ICM to blastocyst among embryos that gave clinical pregnancy was 0.33 +/- 0.05 as against 0.30 +/- 0.09 among embryos that did not give clinical pregnancy (p value – 0.015). Mean area ratio of ICM to blastocyst among embryos that gave clinical pregnancy was 0.14 +/- 0.04 as against 0.13 +/- 0.07 (p value – 0.26). Morphological scoring was calculated from grading as per Istanbul consensus and quantified as 1/ICM score x 1/ Trophoderm score x Expansion score. Mean morphological scoring of embryos that gave clinical pregnancy was 2.45 +/- 1.27 as against 2.04 +/- 1.08 among embryos that did not give clinical pregnancy (p value – 0.03).

Correlation coefficient between morphological scoring and mean diameter ratio of ICM to blastocyst was 0.23 (p = 0.003), showing mean diameter ratio is positively correlated with morphological scoring. Correlation coefficient between mean area ratio of ICM to blastocyst to morphological scoring was 0.14 (p = 0.06).

Area under curve (AUC) for ICM to blastocyst diameter ratio to predict clinical pregnancy was 0.586 (p=0.04), for area ratio was 0.576 (p=0.04) and for morphological scoring was 0.595 (p=0.04). The predictive ability for clinical pregnancy was highest for existing morphological scoring followed by ICM to blastocyst diameter ratio and least for area ratio.

CONCLUSIONS: Ratio between ICM to blastocyst dimensions would serve as a simple, cost-effective tool for selecting embryos prior to transfer in developing countries.

SUPPORT: NIL.

P-114 Tuesday, October 15, 2019 6:30 AM

INCREASED MALE LIVE-BIRTH RATES AFTER BLASTOCYST-STAGE FROZEN-THAWED EMBRYO TRANSFERS COMPARED WITH CLEAVAGE-STAGE: A SOCIETY FOR ASSISTED REPRODUCTIVE TECHNOLOGIES CLINICAL OUTCOMES REPORTING SYSTEM STUDY. Barry E. Perlman, DO, a Kavitha Krishnamoorthy, MD, a Sara S. Morelli, MD, PhD, a Patricia Greenberg, MS, a Sangita K. Jindal, Ph.D., a Peter McGovern, MD, a Rutgers New Jersey Medical School, Newark, NJ; bRutgers School of Public Health, New Brunswick, NJ; cEinstein COM, Montefiore, Hartsdale, OR; dUniversity Reproductive Associates, NJ.

OBJECTIVE: It has recently been described that blastocyst-stage frozen embryo transfer (FET) is associated with higher live-birth rates compared with cleavage-stage FETs, however other outcomes such as gender have not been well studied. Male-to-female sex ratio of offspring born after fresh blastocyst transfers suggest a shift towards males but whether the use of frozen-thawed embryos affects this ratio is not known. The object of this study was to investigate whether there is an increase in live-birth gender in blastocyst-stage compared with cleavage-stage FETs.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All IVF cycles reported to the Society for Assisted Reproductive Technology from 2004 to 2013 were evaluated. Patients included were those with recorded live births who underwent FETs at either the blastocyst-stage (n=56,193) or the cleavage-stage (n=42,941). Main outcome measures were live-birth gender ratios. Demographic criteria from each cycle was also collected. Statistical analysis was performed using SAS and Microsoft Excel. Chi-square analysis for bivariate analysis was performed using Matlab. Correlation coefficients were drawn between dimensions ratio and pregnancy outcome, which can be used to select embryo for transfer in developing countries.
TABLE 1.

<table>
<thead>
<tr>
<th></th>
<th>Single Biopsy/Double Vitrification FETs</th>
<th>Double Biopsy/Double Vitrification FET</th>
<th>Single Biopsy/Single Vitrification FET (Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Age</td>
<td>35.1 ± 3.7ᵃ</td>
<td>37.8 ± 3.8ᵇ</td>
<td>37.3 ± 3.4ᵇ</td>
</tr>
<tr>
<td>Clinical Pregnancy with Fetal Cardiac Activity</td>
<td>63.8%</td>
<td>53.8%*</td>
<td>67.1%</td>
</tr>
<tr>
<td>MAB Rate</td>
<td>5.8%</td>
<td>20.0%*</td>
<td>4.3%</td>
</tr>
<tr>
<td>Live Birth Rate</td>
<td>60.1%</td>
<td>43.0%*</td>
<td>64.3%</td>
</tr>
</tbody>
</table>

ᵃP < 0.0001;ᵇP < 0.01

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Groups were classified according to the number of rounds of biopsy and vitrification that the euploid blastocyst (≥ 3 Grade 3BB) underwent prior to FET at a single infertility clinic: Single biopsy (4-6 cells)/Double vitrification (n=326 FETs), Double biopsy (9-12 cells)/Double vitrification (n=93 FETs), and a control group of Single biopsy (4-6 cells)/Single vitrification FETs (n=93 FETs). Standard protocols for a hormone replacement FET were utilized for all patients. Statistical analysis included ANOVA and Chi-square test where appropriate, significance at P<0.05.

RESULTS: Mean maternal age was significantly lower in the Single Biopsy/Double Vitrification group (Table 1; P<0.0001). Blastocyst grade was comparable across the groups. FET reproductive outcomes revealed a significant decrease in clinical pregnancy and live birth rate, with a significant increase in MAB rate when a euploid blastocyst underwent a double biopsy and double vitrification prior to transfer (Table 1; p<0.01). There were no significant differences in reproductive outcomes between the Single Biopsy/Double Vitrification FET group and the control group with Single Biopsy/Single Vitrification (Table 1).

CONCLUSIONS: In conclusion, for transferrable quality, euploid blastocysts a single biopsy, double vitrification had comparable reproductive outcomes as a single biopsy, single vitrification, thereby supporting the efficacy of double vitrification. In contrast, a double biopsy had a significant impact on the developmental potential of a euploid blastocyst with a decreased probability of establishing and sustaining a viable clinical pregnancy. This novel study highlights the adverse impact of removing too many TE cells with a double biopsy for PGT-A.

SUPPORT: None.

P-117 Tuesday, October 15, 2019 6:30 AM

DEGREE OF RE-EXPANSION FOLLOWING VITRIFICATION/REWARMING OF EUPOLID BLASTOCYSTS IS INVERSELY CORRELATED WITH IMPLANTATION AND ONGOING PREGNANCY/LIVE BIRTH RATES. Sydney Chang, MD,¹ Taraneh Gharib Nazem, MD,³ Dmitry Gounko, MA,² Marlena Duke, MSc, ELD,¹ Christine Briton-Jones, PhD, HCLD,³ Alan B. Copperman, MD,² Beth McAvay, MD,² ¹Icahn School of Medicine at Mount Sinai, New York, NY; ²Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Routine implementation of blastocyst culture, preimplantation genetic testing, and freeze-all cycles has resulted in supernumerary cryopreserved euploid blastocysts available for frozen embryo transfer (FET). Often faced with a selection of chromosomally normal embryos, embryologists and clinicians turn to embryo morphology, morphokinetics, and timing of blastulation and cavitation to develop prognostic criteria. A recent study showed that re-expansion of vitrified/rewarmed blastocysts strongly correlated with implantation compared to blastocysts that did not re-expand.¹ Yet, that study did not incorporate PGT-A and was limited by small sample size. Thus, our objective was to evaluate the association between degree of re-expansion prior to FET and clinical outcomes among euploid blastocysts.

DESIGN: Retrospective, cohort study.

MATERIALS AND METHODS: The study included patients at an academic center who underwent single euploid FET cycle(s) from 2012-2019. Embryo vitrification/rewarming were performed with the Cryotop method (Kitazato). Embryos were classified into 3 groups: (1) fully re-expanded, (2) partially re-expanded, and (3) not re-expanded. Images of embryos recorded as not re-expanded after 3-4 hours post-warming were manually compared to the image taken immediately post-warming to determine whether partial re-expansion had occurred during the culture period. Primary outcome was ongoing pregnancy/live birth (OP/LB) rate. Secondary outcomes were rates of clinical pregnancy (CP) and early pregnancy loss (EPL). Data were evaluated with T-tests, chi-square tests, and generalized estimating equations.

RESULTS: The study included 4440 single euploid FET cycles from 2968 patients. There were 118 cycles (2.7%) where embryos were not fully re-expanded 3-4 hours post-warming. Of these, 58 had partially re-expanded and 59 did not re-expand prior to FET. There was a higher proportion of day 7 embryos (27.1%) in the not re-expanded compared to the fully re-expanded cohort (2.6%). After controlling for confounders, blastocysts that did not re-expand after 3-4 hours were associated with a significant decrease in OP/LB (OR 0.19 [95% CI 0.09-0.40], p<0.0001) and CP (OR 0.19 [95% CI 0.10-0.35], p<0.0001), compared to fully re-expanded blastocysts. There was no significant difference in OP/LB or CP rates between partially and fully re-expanded groups. There was no difference in EPL rate between the 3 groups.

CONCLUSIONS: In this study assessing the contribution of embryo re-expansion after vitrification/rewarming in a single euploid FET model, we showed reduced CP and OP/LB rates in embryos that did not re-expand. Our findings are consistent with Coello et al. who found a lower implantation rate for embryos that did not fully re-expand at FET compared to those that did.¹ Though transfer of blastocysts that did not re-expand resulted in a 76% decrease in OP/LB rate, our study also found no difference in EPL. Patients can therefore be reassured that once implantation has been achieved, there is no demonstrable increase in EPL.


SUPPORT: None.

P-118 Tuesday, October 15, 2019 6:30 AM

PREDICTIVE ABILITY OF A BLASTOCYST GRADE ON REPRODUCTIVE OUTCOMES IN ELECTIVE FRESH EMBRYO TRANSFER. Alyson M. Digby, MD, Bsc;² Lesley Roberts, MD FRCPSC,³ Mary M. Brown, MSc,⁴ Megan Dufton, PhD Sc,⁴ Renda Bouzayen, MD FRCPSC,⁴ ¹IWK Health Centre, Dalhousie University, Halifax, NS, Canada; ²University of Manitoba, Winnipeg, MB, Canada; ³IWK Health Centre Dalhousie University, Halifax, NS, Canada; ⁴Atlantic Assisted Reproductive Technologies, Halifax, NS, Canada.

OBJECTIVE: Within Canada in 2012, 25,782 invitro fertilization cycles were initiated, and 21,054 embryos transferred (1). The clinical pregnancy rate per embryo was 36.6% (2). Transfer typically occurs day 3 at the cleavage stage or day 5 at the blastocyst stage. Allowing embryos to mature prior to transfer permits self-selection of the “best quality” embryos, leading to higher implantation and pregnancy rates. A challenge is identifying which embryo has the highest likelihood of progressing to pregnancy. In 2011, a consensus document reviewed existing evidence for grading and developed a standard guideline. The purpose of this study is to determine if blastocyst stage or grade is predictive of pregnancy(3).

DESIGN: A retrospective cohort study drawing data from the Atlantic Assisted Reproductive Therapies database and patient charts between January, 2005 and June, 2014 was completed.

MATERIALS AND METHODS: Blastocyst grade and expansion stage (ES) was determined by embryo morphology coded by an embryologist. Only fresh, single embryos transferred on day 5 of culture were included. Data was excluded if the embryo transferred was a morula, cleavage stage or complete grading details were absent. Data was excluded if corresponding
to multiple embryo transfer, frozen embryo transfer, transfer of morula or cleavage stage, was missing charted data on morphologic grading criteria, or if transfer occurred on a culture day other than 5. On selected data, logistic regression models were used to test the association between the occurrence of pregnancy and i) each blastocyst grading criteria (ES, trophoectoderm (TD) and inner cell mass score (ICM)) and ii) the total embryo score stratified by blastocyst stage (early blastocyst, blastocyst, expanded blastocyst). All tests were performed at a 5% significance level. The area under the receiver operating characteristic (AUROC) curve was used to evaluate the performance of both TD and ICM in pregnancy prediction.

RESULTS: For each one point increase in score for ES, TD and ICM, there was a statistically significant increase in the odds of pregnancy of 1.78 (95% CI: 1.27 – 2.58), 1.38 (95% CI: 1.18 – 1.63), and 1.41 (95% CI: 1.19 – 1.69), respectively. The AUROC curve was nearly identical for both TD and ICM (0.62) and thus both discriminate similarly in predicting pregnancy. It does not appear that one offers greater predictive ability over the other.

CONCLUSIONS: This study suggests that ES, TD quality, and ICM quality may be useful for predicting clinical pregnancy rates amongst women undergoing transfer of an early blastocyst, blastocyst, or expanded blastocyst on culture day 5. Interestingly, it seems that TD and ICM are equivalent in terms of predictive ability. The importance of blastocyst expansion on the likelihood of pregnancy was demonstrated. When embryo score was stratified by stage, the transfer of an expanded blastocyst was associated with an increased likelihood of pregnancy. Transfer of an early blastocyst or blastocyst was not.


P-119 Tuesday, October 15, 2019 6:30 AM

IS THERE A RELATIONSHIP BETWEEN MITOCHONDRIAL DNA CONTENT AND ABORTION RATE IN PATIENTS UNDERGOING SINGLE EUPLOID FROZEN EMBRYO TRANSFER? Ahmed El-Damen, MSc, Ibrahim Elkhaitib, MSc, Asina Bayram, MSc, Ana Aranz, MSc, Suzan Samir, BVM, Neelke De Munk, PhD, Barbara Lawrenz, MD, PhD, Human M. Fatemi, MD, PhD. IVIRMA Middle East Fertility Clinic, Abu Dhabi, United Arab Emirates.

OBJECTIVE: The mitochondrial DNA (mtDNA) content of trophoectoderm cells is related to the energy supply of the blastocyst, which can affect its ability either to implant in the uterine cavity or not. While it has been demonstrated that euploid blastocysts present a lower mtDNA content as compared to aneuploid blastocysts, there are no data evaluating whether the abortion rate of euploid blastocysts could be associated with their mtDNA content. This information could help maximizing the success rate of single euploid embryo transfers in ART by selecting the blastocysts with the highest potential to achieve a live birth. The aim of this study is to determine whether the mtDNA content is related to the abortion rate in patients undergoing single euploid frozen embryo transfer (SEFET).

DESIGN: A retrospective cohort study of 355 SEFET cycles between April 2017 and December 2018 at a single private fertility center.

MATERIALS AND METHODS: Patients undergoing ART with pre-implantation genetic testing for aneuploidies (PGT-A) revealing the ploidy outcome and mtDNA content using Next Generation Sequencing (NGS), were included for the study. Blastocyst biopsy was performed on day 5 or 6 of development. All biopsied blastocysts were vitrified, and only euploid ones were selected for warming and subsequent SEFET using the Cryotop method and Kitazato media. Embryo transfer (ET) was performed either in a hormonal replacement therapy cycle (HRT) or in a true natural cycle (NC). Pregnancy outcome was defined 10-14 days after SEFET: a pregnancy test was considered to be positive if PhCG concentration in serum was > 15 IU. Ongoing pregnancy was defined as having a visible gestational sac with a fetal heart beat at 8 weeks of pregnancy while an abortion was defined as having a visible gestational sac without heartbeat until 8 weeks of pregnancy. The primary endpoint was to compare the mtDNA content between embryos leading to an ongoing pregnancy or an abortion. Unpaired two-tailed t-Student test was used to compare means of numerical variables and chi-square test for testing independence between categorical variables. A logistic regression model was performed controlling for maternal age, BMI, transfer distance from the fundus, endometrial thickness, cycle regimen and embryo quality. A p-value < 0.05 was considered statistically significant.

RESULTS: 355 euploid blastocysts were selected for SEFET in 314 patients with an average age of (33.7±5.5); 255 of them were biopsied on day 5 (71.8%) and 100 on day 6 (28.2%). Embryo transfer (ET) was performed in an HRT cycle (n=255; 71.8%) or a NC (n=100; 28.2%). A pregnancy rate of 66.2% (235/355) was obtained with ongoing pregnancy and abortion rates of 52.4% and 5.6%, respectively. There was no significant difference in the mtDNA content between pregnant and non-pregnant groups (p=0.095) and between the abortion and ongoing pregnancy group (p=0.15). Multivariable analysis showed the same non-significant relationship except for abortion rate and BMI (p=0.011).

CONCLUSIONS: Mitochondrial DNA content of the human blastocyst is unable to predict the abortion rate of implanted euploid blastocysts.

P-120 Tuesday, October 15, 2019 6:30 AM

FROZEN-THAWED EMBRYO TRANSFER IS BETTER THAN FRESH EMBRYO TRANSFER IN GNRH ANTAGONIST CYCLE IN NORMO-RESPONDERS: A RETROSPECTIVE COHORT STUDY. Xitong Liu. Resident, Haiyan Bai. Physician, Northwest women’s and children’s hospital, Xi’an, China.

OBJECTIVE: To compare the clinical outcome of frozen-thawed embryo transfer and fresh embryo transfer in GnRH antagonist protocol.

DESIGN: A total of 1430 normo-responder women from a single ART center(from January 2015 to January 2019) were enrolled in this retrospective cohort study. Women aged<40 years, no. of oocyte retrieved between 3 and 10, good embryo quality, underwent fresh embryo transfer or frozen-thawed all strategy and transferred in subsequent cycle were included. Endometriosis, PCOS, PCOGG cycles were excluded.

MATERIALS AND METHODS: The primary outcome was clinical pregnancy rate. A logistic regression analysis was performed to determine the variables that could be independently associated with clinical pregnancy rate. Models were adjusted for covariates including female age, fertilization type, infertility type, infertility duration, no. of oocyte retrieved, no. of embryo transferred and D3/D5 embryo transfer.

RESULTS: In total, 495 women were treated with fresh embryo transfer, whereas 935 patients were treated with frozen-thawed embryo transfer.

TABLE 1. Relationship between timing of transfer in different models

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Crude Model</th>
<th>Model I</th>
<th>Model II</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β(95%CI)</td>
<td>P-value</td>
<td>β(95%CI)</td>
</tr>
<tr>
<td>Timing of ET</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fresh ET</td>
<td>1.0</td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>Frozen ET</td>
<td>0.68 (0.55, 0.85)</td>
<td>0.001</td>
<td>0.73 (0.58, 0.92)</td>
</tr>
</tbody>
</table>

ET, embryo transfer; CI, confidence interval
Crude model: we did not adjust other covariants
Model I: we adjusted female age
Model II: we adjusted female age, fertilization type, infertility type, infertility duration, no. of oocyte retrieved, no. of embryo transferred and D3/D5 embryo transfer.
CI confidence interval

FERTILITY & STERILITY® e155
Clinical pregnancy rate (54.50% vs 63.70%, p = 0.001) were significantly higher with frozen embryo transfer compared to fresh embryo transfer. Variables that were found to be independently associated with clinical pregnancy rate were fresh/frozen embryo transfer, female age and no. of embryo transferred. After adjusting for variables, frozen embryo transfer (0.75 (0.59, 0.95), p = 0.016) was protective factor of clinical pregnancy rate.

CONCLUSIONS: Frozen embryo transfer is better than fresh embryo transfer in GnRH antagonist cycle in normo-responders.

P-121 Tuesday, October 15, 2019 6:30 AM

OBJECTIVE: No study has yet unequivocally established significance of ICM gradation, TE gradation and degree of blastocoel expansion/re-expansion in enhancing live-births. Also, most studies have clubbed results from fresh/ frozen and single/double transfer cycles. We aimed to individually assess the relevance of grades of inner cell mass, trophoderm and degree of post-warm blastocoel re-expansion on live-birth rates exclusively in vitrified-warmed single blastocyst transfer cycles.

DESIGN: Retrospective study of vitrified-warmed cycles involving women (n = 380) undergoing elective single blastocyst transfer. Oocyte donation, Embryo-donation, assisted hatching and preimplantation genetic diagnosis cycles were excluded. Ethics Committee of the centre approved this study. All blastocysts were graded as per Gardner and Souchkodraft method of classification as 1-6 for degree of expansion and grades A/B/C for ICM and TE.

MATERIALS AND METHODS: Natural-cycle endometrial preparation was done with hormone supplementation followed by luteal-phase support with micronized progesterone. Endometrial response (thickness and homogeneity) was noted by ultrasound. Single blastocyst was transferred 3 hours after warming. Pre-vitrification grade of blastocyst was compared with the post-warmed status. β-hCG level measured on day 8 of transfer indicated pregnancy. Positive cardiac activity at sixth week confirmed clinical pregnancy. Live-birth was the primary outcome measure.

RESULTS: Women were classified into Live-birth (LB; n = 172) and non-pregnant (NP; n = 208) groups. Age, BMI, infertility period as well as number of oocytes retrieved, rate of formation of good quality cleavage-stage and blastocyst-stage embryos and survival rates post-warming did not differ significantly between the two groups. Same brand of embryo-transfer catheter and same brand and volume of media was used for transfer. However, the degree of re-expansion was significantly higher in LB group than in NP group (Mean ± SD: 3.7 ± 0.9 and 3.0 ± 0.83, P = 0.0052). The Fisher-Exact test odds ratio for achieving a live-birth with 3-4 degree of re-expansion was 3.0 (p = 0.0011) whereas the odds ratio was much lower (0.32) with any other degree of re-expansion. Although ICM grade was higher/better in Live-birth group than in non-pregnant group, the difference remained statistically non-significant (Odds ratio 1.23, p = 0.82). No significant difference was observed in the TE grades between the two study groups (p = 0.2). A notable difference was also observed in the endometrial echopattern (p = 0.03) although the endometrial thickness remained comparable between the two results. Groups suggest that, post-warming degree of re-expansion is the single most decisive factor for live birth rates in such cycles.

CONCLUSIONS: Blastocoel re-expansion to expanded 3/4 stage is a superior morphological indicator than ICM & TE grades for better live-birth rates in vitrified-warmed or blastocyst transfer cycles. However, larger multicentric trials are required to unequivocally establish it as a robust prognosticator of live-birth rates in vitrified-warmed ET cycles.

SUPPORT: None.

P-122 Tuesday, October 15, 2019 6:30 AM
DOUBLE EMBRYO TRANSFERS OF POOR QUALITY BLASTOCYSTS GIVE THE SAME LIVE BIRTH RATE AS A SINGLE EMBRYO TRANSFER OF A GOOD QUALITY BLASTOCYST. Mako Hanada. Associate, Ogikubo hospital Niji clinic, Tokyo, Japan.

OBJECTIVE: How can embryo transfers of poor quality blastocysts lead to good results?


MATERIALS AND METHODS: Using Gardner’s blastocyst grading scale, embryos grade A or B were evaluated as good quality blastocyst and embryos containing C evaluation as poor quality blastocyst. We analyzed the live birth rate, miscarriage rate and multiple pregnancy rate of single embryo transfer of good quality blastocyst (SBT-G), single embryo transfer of poor quality blastocyst (SBT-P), double embryo transfers of good quality blastocysts (DBT-GG), double embryo transfers of good and poor quality blastocysts (DBT-GP) and double embryo transfers of poor quality blastocysts (DBT-PP).

RESULTS: 1379 cycles were included in the study. The mean age (SD) of the whole study population was 37.8 years (±4.0 years). 1020 cycles in women who received SBT-G, 167 cycles in women who received SBT-P, 56 cycles in women who received DBT-GG, 74 cycles in women who received DBT-GP and 62 cycles in women who received DBT-PP. There was no significant difference in the age of each group. The live birth rate (SBT-G: 21.4%, SBT-P: 12.6%, DBT-GG: 32.1%, DBT-GP: 23.0%, DBT-PP: 19.4%) was significantly higher in the SBT-G group and the DBT-GG group than in the SBT-P group. The miscarriage rate (SBT-G: 28.3%, SBT-P: 24.2%, DBT-GG: 17.4%, DBT-GP: 35.7%, DBT-PP: 36.4%) tended to be lower in the DBT-GG, but with no significant difference between each group. The multiple pregnancy rate (SBT-G: 2.9%, SBT-P: 0.6%, DBT-GG: 21.7%, DBT-GP: 3.6%, DBT-PP: 13.6%) was significantly higher in the SBT-G group and the DBT-GG group than in the SBT-P group. And the multiple pregnancy rate was significantly higher in the DBT-PP group than in the SBT-G group.

CONCLUSIONS: In embryo transfer using poor quality blastocysts, the live birth rates of DBT-GP and DBT-PP were almost the same. The live birth rate of SBT-G was also almost the same. From this, it was found that there is no benefit in DBT-GP, in which the live birth rate does not rise despite double embryo transfers, and only the miscarriage rate rises. In addition, although the live birth rate is low if only one poor quality blastocysts is used, the live birth rate is almost equivalent to that of SBT-G and DBT-GP by performing double embryo transfers of poor quality blastocysts. It was found that DBT-PP is an effective method when there are only poor quality blastocysts. However, Double embryo transfers raise the multiple pregnancy rate, so careful consideration is necessary.

P-123 Tuesday, October 15, 2019 6:30 AM
THE IMPACT OF TEMPERATURE AND RELATIVE HUMIDITY ON OUTCOMES OF OVARIAN STIMULATION AND IN VITRO FERTILIZATION USING AN OOCYTE DONATION COHORT. Audrey J. Gaskins, ScD, Zsolt Peter Nagy, MD, PhD, Sarah M. Capelouto, MD, Daniel B. Shapiro, MD, Jessica B. Spencer, MD, MSc, Heather S. Hopp, MD. “Emory University, Atlanta, GA; Reproductive Medicine Associates, Atlanta, GA; “The University of Texas, Southwestern Medical Center, Dallas, TX.

OBJECTIVE: To determine the effect of temperature, humidity, and precipitation prior to oocyte retrieval on ovarian stimulation outcomes among oocyte donors and early in vitro fertilization (IVF) outcomes among recipients.

DESIGN: Retrospective cohort study of data from a frozen donor oocyte bank from 2008 to 2015.

MATERIALS AND METHODS: A total of 350 oocyte donors residing in the metro-Atlanta area underwent 553 ovarian stimulation cycles with an antagonist protocol. Mature oocytes were vitrified and later thawed in individual cohorts among 989 unique recipients. Mean temperature, relative humidity, and precipitation levels were calculated for the 90 days prior to oocyte retrieval using information from the Parameter-elevation Regressions on Independent Slopes Model. The associations between these climate variables and outcomes of ovarian stimulation (e.g. estradiol level at trigger and number of total and mature oocytes retrieved) and early IVF outcomes (e.g. % fertilized oocytes and % usable embryos) were modeled using generalized estimating equations adjusted for donor age, body mass index (BMI), race, retrieval year.

RESULTS: The mean (standard deviation) age and BMI among oocyte donors was 25.4 (2.8) years and 22.6 (2.5) kg/m². Approximately 25% were racial/ethnic minorities and all were non-smokers. Donors exposed to warmer temperatures prior to oocyte retrieval had significantly higher

Vol. 112, No. 3, Supplement, September 2019
stratified levels at trigger (p-trend=0.04) despite no differences in the total dose of gonadotropins. Specifically, women in the highest quartile of temperature (76.0-81.4°F) had an average estradiol level of 3761 pg/mL (95% CI 3403, 4119) compared to 3341 pg/mL (95% CI 3034, 3647) among women in the lowest quartile (38.6-49.6°F). There was no impact of temperature for oocyte counts. Lower temperatures and higher humidity prior to oocyte retrieval were associated with a slightly higher percentage of usable embryos after oocyte warming and fertilization (p-trend=0.03 and 0.04). Greater mean precipitation prior to oocyte retrieval was associated with a slightly higher percentage of mature oocytes retrieved (p-trend=0.06) but was not associated with any of the IVF outcomes.

CONCLUSIONS: While warmer temperatures prior to oocyte retrieval were associated with higher estradiol levels at trigger, the resulting oocytes resulted in a lower percentage of usable embryos once thawed and fertilized among recipients. Vitrified oocyte donation represents an excellent model to determine the impact of environmental exposure such as climate variables on IVF outcomes given that exposures experienced by the donor and recipient are uncorrelated in time and space.

SUPPORT: Supported in part by R01ES026648 from the NIEHS.

P-124 Tuesday, October 15, 2019 6:30 AM

TIMING OF BLASTOCYST DEVELOPMENT IS THE SOLE PREDICTOR OF POSITIVE PREGNANCY OUTCOME IN ADVANCED MATERNAL AGE PATIENTS FOLLOWING SINGLE EUPLOID BLASTOCYST TRANSFER. Mandy G. Katz-Jaffe, Ph.D., Annette Mats, MS, Amy Bartoli, MS, Diane Klepacka, MS, Daniella Young, MS, Emily Anderson, BS, Michelle M. Denomme Tignanelli, PhD, William B. Schoolcraft, MD. Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Improving embryo quality and selection is imperative to achieve a shorter time to pregnancy and successful live birth outcome, specifically for women of advanced maternal age (AMA). Preimplantation genetic testing for aneuploidy (PGT-A) allows for selection of euploid embryos, beneficial for this older population that are at increased risk for oocyte aneuploidy. The purpose of this study was to identify effective predictors of reproductive outcomes for AMA patients in conjunction with a euploid single embryo transfer (SET).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: AMA patients (≥ 38 years; n=847) underwent routine oocyte retrieval, ICSI blastocyst biopsy, PGT-A and subsequent euploid SET at a single large infertility clinic. Patients presented with various infertility diagnoses and without significantly compromised ovarian reserve. Reproductive outcomes were divided into three groups; successful live birth (n=504), positive implantation followed by pregnancy loss (ultrasound + hCG; n=81) and negative/biochemical (negative, or rise and subsequent direct fall of hCG; n=262). Statistical analyses included Chi Square test for independent samples and Mann-Whitney U tests where appropriate, with significance at P<0.05.

RESULTS: Maternal age at oocyte retrieval was significantly associated with the likelihood of an embryo transfer, as the percent of aneuploid-only cycles increased significantly with age; 38-40 years (20%), 41-42 years (46%), 43+ years (76%; P<0.0001). Reproductive outcomes following euploid SET were not associated with any of the following: maternal age at oocyte retrieval (mean 40.0 years), total number of oocytes retrieved, total number of MII oocytes, number of blastocysts available for biopsy, % euploid blastocysts, or the inner cell mass (ICM) and trophoderm grade. Pregnancy outcomes following euploid SET were only significantly associated with the timing of blastocyst development and the appearance of the ICM (P<0.0001). Euploid blastocysts that resulted in a positive/biochemical outcome were significantly over-represented by slower blastocyst development (52.3%) compared to those with live birth (37.5%) and pregnancy loss (38.3%) (P<0.0001). Remarkably, no differences were observed between successful live birth and positive implantation followed by pregnancy loss for any parameters analyzed. Interestingly, a second euploid SET for AMA patients with prior pregnancy loss resulted in 58.3% successful live births (n=36), comparable to the overall first SET live birth rate (59.5%; ns).

CONCLUSIONS: The timing of blastocyst development and the appearance of the ICM was the sole predictor of positive pregnancy in AMA patients following a euploid SET, and thus should be highly considered for euploid blastocyst selection to achieve the fastest time to pregnancy. Further investigations are essential to identify potential predictors of euploid pregnancy loss, and the stochastic occurrence of this adverse outcome.

SUPPORT: None.

P-125 Tuesday, October 15, 2019 6:30 AM

AUTOMATED HALO IDENTIFICATION: A NOVEL PREDICTIVE FEATURE FOR IVF SUCCESS IDENTIFIED THROUGH AN ARTIFICIAL INTELLIGENCE AI ALGORITHM. Marcos Meseguer, PhD,a Ron Uriel Mao, BSc,b Lucia Alegre, PhD,a Raquel Del Gallego, PhD,b Antonio Pellicer, MD, PhD,b Daniel S. Seidman, M.D, MMS,c Daniella Gilboa, MSc,b cIVRMA Global, Valencia, Spain; bAIVF, Tel Aviv, Israel; cThe Foundation For Embryonic Competence, Basking Ridge, NJ; dDepartment of Obstetrics and Gynecology Sheba Medical Center affiliated to The Sackler Faculty of Medicine, Tel Aviv, Israel.

OBJECTIVE: To identify in fertilized oocytes previously unrecognized predictive features for live birth following IVF treatment that can apparently be revealed only by an advanced novel AI algorithm.

DESIGN: The study used AI to analyse TL videos of embryos in their pronuclei stage.

MATERIALS AND METHODS: We analyzed video images of 123 fertilized embryos obtained from a time-lapse system Embryoscope. Of the 123 videos, 111 were clear enough for analysis. All embryos analyzed were graded as Top-Graded embryos and were transferred back to the uterus. Of these embryos 88 (71.5%) successfully implanted and 45 (36.6%) resulted in a live birth.

Using a machine learning algorithm, we were able for the first time to characterize a previously unrecognized feature, the pale cytoplasm creating a "halo" surrounding the nucleus of the fertilized oocyte. The measurable amount of this halo over a range of images was compared to a set threshold. The resulting yes/no decision was assessed in relation to the likelihood of the embryo to implant successfully.

We calculated a relative brightness/smoothness measure, comparing each image to a reference image of the same embryo 7 hours earlier. These measurements were compared to an internal threshold obtained experimentally, with the result reported as above threshold (significant halo identified) or below threshold (no significant halo identified).

RESULTS: The halo was identified in 42% of 49 videos of embryos that successfully implanted versus in only 17% of embryos that failed to implant. There was no difference in the proportion of embryos that implanted, where a halo was identified, according to whether they carried out to a live birth or miscarried.

Using the halo to predict successful implantation of a Top-Graded transferred embryo had a sensitivity of 42% and a specificity of 83%, with a positive predictive value of 85% and a negative predictive value of 46%.

CONCLUSIONS: An AI algorithm identified in video images of fertilized oocytes a previously unrecognized feature that is associated with a high positive predictive value for subsequent successful implantation. The Automated Halo Identification may help improve embryo selection and result in higher live birth rates.

P-126 Tuesday, October 15, 2019 6:30 AM

HIGHER CUMULATIVE LIVE BIRTH RATES (CLBR) ARE EXPECTED WITH A FREEZE-ALL POLICY AS COMPARED TO A FRESH EMBRYOTRANSFER POLICY, WHEN MORE THAN TWO BLASTOCYSTS ARE AVAILABLE. Petroula Tatsi, MSc,a Tatiana Chartomatsidou, MSc,a Christina Vlachou, MSc,a George Michos, MD, PhD,a Robert Najdecki, MD, PhD,a Evangelos Papanikolau, MD, PhD,a Eros Nikitos, MSc,a Evangelia Timotheou, MSc,a aAssisting Nature, Center of Assisted Reproduction and Genetics, Thessaloniki, Greece; b3rd Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Thessaloniki, Greece; cInstitute of Life, Athens, Greece.

OBJECTIVE: The purpose of the study is to evaluate if there is any advantage in terms of pregnancy expressed as CLBR between patients having at least 2 blastocysts, who follow Freeze-all strategy and patients who have first a fresh ET and then subsequent frozen-thawed ETs (FET).

DESIGN: This is a prospective observational study, which includes two groups of patients; Group FRALL: couples which followed freeze-all Policy (no fresh ET) and up to 3 FET and Group FRESH: couples which completed one fresh ET and two subsequent FET. All couples had at least two blastocysts available for ET.

MATERIALS AND METHODS: Women included in the study were younger than 40 and had at least 4 blastocysts available. Exclusion criteria were: Preimplantation Genetic Testing (PGT), Testicular Sperm Extraction (TESE) cycles or poor responders (oocytes <4). Study was performed

FERTILITY & STERILITY®
e157
between 2017 and 2018 in Assisting Nature, Centre of Assisted Reproduction and Genetics, Thessaloniki, Greece. FRALL-Group included 87 couples with a mean female age of 32.8 years, while FRESH-Group included 86 women with an average age of 33.1. The Controlled Ovarian Stimulation (COS) was based in an antagonist protocol.

RESULTS: The total CLBR was estimated for each group of patients, as well as for each ET separately. X² test was used to compare live birth rates between the two groups. In FRALL-Group the Live Birth Rate after the first FET was 57.5% and in FRESH-Group was 39.5%. The LBR was significantly higher in FRALL-group compared to FRESH-Group after the first ET (frozen versus fresh, \( p<0.05 \)). The total CLBR for all the completed ETs was 81.6% in FRALL-Group and 71.3% in group B. Cumulatively, the live birth rates were again higher for the Freeze-all group though not statistically significant (\( p>0.05 \)).

CONCLUSIONS: The CLBR is higher in patients who follow freeze-all strategy compared to those who undergo fresh and then FET. Our results indicate that in case of blastocyst ETs an artificially prepared endometrium (in a frozen cycle) might be superior than that after a stimulation cycle. This indicates that women considered normal or high responders have better chances of achieving live birth, if they follow Freeze-all policy. With appropriate consultation women do not argue about fresh and frozen ET, and once some criteria met, they are happy to follow our instructions. A cut-off of 2 blastocysts might look favorable into freezing all, however, higher number of cases is required in order to confirm the obtained results.

P-127 Tuesday, October 15, 2019 6:30 AM

IMPACT OF MEIOTIC SPINDLE IMAGING ON FERTILIZATION, EMBRYO DEVELOPMENT, CLINICAL OUTCOME AND MORPHOKINETIC PARAMETERS: AN ANALYSIS OF 415 IN-VIVO MATURED AND 317 IN-VITRO MATURED HUMAN OOCYTE SIBLINGS. Yukiko Nakajo, AS,a Nobuya Aono, Ph.D.,b Hiromitsu Hattori, M.Sc.,c Yusuke Nakamura, BS,b Chiyuri Kumao, BS,b Noriyuki Okuyama, M.Sc.,c Tomoko Hashimoto, M.D., Ph.D.,b Mayumi Toya, M.D., Ph.D.,d Hideki Igarashi, M.D., Ph.D.,d Koichi Kyono, M.D., Ph.D.,d Kyono ART Clinic, Sendai, Miyagi, Japan; e158 ASRM Abstracts Vol. 112, No. 3, Supplement, September 2019

OBJECTIVE: To evaluate the relationship between meiotic spindle imaging of in-vivo and in-vitro matured human oocytes and intracytoplasmic sperm injection (ICSI) outcomes.

DESIGN: This study was a retrospective observational study conducted at Kyono ART Clinic in Japan from September 2012 to January 2019.

MATERIALS AND METHODS: This study included a total of 259 ICSI cycles in which were retrieved six or fewer mature oocytes and at least one immature oocyte. ICSI was performed on matured oocytes immediately after denudation. After denudation, MI oocytes were cultured for 4 hours to allow oocyte maturation. We categorized each sibling MI oocyte into an in-vivo matured oocyte group (n=415 oocytes) and an in-vitro matured oocyte group (n=317 oocytes). Both groups, the oocytes’ meiotic spindles were visualized with a Polscope before ICSI. We compared fertilization rate, embryo development and clinical outcome irrespective of ICM and TE grade. These 810 cycles included a total of 119 fresh blastocyst transfers and 691 frozen-thawed blastocyst transfers. Clinical pregnancy was defined as a visible sac by ultrasound. All embryos were partially hatched at the pre-blastocyst stage.

RESULTS: Blastocyst expansion stages of 4 and 5 had a significantly higher (\( p<0.001 \)) clinical pregnancy rate (67.1% and 59.2%, respectively) compared to the expansion stages of 6 (46.4%). The expansion stages of 2 and 3 do not have a statistical significance/difference compared to the expansion stage 6. The expansion score did not have a correlation with spontaneous abortion (table). Our results contradict previously published work that found no correlation between fully hatched (grade 6) and non-hatching or partially hatched blastocysts (Rodriguez-Purata et al., 2016).

CONCLUSIONS: Fully hatched (grade 6) euploid blastocysts had a significantly lower clinical pregnancy rate compared to non-hatching and partially hatched blastocysts (Rodriguez-Purata et al., 2016). This was in agreement with our findings. The non-hatching blastocysts had a significantly lower clinical pregnancy rate compared to fully hatched and partially hatched blastocysts. Artificial hatching could impact expansion rates at biopsy. Future research could focus on determining whether the implantation potential is compromised due to the biopsy procedure itself.

RESULTS: The mean patient age was 39.0±4.1 years (range: 25-45 years). The spindle was detected in 85.3% (325/381) and 22.1% (70/317) of the in-vivo and in-vitro matured oocytes, respectively. In both groups, fertilization, blastocyst formation, and good-quality blastocyst rates were significantly higher when spindles were detected (Table). When the spindle was detected, there were no significant differences in fertilization rate or embryo development competence between in-vivo matured and in-vitro matured oocytes.

Also, there was no significant difference in clinical pregnancy rate in each group (Table). In the morphokinetic parameters analysis, there were no significant differences in time points of cell division (tPNI to t8), interval of cell cleavage (CC2 and S2), or incidence of DUC.

CONCLUSIONS: Meiotic spindle imaging may be useful for prediction in both in vitro and in-vitro-matured oocyte development. When meiotic spindle is detected in matured oocytes, developmental competence may not be influenced by whether maturation occurs in vivo or in vitro.

P-128 Tuesday, October 15, 2019 6:30 AM

CORRELATION BETWEEN BLASTOCYST STAGE OF EXPANSION AND CLINICAL OUTCOME: A RETROSPECTIVE ANALYSIS OF 810 SINGLE EUPOID BLASTOCYST TRANSFER CYCLES AT A SINGLE IVF CENTER. Vikrant V. Reddy, M.Sc.a Qianning Zhao, M.Sc.a Odgerel Badamjav, M.Sc.a Jennifer Dasg, M.Sc.a Jeong Hee Moon, Ph.D.a Yimin Qin, Ph.D.a Ali Masoudi, BS,a Kenney Tuyen, BS,b Barry R. Behr, Ph.D.a Stanford University Medical Center (LPCH), Sunnyvale, CA; cStanford Fertility and Reproductive Medicine Center (LPCH), Sunnyvale, CA; dStanford Fertility and Reproductive Medicine Center, Sunnyvale, CA.

OBJECTIVE: To determine whether a correlation exists between the stage of expansion of an euploid blastocyst and clinical outcome.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: A total of 810 PGT-A euploid single blastocyst transfer cycles between 2014 and 2018, graded using the Gardner criteria (Gardner et al., 1999), were retrospectively analyzed at a single IVF center. The relationship between the stage of euploid blastocyst expansion and clinical outcome irrespective of ICM and TE grade. These 810 cycles included a total of 119 fresh blastocyst transfers and 691 frozen-thawed blastocyst transfers. Clinical pregnancy was defined as a visible sac by ultrasound. All embryos were partially hatched at the pre-blastocyst stage.

RESULTS: Blastocyst expansion stages of 4 and 5 had a significantly higher (\( p<0.001 \)) clinical pregnancy rate (67.1% and 59.2%, respectively) compared to the expansion stages of 6 (46.4%). The expansion stages of 2 and 3 do not have a statistical significance/difference compared to the expansion stage 6. The expansion score did not have a correlation with spontaneous abortion (table). Our results contradict previously published work that found no correlation between fully hatched (grade 6) and non-hatching or partially hatched blastocysts (Rodriguez-Purata et al., 2016).

CONCLUSIONS: Fully hatched (grade 6) euploid blastocysts had a significantly lower clinical pregnancy rate compared to non-hatching and partially hatched blastocysts (Rodriguez-Purata et al., 2016). This was in agreement with our findings. The non-hatching blastocysts had a significantly lower clinical pregnancy rate compared to fully hatched and partially hatched blastocysts. Artificial hatching could impact expansion rates at biopsy. Future research could focus on determining whether the implantation potential is compromised due to the biopsy procedure itself.

TABLE. Fertilization rate, embryo development and clinical outcomes

<table>
<thead>
<tr>
<th>Meiotic spindle in in-vivo matured oocytes</th>
<th>Meiotic spindle in in-vitro matured oocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detected</td>
<td>Not detected</td>
</tr>
<tr>
<td>No. of oocytes</td>
<td></td>
</tr>
<tr>
<td>325</td>
<td>56</td>
</tr>
<tr>
<td>45.2% (19/42)</td>
<td>28.6% (4/14)</td>
</tr>
<tr>
<td>34.3% (12/35)</td>
<td>17.7% (17/96)</td>
</tr>
<tr>
<td>20.1% (41/204)</td>
<td>0.0% (0/14)</td>
</tr>
<tr>
<td>0.0% (0/96)</td>
<td></td>
</tr>
<tr>
<td>8.6% (3/35)</td>
<td></td>
</tr>
<tr>
<td>16.7% (3/18)</td>
<td>8.0% (2/25)</td>
</tr>
</tbody>
</table>

\* \( p<0.05 \)
The field of IVF has focused on embryo selection and PGT-A. Recent techniques have enhanced the selection process, allowing for the identification of embryos with potential for better pregnancy outcomes.

**REFERENCES:**

**P-129 Tuesday, October 15, 2019 6:30 AM**

**PREGNANCY OUTCOMES OF FROZEN THAWED CLEAVAGE STAGE EMBRYOS WITH OR WITHOUT EXTENDED CULTURE TO BLASTOCYST STAGE.** Cindy Chan, MD, Huang Yung Ling, MS, Chi-Huang Chen, MD, PhD, Chi-Ruey Tzeng, MD, MPH. Taipei Medical University Hospital, Taipei, Taiwan.

**OBJECTIVE:** Evaluate pregnancy outcomes of frozen thawed cleavage stage embryos with or without extended culture to blastocyst stage.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** Frozen embryo transfer (FET) cycles from January 2017 to April 2018 that included cleavage stage embryo transfer (D3 FET) were compared to cleavage stage embryos that underwent extended culture after thawing to blastocyst stage before transfer (EC D5 FET) and thawed blastocyst embryo transfer (D5 FET). Pregnancy outcomes such as pregnancy rate, implantation rate, abortion rate and live birth rate were compared. Patients with any of the following were excluded: endometrial thickness less than 0.7 cm, undergoing simultaneous controlled ovarian stimulation or fresh embryo transfer, only day 2/3 embryos available for transfer, or thawing or culture failure.

**RESULTS:** Total of 1182 cycles were reviewed, and, after exclusion, 843 cases with a robust variance estimate. We then combined all variables with a p-value < 0.05 into a multivariable model. Factors predictive of having supernumerary embryos in freeze-all cycles were:

1. Age (< 35) 1.07 (1.02 - 1.13) .037
2. Age (30 – 35) 1.07 (1.02 - 1.13) .037
3. Nulligravida 1.06 (1.01 - 1.15) .037

**CONCLUSIONS:** Several factors are predictive of having supernumerary embryos. Women with AMH > 3 or younger than 35 had more opportunities for frozen transfers such that a selection technique could be applicable.

**REFERENCES:**

**SUPPORT:** None.

**TABLE 1.**

<table>
<thead>
<tr>
<th>Variable (Referent)</th>
<th>Adjusted Risk Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&lt; 35) 35 - 37</td>
<td>1.02 (0.99 - 1.05)</td>
<td>.147</td>
</tr>
<tr>
<td>38 - 40</td>
<td>0.96 (0.93 - 0.99)</td>
<td>.017</td>
</tr>
<tr>
<td>41 - 42</td>
<td>0.87 (0.82 - 0.91)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>4+</td>
<td>0.70 (0.64 - 0.76)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BMI (18.5 – 24.9) &lt; 18.5</td>
<td>1.03 (0.97 - 1.09)</td>
<td>.340</td>
</tr>
<tr>
<td>25.0 - 29.9</td>
<td>0.96 (0.93 - 0.99)</td>
<td>&lt;.006</td>
</tr>
<tr>
<td>&gt; 30</td>
<td>0.97 (0.94 - 1.00)</td>
<td>.063</td>
</tr>
<tr>
<td>AMH (1.0 – 3.0) &lt; 1.0</td>
<td>0.90 (0.86 - 0.95)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&gt; 3.0</td>
<td>1.02 (0.99 - 1.05)</td>
<td>.153</td>
</tr>
<tr>
<td>Nulligravida</td>
<td>1.06 (1.04 - 1.09)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Prior fresh transfer (0)</td>
<td>0.94 (0.91 - 0.98)</td>
<td>.001</td>
</tr>
<tr>
<td>2</td>
<td>0.93 (0.88 - 0.97)</td>
<td>.003</td>
</tr>
<tr>
<td>3</td>
<td>0.93 (0.86 - 0.99)</td>
<td>.037</td>
</tr>
<tr>
<td>4+</td>
<td>0.97 (0.90 - 1.04)</td>
<td>.333</td>
</tr>
<tr>
<td>Prior frozen transfer (0)</td>
<td>1.07 (1.02 - 1.13)</td>
<td>.004</td>
</tr>
<tr>
<td>2</td>
<td>1.07 (1.01 - 1.15)</td>
<td>.034</td>
</tr>
<tr>
<td>3</td>
<td>1.13 (1.04 - 1.23)</td>
<td>.004</td>
</tr>
<tr>
<td>4+</td>
<td>1.09 (0.99 - 1.21)</td>
<td>.084</td>
</tr>
<tr>
<td># eggs retrieved 4 - 8</td>
<td>5.46 (4.56 - 6.54)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>9 - 13</td>
<td>8.42 (7.05 - 10.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>14 - 20</td>
<td>10.3 (8.59 - 12.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>21 - 45+</td>
<td>11.0 (9.18 - 13.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sperm source (partner)</td>
<td>All mature</td>
<td>1.22 (1.18 - 1.27)</td>
</tr>
<tr>
<td>Donor</td>
<td>Some mature</td>
<td>1.18 (1.11 - 1.26)</td>
</tr>
</tbody>
</table>

**FERTILITY & STERILITY® e159**
LIVE BIRTH DATA FROM 498 ELECTIVE AND NON-ELECTIVE AUTOLOGOUS OOCYTE THAW CYCLES (2009-2018). Anne Martini, DO,† Rachel Horowitz, MD,§ Kate Devine, MD,*, Jui-He Tsai, PhD,† Micah J. Hill, DO,† Alan H. DeCherney, MD,*, Joseph Doyle, MD,† Caleb Kallen, MD, PhD,§ National Institute of Child Health and Human Development, NIH, Bethesda, MD;§ Shady Grove Fertility and Lankenau Medical Center, Philadelphia, PA;* Shady Grove Fertility, Rockville, MD.

OBJECTIVE: We present live birth data from 498 autologous treatment cycles using frozen/thawed oocytes. We hypothesized that elective oocyte cryopreservation results in higher live birth rates (LBR) than non-elective (onco-fertility, unanticipated lack of sperm, or limited insemination).

DESIGN: Retrospective Cohort.

MATERIALS AND METHODS: We identified all autologous In Vitro Fertilization (IVF) cycles using frozen oocytes (2009-2018). Ovarian stimulation, oocyte freeze/thaw, IVF, intracytoplasmic sperm injection (ICSI), embryo culture/transfer/vitrification were performed using published protocols. Primary outcome was live birth per thaw cycle. Secondary outcomes were stratified by indication for oocyte freezing, age at oocyte retrieval and by utilization of preimplantation genetic testing (PGT). Cumulative LBRs were compared using age-adjusted logistic regression.

RESULTS: In 498 thaw cycles involving 4,554 MII oocytes (average 9.1 oocytes/thaw), oocyte survival and fertilization rates were similar across all ages and indications for freezing (85.7% and 69.5% in aggregate). More than half of patients had a fresh embryo transfer (ET) and 48% had at least one embryo for vitrification (average 1.7 blastocysts frozen/thaw). Ten percent of thaw cycles had zero embryos for transfer or vitrification. On average, elective egg freezing patients thawed more MIIs (11.4 vs 7.4) and generated more vitrified blastocysts compared to grade 3 embryos (16.1% vs 7.7%, p = 0.048). The live birth rates were comparable by origin of blastocysts. Patients were statistically older and had lower anti-Mullerian hormone (AMH) levels than the control group, composed of >270 poor quality D3 embryos. Blastulation rates were statistically lower than in the control group (23.5% vs. 37%, p > 0.005). The rates of usable blastocysts and rates of live birth did not differ between the two groups. In the control group, the rate of usable blastocysts was also higher for slow-developing embryos compared to grade 3 embryos (16.1% vs. 7.7%, p = 0.048).

CONCLUSIONS: Despite the absence of good quality D3 embryos, a cohort composed entirely of "rejected" embryos can result in a transferable blastocyst and live birth. It appears that the high fragmentation rate of blastomeres is associated with a poorer prognosis than the decreased number of cells on D3. This study could improve the counseling of couples facing this situation.
RESULTS: Compared with Group A, the female patients in Group B was younger (31.37 ±4.42 VS 31.95 ±4.63, P<0.05). There was no significant difference in male age, thickness of endometrium, endometrial preparation methods and the proportion of primary infertility patients between Group A and Group B. The rate of single blastocyst transfer (SBT), clinical pregnancy rate (cPR) and implantation rate in Group B were significantly higher than those in Group A (84.2% VS 65.8%, 66.0% VS 40.9%, 62.1% VS 35.1%, P<0.001), and the early miscarriage rate and multiple pregnancy rate in Group B were significantly lower than those of Group A (11.2% VS 17.9%, 8.9% VS 15.1%, P<0.001). The cPR and implantation rate in Group C were significantly higher than those in Group D (55.3% VS 37.3%,44.8% VS 32.6%, P<0.001). No significant differences were found between Group C and Group D in terms of early miscarriage rate and multiple pregnancy rate. The rate of SBT, cPR and implantation rate in Group B were significantly higher than those in Group C (84.2% VS 61.2%, 66.0% VS 55.3%,62.1% VS 44.8%, P<0.05), and the early miscarriage rate in Group B was significantly lower than that of Group C (11.2% VS 21.1%, P<0.05).

CONCLUSIONS: Transfer the blastocysts on 5 days, instead of 6 days after ovulation or progesterone use in HRT cycle, could improve the cPR and implantation rate of the blastocysts on day 6 in frozen-thawed cycles. The cPR and implantation rate of blastocysts fertilized on day 5 are significantly higher compared with blastocysts fertilized on day 6, and the early miscarriage rate is lower, no matter the timing to transfer blastocysts on day 6. The Hospital Project of Fujian Provincial Maternity and Children Hospital(grant no.2018YFC10002105).

SUPPPORT: National Key R&D Program of China(grant no.2018YFC10002105).

P-134 Tuesday, October 15, 2019 6:30 AM

DOES THE DAY OF FINAL OOCYTE MATURATION INJECTION PREDICT OUTCOMES IN COUPLES UNDERGOING IN VITRO FERTILIZATION/INTRACYTOPLASMIC SPERM INJECTION — AN ANALYSIS BASED ON AGE AND INDIVIDUAL CONTROLLED OVARIAN STIMULATION PROTOCOL. Abye Aapen, MBBS DRCOG PhD, Amy E. Sparks, PhD, Yunshu Zhou, MS, Karen M. Summers, MPH, CHES, Patrick Ten Eyck, MS PhD, Eyup Hakan Duran, MD University of Iowa, Iowa City, IA.

OBJECTIVE: Optimizing outcomes for assisted conception treatment remains a clinical challenge. Previous studies have evaluated the role of oocyte number, stage and number of embryos transferred, and the endometrium. The goal of this study was to evaluate the impact of treatment cycle duration and the influence of maternal age in individual controlled ovarian stimulation (COS) protocols on predicting live birth outcomes in in-vitro fertilization (IVF) treatment.

DESIGN: Retrospective study using data from a single academic center.

MATERIALS AND METHODS: Demographic and outcome data for 1831 IVF cycles performed between Jan 2014 and Jun 2018 were analyzed. Cycle duration was defined as the number of days of gonadotrophin treatment until the day of final oocyte maturation injection. Live birth rate (LBR) was the primary outcome and logistic regression was used for all models. The main predictor was treatment cycle duration. Cycles were analyzed in total, and in categories of COS protocol used and maternal age (<38 and ≥ 38 years). Secondary outcomes included biochemical and clinical pregnancy. Cycle duration was analyzed as a continuous variable. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, USA).

RESULTS: We included 1314 treatment cycles using autologous oocytes which resulted in fresh embryo transfers, without the use of pre-implantation genetic testing. There were 617 live births with an overall LBR of 47%. A total of 475 (36.1%) utilized a long agonist (LA) protocol, 346 (26.3%) utilized an antagonist protocol with human chorionic gonadotropin (hCG) trigger, 335 (26%) utilized an antagonist protocol with gonadotropin releasing hormone (GnRH) antagonist, 218 (17.5%) utilized a GnRH agonist flare protocol. On analysis of individual protocols, increasing cycle duration was a strong negative predictor for LBR in women <38 using a LA protocol (OR 0.80; 95% CI[0.69-0.92], P=0.001) and also in women ≥38 using an antagonist protocol with hCG trigger (OR 0.72; 95% CI[0.54-0.96], P=0.022). A combined analysis of all treatment protocols and ages also suggested a significant negative association increasing cycle duration with IVF outcome (OR 0.83; 95% CI[0.78-0.89], P<0.001). For other types of COS treatment protocols, increasing cycle duration was not a statistically significant predictor of LBR.

CONCLUSIONS: Our large retrospective study suggests a relationship between IVF cycle duration, individual COS protocol and LBR. Our study while adding evidence to the existing body of evidence on detrimental effects of prolonged ovarian stimulation, can also aid in clinical decision making on an ‘optimal’ day for final oocyte trigger injection based on maternal age and the individual type of COS protocol.

Statistical analysis for other age/treatment combinations: (Protocol, Age, OR, 95%CI, P value)
1. LA ≥38 - 1.02; [0.74-1.40], 0.91
2. Antagonist -hCG <38 - 0.90; [0.78-1.05], 0.17
3. Antagonist -agonist <38 - 0.87 [0.75-1.02], 0.08
4. Antagonist -agonist ≥38 - 0.88 [0.51-2.49], 0.80
5. Flare <38 - 0.98 [0.79-1.22], 0.85
6. Flare ≥38 - 0.98 [0.76-1.25], 0.88


SUPPPORT: Funding support: A statistical analysis for this project was supported by the Clinical and Translational Science Award (CTSA) from the National Center for Advancing Translational Sciences at the National Institutes of Health (NIH).

P-135 Tuesday, October 15, 2019 6:30 AM

ASSISTED HATCHING: IS IT ALL IT’S CRACKED UP TO BE? Charis E. Ng, BHSc, a Marta Wais, MD, b Crystal Chan, MD, MSc. a University of Toronto, Toronto, ON, Canada; bLunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital, Toronto, ON, Canada.

OBJECTIVE: Observational studies show that blastocyst embryos must spontaneously hatch from their surrounding zona pellucida in order to implant. In IVF, assisted hatching (AH) is a laboratory procedure that intentionally breaches the embryo’s zona pellucida prior to transfer. The putative benefit is to augment an embryo’s ability to implant; however, there is still clinical equipoise regarding whether AH improves IVF outcomes, particularly for frozen-thawed embryos at the blastocyst stage. AH has also been associated with an increased risk of monozygotic twinning (MZT), although this is also controversial due to the small sizes of previous studies and the rare nature of this outcome. This study aims to determine the effect of AH on pregnancy outcomes in IVF patients undergoing frozen-thawed blastocyst stage embryo transfers.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All frozen-thawed embryo transfers that occurred at Mount Sinai Fertility between Jan 2013 and Dec 2017 were included. Exclusion criteria included: cancellation of cycle prior to transfer, use of preimplantation genetics testing of the embryo, and ≥ 2 embryos transferred with discordant use of AH. The primary outcome was clinical pregnancy rate. Secondary outcomes included biochemical pregnancy, early pregnancy loss, live birth, and MZT rates. RR ratios, 95% CI, and p-values were calculated.

RESULTS: A total of 2165 transfer cycles were carried out. The AH group (n=1986) had similar biochemical pregnancy (38.7% vs 42.1%, aRR 0.92, CI 0.77-1.10), clinical pregnancy (29.1% vs 30.3%, aRR 0.96, CI 0.76-1.21), early pregnancy loss (43.5% vs 40.9%, aRR 1.06, CI 0.79-1.44), and live birth (19.9% vs 20.5%, aRR 0.97, CI 0.71-1.32) rates when compared to the control. MZT rates were comparable between groups (1.8% vs 1.85%, RR 0.76, CI 0.1-5.95) although the low numbers of events in this outcome limits interpretation. Interestingly, six pairs of dichorionic/diamniotic (di/di) twins resulted from single blastocyst embryo transfers. Subgroup analyses of single embryo transfers (n=1599) demonstrated that AH in embryos with expansion grades ≤3 was associated with a statistically significant decrease in biochemical pregnancy (32.5% vs 44.3%, aRR 0.45, CI 0.23-0.84), and clinical pregnancy (MZT risk vs 32.4%, aRR 0.00, CI 0.00-5.87). There were no statistically significant differences in early pregnancy loss and live birth rate in this population, nor any pregnancy outcomes for embryos with expansion grades of 4.

CONCLUSIONS: This study demonstrates that AH of frozen-thawed blastocyst stage embryos resulted in similar outcomes to transfers that did not use this technique. AH was not associated with any improvement in pregnancy.
outcomes including implantation, clinical pregnancy, early pregnancy loss, and live birth. The identification of d/di twins from single blastocyst embryo transfers challenges previously held notions that d/di MZT only occurs from division prior to the blastocyst stage. This study also demonstrates that AH of embryos with expansion grades ≤5 may be associated with poorer rates of beta pregnancy and clinical pregnancy.

P-136 Tuesday, October 15, 2019 6:30 AM

RELATIONSHIP BETWEEN THE PREGNANCY AND THE SIZE OF ARRESTED BLASTOMERE DERIVED FROM ABNORMAL CYTOKINESIS IN BLASTOCYST TRANSFER CYCLES. Hiroki Izumi, M.S.; Manabu Satoh, Ph.D.;1 Shu Hashimoto, Ph.D.; Yoshihara Nakaoka, MD, Ph.D.;2 Yoshiharu Morimoto, MD, PhD. 1IVF NAMBA CLINIC, Osaka, Japan; 2Reproductive Science, Osaka City University Graduate School of Medicine, Osaka, Japan; 3HORAC Grand Front Osaka clinic, Osaka, Japan.

OBJECTIVE: From observation continual morphological changes, about 25% of normally-fertilized ova shows abnormal cytokinesis at 1st mitosis (AC). The abnormal cytokinesis is a marker to be eliminated from transfer due to chromosomal aberration and low developmental competence. However, it has been shown that a few AC embryos develop to morphologically-good blastocysts, showing implantation potential comparable to blastocysts derived from normally-cleaved embryos. Chromosome abnormality of blastocysts derived from AC-embryos is equivalent to that of blastocysts derived from normally-cleaved embryo. Some of infertility couples have only morphologically-good blastocysts, showing abnormal cytokinesis at 1st mitosis.

DESIGN: Clinical research

MATERIALS AND METHODS: Retrospective study of single blastocyst transfer (vitriified-warmed 415 blastocysts) between February 2018 and January 2019 were conducted. Blastocysts were separated three groups: embryos which underwent normal cytokinesis at both 1st and 2nd mitoses (control; n=108), embryos which had abnormal cytokinesis at 1st mitosis (1st abnormal; n=108) and embryos which had abnormal cytokinesis at 1st and 2nd mitoses (2nd abnormal; n=108). Blastocysts developed from AC embryos were classified according to the diameter of arrested blastomere (30 and greater than 30 mm: SAB and over 30 mm: LAB). Morphological changes of embryos have been recorded using a commercial time-lapse incubator (CCM-IBIS, ASTEC). Cleavage patterns and the diameter of arrested blastomeres were determined by time-lapse data analyzing. Blastocyst quality were scored by blastocyst score quality score (BQS) according to the Gardner grading system. Clinical pregnancy and miscarriage rates were compared. Tukey-Kramer, t- and chi-squared tests were used for statistical analysis

RESULTS: There was no significant difference in pregnancy rates (control: 50.4%, 1N: 67.8%, 1A: 44.4%) after single blastocyst transfer and miscarriage rates (control: 22.7%, 1N: 25.0%, 1A: 22.9%) among 3 groups. The BQS (26) of control blastocysts was significantly higher than 1N (18) and 1A (19, P < 0.05). Pregnancy rates of SAB in 1N was significantly higher than that of LAB (64.9% vs. 25.0%, P < 0.05). Pregnancy rates of SAB in 1A was significantly higher than that of LAB (50.0% vs. 12.5%, P < 0.05). Miscarriage rates of SAB in 1N was significantly lower than that of LAB (4.2% vs. 100%, P < 0.05). Miscarriage rates of SAB in 1A was significantly lower than that of LAB (19.6% vs. 100%, P < 0.05).

CONCLUSIONS: In some of embryos which underwent abnormal cytokinesis at 1st mitosis, abnormal cytokinesis might be occurred by fragmentation and their chromosomes normally separated. In this case, if embryos lost large volume of cytoplasm as fragmentation, their pregnancy potential would be decreased. Observing the size of arrested blastomere can predict pregnancy non-invasively in the case of morphologically-good blastocyst transfer developed from AC embryos.

P-137 Tuesday, October 15, 2019 6:30 AM

EMBRYO SELECT ASSAY: A NON-INVASIVE, DIPSTICK ELISA STRIP ASSAY TO IDENTIFY THE MOST COMPETENT EMBRYO FROM THE COHORT. Elyse Elizabeth Puseck, MD, MS, MBA; Michael J. Kirk, E.L.D., E Antony Anderson, D.H.Sc.; Milica Ivanovic, B.S.; Seth Levant, M.D.; Aleksandra Lazarevic, B.A.; Rajasigam Jayendran, Ph.D, HCLD; Wayne State University, Detroit, MI; Michigan Center for Fertility and Women’s Health, Warren, MI; Aspire Fertility San Antonio, San Antonio, TX; Andrology Laboratory Services, Chicago, IL; Partners in Reproductive Health, Temple Park, IL; Andrologic Inc, Chicago, IL.

OBJECTIVE: Identifying the single best embryo for transfer in vitro fertilization (IVF) frozen embryo transfer (FET) is critical to improve pregnancy rates and decrease multiple gestations. To date, embryo selection has relied on embryo morphology (quality) and sometimes genetic data from pre-implantation genetic testing (PGT). Early in pregnancy, the trophoderm of the developing embryo secretes hCG which enters the maternal blood stream to signal implantation and is detectable in maternal serum about 8-12 days after embryo transfer. Previous work by Dr. Edwards and others have shown hCG levels can be identified in spent culture media (approximately 0.2 mIU/mL on day 2, 0.5 mIU/mL on day 3, and 1.4 mIU/mL on day 5). We developed a dipstick, enzyme linked immunosorbent assay (ELISA) to measure hCG in the spent embryo culture media or spent embryo fluid after the embryo is biopsied. The objective is to identify the most competent embryo with the highest reproductive potential from its cohort—rapidly, non-invasively, and cost effectively.

DESIGN: Experimental.

MATERIALS AND METHODS: The embryo select assay is a dip stick strip assay which is able to quantitatively measure small amounts of hCG using a chemiluminescent substrate and SpectrumX L. We performed 2 studies to evaluate this method. The first study evaluated embryo biopsy fluid to measure the concentration of hCG using this method. The second study evaluated hCG levels from embryo spent media of individual embryos obtained from the same couples to determine if this method can determine the most competent (metabolically functional) embryo with the highest reproductive potential from its cohort. Non-parametric Kruskal-Wallis Test was used to examine differences in hCG levels by embryo grade and PGT outcome. Analyses were performed using SAS (v9.4) and p-values < 0.05 are statistically significant.

RESULTS: For Study 1, we collected fluid from 101 embryo biopsies and measured the hCG levels. Quantitative hCG levels were detected in 60.4% of 101 samples; no hCG in 39.6%. In study 2, individual embryo biopsy fluid media from 51 embryos obtained from 15 couples were assessed to compare with current embryo selection methods (embryo quality and PGT results). 5 embryos had no detectable hCG level, which may indicate the embryos did not make hCG and would not implant. Alternatively, it may indicate that there was dropout in the assay. The other 46 samples had measurable hCG levels. There was no association between hCG levels and embryo grade (p = 0.19) or PGT outcome (p = 0.14).

CONCLUSIONS: Embryos need to make hCG in order to survive as an implanting embryo. This rapid, quantitative, novel “dipstick” assay of individual embryos provides new information regarding the embryo’s metabolic function, independent of current methods (embryo morphology and PGT). Future studies of live birth outcomes using these embryos in FETs will corroborate whether this method helps to identify the best, reproductively competent embryo for transfer.

SUPPORT: None.

P-138 Tuesday, October 15, 2019 6:30 AM

SINGLE VITRIFIED-WARMED BLASTOCYST TRANSFER: WHAT ARE THE BEST PREDICTIVE FACTORS FOR SUCCESS? Evelyne Boulet, B.Sc, Jason Ka Man Au, M.Sc, Jill Anne Mellom, M.Sc, Jon Havelock, MD, Pacific Centre for Reproductive Medicine, Burnaby, BC, Canada.

OBJECTIVE: To determine if the endometrial thickness, the blastocyst expansion, the inner cell mass (ICM) quality and trophectoderm (TE) quality, or day of embryo freezing (5 vs 6), while controlling for the patient age at freezing, is a good indicator in predicting the clinical pregnancy outcome for single vitrified-warmed embryo transfers.

DESIGN: A retrospective observational study.

MATERIALS AND METHODS: From Jan 2016 to Dec 2018, a total of 771 frozen embryo transfers (FETs), where only a single autologous blastocyst was transferred, were analyzed. Exclusion criteria include patients over 42 years of age and cycles with preimplantation genetic testing and gestational carriers. All embryos were vitrified and warmed with the Vitrolife RapidVi/ RapidWarm on Rapid-i24 devices. All embryos were graded with the Gardner’s scoring system immediately prior to transfers. We excluded 38 cycles (4.9%) from the analysis due to their small numbers – blastocyst expansion size-1, size-5, size-6, and embryos frozen on day 7. Continuous variables were analyzed with the student’s t-test and categorical variables with the Pearson’s chi-squared test. The discriminatory ability of each variable was evaluated with the multivariate logistic regression analysis.

RESULTS: 733 FETs were analyzed and divided into 4 groups: positive and negative implantation. The comparison results and the regression analysis results are shown in Table 1. For categorical variables, CFPs were compared between groups while controlling for patient age at freezing. Day 5 frozen embryos had a CPR of 50.3% vs day 6 of 41.2% (P = 0.12). Embryos with size-4 expansion had a CPR of 51.5% vs size-3 of 44.3% vs size-2 of 32.5% (P < 0.003 for
MATERIY OF CUMULUS OOCYTE COMPLEX (COC) PREDICTS THE OUTCOME OF ART. ~ FOCUS ON DYSMATURE ~, Mitsuyoshi Amita, M.D., Ph.D., Eri Ishida, M.Sc., Kuniko Tatsumi, M.Sc, Yoko Yoshitake, M.D., Ryosuke Akino, M.D., Takakazu Saito, M.D., Ph.D. National Center for Child Health and Development, Okura, Setagaya, Tokyo, Japan.

OBJECTIVE: Cumulus oocyte complex (COC) at oocyte retrieval with assisted reproductive technology (ART) can be easily classified in a visual manner by its maturity. We have classified them into three categories, mature, immature, and dysmature, for more than ten years. Dysmature COC is thought to be taken from atretic follicles. Although the classification has been generally used for over three decades, there is little study to identify whether the maturity of COC affect the results of ART, such as fertilization rate, implantation rate, and pregnancy rate. In this study, we present that the maturity of COC at oocyte retrieval may be used as an indicator to predict outcome of ART.

MATERIALS AND METHODS: The infertile patients who underwent in vitro fertilization (IVF) / intracytoplasmic sperm injection cycles between March 2014 and December 2017 and performed frozen / thawed embryo transfer (ET) by August 2018 participated in the study. After institutional review board approved the study and individual patients provided informed consent prior, 292 patients, 527 cycles are investigated. COCs at oocyte retrieval observed with a stereoscopic microscope were classified into three categories, mature (M group), immature (IM group), and dysmature (D group), then following fertilization rates, ET rates, and pregnancy rates of fresh ET cycles or frozen/thawed ET cycles were calculated. Statistical analysis was performed with Chi-square test, P < 0.05 were considered significant.

RESULTS: The total number of COCs retrieved was 2924 (1611 M group, 939 IM group, and 374 D group). The fertilization rate per COC number was significantly higher in M group (63.6%), and lower in D group (36.9%). The rate of fresh ET per COC was significantly higher in M group (8.0%), and lower in D group (3.1%), and there was no pregnancy in D group with fresh ET cycles. The rate of the number of frozen embryos per COC was significantly higher in M group (42.4%), and lower in IM group (33.7%) and D group (19.5%). The pregnancy rate per thawed ET cycle was significantly higher in D group (38.9%) compared to M group (21.6%) and IM group (19.7%).

CONCLUSIONS: The maturity of COC at oocyte retrieval may be used as an indicator to predict outcome of ART. Dysmature COC resulted in poor fertilization rate, ET rate and embryo freezing rate. But, frozen embryo from dysmature COC may not worse in pregnancy rate compared to those from mature COC. SUPPORT: None.
P-141 Tuesday, October 15, 2019 6:30 AM

ENDOMETRIAL THICKNESS IN PREDICTION OF PREGNANCY OUTCOME IN FRESH EGG DONATION CYCLES: A RETROSPECTIVE COHORT ANALYSIS. Jakob Doblinger, MD, Elena Labarta, MD PhD, Ernesto Bosch, MD, PhD. IVIRMA Valencia, Valencia, Spain; IVIRMA, Valencia, Spain.

OBJECTIVE: To analyse the relationship between endometrial thickness and pregnancy outcome in fresh oocyte donation cycles.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: Single centre retrospective cohort analysis of 1928 fresh single embryo transfer oocyte donation cycles. Treatment took place at a private infertility clinic (IVIRMA Valencia, Spain) between January 1st, 2016 and December 31st, 2017. We included women under 50 years old undergoing fresh oocyte-donation treatment in the context of a hormone replacement therapy (HRT) cycle for endometrial preparation. Only women with a normal uterus on the 2D ultrasound and accepting a single transfer of a day 5 blastocyst were included. Only one good quality blastocyst according to the Spanish ASEBIR classification was transferred after 5 days of progesterone administration (Micronized Progesterone, 400 mg/12h. vaginally). We excluded cases in which an endometrial preparation under a natural cycle was performed, when more than one embryo was transferred, or any good quality blastocyst was available.

RESULTS: Mean age was 42.5 ± 4.8 and BMI was 23.0 ± 3.6. The overall live birth rate was 45.6%. The mean endometrial thickness was 8.7±1.7 mm, ranging from 3.0 to 17.0 mm. The distribution by percentiles is as follows: p10=6.9mm; p25=7.5mm; p50=8.5mm; p75=9.5mm; p90=11.0mm. For the purpose of the analysis, patients were categorized in 6 groups defined by percentiles. LBR in women with endometrium ≤ p10, (≤ 6.9 mm), was significantly reduced compared to the rest of the population (36.7% vs 46.2%; p<0.015).

When submitted to a multivariate logistic regression analysis in which all variables related to live birth were included (i.e. age, BMI, number of oocytes, number of fertilized oocytes and number of good quality blastocysts available), endometrial thickness remained as an independent factor related to live birth. An endometrial thickness ≤ 6.9 mm was associated with a significantly reduced probability of live birth compared with patients with an endometrial thickness of 7 mm or more (OR: 0.70; 95% CI: 0.50-0.97).

CONCLUSIONS: Our results indicate a reduction of live birth rate for more than 9% with an endometrial thickness lower than 7 mm. This finding even remains as an independent factor after multivariate logistic regression analysis controlling for all potentially relevant confounders. To our best knowledge this study seems to represent the largest cohort investigating live birth rate in fresh oocyte donation cycles and including only single embryo transfers.


P-142 Tuesday, October 15, 2019 6:30 AM

WHAT IS THE CLINICAL IMPACT OF THE ENDOMETRIAL RECEPTIVITY ARRAY IN PG-T AND OOCYTE DONATION CYCLES? Francisca Martinez, PhD,a Ana Raquel Neves, MD, Marta Devesa, PhD,c Sandra García-Martínez, Scb,d Buenaventura Coroleu, PhD, MD,e Instituto Universitario Dexeus, Barcelona, Spain; fCoimbra Hospital and University Centre, Coimbra, Portugal; gHospital universitario Dexeus, Barcelona, Spain.

OBJECTIVE: Despite the extensive investigation in the field of assisted reproduction, implantation still remains a challenge. The endometrial receptivity array (ERA) has been studied in both implantation failure (IF) and non-IF populations yielding conflicting results. We hypothesized that controlling for the embryonic factor might allow for a more accurate interpretation of the endometrial assessment.

Our aim was to evaluate the influence of the ERA test on the implantation rate (IR) and pregnancy rate (PR) in patients with previous failed euploid embryo transfers (EET) and previous failed oocyte donation embryo transfers (RET). We also compared patients who underwent the ERA test to those who did not.

METHODS: Single centre retrospective study. We conducted an inter-y 2018 analysis of a cohort of 87 patients submitted to fresh EET (n=79) or RET (n=32) who underwent a test and a post-ERA euploid embryo transfer (EET) or oocyte donation embryo transfer (RET) between 2012-2018. Controls were patients with at least 1 previously failed EET (n=119) or 2 failed RET (n=158) who underwent EET or RET during the same period without undergoing an ERA test. Results were compared using a Chi-square test.

RESULTS: There were 98 clinical pregnancies (CP) among 143 EET (14CP among 24 EET in ERA group, and 84 CP among control group) and 114 CP among 190 RET (11CP among 32 ERA group, and 103 CP among control group).

There was no statistically significant difference regarding IR (55.6% [34.6%-76.5%] vs. 65.0% [56.9%-73.1%]) and PR (58.3% vs.70.6%, p=0.238) in the ERA vs. control group. In the EET arm both IR (26.8% [12.3%-41.4%] vs. 57.2% [50.1%-64.3%]) and PR (34.4% vs. 65.2%, p=0.001) were significantly lower in the ERA group. Multivariate logistic regression confirmed the fact that the performance of an ERA test did not significantly influence the IR and PR rates both in EET and RET. In the ERA group, 41.1% patients were non-receptive (NR). No significant difference was found regarding IR or PR in NR vs. receptive patients in both EET and RET arms.

CONCLUSIONS: In our sample, the performance of an ERA test did not improve pregnancy outcomes. Future prospective studies in larger samples are needed to confirm the role of the ERA test in EET and RET.

P-143 Tuesday, October 15, 2019 6:30 AM

INTENTIONAL ENDOMETRIAL INJURY TRYING TO IMPROVE CLINICAL OUTCOMES OF AN OOCYTE DONATION PROGRAM IN PATIENTS WITHOUT RIF. INTERIM ANALYSIS OF A RANDOMIZED CONTROLLED TRIAL. Carmen Vidal, M.D., Ph.D., Juan Giles, M.D., Ph.D., Elena Labarta, M.D. PhD, Gemma Castillon, M.D., Ph.D., Javier Martinez-Salazar, M.D., Laura Fernández, M.D., Yanira Ayllon, Sr., M.D., Manuel Muñoz, M.D., Jose Bellver, M.D PhD, Antonia Tocino, Sr., M.D., Elkin Muñoz, M.D., Ph.D., Antonio Pellicer, M.D. PhD, Nicolas Garrido, PhD# IVIRMA Valencia, Valencia, Spain; #IVI-MA Valencia, Valencia, Spain; #IVI-MA Valencia, Valencia, Spain; #IVI-MA Barcelona, Barcelona, Spain; #IVI- Madrid, Madrid, Spain; #IVI Murcia, Murcia, Spain; #IVIRMA, Las Palmas de GC, Spain; #IVIRMA ALICANTE, Alicante, Spain; #Affiliation not provided; #IVI-MA Sevilla, SEVILLA, Spain; #IVI-MA Vigo, Vigo, Spain; #IVI Foundation, IIS La Fe, Valencia, IIS, Spain.

OBJECTIVE: Oocyte donation program (OD) provides the ideal setting for investigate if endometrial scratching improves 10% the ongoing implantation rate, as the recipient’s endometrial priming guarantees the homogeneity of the endometrium and also the equality of quality of the transferred embryos and limiting the confounding factors.

DESIGN: A multicentric, open-label, randomized, controlled trial has been conducted in a private setting since Oct 2013. Eligible recipients were...
CORTICOSTEROIDS AND ANTIBIOTICS BEFORE ENDOMETRITIS BENEFIT FROM DO PATIENTS WITH A HISTORY OF CHRONIC BLEEDING? Sydney Chang, MD, a Lily Ottenboser, BA, b Sass Wodoslawsky, BA, b Dmitry Gounko, MA, b Joseph A. Lee, BA, b Alan B. Copperman, MD, a Beth McAvey, MD, a Icahn School of Medicine at Mount Sinai, New York, NY; b Reproductive Medicine Associates of New York, New York, NY. OBJECTIVE: Subchorionic hematoma (SCH) is observed in 4-48% of early pregnancies. Although the etiology is unknown, SCH is believed to result from partial detachment of the chorion from the uterine wall, and frequently present with vaginal bleeding (VB). Some studies have suggested that the incidence of SCH is higher in pregnancies that result from in vitro fertilization (IVF), but the mechanism and clinical significance are unclear.

The endometrial lining proliferates under the influence of estradiol (E2) during synthetic preparation for a frozen embryo transfer (FET) cycle. Whether there is an endometrial thickness (EnT) beyond which the endometrium begins to outgrow its blood supply has yet to be discovered. Given that E2 levels are often supraphysiologic and EnT maximized during synthetic preparation, we asked whether there is an association between EnT and the incidence of SCH/VB in pregnancies achieved following single euploid FETs. DESIGN: Retrospective, cohort study.

MATERIALS AND METHODS: The study included patients at a single, academic ART center who achieved a pregnancy following a synthetically prepared single euploid FET cycle from 2012 to 2019. Natural endometrial preparation cycles were excluded. Natural language processing was performed to identify pregnancies complicated by SCH. Blind review of the database was conducted by two independent reviewers to verify data quality. EnT was treated as a continuous variable. The primary outcomes of the study were incidence of SCH and VB. The secondary outcomes were rates of ongoing pregnancy rate/live birth (OP/LB) and clinical pregnancy loss were not significantly different in patients who had not had an EMB (Un-tested), or in patients who were tested for CE and found to be negative. In patients with a history of CE there was a small but significant increase in IUP in Post (n=61, 54%) compared to Pre (n=46, 37%) \(X^2(2, N=238)=9.31\ P<0.05\).

CONCLUSIONS: Overall, treatment with AC was not associated with higher IUP rates. The use of AC did not improve outcomes in patients with a history of CE, and unexpectedly resulted in lower IUP rates.

TABLE 1. Pregnancy outcomes after STEET by treatment with AC (Pre) vs without AC (Post). Results were divided into 3 groups: Untested, CE positive (+CE) vs CE negative (CE-). \(X^2 = Chi Squared, DF = Degrees of Freedom, SIG = significant difference, NS = Non-significant difference.\)

<table>
<thead>
<tr>
<th>All Pre</th>
<th>n</th>
<th>%</th>
<th>All Post</th>
<th>n</th>
<th>%</th>
<th>X2</th>
</tr>
</thead>
<tbody>
<tr>
<td>NP+E</td>
<td>439</td>
<td>23%</td>
<td>NP+E</td>
<td>123</td>
<td>17%</td>
<td>4.23</td>
</tr>
<tr>
<td>IUP</td>
<td>1247</td>
<td>67%</td>
<td>IUP</td>
<td>628</td>
<td>69%</td>
<td>DF = 2</td>
</tr>
<tr>
<td>BP</td>
<td>184</td>
<td>10%</td>
<td>BP</td>
<td>79</td>
<td>9%</td>
<td>NS</td>
</tr>
<tr>
<td>Post +CE</td>
<td>n</td>
<td>%</td>
<td>Post -CE</td>
<td>n</td>
<td>%</td>
<td>X2</td>
</tr>
<tr>
<td>N=126</td>
<td></td>
<td></td>
<td>N=112</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NP+E</td>
<td>80</td>
<td>40%</td>
<td>NP+E</td>
<td>33</td>
<td>31%</td>
<td>2.23</td>
</tr>
<tr>
<td>IUP</td>
<td>46</td>
<td>36%</td>
<td>IUP</td>
<td>61</td>
<td>54%</td>
<td>DF = 2</td>
</tr>
<tr>
<td>BP</td>
<td>29</td>
<td>23%</td>
<td>BP</td>
<td>13</td>
<td>12%</td>
<td>SIG</td>
</tr>
</tbody>
</table>

Support: None.
trial preparation improves IVF outcomes in women suffering from RIF. There was no statistically significant association between EnT at time of FET and incidence of SCH (OR 0.97 [95% CI 0.91-1.03], p=0.32) or VB (OR 0.97 [95% CI 0.93-1.06]) when controlling for oocyte age, BMI, and EnP. There was no difference between rates of OP/LB (89.04 % vs. 86.62 %, p=0.30) or clinical pregnancy loss (10.96 % vs 13.38 %, p=0.63) amongst patients with and without SCH.

CONCLUSIONS: In the largest study to evaluate the association between EnT and SCH using a single euploid FET model, we demonstrated no increase in the incidence of SCH or VB with increasing EnT in synthetically prepared FET cycles. Clinicians can be reassured that patients undergoing synthetic preparation for FET are not being placed at a higher risk for SCH or VB as a result of having a thicker endometrium. While EnT does not appear to be correlated with SCH, future studies that identify risk factors at the molecular level—such as markers of placental invasion—would offer a deeper look at the pathophysiology of SCH and help elucidate interactions at the maternal-fetal interface.


Support: None.

P-144 Tuesday, October 15, 2019 6:30 AM

ENDOMETRIAL PREPARATION WITH ETANERCEPT INCREASES EMBRYO IMPLANTATION AND LIVE BIRTH IN WOMEN SUFFERING FROM IMPLANTATION FAILURE DURING IN VITRO FERTILIZATION.

OBJECTIVE: Repeated implantation failure (RIF) plague many women undergoing in vitro fertilization (IVF). The exact cause and definition are currently under debate. Carrying out >3 failed IVF cycles with the accumulated transfer of at least 8 embryos is considered an initial definition of RIF. Typical RIF patients under 40 years with good ovarian reserve, normal endometrial morphology, normal karyotypes, anti-cardiolipin, and normal lupus anticoagulant as well as common thrombophilias. During implantation, Tumor Necrosis Factor-a (TNFa) stimulates MMP9 for endometrial invasion by the embryo, stimulates the expression of MUC1, gives embryo protection effects on teratogenic stress, and induces COX-2 response. Etanercept, a TNFa antagonist, has been shown to improve pregnancy rates in women with recurrent reproductive failure and with endometriomas. The aim of this study was to determine the effectiveness of etanercept treatment in IVF outcomes in women with RIF.

DESIGN: Single-arm, prospective study.

MATERIALS AND METHODS: Sixty-seven women suffering from RIF were recruited from the Ingenes Institute in Mexico City. All patient underwent a similar IVF protocol. Each woman received Etanercept (4 x 25 mg every 3 days) during endometrial preparation and at embryo transfer (25 mg). IVF outcomes that were assessed were embryo implantation (h-BCH >10 mg/ml at Day 14), the presence of gestational sacs at week 8 by ultrasound, and live birth.

RESULTS: All women reported no side-effects associated with the treatment. 70.1% of the cohort achieved embryo implantation, 67.2% developed gestational sacs; however, the live birth rate was at 44.8%. Frozen cycles (n=26) did perform better than fresh cycles (n=41) for implantation (75.6% vs 61.5%), gestational sac (73.2% vs 57.7%), and live birth rate (48.8% vs 38.5%, respectively); however, these results were not significant.

CONCLUSIONS: Here, we showed that using Etanercept during endometrial preparation improves IVF outcomes in women suffering from RIF.

Support: None.

P-147 Tuesday, October 15, 2019 6:30 AM

CHRONIC ENDOMETRITIS SCREENING IN PATIENTS WHO EXPERIENCE EUPLOID EMBRYO IMPLANTATION FAILURE DOES NOT IMPROVE IVF OUTCOMES AFTER A SUBSEQUENT EUPLOID FET.

OBJECTIVE: Infertile women who experience recurrent implantation failure (RIF) is commonly diagnosed with Chronic Endometritis (CE). Recent studies have shown that CE may affect endometrial decidualization and alter expression of proteins involved in endometrial-embryo receptivity. Therefore, CE is considered as a potential etiology of failed euploid embryo implantation when no other clinical cause is evident. There are limited findings to draw conclusions about the value of performing an endometrial biopsy (EB) for CE screening; especially among patients who have experienced a failed euploid embryo transfer (1). The aim of this study is to assess the clinical benefit of patients who undergo an endometrial biopsy and chronic endometritis screening following a failed euploid embryo transfer and prior to undergoing further ART treatment.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: This study included infertile patients who had failed a euploid embryo transfer and, thereafter, underwent an endometrial biopsy for CE screening, received antibiotic treatment (if indicated), and had a subsequent single euploid embryo transfer from January 2016 to December 2018. Cohorts were segregated as it follows: Group 1: patients that underwent a EB and were diagnosed with CE and received antibiotic treatment; Group 2: Patients who underwent EB and were negative for CE; and Group 3: a control group of patients without an EB. Demographic characteristics and IVF outcomes were compared among cohorts. ANOVA, χ2 test, and an adjusted multivariate regression analysis with a GEE model were used for data analysis.

RESULTS: A total of 1109 patients with a failed euploid FET were included in the analysis, Group 1 (n=124); Group 2 (n=90) and Group 3 (n=985). Significant differences were found in BMI (Group 1: 24.6, Group 2: 24.5, Group 3: 23.5, p=0.01), prior number of euploid FET cycles (1.8, 1.67, 1.55, p=0.006), and days between EB and FET (Group 1: 63.1, Group 2: 94.3, p=0.001). No significant differences were found on implantation rate (69.3%, 71.1%, 64.4%, p=0.5), clinical pregnancy rate (52.4%, 54.4%, 54.8%, p=0.9), live birth rate (LBR) (45.1%, 46.6%, 42.4%, p=0.65) and clinical loss rates (7.2%, 7.7%, 11.3%, p=0.24) among cohorts. After adjusting for age, BMI, AMH, embryo quality and day of embryo biopsy, there was no association between patients who received CE diagnosis (OR 1.5, CI95% 0.8-2.8, p=0.1), and for those who received a normal EB result (OR1.1, CI95% 0.6-1.7, p=0.6) with lower odds of LBR when compared to the control group.

CONCLUSIONS: Understanding the potential advantages of CE screening on embryo implantation outcomes is of critical importance for modern ART specialists. To date there is no high quality evidence to support performing endometrial biopsies for CE screening in patients who experienced a failed euploid implantation.

Our study suggests that undergoing an endometrial biopsy, regardless of results, does not result in improved IVF outcomes in subsequent euploid FETs compared with patients who were not tested for chronic endometritis.


Support: None.

P-148 Tuesday, October 15, 2019 6:30 AM

VALUE OF ENDOMETRIAL ECHO PATTERN TRANSFORMATION AFTER hCG TRIGGER IN PREDICTING IVF PREGNANCY OUTCOME: A PROSPECTIVE COHORT STUDY.

OBJECTIVE: To investigate if the endometrial echo pattern transformation after hCG trigger affect IVF pregnancy outcome.

DESIGN: Prospective cohort study.
MATERIALS AND METHODS: In an academic center for reproductive medicine, a series endometrial echo pattern monitoring were carried out in 146 patients after hCG trigger: hCG day, from 1 through 3 days after ovum pick-up (OPU+1, OPU+2, OPU+3). The endometrial echogenicity value was obtained by ImageJ software. Patients were compared according to their pregnant status. For further analysis, endometrial echogenicity value was sorted into five groups: ≤60%, 61%-70%, 71%-80%, 81%-90%, and >90%. And Clinical pregnancy rate and embryo implantation rate were compared among the five echogenicity groups.

RESULTS: The endometrial echogenicity value was calculated as the ratio of the hyperechogenic endometrial area over the whole endometrial area. The endometrial echogenicity value on OPU+1,2,3 were differed markedly between clinical pregnant group and non-pregnant group (P<0.001). Clinical pregnancy rate and embryo implantation rate had positive relationship with echogenicity value. The ROC curve analysis of endometrial echogenicity for pregnancy showed the area under curve was greatest on OPU+2 (0.738, 0.765, 0.714 respectively). Endometrial echogenicity value on the OPU+2 had the most predictive value, and the cutoff value was 76.5%. The sensitivity was 63.1% and specificity was 82.0%.

Endometrial echogenicity values after hCG trigger in the two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>HCG</th>
<th>OPU+1</th>
<th>OPU+2</th>
<th>OPU+3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant</td>
<td>65</td>
<td>0.54±0.14</td>
<td>0.75±0.12</td>
<td>0.78±0.12</td>
<td>0.81±0.11</td>
</tr>
<tr>
<td>Non-pregnant</td>
<td>65</td>
<td>0.45±0.17</td>
<td>0.67±0.14</td>
<td>0.68±0.14</td>
<td>0.72±0.14</td>
</tr>
</tbody>
</table>

*p value <0.001, <0.001, <0.001

OBJECTIVE: To determine the clinical utility of the Endometrial Receptivity Array (ERA) in women with ≥1 prior failed embryo transfer (ET).

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: This study included 214 women who underwent an ERA biopsy with a subsequent frozen ET between January 2016 and February 2019. Those with a nonreceptive endometrium were exposed to an ERA biopsy with a subsequent frozen ET between January 2016 and February 2019. Those with a nonreceptive endometrium were exposed to an ERA biopsy with a subsequent frozen ET between January 2016 and February 2019. Those with a nonreceptive endometrium were exposed to an ERA biopsy with a subsequent frozen ET between January 2016 and February 2019.

CONCLUSIONS: Women with ≥1 failed ET had a similar prevalence of non-receptive endometrium compared to the reference group. The pregnancy outcomes in a subsequent ET cycle between the two groups were similar. Among women with ≥1 failed ET, adjustment in progesterone exposure for those with non-receptive endometrium resulted in pregnancy outcomes comparable to those with a receptive endometrium. To further clarify the clinical utility of the ERA, studies are needed to compare outcomes in women who underwent the ERA prior to another transfer versus women who opt to proceed directly to the next transfer attempt.

SUPPORT: None.

P-150

WITHDRAWN

P-151 Tuesday, October 15, 2019 6:30 AM

PROGNOSTIC VALUE OF UTERINE NATURAL KILLER (uNK) CELLS DENSITY IN PERI-IMPLANTATION ENDOMETRIUM FROM WOMEN WITH RECURRENT IMPLANTATION FAILURE.

Xiaoyan Chen, PhD. The Chinese University of Hong Kong, Hong Kong, Hong Kong.

OBJECTIVE: CD56+ uterine natural killer (uNK) cells constitute major components in human endometrium and play an important role around the time of implantation. The aim of this study is to investigate the prognostic value of uNK cells density for subsequent pregnancy outcome in women with recurrent implantation failure (RIF) after IVF-ET treatment.

DESIGN: It is a prospective cohort study carried out in a university-affiliated IVF center.

MATERIALS AND METHODS: A total of 59 women with RIF participated in the study. Endometrial biopsies were obtained precisely 7 days after luteinization hormone surge in the natural cycle preceding frozen embryo transfer. Endometrial sections were immunostained for CD56 and cell counting was performed by a standardised protocol. Results were expressed as percentage of positive uNK cell/ total stromal cells.

RESULTS: No significance difference in uNK cell density was observed between women who did not get pregnant (n=31; median 2.2% range 0.3-7.2%) and women who get pregnant (n=28; median 1.9% range 0.2-8.5%). There was also no significant difference in uNK cell density between women who miscarried (n=9; median 2.2% range 1.0-8.5%) and women who had a live birth (n=19; mean 2.0% range 0.2-7.9%) in a subsequent pregnancy.

CONCLUSIONS: Uterine NK cells density in the peri-implantation endometrium is of no predictive value for subsequent pregnancy outcome in women with RIF.

SUPPORT: This study was supported by Hong Kong Health and Medical Research Fund.

P-152 Tuesday, October 15, 2019 6:30 AM

IMPACT OF ENDOMETRIAL PREPARATION IN CRYOPRESERVED-WARMED EMBRYO TRANSFER (FET) CYCLES ON PERINATAL OUTCOME.

Anna Sokalska, MD, PhD, Nathanael C. Koelper, MPH, Charkiea Kalliora, MD, Monica Maingi, MD, Christos Coutifaris, MD, PhD, Suneeata Senapati, MD, MSCE. University of Pennsylvania, Philadelphia, PA.

OBJECTIVE: There is clinical equipoise regarding the safety and superiority of the cryopreserved-warmed (FET) over fresh embryo transfer cycles with respect to perinatal outcomes. Prior studies suggest, that elevated estradiol (E2) level leads to abnormal placentation and preeclampsia (PEC). Recent data demonstrate a potential increased risk of PEC in FET (physiologic E2 level) compared to fresh embryo transfer cycles (supraphysiologic E2 level).

Prior failed ET Reference

<table>
<thead>
<tr>
<th>Group</th>
<th>N=124</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conception</td>
<td>88 (71%)</td>
<td>0.282</td>
</tr>
<tr>
<td>Clinical Pregnancy</td>
<td>74 (60%)</td>
<td>0.643</td>
</tr>
<tr>
<td>Ongoing Pregnancy or Live Birth</td>
<td>54 (44%)</td>
<td>0.265</td>
</tr>
</tbody>
</table>
Specifically, the absence of a corpus luteum may play a role in disorders of placentation, however the mechanism is not well understood. The aim of this study was to evaluate the factors influencing pregnancy and perinatal outcomes in natural FET cycles (nFET) and programmed FET cycles (pFET).

RESULTS: Of 836 GCs, 101 were eligible for inclusion in this study. Average BW of index GC pregnancies was 7.83 lbs (SD 3.01) and 7.68 lbs (SD 1.01) for the GC’s most recent own singleton delivery. Average gestational age at delivery was 39.13 years (SD 0.993) vs. 39.1 (SD 0.993) for the GC’s most recent own singleton delivery. Average BW of singleton births was 7.62 lbs (SD 1.05). While average birth weight of all the GC’s prior singleton deliveries was not correlated with the birth weight of the index GC pregnancy (r = 0.051, P = 0.623), the birth weight of the GC’s most recent own singleton birth was significantly correlated with the birth weight of the index GC pregnancy (r = 0.298, P = 0.003). Birth weight of the index GC pregnancy was not correlated with GC BMI (r = 0.423). Mean gestational age at delivery was significantly shorter (P = 0.003) for singleton births as compared to the birth weight of the index GC pregnancy (P = 0.001).

CONCLUSIONS: While birth weight and gestational age at delivery are likely multifactorial and impacted by both genetic and environmental factors, we found that in singleton GC pregnancies birth weight and gestational age are correlated with birth weight and gestational age of a GC’s last own delivery. This data is of value when counseling both intended parents and evaluating candidacy for potential surrogacy.

EIV OUTCOME PREDICTORS - GESTATIONAL CARRIERS

P-154 Tuesday, October 15, 2019 6:30 AM

CAN BIRTH WEIGHT AND GESTATIONAL AGE AT DELIVERY OF SINGLETON GESTATIONAL CARRIER PREGNANCIES BE PREDICTED BY THE GESTATIONAL CARRIER’S OWN PREVIOUS SINGLETON PREGNANCIES? Rachel S. Mandelbaum, MD, Meghan B. Smith, MD, Jacqueline Ho, MD MS, Kristin Bendikson, M.D., Richard J. Paulson, MD, MS. University of Southern California, Los Angeles, CA.

OBJECTIVE: Gestational carriers (GC) represent a unique population in which to study the effect of assisted reproductive technology on obstetric outcomes, as they are not infertile and have usually had favorable obstetric outcomes in the past. In GC pregnancies, important questions remain regarding how perinatal outcomes are differentially impacted by the genetic parents versus the GC. This study sought to compare birth weight and gestational age at delivery between a GC’s prior own pregnancies versus the current GC pregnancy.

DESIGN: A retrospective analysis of all GC singleton deliveries from a single agency between 2008-2019.

MATERIALS AND METHODS: Data from a large surrogate agency that consisted of matched GCs and intended parent couples for an index GC pregnancy were reviewed. GCs with a history of or current multiple gestation as well as with a history of or current preterm delivery were excluded. All available birth weights of the GCs own children as well as the gestational age at delivery for the GC’s last own birth were collected. Both average birth weight and last singleton birth weight of the GC’s prior own deliveries were correlated to the birth weight of the index GC pregnancy. Gestational age at delivery of the GC’s last own delivery was compared to the gestational age at delivery for the index GC pregnancy.

RESULTS: Of 836 GCs, 101 were eligible for inclusion in this study. Average age of GCs at time of delivery was 34.9 years (SD 4.4) and their average BMI was 24.3 (SD 3.13). 93 GCs (76.9%) had a prior parity of ≥ 3, and 27 (22.3%) had grand multiparity (≥ 5). The average birth weight of all GC’s prior spontaneously conceived singleton births was 7.83 lbs (SD 3.01) and 7.68 lbs (SD 1.01) for the GC’s most recent own singleton delivery. Average BW of index GC pregnancies was 7.62 lbs (SD 1.05). While average birth weight of all the GC’s prior singleton births was not correlated with the birth weight of the index GC pregnancy (r = 0.051, P = 0.623), the birth weight of the GC’s most recent own singleton birth was significantly correlated with the birth weight of the index GC pregnancy (r = 0.298, P = 0.003). Birth weight of the index GC pregnancy was not correlated with GC BMI (r = 0.423). Mean gestational age at delivery was similar between the GC’s last own singleton delivery and the index GC pregnancies (mean 39.1 (SD 0.993) vs. 39.1 (SD =0.983), P<0.001). Gestational age at delivery of the GC’s last own singleton pregnancy was also significantly associated with the gestational age at delivery for the index GC pregnancy (P<0.001).

CONCLUSIONS: While birth weight and gestational age at delivery are likely multifactorial and impacted by both genetic and environmental factors, we found that in singleton GC pregnancies birth weight and gestational age are correlated with birth weight and gestational age of a GC’s last own delivery. This data is of value when counseling both intended parents and evaluating candidacy for potential surrogacy.

P-155

WITHDRAWN
OBJECTIVE: Published data suggest that clinical pregnancy and live birth rates are higher in cycles using gestational carriers (GC) compared to non-GC GC IVF cycles. This data includes fresh and frozen, Day 3 and Day 5 transfers of both tested and untested embryos, preventing effective isolation and evaluation of the uterine factor. Studies to date have not evaluated clinical outcomes between GC and non-GC GC euploid elective single embryo transfers (eSETs) in programmed frozen embryo transfer (FET) cycles. Our objective was to compare clinical outcomes of euploid eSETs in programmed FET cycles in GCs with non-GC cycles.

RESULTS: A total of 115 GC and 428 non-GC FET cycles met inclusion criteria. There was no statistically significant difference in embryo day (63% Day 5 vs GC vs 69% Day 5 for non-GC, p=0.39) between the GC and non-GC GC FET groups. Statistical analysis was performed using the student t-test and chi-square, where applicable.

RESULTS: The study included patients who underwent embryo transfer of a single Day 5 or Day 6 euploid embryo in a programmed FET cycle at a single IVF center in 2018. Preimplantation genetic testing for aneuploidy was performed following trophoderm biopsy and next generation sequencing. FET cycle outcomes were compared between the GC and non-GC FET groups. Statistical analysis was performed using the student t-test and chi-square, where applicable.

RESULTS: The study included patients undergoing single euploid FET from 2012 to 2019. Endometrial preparation was performed using oral, vaginal, transdermal E2, or a combination of these routes. Cycles involving ovum donation, natural endometrial preparation, intramuscular E2, 21 days of E2 stimulation, or an endometrial thickness <8 mm were excluded. Preimplantation genetic testing for aneuploidy (PGT-A) was performed using quantitative polymerase chain reaction, array comparative genomic hybridization, or next generation sequencing. Supraphysiologic E2 levels were defined as the mean+2SD of natural FET cycles occurring in the same time period. E2 exposure was measured using area under the curve (AUC). Supraphysiologic E2 was calculated as AUC E2 ≥ 7,136.4 pg/mL. The primary outcome of the study was OP/LB. Secondary outcomes included clinical pregnancy (CP) and early pregnancy loss (EPL) rates. Data were evaluated using t-tests, chi-square tests, and general estimating equations.

RESULTS: The study included 3876 single euploid FET cycles from 2707 patients. CP and OP/LB were 61.9% and 54.1% in the physiologic E2, and 53.9% and 47.3% in the supraphysiologic E2 groups, respectively. Unvariable analysis identified BMI and embryo morphology ≥4BB as possible confounders. After controlling for these confounders, there was a decreased CP rate in cycles that had supraphysiologic compared to physiologic E2 levels (OR 0.72 [95% CI 0.52-0.99], p=0.04), but no difference in OP/LB rate (OR 0.78 [95% CI 0.57-1.06], p=0.12) or EPL rate (OR 1.07 [95% CI 0.77-1.41], p=0.47).

CONCLUSIONS: In this study evaluating the association between E2 levels and pregnancy outcomes in a single euploid FET study model, we found that CP, but not OP/LB, is significantly lower in the presence of supraphysiologic E2 levels. This study found no difference in biochemical or clinical pregnancy loss following FET of a euploid embryo in the setting of supraphysiologic E2, suggesting that patients can be reassured that after implantation there is no demonstrable increase in EPL. Future studies might focus on pharmacogenomic markers that can identify women who will respond to equivalent doses of E2 with demonstrable increase in EPL. Future studies might focus on pharmacogenomic markers that can identify women who will respond to equivalent doses of E2 with demonstrable increase in EPL. Future studies might focus on pharmacogenomic markers that can identify women who will respond to equivalent doses of E2 with demonstrable increase in EPL. Future studies might focus on pharmacogenomic markers that can identify women who will respond to equivalent doses of E2 with demonstrable increase in EPL. Future studies might focus on pharmacogenomic markers that can identify women who will respond to equivalent doses of E2 with demonstrable increase in EPL. Future studies might focus on pharmacogenomic markers that can identify women who will respond to equivalent doses of E2 with demonstrable increase in EPL. Future studies might focus on pharmacogenomic markers that can identify women who will respond to equivalent doses of E2 with demonstrable increase in EPL.
(PRG) frozen embryo transfer (FET) cycles; compared to natural (NAT) FETs where estradiol (E2) levels were lower. We analyzed whether E2 levels were associated with an increased incidence of SCH formation.

**DESIGN:** Retrospective cohort study of all single thawed euploid embryo transfer cycles resulting in clinical pregnancy from 1/2016 to 12/2018 at our center.

**MATERIALS AND METHODS:** All single euploid (by Next Generation Sequencing) FETs resulting in clinical pregnancy (presence of a gestational sac) were included. FET cycles with ploidy determined by aCGH, or cycles in which untested, mosaic, or multiple embryos were transferred were excluded. PRG cycles were defined by treatment of oral E2 daily followed by progesterone (P4); either 50-75mg intramuscular in oil or vaginal suppository. A NAT cycle, with and without with luterozole, was defined by monitoring until a dominant follicle reached >18mm and ovulation was confirmed, followed by supplementation with vaginal P4 suppository. SCH was defined as a measurable clot behind the gestational sac at time of luteal ultrasound. The primary outcome was E2 levels in patients with SCH. Statistical analysis included Shapiro-Wilk test for normality for continuous variable, Mann-Whitney U and Fisher’s Exact tests where appropriate. Median values are presented, as continuous variables were not parametric. A p-value <0.05 was considered significant.

**RESULTS:** 1273 cycles were identified and included; 213 NAT and 1060 PRG. Age (p=0.73), endometrial thickness (p=0.65), P4 level on cycle day (CD) 28 (p=0.82) and CD of SCH diagnosis (p=0.78) were similar between groups, though first hCG levels were lower in PRG cycles (196 vs 164 mIU/mL, p<0.001). The formation of SCH was significantly lower in NAT cycles compared to PRG cycles (24.8 - 0.78, p<0.001). There was no association with SCH incidence by P4 type (IM vs vaginal, p=0.40) in PRG cycles. Additionally, E2 levels were significantly higher in PRG cycles on day of P4 start (351.5 vs 268.5, p<0.001) and CD 28 (356.5 vs 249, p<0.001). However, there was no relationship between SCH formation and continuous E2 levels on day of P4 start (NAT p=0.76 PRG p=0.44) or on CD 28 (NAT p=0.71, PRG p=0.11) in either protocol. Within PRG cycles, SCH incidence was not associated with the change in E2 from day of P4 initiation to CD28 (p=0.25). E2 levels were then reclassified as high (>249pg/mL) or low based on the median E2 at day of P4 initiation (249 pg/mL). There was no association between rate of SCH formation in PRG cycles with high E2 (RR 1.10 (0.72-1.65), p=0.09) or with high E2s on CD 28 (RR 1.10 (0.72-1.65), p= 0.38). Interestingly, in NAT FET cycles, patients with high E2 levels were more likely to have SCH formation (RR 3.23 (1.0-10.83), p<0.04).

**CONCLUSIONS:** Both SCH formation and serum E2 levels are higher in PRG FETs. However, high E2 levels was not associated with SCH formation. Further analysis is needed to determine the physiologic cause for an increased rate of SCH formation in PRG cycles and an estimation of obstetrical risk.


**TABLE 1. Results of Follicles, Mature oocyte and Pregnancy rates in Fresh,Frozen Embryo Transfer**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Fresh-ET</th>
<th>Frozen-Thawed ET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicles</td>
<td>Mature oocyte (%)</td>
<td>P.R*</td>
</tr>
<tr>
<td>0~1000</td>
<td>6.3 ± 4.2</td>
<td>47</td>
</tr>
<tr>
<td>1000~2000</td>
<td>11.0 ± 5.0</td>
<td>42</td>
</tr>
<tr>
<td>2000~3000</td>
<td>14.5 ± 5.0</td>
<td>40</td>
</tr>
<tr>
<td>3000~4000</td>
<td>17.2 ± 5.0</td>
<td>39</td>
</tr>
<tr>
<td>4000~5000</td>
<td>18.9 ± 4.6</td>
<td>39</td>
</tr>
<tr>
<td>5000~6000</td>
<td>19.5 ± 4.6</td>
<td>39</td>
</tr>
<tr>
<td>6000~7000</td>
<td>21.3 ± 4.6</td>
<td>40</td>
</tr>
<tr>
<td>7000~</td>
<td>21.5 ± 4.1</td>
<td>39</td>
</tr>
</tbody>
</table>

*P<0.05; Pregnancy rates column analyzed by T-test; p<0.05; Pregnancy rates in Fresh ET and Frozen-thawed ET analyzed by χ²-test; p<0.05; Pregnancy rates

**P-160 Tuesday, October 15, 2019 6:30 AM**

"PREDICTIVE VALUE OF SERUM PROGESTERONE LEVEL ON DAY 4, DAY 7 AND DAY 11 AFTER BLASTOCYST TRANSFER IN A HORMONAL REPLACEMENT THERAPY CYCLE.** Elena Labarta, MD PhD,a Giulia Mariani, MD,a Ernesto Bosch, MD PhD,a *IVI-RMA, Valencia, Spain; bIVI-RMA, Valencia, Spain, Spain.

**OBJECTIVE:** Recent studies have suggested that low serum progesterone (P) levels on day of embryo transfer (ET) are associated with poorer pregnancy outcome. Determination of serum P in hormonal replacement therapy (HRT) cycles reflects the absorption of exogenous P because no endogenous production exists until pregnancy week 5-6. It is of interest to know if serum P levels during mid and late luteal phase are related with the risk of miscarriage or of ongoing pregnancy.

In this study, we wanted to evaluate the predictive value of P levels from mid luteal phase (4 and 7 days after ET) to the day of the β-hCG check (11 days after ET) for ongoing pregnancy in HRT cycles.

**DESIGN:** Prospective cohort study performed between June 2017 and August 2018 in IVI-RMA Valencia,Spain.

**MATERIALS AND METHODS:** Eligible patients were aged between 18-42 years, with a normal uterus, and being transferred 1-2 good quality blastocysts from own or donated eggs after an HRT cycle with estradiol valerate and vaginal progesterone (P400mg/12h).

Serum P levels were measured three times during the mid and late luteal phase on the 4th, 7th and 11th day after ET.

**Correlation between pregnancy results and hormonal time 2-degree polynomial fitted data was analyzed by linear model. A logistic linear model and ROC analysis were performed to assess P polynomial coefficients as a predictive test for ongoing pregnancy.

**RESULTS:** A total of 150 patients were included. Mean age was 38.1±3.9y, with a BMI of 23.4±3.6kg/m² and endometrial thickness before introducing exogenous progesterone of 9.1±1.6mm. The overall ongoing pregnancy rate was 47.3% (95%CI=39.3-55.3).

The AUC for P exposure during the luteal phase was significantly higher in ongoing pregnancies (101.2ng/ml (95%IC=90.8-111.6)) when compared with negative β-hCG cases (79.4ng/ml (95%IC=66.5-92.4)), p=0.027.
On ET+11, ongoing pregnancies showed a significantly higher serum P levels when compared with negative β-hCG (mean difference 5.5 ng/ml (95%CI=2.6-8.3), p<0.001).

The ROC curve showed that there is a significant predictive value of serum P levels for ongoing pregnancy rate, being the AUC (95% CI) = 0.63 (0.54-0.72) on ET+4; 0.65 (0.56-0.74) on ET+7; and 0.73 (0.65-0.81) on ET+14 with best cutoff values of 9.95, 21.3 and 11.6 ng/ml, respectively.

CONCLUSIONS: In HRT cycles in which vaginal progesterone is used, P levels across luteal phase days are associated with pregnancy outcome. Ongoing pregnancies showed a higher exposure to P. These results suggest that absorption to vaginal P can vary among patients and this can influence on the results.

SUPPORT: None.

P-161 Tuesday, October 15, 2019 6:30 AM
THE PREDICTIVE VALUE OF FSH BASAL LEVELS FOR ART OUTCOMES IS AGE DEPENDENT. Jose Buratini, DVM, PHD, Claudio M. M. Brigante, MD, Silvana Gippone, MD, Mara Zanirato, MD, Maria Cristina Guglielmo, BSCI, PHD, Mariabeatrice Dal Canto, BSCI, PHD, Mario Mignini Renzini, MD, Rubens Fadini, MD. Biogenesi Reproductive Medicine Center, Monza, Italy.

OBJECTIVE: Studies with robust numbers of patients to clarify the predictive value of FSH levels for ART outcomes are still needed. In this study, we examined a large cohort of ICSI patients aiming to assess across different maternal age groups the association of FSH basal levels with implantation, clinical pregnancy and abortion rates.

DESIGN: We performed a retrospective analysis of data collected since 2016 including 2503 autologous ICSI cycles. Each ICSI cycle represents a distinct patient. Patients were grouped according to FSH plasma concentrations measured on the second or third day of the ICSI cycle (FSH groups: <7.5; 7.5 to 10; >10 IU/L), and age (Age groups: <34; 34 to 37; ≥38; ≥40).

MATERIALS AND METHODS: Patients ageing 20 to 45 years with unexplained, male-related or tubal sub-fertility were subjected to controlled ovarian stimulation utilising a GnRH antagonist protocol, with FSH dose individually adjusted and oocyte maturation triggered with hCG 36 hours before oocyte collection. Matured oocytes were subjected to ICSI and one single FSH measurement or clinically not perceived due to their interaction to clarify the mechanisms linking higher FSH levels with impaired fertility in young age women undergoing ART.

RESULTS: Across different maternal age groups, FSH basal levels only significantly affected implantation and pregnancy rates, but not with abortion rate. For patients under 34 years with basal FSH ≤7.5 IU/L, pregnancy rates were 9.9% (41/416), 9.2% (26/284) and 6.7% (19/283; P = 0.023), respectively. As expected, implantation and clinical pregnancy rates decreased progressively with age, but did not consistently vary with FSH levels in patients older than 34. For patients older than 40 years with basal FSH <7.5, 7.5 to 10 and >10 IU/L, clinical pregnancy rates were 9.9% (41/416), 9.2% (20/284) and 6.7% (19/283; P = 0.035), and implantation rates were 9.9% (73/741), 10.1% (48/476) and 9.5% (42/443; P = 0.96), respectively.

CONCLUSIONS: Higher FSH basal levels are associated with poorer ART outcomes in patients under 34 years and thus represent a useful ART prognostic tool for this age group. Interestingly, the predictive value of FSH basal levels for ART outcomes seems to fade as maternal age advances. New studies are needed to clarify the mechanisms linking higher FSH levels with impaired fertility in younger patients, and whether these mechanisms are absent, not reflected by a single FSH measurement or clinically not perceived due to their interaction with other age-related modifications in older patients.

P-162 Tuesday, October 15, 2019 6:30 AM
THE IMPACT OF SPONTANEOUS LH SURGE DURING A NATURAL CYCLE FROZEN EMBRYO TRANSFER. Jasmyne K. Johal, MD, MSc, Brindha Bavan, MD, Ruth B. Lathi, MD, Amin A. Millki, MD, Stanford University, Stanford, CA; Stanford Fertility and Reproductive Medicine Center, Sunnyvale, CA.

OBJECTIVE: This study aims to assess outcomes of natural cycle frozen embryo transfers (NC-FET) in women who had spontaneous LH surge compared to women without detected LH surge on the day of HCG trigger; we hypothesize there is no difference in pregnancy rates between the two groups.

DESIGN: Institutional Review Board-approved retrospective cohort study.

MATERIALS AND METHODS: All patients who underwent NC-FET with euploid blastocysts at a single academic institution from 5/1/2016 to 11/15/2017 were reviewed. Previous workup included confirmation of normal uterine cavity. Standard protocol for NC-FET included ultrason sound monitoring and HCG trigger when the dominant follicle was ≥18 mm and endometrial lining was ≥7 mm. Patients had serum LH, estradiol, and progesterone checked on the day of HCG trigger. If LH was ≥20 mIU/mL, FET was performed 6 days after surge (LH+6), with the intent of transferring a thawed blastocyst 5 days after ovulation. If LH was <20 mIU/mL, FET was performed 7 days after HCG trigger (HCG+7).

Vaginal progesterone supplementation was started 3 days after spontaneous LH surge or 4 days after HCG trigger. Demographic information and pregnancy rates for both groups were recorded in a secure REDCap database and compared using t-test and chi-squared statistical analyses.

RESULTS: A total of 226 NC-FETs were included. Mean age at transfer was 36, and mean BMI was 25. Overall, the pregnancy rate (PR), defined by positive beta HCG, was 75% and live birth rate (LBR) was 57%. Baseline characteristics between those patients who were transferred at LH+6 (n = 91) and those transferred at HCG+7 (n = 135) are provided in Table 1. Women in the LH+6 group had a PR of 79% and LBR of 59%. Women in the HCG+7 group had a PR of 71% and LBR of 56% (P = 0.26 and p = 0.57, respectively).

CONCLUSIONS: HCG triggered NC-FETs have been shown to have similar pregnancy rates as hormone replacement cycles; however, there is a paucity of data regarding monitored NC-FET timing and success in the setting of a spontaneous LH surge. In our study cohort, patients undergoing NC-FETs based on LH+6 timing had similar pregnancy and live birth rates when compared to those patients who did not have a spontaneous LH surge and transferred at HCG+7.

SUPPORT: None.

P-163 Tuesday, October 15, 2019 6:30 AM
THE RELATIONSHIP BETWEEN ANTI-MULLERIAN HORMONE AND ANEUPLOIDY IN REPRODUCTIVE-AGE WOMEN UNDERGOING PREIMPLANTATION GENETIC TESTING; IS THERE A CORRELATION? Monica Pasternak, MD, Micha Thompson, BA, Steven Spandorfer, MD, Ronald O. Perlman and Claudia Cohen Center for Reproductive Medicine, New York, NY; The Ronald O. Perlman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: The primary objective of this study was to investigate whether there is a correlation between serum anti-Mullerian hormone (AMH) levels and embryo chromosomal abnormality as determined by pre-implantation genetic testing for aneuploidy (PGT-A), and whether this differs by patient age.

DESIGN: This is a retrospective single-institution study. Demographics of patients undergoing in vitro fertilization (IVF) with PGT-A during a 4-year period were recorded, as well as characteristics of their resultant embryos.

MATERIALS AND METHODS: There were 1653 IVF/PGT-A cycles performed by patients who also had a serum AMH assay measured at our

<table>
<thead>
<tr>
<th>TABLE 1.</th>
<th>NC-FET at LH+6</th>
<th>NC-FET at HCG+7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics/Outcomes</td>
<td>(n=91)</td>
<td>(n=135)</td>
</tr>
<tr>
<td>Mean age at transfer (y)</td>
<td>35</td>
<td>37</td>
</tr>
<tr>
<td>Mean BMI (kg/m2)</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Nulliparous (n)</td>
<td>70 (76%)</td>
<td>77 (57%)</td>
</tr>
<tr>
<td>Non-smoking (n)</td>
<td>87 (96%)</td>
<td>10 (93%)</td>
</tr>
<tr>
<td>Endometrial thickness (mm)</td>
<td>9.0</td>
<td>8.9</td>
</tr>
<tr>
<td>Mean LH value (mIU/mL)</td>
<td>45.0</td>
<td>40.5</td>
</tr>
<tr>
<td>Mean peak estradiol value (pg/mL)</td>
<td>376</td>
<td>286</td>
</tr>
<tr>
<td>Mean progesterone value (ng/mL)</td>
<td>0.8</td>
<td>0.4</td>
</tr>
<tr>
<td>Pregnancy rate (n)</td>
<td>72 (79%)</td>
<td>96 (71%)</td>
</tr>
<tr>
<td>Live birth rate (n)</td>
<td>54 (59%)</td>
<td>75 (56%)</td>
</tr>
</tbody>
</table>
institution; patients who had AMH drawn elsewhere were not included in this study. The percent of euploid embryos per number of embryos biopsied and cryopreserved at day 5/6 of embryogenesis was calculated for each IVF cycle. Patients were separated into two age groups: less than 39 yo and greater than or equal to 39 yo. AMH values were classified as low if <1.0 and normal if ≥1.0. Statistical analysis was performed by using the Kruskal-Wallis and Chi-square tests as appropriate.

RESULTS: Of the 1653 IVF/PGT-A cycles analyzed, 1266 cycles included patients who had an AMH ≥1.0, and 387 had an AMH <1.0. We further stratified the patients by age (<39 and ≥39 yr). A total of 735 cycles included patients who were <39 yr, and 531 were ≥39 yr. For women who were <39 yr, there was an average of 48.9% euploid embryos per IVF/PGT-A cycle for those with an AMH ≥1.0 compared to women <39 yr with an AMH <1.0 for whom there was an average of 40.1% euploid embryos per cycle (p = 0.01). For women ≥39 yr with an AMH ≥1.0, there was an average of 16.9% euploid embryos per IVF/PGT-A cycle, compared to those with an AMH <1.0 for whom there was an average of 15.4% euploid embryos per cycle (p = 0.062).

CONCLUSIONS: The relationship between serum AMH levels and embryos chromosomal abnormality in patients undergoing IVF with PGT-A has yet to be determined. Previous studies have limited data pertaining to the relationship between AMH and aneuploidy prior to embryo transfer (ET) and conception in patients utilizing IVF. Most research on this subject has been disparate in terms of how and when these serum assays were obtained, and without controlling for the use of IVF. Additionally, most studies measured AMH during a clinical pregnancy, at which time AMH levels will be suppressed physiologically. The results from our study found that in women less than 39 yo, AMH is significantly correlated with percent euploid embryos per the number of embryos biopsied in a given IVF/PGT-A cycle. No significant difference was found in women greater than or equal to 39 yr. Therefore, it is reasonable to expect that women of younger reproductive age to have a disparity in terms of yield of euploid embryos after IVF/PGT-A depending on ovarian reserve as determined by AMH level, and to discuss it with our patients as part of IVF/PGT-A counseling.

SUPPORT: None.

P-165 Tuesday, October 15, 2019 6:30 AM

COMPARING FROZEN EMBRYO TRANSFER OUTCOMES WITH BASELINE LH LEVELS. Ariel Z. Benor, M.D., Richard Grazi, M.D. Maimonides Medical Center, Brooklyn, NY.

OBJECTIVE: To see if, during a programmed frozen-embryo transfer (FET) cycle, an endogenous rise in the LH level prior to initiation of progesterone supplementation may influence live birth rate (LBR). In the absence of concomitant pituitary suppression, high estradiol (E2) levels will often stimulate luteinizing hormone (LH) to rise to levels commonly associated with the periovulatory LH surge. In our study, we sought to correlate the live birth rates following FET when LH rose beyond a threshold level prior to supplementation with progesterone (P).

DESIGN: This was a single-center, retrospective cohort study from 2016-2018.

MATERIALS AND METHODS: The programmed preparation of endometrium started with estradiol pretreatment for a minimum of 14 days followed by five days of P given by intramuscular or vaginal route, or both, with FET performed on day 6 of P replacement. Two groups were stratified by LH levels <15 mIU/mL and LH >15 mIU/mL. Patients who were found to have a periovulatory follicle were excluded from the analysis.

RESULTS: One hundred fifty-five patients who underwent a frozen embryo transfer had LH levels drawn prior to the start of progesterone supplementation (pre-P). Seventy patients had a live birth and 111 patients did not. Of the 70 with a live birth, the mean LH level was 14.5 mIU/mL and of the 111 without a live birth, the mean LH was 14.2 mIU/mL. Whether pre-P LH levels were <15 or >15 mIU/mL made no difference to the LBR (p = 0.7). There was no pre-P LH level beyond which a decrease in LBR was seen. Of those patients who live birth, 40% had an LH range of 15-61.5, while 60% had an LH >15 (range of 0-14.3); the mean LH level was 14.5 (95% CI, 12.0-17.0). Of those without a live birth, 63% had an LH >15 (range of 0-14.8), while 37% had an LH <15 (range of 15.2-33.8); the mean LH level was 14.3 (95% CI, 12.3-16.3). We found that regardless of what threshold level was set for LH, no level was predictive of an effect on LBR.

CONCLUSIONS: LH levels that exceed 15 mIU/mL prior to initiating P supplementation in a programmed FET cycle have no significant effect on LBR. In the absence of a maturing follicle, there appears to be no threshold beyond which LH levels affect LBR.

References: None.

SUPPORT: None.

P-166 Tuesday, October 15, 2019 6:30 AM

SERUM hCG LEVEL MEASURED 5 DAYS AFTER SINGLE THAWED BLASTOCYST TRANSFER AS A PREDICTOR OF OUTCOME. Angela H. Liu, M.D.,* Ankita Raman, M.D.,* Carrie E. Bedient, M.D.,* Leah A. Kaye, M.D.,* Forest C. Garner, MS, b Bruce Shapiro, M.D., Ph.D., H.C.L.D.,* *University of Nevada, Las Vegas, Las Vegas, NV; bFertility Center of Las Vegas, Las Vegas, NV.

OBJECTIVE: Investigate serum hCG level measured 5 days after vitrified-warmed single-blastocyst transfer as a predictor of transfer outcomes.

CONCLUSIONS: Contrary to previous low powered studies, we demonstrated that P4 levels at or above 10 ng/mL on the day of embryo transfer are not associated with statistically significant improvements in biochemical pregnancy, clinical pregnancy or live birth rates. Therefore, this finding en- hances our limited understanding of transfer day P4 levels in predicting pregnancy outcomes for universally utilized artificial FET cycles and highlights the need for further research in this area.


Determined the impact changes in these metabolites have on embryology outcomes in overweight patients. The tested metabolites were adipokines (resistin, leptin and adiponectin), pro-inflammatory cytokines (IL6, IL18, TNFα, CRP, chemerin, prolactin and insulin) and chemerin). All samples and standards were assayed in duplicate (MACS-TNFα). Linear regression was considered significant.

RESULTS: There were 932 single-blastocyst transfers in the 5-year study period. Among all 932 transfers, a day 5 hCG level 5 IU/L was predictive of each outcome except multiple pregnancy. Sensitivity, specificity, positive predictive value, and negative predictive value, and P-values are shown in Table 1. The live birth rate among transfers with day 5 hCG level 5 IU/L was 77.0%; while failure to achieve that criterion was associated with a live birth rate of only 12.0%. The area under the ROC curve for day 5 hCG level as a predictor of live birth was 0.830.

CONCLUSIONS: Serum hCG level measured 5 days after blastocyst transfer is a useful early predictor of outcome following single thawed blastocyst transfers in artificially prepared cycles. However, the sensitivity for predicting ongoing pregnancy and live birth was only 94%, indicating that a later confirmatory test is still required. The correlation between day 5 hCG and outcome highlights the importance of early implantation and the putative peri-implantation period in artificial cycles.

FERTILITY & STERILITY

IVF OUTCOME PREDICTORS - LUTEAL SUPPORT

P-168 Tuesday, October 15, 2019 6:30 AM
IN PATIENTS WITH SUB-OPTIMAL ENDOMETRIAL LINING, DOES THE ROUTE OF ADMINISTRATION OF SUPPLEMENTAL ESTROGEN CORRELATE WITH FROZEN EMBRYO TRANSFER OUTCOMES? Devora Aharon, MD, a Sass Wodoslawsky, BA, b Ariel Megan Schnur, RN, BSN, b Jordyn Banks, RN, b Melissa Bell, RN, b Margaret Daneyko, RN, b Lawrence Gunfled, MD, a Alan B. Copperman, MD, a Icahn School of Medicine at Mount Sinai, New York, NY; b Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Patients routinely receive supplemental oral estrogen in preparation of the endometrial lining prior to a frozen embryo transfer (FET). In patients with suboptimal growth, additional vaginal or transdermal estrogen supplementation may be prescribed in attempt to increase estrogen absorption and optimize uterine lining thickness. To date, there are limited data analyzing the clinical utility of either route. This study aims to evaluate the correlation of vaginal or transdermal estradiol supplementation with patient FET cycle outcomes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The study included patients who underwent an autologous or donor egg FET cycle with an endometrial thickness of <7mm on cycle day 10-15 from November 2005-April 2019. Patients were separated into groups by route of additional E2 supplementation (vaginal estradiol tablets (E2 PV group); transdermal estrogen patch (E2 TD group)). Baseline demographics and cycle characteristics were collected. Outcomes included endometrial stripe (EMS) at embryo transfer, chemical pregnancy rate, clinical pregnancy rate, and live birth rate. A sub-analysis of euploid FET was performed. A sub-analysis was performed in patients with a structural uterine factor (as identified by an initial hysterosalpingogram (HSG) or saline infusion sonohysterography (SIS)). Statistical significance was calculated using chi-square test and t-test. A p-value of 0.05 was set for statistical significance.

RESULTS: A total of 414 patients underwent 461 FET cycles within the study, including 396 E2 PV cycles and 65 E2 PV cycles. Baseline demographics were similar between the two groups. A statistically significant increase in EMS at transfer was seen in the E2 PV group compared to the E2 TD group, however, the absolute difference was 0.01 mm (E2 TD 8.34 (4.6-15.5, SD = 1.57 vs E2 PV 8.35 (5.1-15.6, SD = 2.23), p = 0.0002). No statistically significant differences in chemical pregnancy, clinical pregnancy, or live birth rates were seen. In the sub-analysis of euploid FETs, EMS at transfer was significantly greater in the E2 PV compared to E2 TD group (8.66 (5.1-15.6, SD 2.06) vs. 8.32 (5.3-13.7, 0.0001).
A significant increase in chemical pregnancy rate was seen in the E2 PV compared to E2 TD group (75% vs. 59.4%, p=0.05). However, clinical pregnancy rates and live birth rates were similar. In the sub-analysis of patients with an initially abnormal SIS or HSG, EMS at transfer was significantly lower in the E2 PV compared to E2 TD group (7.05 [5.2-9.0, SD ± 1.13] vs. 8.11 [5.12-12.46, SD ± 1.65], p=0.049). No significant differences were seen in clinical pregnancy, chemical pregnancy, and live birth rates.

CONCLUSIONS: Supplemental vaginal and transdermal estradiol were equally effective in achieving endometrial thickness >7mm, and both methods resulted in similar pregnancy outcomes. Patients can be comforted in knowing that both routes of estrogen supplementation are effective in supporting the endometrial lining prior to FET, and choice of method may be based on patient and provider preference. Reference: None. SUPPORT: None.

P-169 Tuesday, October 15, 2019 6:30 AM

NATURAL FROZEN EMBRYO TRANSFER WITH hCG BOOSTER FOR OPTIMIZATION OF CYCLE OUTCOMES: A RETROSPECTIVE COHORT STUDY. Claire Stewart, BA, David Reichman, MD, Zev Rosenwaks, MD, Weill Cornell Medical College, New York, NY; aWeill Cornell Medicine, New York, NY; bThe Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To determine whether luteal support with intramuscular injection of human chorionic gonadotropin 1-day post-luteinizing hormone (LH) surge in natural cycle frozen embryo transfers (FET) increases ongoing pregnancy rates.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All patients undergoing natural cycle FET with transfer of a single euploid blastocyst between January 2017 and December 2018 were reviewed for inclusion. Patients were divided into two groups based on whether they received one bolus dose of hCG (typical dose, 3300 IU) 1-day after identification of the LH surge. All patients received vaginal progesterone support after transfer. Groups were further stratified by embryo quality. Patients with uterine factor infertility were excluded. The primary outcome of this study was ongoing pregnancy rate. Secondary outcomes included first trimester miscarriage and biochemical pregnancy rates. Outcomes were analyzed with Chi-squared test, Fisher exact test, and logistic regression where appropriate. Odds ratios (OR) with 95% confidence intervals (CI) were calculated and adjusted for patient age at time of transfer, embryo quality assessed by blastocyst grade, BMI, gravidity, parity, and peak endometrial thickness. 

RESULTS: A total of 529 FET cycles were included. Patients receiving hCG (n = 146) had a statistically significant higher ongoing pregnancy rate than those without treatment (n = 383) (69.9% vs. 57.4%, adjusted odds ratio 1.72; 95% CI, 1.13-2.65). There were no significant differences observed in the rates of first trimester miscarriage or biochemical pregnancy (Table).

CONCLUSIONS: This study provides evidence that natural cycle FET in which the luteal phase is buttressed with both a single hCG injection after the endogenous LH surge, as well as vaginal progesterone after transfer, are associated with higher clinical success rates with minimal negative impact on the patient experience.

P-170 Tuesday, October 15, 2019 6:30 AM

LUTEAL PHASE SUPPORT USING GONADOTROPIN RELEASENING HORMONE AGONIST (GNRHA) VERSUS ESTROGEN AND PROGESTERONE SUPPLEMENTATION IN HIGH RESPONDERS FOLLOWING GNHRHA TRIGGERING – A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL. Lilach Marom Haham, M.D, Yariv Shlomo Gidoni, M.D, Ovad Baruchin, M.D, MHA, Jonathan Barkat, M.D, Ariel Revel, M.D, Ido Ben-Ami, M.D, PhD, Shamir medical center, Tel Aviv university, Beer Yakov, Israel; Shamir Medical Center, Be'er Ya'akov, Israel; Tel Aviv university, Tel Aviv, Israel.

OBJECTIVE: GNRHAs triggering is used as an alternative to hCG in GnRH antagonist protocols to almost eliminate the risk of OHSS. However, its main disadvantage is a significant lower pregnancy rate which is thought to be caused due to luteolysis. In order to preserve high pregnancy rates, several luteal support regimens were investigated including an intensive estrogen and progesterone supplementation and daily GnRHa treatment. However, no study, so far, compared the efficacy of these two regimens. Our aim was to compare the efficacy of GnRHa versus intensive estrogen and progesterone supplementation for luteal phase support in high responders following GnRHa triggering.

DESIGN: A prospective randomized controlled trial MATERIALS AND METHODS: High responder patients defined as either reaching a serum estradiol levels of ≥3500 pg/ml on the day of trigger or having ≥15 oocytes retrieved, were recruited between October 2017 until March 2019. The patients were randomly assigned to either daily intranasal GnRHa (nafarelin 200 micrograms daily), or a combination of estrogen and progesterone (E2 4 mg twice daily, vaginal Endometrin 300 mg daily and intramuscular injection of progesterone retard 250 mg once every five days) for luteal support. The GnRH antagonist protocol using GnRHa triggering was initiated. Patients with a BMI >35 or <19, recurrent implantation failure, moderate to severe endometriosis or hydroalpinx were excluded. Study groups’ characteristics were compared using independent t-test. Implantation rates and clinical pregnancy rates were compared using chi square test.

P-171 Tuesday, October 15, 2019 6:30 AM

INTRAMUSCULAR INJECTION OF HUMAN CHORIONIC GONADOTROPIN BEFORE SECRETORY TRANSFORMATION SIGNIFICANTLY IMPROVES THE IMPLANTATION AND PREGNANCY OUTCOMES IN FROZEN EMBRYO TRANSFER CYCLES. Ling Deng, bachelor, Xin Chen, PhD, Shi-ling Chen, PhD, De-Sheng Ye, doctor, Ling Deng, bachelor, Xi Jinping, Hong, PhD, Chi Zhaoyang, M.D, Shi-qing Chen, PhD, Yu-hua Tan, M.D, Da-xin Guo, M.D, Shuang-feng Wang, MD, Ya’akov, Israel; Tel Aviv university, Tel Aviv, Israel.

OBJECTIVE: To explore the effect of intramuscular injection of human chorionic gonadotropin (hCG) before secretory transformation on pregnancy outcomes of hormone replacement treatment frozen embryo transfer cycles (HRT-FET).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Infertility patients younger than 43 years and performing HRT-FET cycles in center for Reproductive Medicine were recruited in this study. Patients suffering from adenomyosis were excluded. And a total of 904 HRT-FET cycles were analyzed, 404 cycles in the hCG group and 500 in the control group, respectively. Patients in the hCG group received intramuscular injection of 10,000 IU hCG before secretory transformation. The control group performed FET without hCG administration before secretory transformation. We compared the implantation rate (IR), clinical pregnancy rate (CPR), ongoing pregnancy rate (OPR) and live birth rate (LBR).

RESULTS: The basic characteristics and clinical parameters were comparable between the two groups. The CPR (58.7% vs. 49.6%; odds ratio (OR), 1.4; 95% confidence interval (CI), 1.1–1.8; P = 0.007), OPR (50.0% vs. 41.2%; OR, 1.4; 95% CI, 1.1–1.9; P = 0.008), LBR (47.5% vs. 38.2%; OR, 1.5; 95% CI, 1.1–1.9; P = 0.005) and IR (43.8% vs. 34.6%; P = 0.000) were statistically significantly higher in the hCG group as compared with the control group. After adjusting confounding factors (age at index IVF/ICSI cycles, duration of subfertility, body mass index, number of embryos transferred and good-quality embryos transferred, and cycles of previous transfer), the use of hCG was still a significant factor predictive of LBR in HRT-FET cycles (adjusted OR 1.5; adjusted 95% CI 1.1-2.1; P = 0.002). When the analysis was restricted in the patients with age <39 years old and with at least one good embryo transferred in the included cycles, the pregnancy rates in the hCG group were more superior to the control group with statistically significant difference (CPR: 64.3% vs. 52.3%; adjusted OR, 1.6; adjusted 95% CI, 1.2-2.3; P = 0.001), OPR 56.5 % vs. 45.4%; adjusted OR, 1.6; adjusted 95% CI, 1.2-2.2; P = 0.002), LBR: 53.7% vs. 41.7%; adjusted OR, 1.7; adjusted 95% CI, 1.2-2.3; P = 0.001).

CONCLUSIONS: Intramuscular injection of 10,000 IU hCG before secretory transformation statistically significantly improved IR and pregnancy outcomes in HRT-FET cycles.
RESULTS: A total of 47 women were allocated, 23 were assigned to the GnRHa arm and 24 were assigned to estrogen and progesterone treatment arm. Patients’ characteristics including age, BMI, gravidity, parity as well as basal FSH levels didn’t differ significantly between the study groups. Treatment’s characteristics including the FSH dosage, duration of stimulation, peak estradiol levels, number of oocytes retrieved, fertilization rates and number of embryo transferred also didn’t differ significantly between the study groups. The implantation rate was 56.5% and 37.5% in the GnRHa arm and in the estrogen and progesterone arm, respectively (P = 0.1). The clinical pregnancy rate was higher in the GnRHa treatment group compared to the estrogen and progesterone group although the difference was not statistically significant (60.8% vs. 50%, P = 0.45). Of note, no cases of OHSS were observed in both study groups.

CONCLUSIONS: Luteal support using GnRHa alone is as effective and safe as using intensive estrogen and progesterone supplementation following GnRHa triggering in high responders. This new approach in fresh embryo transfer in high responders after GnRHa triggering offer a more convenient luteal support without compromising implantation and clinical pregnancy rates.

P-172 Tuesday, October 15, 2019 6:30 AM
PROSPECTIVE ANALYSIS OF PROGESTERONE DURATION IN PROGRAMMED SINGLE THAWED EUPLOID EMBRYO TRANSFER CYCLES. Carly I. Hirschberg, MD, a Jennifer K. Blakemore, MD, a Mary Elizabeth Fino, MD, a James A. Grifo, MD, PhD, b NYU Langone School of Medicine, New York, NY; c NYU Langone Fertility Center, New York, NY; d NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: In the era of personalized medicine and the simultaneously increasing use of frozen embryo transfer (FET), assays of the endometrium’s receptivity prior to transfer has gained popularity, especially among patients. However, the optimal timing for single thawed euploid embryo transfers (STEET) in a programmed FET has yet to be determined. We sought to examine the outcomes of euploid FETs by length of progesterone (P4) exposure at our clinic.

DESIGN: Prospective cohort study of all programmed FETs of single euploid embryos between 6/1/2018 and 12/18/2018 at our center.

MATERIALS AND METHODS: All patients undergoing FET in the inclusion time period were asked to write down the exact time of P4 initiation and then report the start time on the day of P4 serum level check (2 days later) prior to embryo transfer. All FETs were then reviewed. Programmed FET cycles were defined as treatment of oral estradiol daily followed by either 50-75mg intramuscular P4 in oil or vaginal P4 suppository with transfer of a euploid embryo (tested by either array comparative genomic hybridization or Next Generation Sequencing). Programmed FETs with untested, mosaic chromosomal FETs were excluded from this study.

RESULTS: A total of 47 women were allocated, 23 were assigned to the GnRHa arm and 24 to the estrogen and progesterone arm. Patients’ characteristics including age, BMI, gravidity, parity as well as basal FSH levels didn’t differ significantly between the study groups. Treatment’s characteristics including the FSH dosage, duration of stimulation, peak estradiol levels, number of oocytes retrieved, fertilization rates and number of embryo transferred also didn’t differ significantly between the study groups. The implantation rate was 56.5% and 37.5% in the GnRHa arm and in the estrogen and progesterone arm, respectively (P=0.1). The clinical pregnancy rate was higher in the GnRHa treatment group compared to the estrogen and progesterone group although the difference was not statistically significant (60.8% vs. 50%, P=0.45). Of note, no cases of OHSS were observed in both study groups.

CONCLUSIONS: Luteal support using GnRHa alone is as effective and safe as using intensive estrogen and progesterone supplementation following GnRHa triggering in high responders. This new approach in fresh embryo transfer in high responders after GnRHa triggering offer a more convenient luteal support without compromising implantation and clinical pregnancy rates.

P-173 Tuesday, October 15, 2019 6:30 AM
A NOVEL PROGESTERONE RELEASING INTRAVAGINAL RING FOR LUTEAL PHASE SUPPORT: PHARMACOKINETICS AND SAFETY IN A SHEEP MODEL. David R. Friend, PhD. Dare Bioscience, Inc., SAN DIEGO, CA.

OBJECTIVE: To evaluate the in vitro release and in vivo pharmacokinetics and local tolerability of a novel, segmented ethylene-vinyl acetate (EVA) intravaginal ring (IVR) (DARE-FRT1) delivering progesterone (P) in a drug-naïve female Dorset crossbred sheep. These rings are being developed to provide luteal phase support and supplementation during ART cycles and early pregnancy.

DESIGN: IVRs capable of releasing P at 4 mg/d, 8 mg/d and 12 mg/day were administered to female sheep to assess the pharmacokinetics and safety compared to vaginal administration of Crinone 8% gel or Prometrium (200 mg) capsules.

MATERIALS AND METHODS: IVRs were prepared by hot-melt extrusion to create segments of varying length and drug content. The appropriate segments were used to create segmented IVRs capable of releasing P at rates of approximately 4, 8, and 12 mg/day. Release rates of P from the three IVR formulations were measured in vitro to determine whether the target release rates had been attained. Release rates were tested using 200 mL 0.5% sodium dodecyl sulfate as a release medium, in shakers at 37°C. Sampling (2 mL) was conducted on Days 1-4, 7-11, and 14. Animals were randomized into one of six treatment groups: Group 1) Crinone® 8% gel (90 mg); group 2) Prometrium® 200 mg capsules; group 3) placebo IVR; group 4) P IVR 4 mg/day; group 5) P IVR 8 mg/day; and group 6) P IVR 12 mg/day. All IVRs were inserted on Day 1 remained in place through Day 14; the rings were removed and a new ring inserted on Day 15. The second ring remained in place until Day 29. Blood samples were taken at scheduled times for pharmacokinetic (PK) analysis. Concentrations of P in plasma were measured using a validated LC/MS/MS method. Postmortem examinations performed on all IVR groups included vaginal irritation, macroscopic and microscopic evaluations, including irritation scoring and histopathology.

RESULTS: Following a relatively large amount of released P on Day 1, in vitro release rates confirmed that P was released at approximately 4, 8, or 12 mg/d over Days 2-14. IVRs were retained over 28 days in all animals with two exceptions. Clinical observations showed no significant abnormal findings in any group. PK analysis in animals showed sustained release of P from Days 0 through 14 of ring use. PK parameters from the three different IVRs were consistent with the in vivo release rates. Cmax increased in a dose-related manner, with mean values of 455, 682, and 1,040 pg/mL for the 4, 8 and 12 mg/day IVR groups, respectively. The lower dose Crinone gel (90 mg P) showed substantially greater relative bioavailability compared with the higher dose Prometrium capsules (200 mg P). Irritation scores and microscopic assessments were consistent with the IVRs being well tolerated following 28 days of exposure.

CONCLUSIONS: The data obtained from this study demonstrate that the segmented DARE-FRT1 EVA-based IVRs are capable of sustained release of P at different rates over a 14-day period. The rings were well tolerated with minimal to mild local irritation. These results suggest the rings are suitable for evaluation in a Phase 1 clinical study in women for PK and safety.

IVF OUTCOME PREDICTORS - OOCYTES

P-174 Tuesday, October 15, 2019 6:30 AM
INCREASED NUMBER OF OOCYTES RETRIEVED IN FROZEN DONOR OOCYTE CYCLES DOES NOT HAVE A NEGATIVE IMPACT ON OUTCOMES. Rita Ann Fields, MS, a Andrew Dorffmann, MS, a Laurence Udooff, MD, b Fairfax EggBank, Fairfax, VA; Genetics and IVF Institute, Fairfax, VA.
OBJECTIVE: There is mounting evidence that outcome parameters from retrievals that yield high numbers of oocytes are not negatively impacted compared to cycles where fewer oocytes are retrieved. However, the perception persists that when many oocytes are retrieved, the oocytes are of poorer quality and lead to inferior embryo development and pregnancy rates. This research aims to determine if the number of oocytes retrieved in frozen donor egg cycles is correlated with IVF outcomes as measured by the following parameters: oocyte survival after vitrification, fertilization, blastocyst development and clinical pregnancy rate.

DESIgn: Retrospective cohort study.

MATERIALS AND METHODS: Oocytes were retrieved from anonymous egg donors at 12 IVF clinics for use in a commercial egg bank between 2016-2018. Mature eggs were vitrified using a commercially available vitrification media from Repro Life. Retrieved, mature oocytes were divided into cohorts of 6-8 oocytes for use by multiple recipients. Egg warming was performed using Repro Life warming media at 195 different recipients’ clinics. All reported warmings were from the retrieval period were included. Retrievals were sorted by total egg number retrieved and divided into 4 groups: <13, 13-24, 25-32 and >32 oocytes retrieved. Outcomes were evaluated t-test between percent. For pregnancy outcomes, only primary transfers were assessed.

RESULTS: A total of 714 retrievals and 1721 warmings were assessed. There was a statistically significant difference between groups 2-4 for oocyte survival, fertilization, blastocyst conversion or clinical pregnancy rate. There was a statistically significant difference between group 1 compared to groups 3 and 4 for oocyte survival, but this was not considered clinically meaningful.

CONCLUSIONS: Analysis of the data from this study supports the hypothesis that the number of oocytes retrieved from donors does not have a negative impact on embryo or cycle outcomes. Because blastocyst conversion rates and clinical pregnancy rates are similar between all groups, it reflected in the current practice after confirming non-detrimental effects in the offspring.

SUPPORT: None.

P-175 Tuesday, October 15, 2019 6:30 AM

ARTIFICIAL OOCYTE ACTIVATION (AOA) TREATMENT OFFERS A NEW OPTION IN PREVIOUSLY UN-SUCCESSFUL CASES DUE TO POOR FERTILIZATION HISTORY; A PAIRED COHORT STUDY. Alberto Tejera, Sr., PhD; Lucia Alegre, PhD; Arantza Delgado, PhD; Jose Maria De los Santos, Sr., PhD; Jose Alejandro Remohi, MD, PhD; Marcos Meseguer, PhD; Embryologist, Valencia, Spain; IVIRMA Global, Valencia, Spain; IVIRMA Valencia, Valencia, Spain; Affiliation not provided; IVIRMA Valencia, Valencia, Spain; IVIRMA Global, Valencia, Spain, Tel Aviv, Israel.

OBJECTIVE: To improve of treatment outcome in terms of fertilization, implantation and pregnancy rates as well as cancelation rate after applying AOA in the following treatments for those patients with previous very low or failed fertilization attempts. Additionally were tested both delivery rate and obstetric outcomes in children born after AOA use.

DESIGN: Retrospective Cohort Study.

MATERIALS AND METHODS: Period included between April 2013 and December 2018. The total number of oocytes included in the study was 1125 distributed in two groups: the control group formed by 509 oocytes from 66 patients who were injected without AOA, acquiring either a failure or unusually low fertilization values (<30%) and the study group consisted of oocytes from the same patients (66) in a second attempt but using AOA. Injection technique with AOA is comparable to conventional injection (ICSI) but in this case each oocyte was injected by spermatozoon together with a previous phase of buffered medium mixed with ionophore calcium (ICAs) aspirating it up to filling one third of the overall length of the pipette under 40x microscope magnification. Just after, the pipettes were kept for ten minutes with Ica into benchtop incubator and finally were incubated under the same culture conditions (37°C, 6% CO2, 5% O2 atmosphere) Fertilization, pregnancy, implantation and abortion rates were analysed and compared in both groups by X², t-Student and ANOVA tests. Both live birth and neonatal outcome was also reported.

RESULTS: After applying AOA, we observed a significant increase in the fertilization rate (51% vs 13.1%), ongoing pregnancy rate (47% vs. 21.7%) as well as implantation rate (31% vs 13.1%) and lower chances of cancellation (22.7% vs 69.3%). Additionally, no adverse obstetric and perinatal outcomes effects were found after the use of AOA compared to conventional ICSI.

CONCLUSIONS: Our findings support the use of AOA for a specific population of patients with previous very low fertilization or fertilization failure and in consequence, the outcome was impaired. After applying AOA, the reproductive success was significantly enhanced, mainly by the significant increase in the fertilization rate, the number of embryos available for selection, reducing dramatically the cancellation rate. The safety of AOA is reflected in the current practice after confirming non-detrimental effects in the offspring.

SUPPORT: None.

P-176 Tuesday, October 15, 2019 6:30 AM


OBJECTIVE: Using a time-lapse monitoring system, we observed that the oocyte cytoplasmic volume altered in the duration between sperm penetration and pronuclear (PN) fusing. The present study aimed to determine the oocyte cytoplasmic volume at 5 morphokinetic events during fertilization and whether its regulation influences the clinical outcomes.

DESIGN: Retrospective, single-center, cohort study.

MATERIALS AND METHODS: A total of 311 patients (311 cycles; mean age: 35.1 ± 3.7 years) that underwent minimal-stimulation in vitro fertilization (mini-IVF) followed by freshly cleaved single-embryo transfer (SET) from August 2017 to September 2018 were retrospectively analyzed. Retrieved oocytes were inseminated by intracytoplasmic sperm injection (ICSI) after meiotic spindles were confirmed. Oocytes were cultured in a time-lapse incubator (EmbryoScope+, Vitrolife) after ICSI. The oocyte cytoplasmic volume corresponded to the oocyte major axis cross-sectional area (µm²). Measurements were recorded at 5 morphokinetic events: after ICSI (tICSI), time before 2nd polar body (PB) extrusion (tPB2b), time of 2nd PB extrusion (tPB2b), time before PN fusing (tPNf), and time of PN fusing (tPNf). The mean areas of oocytes at the morphokinetic events were compared (Study 1). In addition, the rates of change of oocyte cytoplasmic volume from tPB2b to tPNf (area of tPNf / tPB2b; group A), tPB2b to tPNf (area of tPNf / tPB2b; group B), and tPNf to tPNf (area of tPNf / tPNf; group C) were calculated. A multivariable logistic regression analysis was performed, which includes the significant confounding factors and yields adjusted odds ratios (aORs) and 95% confidence intervals (CIs), to evaluate the correlation between oocyte cytoplasmic volume change and clinical pregnancy (gestational sac observation) after SET (Study 2). P-values <0.05 were considered statistically significant.

RESULTS: Study 1: The mean area of oocytes at tICSI, tPB2b, tPNf, and tPNf were 11.452, 10.826, 10.587, 10.237, and 10.308 µm². The offspring.
respectively. The oocyte areas at tPNb and tPNf were significantly smaller than those at tICSI, tPB2b, and tPB2 ($p < 0.05$). Study 2: The multivariable logistic regression analysis showed that clinical pregnancy had significant associations with group A (area of tPNb / tPB2b, aOR: 4.8, 95% CI: 1.07–23.08, p = 0.035) and group C (area of tPNf / tPNf, aOR: 7.3, 95% CI: 1.22–47.58, p = 0.05), but not with group C (area of tPNf / tPNf, aOR: 2.08, 95% CI: 0.30–14.1, p = 0.4549).

CONCLUSIONS: A significant decrease in oocyte cytoplasmic volume was observed from sperm penetration to PN fading. In addition, there were significant associations between clinical pregnancy and the degree of cytoplasmic volume change from 2nd PB fertilization to PN fading. These results suggest that the regulation of oocyte cytoplasmic volume during fertilization would influence oocyte competence, which may predict successful pregnancy after SET.

SUPPORT: None.

P-178 Tuesday, October 15, 2019 6:30 AM

IVF OUTCOME IN WOMEN WITH ENTIRE COHORT OF OOCYTES WITH COARSE GRANULATION IN PERIVITELLINE SPACE

Raiza Ashraf, M.B.B.S., Aswathy Shanavas, M.S., D.N.B., Alex C. Varghese, Ph.D., Sankalp Singh, M.D., D.N.B., MRCOG, Mohamed Ashraf, M.D., D.G.O, DPS, Nounish Abdul Majidy, M.D, MRCOG, MRCPE. Indian Medical Association, THRISSUR, India; INDIAN MEDICAL ASSOCIATION, KOLLAM, India; Astra Fertility Clinic, Mississauga, ON, Canada; craft hospital, kodungallur, India; chairman of CRAT hospital & Research center, Kudungallure, India; Rcog,RCPI, TRAVENCORE MEDICAL COUNCIL, INDIAN MEDICAL ASSOCIATION, thrissur, India.

OBJECTIVE: The purpose of this study aims to compare embryo quality, clinical pregnancy rate (CPR) and implantation rate(IR) between the the patients having all oocytes with single abnormality i.e coarse granulation in PVS( study N=52) against patients with all oocytes having normal morphology (control N=49).

DESIGN: This is a retrospective case control study conducted during the period from June 2015 - February 2018 at CRAFT Hospital and Research centre, Kerala, India.

MATERIALS AND METHODS: The study protocol has been approved by the Institutional review board (IRB).

The inclusion criteria :maternal age ≤40yrs and male partners with normal semen parameters were selected. Exclusion criteria: Patient with history of recurrent implantation failure, chromosomal abnormalities or uterine abnormalities and those having oocytes with coarse granularity in pvs with other morphological abnormalities were excluded to avoid the bias factor.

Controlled ovarian stimulation was done with flexible antagonist protocol with individualised dose of gonadotrophin started from day 2.On the day of ICSI the oocytes were denuded and checked for their morphology based on ISTANBUL consensus 2011 such as intracytoplasmic and extracytoplasmic dysmorphisms.

Patients with entire cohort of oocytes having coarse granulation in PVS with no other oocyte abnormalities were taken into the study.

After ICSI oocytes were cultured in 6%co2 and 5%O2. On Day 3 embryo morphology was assessed based on the Istanbul consensus as Grade1,2 and 3.

Grade 1 embryos were vitrified on day 3 followed by endometrial prepara-
tion and frozen embryo transfer.

The primary outcome was to compare CPR. Secondary outcome was to assess day 3 grade1 embryos, IR between the two groups.

Sample Size Calculation and Statistical Analysis: The IBM SPSS statistics version 21 was used for statistical calculations. Sample size based on the result of Clinical pregnancy rate among control (32%) and test group (33.66%) and with 80%power and 95%confidance, the minimum sample size comes to 80(40 in each group).

Statistical analysis: Chi-square test was used to compare Fertilisation rate(FR),CPR. IR between study and control group.

RESULTS: The baseline characteristics did not differ significantly between two groups. A total of 1204 oocytes retrieved 577 oocytes belonged to study and 663 oocytes in control group.When compared between two groups, FR (67.38% vs 82.53%), CPR( 18% vs 54.16%) IR (10.58% vs 33.66%). Live birth rate (14% vs 48%) showed statistically significant difference (p value<0.05). Though Day 3grade1 embryo quality was not statistically significant(33% vs 40.75%) control group showed better embryo quality. Limitation of this study is that sample size is small and that it was powered to detect CPR and not live birth rate.

CONCLUSIONS: Coarse granulation in PVS shows low fertilisationclinical pregnancy and implantation rate.Study intends to show that coarse granulation in perivitelline space may predict poor ART outcome and patients can be counselled regarding the same.


SUPPORT: None.
THE CAUSAL EFFECT OF DYNAMIC FERTILITY TREATMENT STRATEGIES ON THE PROBABILITY OF PREGNANCY: A NOVEL APPLICATION OF MARGINAL STRUCTURAL MODELS (MSMS)

OBJECTIVE: To estimate the probability of clinical pregnancy, had all patients or subgroups of patients (based on age) followed a specific treatment strategy: eg, 4 cycles of ovulation induction (OI, with/without intrauterine insemination) using clomiphene or letrozole (OI Oral), 3 cycles of OI + Gonadotropin (OI Gn), or 1 cycle of assisted reproductive technology (ART) with fresh or cryopreserved embryo transfer.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Electronic medical record data from 84,301 US patients who underwent multiple treatments (219,925 cycles) in 2000-2016 were examined. Female patients included were initially treatment-naïve; patients with an initial diagnosis of male infertility were excluded. Inverse Probability (IP) of Censoring Weighting adjusted for stoppage treatment before getting pregnancy and IP of Treatment Weighting adjusted for patient characteristics (eg, diminished ovarian reserve) that excluded. Inverse Probability (IP) of Censoring Weighting adjusted for stopping treatment before getting pregnancy and IP of Treatment Weighting adjusted for patient characteristics (eg, diminished ovarian reserve) that made them more likely to choose a treatment strategy (eg, 1 ART over 4 OI Gn cycles).

RESULTS: In either age group, patients needed >4 OI Gn cycles, or to switch to 1 OI Gn cycle after 3 failed OI Oral cycles to have a similar chance of pregnancy rates with 1 ART cycle. Chance of pregnancy was below 50% for 4 cycles of OI Oral cycles, or to switch to ART sooner rather than repeating multiple cycles of OI. For patients <35 y, the estimated chance of pregnancy with 4 OI Oral cycles is close to 1 ART cycle. Evaluation of real-world data using MSMSs to account for patient dropout and changes in patient characteristics and prognosis over time can provide important insights into treatment-decision trends and evidence for improving personalized medicine.


SUPPORT: Study sponsored by EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany), Rockland, MA, USA.

---

ECTOPIC/HETEROTOPIC PREGNANCY OUTCOMES AFTER BLASTOCYST-STAGE FROZEN-THAWED EMBRYO TRANSFERS COMPARED WITH CLEavage STAGE: A SART-CORS STUDY

OBJECTIVE: It is well established that fresh embryo transfers at the blastocyst stage result in improved pregnancy outcomes compared with cleavage-stage embryo transfers. The Society for Assisted Reproductive Technologies Clinical Outcomes Reporting System (SART CORS) dataset, we have recently shown that blastocyst-stage frozen embryo transfer (FET) is also associated with higher live-birth rates compared with cleavage-stage FETs. However, other outcomes such as ectopic and heterotopic pregnancy rates between cleavage-stage and blastocyst-stage FETs have not been well studied. The objective of this study was to investigate whether there is a difference in ectopic/heterotopic pregnancy rates in blastocyst-stage FETs compared with cleavage-stage FETs.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All in vitro fertilization (IVF) cycles reported to the Society for Assisted Reproductive Technology from 2004 to 2013 were evaluated. Patients included were those with recorded treatment and pregnancy outcomes undergoing FETs at either the blastocyst-stage (n=118,616) or the cleavage-stage (n=137,671). Main outcome measures were pregnancy outcomes, specifically ectopic pregnancy rates and heterotopic pregnancy rates. Demographic criteria from each cycle was also collected. Statistical analysis was performed using SAS and Microsoft Excel. Chi-square analysis for bivariate associations and generalized estimating equations for adjusted associations were used with p<0.05 considered as statistically significant.

RESULTS: There was a statistically significant increase in pregnancy rates with blastocyst-stage FETs compared with cleavage-stage FETs (60.6% vs. 41.0%; p<0.001). Among those who became pregnant, there was a significantly lower incidence of ectopic/heterotopic pregnancy rates in blastocyst-stage FETs vs. cleavage-stage FETs (0.8% vs. 1.1%; p<0.001). Differences in ectopic/heterotopic pregnancy rates remained statistically significant after controlling for confounders such as tubal factor infertility and number of embryos transferred.

CONCLUSIONS: Blastocyst-stage frozen embryo transfer is associated with lower ectopic/heterotopic pregnancy rates compared with cleavage-stage frozen embryo transfer.
**P-187** Tuesday, October 15, 2019 6:30 AM

**LEVERAGING A COMPOSITE OVARIAN RESERVE SCORE IN A MACHINE LEARNING MODEL OF LIVE BIRTH OUTCOMES IN IVF.** Karen Hunter Cohn, PhD.a Cameron Wellock, PhD.a Piraye Yurttas Beim, PhD.a Polaris Data Network; bCelmatix, NEW YORK, NY.

**OBJECTIVE:** As the number of predictive measures for IVF prognosis proliferates, there is a growing need for machine-driven tools to aid patients and their healthcare providers in navigating the complex landscape of decision making. In previous work, we identified that multiple indirect measures of ovarian reserve (baseline FSH, LH, E2, BAFC, AMH) can be combined to measure a latent variable representing a patient’s overall ovarian reserve. Here, we aimed to develop a predictive model that utilizes a composite ovarian reserve score to predict cumulative live birth (LB) outcomes and risk of multiples based on the number of transferred embryos.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** 48,357 cycles were included from 34,734 patients age 25-45 undergoing autologous IVF treatment between 2010-2017 at 13 fertility centers in the US. We excluded cycles using pre-implantation genetic testing and transfer of 3 or more embryos. The dataset was divided into 2/3 for training (36,401 cycles), with the remaining 1/3 set aside as an independent validation set. We used a Bayesian approach because, in contrast to traditional regression models, this allowed us to incorporate the unobserved, but clinically relevant, composite variable of ovarian reserve as a feature of the model for cumulative LB rate and risk of multiples. Accordingly, the number of LBs per initiated cycle was modeled using a zero-inflated binomial distribution to account for patient cancellation prior to transfer, and ovarian reserve was represented in the model as a latent variable dependent on baseline levels of FSH, LH, AMH, and BAFC. To compensate for nonrandom patient dropout across multiple cycles, inverse probability of censoring weighting (IPCW) was used to more accurately predict later cycles. Considered variables in the larger model included patient age, ovarian reserve, BMI, diagnosis, number of transferred embryos, and partner semen analysis.

**RESULTS:** When our model was tested with an independent validation set, we found that our model had an AUC of 0.73 for prediction of a LB and an AUC of 0.82 for prediction of multiples. The most important features of the model included patient age, number of transferred embryos, number of previous failed cycles, and BMI.

**CONCLUSIONS:** For machine-driven tools to truly augment traditionally expert-driven decisions, it is important for the underlying models to grow in sophistication with the growing list and varying importance of prognostic measures. The use of Bayesian models to better determine likely number of LBs can bring better transparency and consistency to patient care and counseling during IVF treatment.

**SUPPORT:** Celmatix.

**P-188** Tuesday, October 15, 2019 6:30 AM

**A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTI-CENTER, PHASE 2 TRIAL TO INVESTIGATE THE EFFECT OF BARUSIBAN ON IMPLANTATION IN IVF/ICSI PATIENTS.** Ernesto Bosch, MD PhD.a Heidi Aasted, MSc.b Bjarkie M. Klein, PhD.b Joan-Carles Arce, MD, PhD.b,c and the BASIC Study Group. dIVI Valencia, Valencia; Valencia; eFerring Pharmaceuticals Inc., Parsippany, NJ; fFerring Pharmaceuticals, Copenhagen, Denmark.

**OBJECTIVE:** To evaluate the effect of the selective oxytocin antagonist barusiban, administered on the day of transfer, on ongoing implantation rate in IVF/ICSI patients.

**DESIGN:** Randomized, double-blind, placebo-controlled, phase 2 trial (BASIC) in 255 IVF/ICSI patients, 18-37 years, with a history of repeated implantation failures. Uterine pathology and thrombophilia disease were excluded. Patients had undergone controlled ovarian stimulation, hCG triggering, oocyte retrieval, and luteal phase progesterone supplementation.

**MATERIALS AND METHODS:** Women were randomized 1:1 on the day of transfer to barusiban (40 mg 45min pre-transfer + 10 mg 15min post-transfer) (n=130) or placebo (n=125), administered subcutaneously. Randomization was stratified by day of transfer (day 3 or 5) and number of embryos/blastocysts transferred (1 or 2). In total, 440 good-quality embryos/blastocysts were transferred (barusiban: 225; placebo: 215). Ongoing implantation (primary endpoint) and pregnancy were assessed 10-11 weeks after transfer. To adjust for imbalances in baseline characteristics between groups, the effect of barusiban was tested using a logistic regression model with treatment, embryo/blastocyst quality, reason for infertility, and center as factors. There were more transfers of excellent-quality blastocysts in the placebo group than in the barusiban group (51% vs 29%) as well as more couples in the placebo group with male factor infertility (51% vs 35%), supporting the value of the adjusted analyses. Both unadjusted and adjusted analyses were performed, and the latter are presented.

**RESULTS:** There was no significant difference in overall ongoing implantation rate between barusiban and placebo with rates of 27.9% and 23.1%, respectively [odds ratio 1.11 (95% CI: 0.69; 1.78), p=0.663]. However, the day of transfer had a significant interaction on the primary endpoint. A significantly higher ongoing implantation rate was observed for barusiban over placebo for day 5 transfers, with 41.3% for barusiban versus 23.2% for placebo [odds ratio 2.34 (95% CI: 1.13; 4.84), p=0.022], but not for day 3 transfers (11.8% versus 17.6% [odds ratio 0.63 (95% CI: 0.30; 1.34), p=0.227]).

The overall ongoing pregnancy rates were 34.1% for barusiban and 35.1% for placebo, with 49.7% for barusiban and 33.4% for placebo for day 5 transfers, and 19.2% and 29.9% for day 3 transfers, respectively.

More mild/moderate injection site reactions were observed with barusiban than with placebo, but there was no difference in severe reactions. No serious drug reactions were reported, and neonatal outcome was comparable between groups.

**CONCLUSIONS:** The present trial was unable to demonstrate the efficacy of barusiban in patients with a history of repeated implantation failures, but it revealed a time window for a clinically relevant effect of barusiban. Barusiban increased the implantation of blastocysts when administered closer to the time of the actual implantation, but not when administered in the early luteal phase during transfer of cleavage-stage embryos. Subcutaneous administration of 50 mg barusiban was well-tolerated.

**SUPPORT:** Ferring Pharmaceuticals.

**P-188** Tuesday, October 15, 2019 6:30 AM

**INCREASED OCCURRENCE OF TWIN AND VERY PRE-TERM BIRTHS IN PATIENTS UNDERGOING IN VITRO FERTILIZATION (IVF) USING FROZEN DONOR OOCYTES.** Luke Y. Ying, M.D.a,b James Baron, M.D.a,b Mark D. Sanchez, M.D.a,b Ying Ying, Ph.D.b aHCA West Florida GME Consortium/Brandon Regional Hospital, Brandon, FL; bUniversity of South Florida Department of Obstetrics and Gynecology, Tampa, FL.

**OBJECTIVE:** To compare pregnancy outcomes in patients undergoing IVF with elective single embryo transfer (eSET) using fresh vs frozen donor oocytes.

**DESIGN:** Retrospective cohort Society for Assisted Reproductive Technology (SART) data study.

**MATERIALS AND METHODS:** A retrospective cohort study was conducted using the publicly available data in the SART National Summary Report from 2014 to 2016. Cycle inclusion criteria were as follows: eSET, fresh donor oocytes, and frozen donor oocytes. Exclusion was use of gestational carrier. Pregnancy outcomes included live births (divided into singleton, twins, or triplets or more) and gestational age at delivery (divided into term, pre-term, and very pre-term). Term was defined as occurring after 37 weeks, pre-term as between 32 and 37 weeks, and very pre-term as before 32 weeks gestation. χ² test was used to compare variables between groups. A P value <0.05 was considered statistically significant.

**RESULTS:** A total of 8997 elective single embryo transfers were analyzed, including 6113 transfers using fresh donor oocytes and 2884 using frozen oocytes. Live birth rate in the frozen oocyte group was significantly lower compared with that in the fresh oocyte group (46.1% vs 53.4%, P < 0.0001, Table 1). Twin birth rate was significantly higher when using frozen oocytes compared to fresh oocytes (3.0% vs 1.1%, P < 0.0001). Total pre-term births (pre-term plus very pre-term) were increased in cycles using frozen oocytes.

**TABLE 1. Pregnancy outcome comparison in patients using fresh vs frozen donor oocytes.**

<table>
<thead>
<tr>
<th></th>
<th>Fresh donor oocytes</th>
<th>Frozen donor oocytes</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of eSETS</td>
<td>6113</td>
<td>2884</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Live birth rate per transfer</td>
<td>53.4%</td>
<td>46.1%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Singletons</td>
<td>98.9%</td>
<td>97%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Twins</td>
<td>1.1%</td>
<td>3.0%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Term delivery</td>
<td>84.6%</td>
<td>82.5%</td>
<td>0.08</td>
</tr>
<tr>
<td>Pre-term delivery</td>
<td>13.5%</td>
<td>13.7%</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Very pre-term delivery</td>
<td>1.9%</td>
<td>3.7%</td>
<td>0.0003</td>
</tr>
</tbody>
</table>
but not statistically different (17.4% vs 15.4%, P = 0.08). There was no significant difference in percentage of pre-term births between frozen and fresh oocytes (13.7% vs 13.5%, P > 0.05). However, frozen donor oocytes were associated with significantly increased percentage of very pre-term births compared to fresh donor oocytes (3.7% vs 1.9%, P = 0.0003).

CONCLUSIONS: The use of fresh donor oocytes in IVF treatment has become increasingly commonplace, but knowledge of related pregnancy outcome risks is currently sparse. This study using the largest SART data available so far shows that IVF patients using frozen donor oocytes had a lower live birth rate and have a significantly increased twin birth rate even with eSET when compared to fresh donor oocytes, which is likely a strong contributing factor in the significantly increased occurrence of very pre-term births and should be taken into account when counseling patients about to undergo IVF treatment.

P-184 Tuesday, October 15, 2019 6:30 AM

OBJECTIVE: The use of PGT-A and vitrification to select euploid embryos for transfer has led to improved live birth success in IVF; however, some euploid embryos fail to implant. Our objective was to compare parameters from 1) the retrieval cycle (IVF) in which blastocysts were biopsied and vitrified, 2) the frozen embryo cycle (FETu) during which the uterus was prepared for transfer, 3) the embryo transfer (FETt), and 4) the embryology (Lab) records all consolidated to determine what best predicts implantation following single thawed euploid embryo transfer (STEET).

DESIGN: Multivariate analysis of 45 parameters from IVF, FETu, FETt, and Lab and their association with a positive pregnancy test (CPR). MATERIALS AND METHODS: Data were collected from our electronic records for patients with transfers of thawed single euploid embryos diagnosed as euploid by Next Generation Sequencing during the IVF cycle. Parameters from IVF (17), FETu (5), FETt (4), and Lab (19) were considered. All 908 cases of STEET using NGS prior to 2018 with the required fields were examined. There were 704 STEETs (77.5%) with CPR. All +HCgs were considered implantations since 1) patients believe they are pregnant when they have a +HCg result and 2) no interfering +HCg was administered to these patients. Stepwise multiple logistic regression (197 combinations of parameters) was performed using the Akaike Information Criterion (AIC) to select significant parameters.

RESULTS: Parameters associated with better implantation (in descending magnitude of standard partial regression coefficient) were: Thicker Endometrium (FETu); higher endogenous serum Estradiol at Start of the IVF Cycle (FETu); Higher Progesterone at Day of Embryo Transfer (FETt); more embryos vitrified (IVF); the re-expansion of the blastocyst after warming (Lab); and less expansion of blastocysts prior to biopsy (Lab). Age at retrieval, embryo grades, as well as many other parameters were not associated with implantation.

CONCLUSIONS: Parameters from 3 of the 4 treatment categories were associated with establishment of +HCg. Of these, some may be under our control: Thicker endometrium, higher Progesterone levels on day of embryo transfer, and less expansion of the blastocyst prior to biopsy. However, the possibility remains that these parameters may be aliases for other features such as rate of uterine proliferation, rate of blastocyst development, patient weight. FETt (embryo transfer) was the category with no parameter associated with implantation. Also notable was the lack of association between embryo grades and +HCg.

SUPPORT: None.

P-185 Tuesday, October 15, 2019 6:30 AM
EFFECT OF VARIATION IN LABORATORY AND CLINICAL PRACTICES DURING THE LAST DECADE ON IVF OUTCOME. Maria Teresita W. Lao, MSc, Rajput Ishia, M.Med Sci, Essam S. N. Michael, M.D., Alex C. Varghese, Ph.D., Kannamannadi Jayaprakasan, Ph.D.1, 2 Astra Fertility Clinic, Mississauga, ON, Canada; 1Department of Obstetrics and Gynaecology, Royal Derby Hospital and University of Nottingham, United Kingdom.

OBJECTIVE: To evaluate the effect of changes in laboratory and clinical practices on IVF outcome and to estimate trend of pregnancy rates over a period of 12 years.

DESIGN: A review of prospectively collected data.

MATERIALS AND METHODS: Review of prospectively collected data at a tertiary fertility centre. Regression analysis used to study trend in the percentage of pregnancy outcome over a period of 12 years (January 2006 to December 2018).

RESULTS: Total number of IVF/ICSI cycles (fresh and frozen) during 12-year period (2006-2018) was 6401. Women’s age ranged from 19-51 years (mean ±SD, 35.58 ± 4.64). Overall clinical pregnancy rate (CPR) during this period was 34.3% (n = 2198). CPR in fresh cycles was 36.7% (1397/3806) which was similar to CPR in frozen cycles 36.5% (1092/2984) (p = 0.94). While there was no trend (R² = 0.76) observed in CPR for fresh embryo transfer (ET) over 12 years, a significant increasing trend (R² = 0.89) was noted in CPR with frozen ET (p < 0.05). In fresh ET cycles, a significant increase in CPR was noted after a switch over from slow freezing to vitrification method in 2008 (p < 0.001). The CPRs were 18% (68/377) during slow freezing (2006-2008), 35.1% (248/706) during transition period (2009-2012) and 40.2% (671/1660) during complete switch to vitrification method (2013-2018). The overall embryo survival rate post thaw was 94.5% (3578/3876). Blastocyst (day 5-7) transfer showed significantly favourable outcome CPR of 40.9% (1461/3568) when compared to cleavage stage embryo (day 2-4) ET with CPR of 37.08% (574/1548), in both fresh and frozen cycles (p < 0.005). Embryo culture in sequential media in bench top incubators versus single step in time-lapse incubators showed a similar CPR 36.2% (235/659) versus 38.6% (249/645) (p = 0.71), although there was increasing trend.

CONCLUSIONS: CPR in frozen embryo transfer cycles showed an increasing trend, mainly due to successful introduction of vitrification method of cryopreservation. Use of tri-gas incubators for embryo culture and blastocyst transfer positively affected CPR. However, introduction of embryo culture in time-lapse incubators did not show any significant change, albeit an increasing trend, in outcome.

P-186 Tuesday, October 15, 2019 6:30 AM
CONCENTRATIONS OF STROMAL CELL-DERIVED FACTOR-1 IN HUMAN FOLLICULAR FLUIDS ARE ASSOCIATED WITH CLINICAL IN VITRO FERTILIZATION OUTCOMES. Hidetaka Okada, MD, Akemi Nishigaki, PhD Kansai Medical University, Hirakata, Japan.

OBJECTIVE: To investigate the association between individual concentrations of stromal cell-derived factor-1 (SDF-1) and vascular endothelial growth factor (VEGF) and sex steroid hormones in human ovarian follicles and IVF outcomes. SDF-1 and VEGF are angiogenic factors that have possible roles in ovarian function.

DESIGN: Prospective Study.

MATERIALS AND METHODS: A total of 31 ICSI patients considered for blastocyst (BL) culture until day 5 were included in this study. Follicular fluid (FF) samples were obtained at the time of oocyte retrieval following ovarian stimulation from 38 year or less women with normal body mass index. Concentrations of SDF-1 and VEGF in 261 FF samples were measured with enzyme-linked immunosorbent assay. Concentrations of progesterone (P4) and estradiol (E2) were measured with a commercially available fluorescence immunassay. FF parameters were included in fertilization rate, cleavage rate, embryo morphology on day 3, and blastocyst morphology on day 5. We calculated the number of BL forming 3 or more per total number of cleavage embryo as the rate of full BL and the number of BL forming 3BB or more as the rate of good-quality BL. Differences in the measured parameters across the different groups were statistically assessed using ANOVA followed by Dunnett’s test and a level of P < 0.05 was considered statistically significant.

RESULTS: The FF concentrations of SDF-1 and VEGF were positively correlated with P4 concentrations in FF (r = 0.51, P < 0.01 and r = 0.71, P < 0.01, respectively), but not correlated with E2 concentrations in FF. Of the 261 oocytes at the MII stage, 200 were successfully fertilized; all these 200 oocytes had 2 pronuclei (PN) and developed into growing embryos. Of the 61 residual oocytes, 18 had 3 or 1 PN, 17 failed to fertilize, and 26 degenerated after ICSI. A possible relation between the concentrations of these
factor and IVF outcomes was evaluated by dividing SDF-1 (<125, 125-200, 200-275, 275-350, and >350 pg/ml) and VEGF (<180, 180-270, 270-360, 360-450, and >450 pg/ml) concentrations into five intervals creating five approximately similar sized groups. The follicular concentration of SDF-1 and VEGF were not significantly associated with fertilization and cleavage outcome, and embryo morphology. The rates of full blastocysts and good-quality blastocysts were significantly higher in follicles with an SDF-1 concentration of 275–350 pg/ml than in the follicles with SDF-1 concentrations of <200 pg/ml and >350 pg/ml (P < 0.05). The follicular concentration of VEGF was not associated with the blastocyst morphology. CONCLUSIONS: Our findings suggest that SDF-1 plays important modulatory roles in early luteinization and its follicular concentration may be a valuable biochemical marker of blastocyst development.

P-187 Tuesday, October 15, 2019 6:30 AM

PREDICTIVE FACTORS FOR OCYOTE RETRIEVAL FAILURE IN TREATMENT CYCLES WITH ASSISTED REPRODUCTIVE TECHNOLOGY: A RETROSPECTIVE COHORT STUDY USING THE NATION-WIDE ART REGISTRY OF JAPAN. Toshifumi Takahashi, M.D., Kuniaki Ota, M.D., Fukushima Medical University, Fukushima, Japan.

OBJECTIVE: The purpose of this study was to evaluate the prognostic factors for oocyte retrieval failure in patients undergoing assisted reproductive technology (ART) treatment cycles.

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: The present study was approved by the Ethical Committee on subjects. The data analyzed in this study were part of the Japanese ART registry database, which was collected by the Japan Society of Obstetrics and Gynecology from 2010 to 2012. We analyzed the data of 464,480 fresh cycles with transvaginal oocyte aspiration. The cycles with oocyte retrieval failure and those with one or more oocytes retrieved were compared to determine predictive factors for oocyte retrieval failure using multivariate logistic regression analyses.

RESULTS: The number of cycles with oocyte retrieval failure was 36,600 (7.9%). According to the multivariate analysis, age, cause of infertility, and controlled ovarian hyperstimulation (COH) were the independent prognostic factors for oocyte retrieval failure. The percentages of oocyte retrieval failure in the age groups of 29 years old and under, 30-34 years old, 35-39 years old, 40-44 years old, and over 45 years old were 3.2%, 4.2%, 5.9%, 10.2%, and 18.6%, respectively. The odds ratios of patients in their 30’s and 40’s were 1.7 and 4.0 times those of the patients in their 20’s, respectively. The percentages of oocyte retrieval failure that corresponded to infertility cause by a male factor, tubal factor, endometriosis, and unknown factors were 5.6%, 7.3%, 8.0%, and 9.2%, respectively. The odds ratios for oocyte retrieval failure in the tubal factor, endometriosis, and unknown groups were 1.3, 1.4, and 1.7 times those in the male factor group, respectively. The percentages of oocyte retrieval failure in the COH cases using aromatase inhibitor or clomiphene (AI+CC), GnRH agonist, and GnRH antagonist were 10%, 1.5%, and 3.5%, respectively. The odds ratios for oocyte retrieval failure in the GnRH antagonist and AI+CC protocols were 2.4 and 5.3 times those for the GnRH agonist protocol, respectively. The percentage of oocyte retrieval failure in the natural cycles was 21%.

CONCLUSIONS: The predictive factors for oocyte retrieval failure might be related to a patient’s age, particular causes of infertility, and COH protocols. These results provide information that may be useful for counseling patients before ART treatments.

P-188 Tuesday, October 15, 2019 6:30 AM


Recent years have seen a dramatic rise in the number of frozen-thawed embryo replacement (FER) cycles. Between 2012 and 2016, the annual number of FETs in the UK increased by 77%, while the number of fresh cycles declined by 2%. Despite FER accounting for 30% of UK IVF workload, the optimum method of endometrial preparation for FER is unknown. OBJECTIVE: This study assesses current UK trends in endometrial preparation for FER and compares the outcomes of women undergoing medicated FER with GnRH-agonist and GnRH-antagonist pituitary suppression.

RESULTS: The first national UK survey of practice on endometrial preparation for FER and a retrospective cohort study comparing GnRH-antagonist with GnRH-agonist pituitary suppression in FER.

MATERIALS AND METHODS: All 84 UK IVF clinics were asked to complete an online survey between September 2018 and January 2019. RESULTS: Sixty-five clinics (77%) responded, together undertaking approximately 24,419 FERs annually. The preferred developmental stage of cryopreservation is blastocyst, favoured by 98% of clinics. In the UK 77% of FETs are medicated, 18% natural cycle, 5% modified natural cycle and <1% ovaulation induction. In ovulatory women 69% of clinics favour medicated, 26% natural cycle and 5% modified natural cycle FER. In natural cycle FER, 31% always, 44% sometimes and 25% never prescribe luteal support. Fifty-one percent of clinics transfer a thawed blastocyst on the fifth day after the predicted day of ovaulation, 21% on the fourth, 14% on the third, 9% on the second and 5% on the seventh.

In medicated FER, 2% of clinics undertake blastocyst transfer on the third day of progesterone, 3% on the fourth, 21% on the fifth, 61% on the sixth and...
13% on the seventh. Luteal support is continued from six to beyond twelve weeks’ gestation, with the majority (69%) stopping at 12 weeks. The use of pituitary suppression in medicated FER varies widely. Fifty-five percent of clinics favour GnRH-agonist down-regulation, 11% GnRH-antagonist and 34% no supplementary pituitary suppression.

Consequently, we analysed all women undergoing medicated FER of one or two unbiopsied blastocysts at a UK IVF clinic between January 2014 and June 2016 comparing GnRH-antagonist with GnRH-agonist medicated FER. 578 patients (188 antagonist, 390 agonist) were included. Baseline characteristics were similar. Live birth (36.7% (antagonist) vs. 39.5% (agonist), p<0.519), clinical pregnancy (59.5% vs. 60.5%, p=0.482) and miscarriage rates (33.3% vs. 34.5%, p=0.857) were similar. In the antagonist group there were less clinic visits (median (range): 2(5) vs. 3(5), p<0.01) and ultrasound scans (1(3) vs. 2(5), p<0.01).

CONCLUSIONS: Wide variation exists in the preferred method of endometrial preparation for FER, emphasising the need for more research to determine the optimum protocols. The survey results highlight particular inconsistency in approach to pituitary suppression in medicated FER. Our cohort study historically categorical benefits to GnRH-agonist as an alternative to GnRH-antagonist for pituitary suppression in medicated FER. However, more research is needed to confirm similar clinical outcomes.

P-191 Tuesday, October 15, 2019 6:30 AM

FRESH VERSUS FREEZE-ALL STRATEGY IN ASSISTED REPRODUCTIVE TECHNOLOGY – A COCHRANE REVIEW. Tjitske Zaart, MD. (MSc), Miriam S. Zagers, MSc., Femke Mol, M.D., PhD, Mariette Goddijn, Prof. Dr. MD. PhD., M. van Wely, Dr. PhD., Sebastiaan Mastenbroek, PhD. Amsterdam UMC, University of Amsterdam, Center for Reproductive Medicine, Amsterdam Reproduction & Development Research Institute, Meibergdreef 9, Amsterdam, Amsterdam, Netherlands.

OBJECTIVE: In vitro fertilisation (IVF) treatments imply a fresh embryo transfer, possibly followed by one or more frozen-thawed embryo transfers in subsequent cycles. Alternatively, one can opt to freeze all suitable embryos and transfer frozen-thawed embryos in subsequent cycles only, which is also known as the freeze-all strategy. We compared the effectiveness and safety of these treatment strategies.

DESIGN: We searched the Cochrane Gynaecology and Fertility Group Trials Register, the Cochrane Central Register of Studies (CRSO), MEDLINE, Embase, PsycINFO, CINAHL, and two registers of ongoing trials in February 2019 for relevant studies, and checked references and contacted study authors in the field to obtain additional data.

MATERIALS AND METHODS: We used standard methodological procedures as recommended by Cochrane for our search, data extraction, and analyses. The primary outcome was cumulative live birth rate (cLBR). Secondary outcomes included ovarian hyper stimulation syndrome (OHSS), pregnancy complications, and time to pregnancy.

RESULTS: We included six RCTs in our meta-analyses, that together reported on 4324 women. The studies compared the freeze-all strategy to IVF with fresh transfer in women with a high risk of OHSS, in ‘good prognosis’ women based on the number of follicles, in women with PCOS, and in young women without PCOS. The evidence was of moderate to low quality due to serious risk of bias, serious imprecision for four studies, and serious unexplained heterogeneity for one study.

For cLBR we found an OR of 1.0 (95% CI 0.97 to 1.24; 6 RCTs; 4324 women; I² = 42%); moderate quality of evidence) for the freeze-all strategy versus IVF with fresh transfer of embryos. These data suggest that for a cLBR of 63% following IVF with fresh transfer of embryos, the cLBR following the freeze-all strategy would be between 62% and 67%.

Women developed less OHSS after the freeze-all strategy compared to IVF with fresh transfer of embryos (OR 0.29, 95% CI 0.19 to 0.44; 4 RCTs; 4065 women; I² = 5%, low quality evidence). These data suggest that for an OHSS rate of 31% following the freeze-all strategy, the rate following the freeze-all strategy would be between 1% and 2%.

The risk of maternal hypertensive disorders and having a large for gestational age baby was increased following the freeze-all strategy compared to IVF with fresh transfer of embryos (OR 2.15, 95% CI 1.42 to 3.25; 3 trials; 3940 women; I² = 97% and OR 1.87, 95% CI 1.43 to 2.44; 3 trials; 3119 women; I² = 0%, respectively, both low-quality evidence). The risk of having a small for gestational age baby was lowered following the freeze-all strategy (OR 0.68, 95% CI 0.53 to 0.89; 3 trials; 3119 women; I² = 56%, low-quality evidence).

One trial reported on time to conception and one trial reported on time to live birth which were both longer in the freeze all strategy.

CONCLUSIONS: We did not find a clear difference in cLBR between the two strategies. The freeze-all strategy lowered the risk of OHSS, increased the risk of maternal hypertensive disorders of pregnancy, increased the risk of a large for gestational age baby, and lowered the risk of a small for gestational age baby. The time to pregnancy was longer in the freeze-all strategy. Reference: NA. SUPPORT: None.

P-192 Tuesday, October 15, 2019 6:30 AM

PREDICTING CUMULATIVE LIVE BIRTH RATE FOR THE FIRST CYCLE OF IN VITRO FERTILIZATION. Yao Lu, M.D., Guiguang Wang, M.D., Steven R. Lindheim, M.D., Yun Sun, M.D. "Center for Reproductive Medicine, Ren J Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China.

OBJECTIVE: To determine the independent predictors of cumulative live birth (CLB) for women undergoing first in vitro fertilization (IVF) cycle.

MATERIALS AND METHODS: We conducted a retrospective cohort study of 6016 women aged 21-42 years old who underwent IVF cycle in the first time, in a single center in Shanghai, China, from January, 2011 to December, 2016. The results of all cycles were included. Logistic regression was used to estimate the effect of individual predictors on CLB. The predictors included age, BMI, smoking status, smoking amount, infertility etiology, and number of retrieved oocytes.

RESULTS: The cumulative live birth rate (CLB) was 44.6% in total population. The cumulative live birth rate was significantly lower in women older than 37 yrs (OR=0.58, 95% CI 0.49-0.70). Furthermore, women with poor ovarian reserve (OR=0.69, 95% CI 0.57-0.83) and poor endometrial thickness (OR=0.58, 95% CI 0.47-0.72) had a lower CLB. Women who had undergone previous infertility treatments had a lower CLB (OR=0.78, 95% CI 0.66-0.92). The results indicated that women with a higher number of retrieved oocytes had a higher CLB (OR=1.09, 95% CI 1.06-1.12) compared to women with less than 15 retrieved oocytes.

CONCLUSIONS: Age, ovarian reserve, endometrial thickness, infertility etiology, and number of retrieved oocytes are independent predictors of CLB in IVF cycles.
OBJECTIVE: To develop a prediction model to estimate the chances of cumulative live birth following the first cycle of in vitro fertilization (IVF) and cumulative embryo transfers based on female demographics and cycle stimulation characteristics.

DESIGN: Retrospective study.

MATERIALS AND METHODS: All women at the age of 20-50 years old who underwent their first IVF treatment in the reproductive center of Ren Ji hospital from Jan 2014 to Dec 2015 were screened. Cumulative live birth was defined as first live birth from all fresh and frozen thawed embryo transferred within 2 years after oocyte retrieval. A multiple fraction polynomial (MFP) regression model was used to predict the probability of live birth for an individual woman. Two clinical prediction models were developed: pre-treatment model using information available before starting ovarian stimulation and the post-treatment model based on additional information collected after oocyte retrieval.

RESULTS: After excluding cycles with PGT and oocyte freezing, 7796 women with 7796 cycles were included. In total 5146 (66.0%) cumulatively had a live birth following their first IVF retrieval. Key pre-treatment predictors of live birth were the woman's age (≥ 35 vs < 35 years; adjusted odds ratio 0.34, 95% confidence interval, 0.29 to 0.38), BMI (≥ 24 vs. < 24; 0.82, 0.72 to 0.92), and a basal FSH (≥ 10 vs. <10 IU/L; 0.54, 0.46 to 0.64). Post-treatment predictors included number of fertilization (1.03, 0.99 to 1.08), basal FSH (≥ 10 vs. < 10 IU/L; 0.89, 0.83 to 0.99), woman's age (≥ 35 vs. <35 years; 0.69, 0.55 to 0.84), endometrial thickness on the day of trigger (≥ 7.5 vs. <7.5 mm; 1.19, 1.01 to 1.49) and cumulative number of embryos transferred (≥ 2 vs. <2; 1.83, 1.40 to 2.40). A pre-treatment model of a 32 year old woman with a BMI of 21.1 kg/m² and basal FSH 7.5 IU/L, has a 62.9% cumulative chance of having a live birth after her first cycle. A post-treatment model for the same woman with 6 fertilized oocytes and an endometrial thickness of 9 mm, has an estimated 77.6% of having a live birth.

CONCLUSIONS: This study provides an individualized estimate of a couple’s cumulative chance of having a live birth after the first IVF cycle both before treatment and after oocyte retrieval. This may help physicians better counsel couples in preparation for their IVF journey both emotionally and financially.

P-193 Tuesday, October 15, 2019: 6:30 AM

PRO CASPASE-3 AND CLEAVED CASPASE-3 GENE AND PROTEIN EXPRESSION IN HUMAN GRANULOSA CELLS CORRELATED WITH COS DURATION, LENGTH OF INFERTILITY AND PROPORTION OF MATURE OOCYTES RETRIEVED. Camila P. Almeida, Ms,a Camila O. Silveira, MD, Ms, Enio F. Ferreira, Sr, PhD, Marcia C. Ferreira, MD, PhD, Gabriele Graças Oliveira, Ms, Emerson S. Veloso, Ms, Felipe H. S. Silva, Sr, Ms,a, SANTUZA S. COELHO, MS,a, Leonardo M. Moraes, MD, MS, Fernando M. Reis, MD, PhD, Helen L. Del Puerto, PhD,a *UFMG, Belo Horizonte, Brazil; ‡Fertilhaby, Belo Horizonte, Brazil.

OBJECTIVE: To evaluate the clinical correlates of pro-caspase-3, cleaved caspase-3 and other apoptosis related genes expressed in human granulosa cells (GCs) of patients undergoing controlled ovarian stimulation (COS).

DESIGN: Luteinized GCs obtained from in vitro fertilization (IVF) and fertility preservation patients were evaluated for their expression of pro-caspase-3, cleaved caspase-3 and gene expression of BAX, BCL2, CASPASE3 and CASPASE8, that later were correlated with patient’s clinical data, such as length of infertility, length of COS and proportion of mature oocytes.

MATERIALS AND METHODS: Follicular fluid (FF) samples were collected from 35 patients referred to a private clinic for couple infertility treat- ment and female fertility preservation between March and September 2018. The study was approved by the institutional Ethics Committee for Research on Human Subjects (COPH No 1.979.648) and the participants provided written informed consent to be enrolled in the study. Luteinized GCs were isolated from FF aspirates using a Histopaque gradient. Recovered GCs were partly fixed in 10% buffered formaldehyde and included in paraffin for further Hematoxylin/Eosin (HE) staining and immunocytochemical procedures, and partly kept frozen in 500 μL of TRI Reagent until RNA isolation. Immunocytochemical staining of cellblock sections was performed for pro-caspase-3 and cleaved caspase-3, according to the peroxidase reaction method with a polyclonal secondary antibody for identification. Total RNA was isolated from GCs, first-strand complementary DNA (cDNA) was synthesized following SuperScript III reverse transcriptase Kit manufacturer’s protocol, and real-time PCR was carried out for BAX, BCL2, CASPASE3, CASPASE8, and S26 as a normalization gene, using Sybr green master mix kit. Data distribution was evaluated by the Shapiro-Wilk test, clinical data and gene and protein expression linear correlations were analyzed by Pearson’s or Spearman’s rank correlation coefficient using prism 8 computer software.

RESULTS: Cleaved caspase-3 correlated positively with the length of COS (r = 0.445, p < 0.05) and the length of infertility (r = 0.476, p < 0.05). However, only pro-caspase-3 expression presented a positive correlation with the proportion of mature oocytes collected (r = 0.427, p < 0.05). Gene expression of CASPASE 3 and CASPASE 8 also correlated directly with the length of COS (r = 0.462, p < 0.05; r = 0.420, p < 0.05, respectively).

CONCLUSIONS: These findings suggest that pro-caspase-3 is constitutively expressed in human granulosa cells and correlates with the proportion of mature oocytes retrieved, therefore it better indicates granulosa cell integrity than immature cell death by apoptosis. Conversely, the activation of caspase-3 in granulosa cells is associated with a longer time of infertility and longer duration of COS in IVF patients.

SUPPORT: PRq UFMG. Fapemig. CNpq.
APOTOPSIS OF CUMULUS GRANULOSA CELLS IS HIGHER IN NON-PREGNANT GROUP IN PATIENTS UNDERGOING IVF/ICSI

OBJECTIVE: To evaluate apoptosis of granulosa cells in clinical pregnant group versus non-pregnant group in women undergoing in-vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI).

DESIGN: A prospective cohort study.

MATERIALS AND METHODS: A prospective cohort study was initiated at a single IVF center involving a total of 164 women undergoing IVF/ICSI cycles. Mural and cumulus granulosa cells, and follicular fluid were collected during oocyte retrieval. Annexin V-FITC/PI apoptosis staining and flow cytometry analysis were performed to evaluate apoptosis rate of mural granulosa cells and cumulus cells. Serum and follicular fluid hormones including estradiol (E2), progesterone (P), testosterone (T), anti-Mullerian hormone (AMH) were measured by ECLIA. Laboratory and clinical outcomes were analyzed.

CONCLUSIONS: A significantly higher apoptosis rate of mural granulosa cells was associated with worse ovarian response, with fewer egg and embryo numbers in IVF/ICSI as well as with age. Early apoptosis rate of cumulus cells might also have influence on clinical pregnancy.


5. Bencomo E, Pérez R, Artagea MA, Acosta E, Peña O, Lopez LA, Avila I, Palumbo A. Apoptosis is a culture-dependent granulosa-lutein A

---

DOES MASSAGE THERAPY IMMEDIATELY PRIOR TO EMBRYO TRANSFER IMPROVE CLINICAL PREGNANCY RATE IN IVF-PGT-A (IN-VITRO FERTILIZATION-PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY) CYCLES?

OBJECTIVE: Prior retrospective research (1) has suggested improved implantation rate in FET (frozen embryo transfer) cycles with untested blastocysts. This purpose of this study is to evaluate whether massage therapy immediately prior to SET (single embryo transfer) of PGT-A euploid embryos improves clinical pregnancy rate.

RESULTS: There was no significant difference in age, body mass index, underlying fertility diagnosis, number of prior embryo transfers (0 vs 1), or endometrial thickness between the two groups. All patients had trilaminar endometrium of at least 7 mm thickness by ultrasound prior to progesterone start. Implantation rate (positive quantitative beta human chorionic gonadotropin 14 days post SET) was 80.6% (n = 25) in the treatment group and 64.3% (n = 21) in the control group, p = 0.09. The live birth rate was 64.5% (n = 20) in the treatment group and 47.1% (n = 16) in the control group, p = 0.16.

CONCLUSIONS: Despite advances in modern fertility treatment, clinical pregnancy rates remain well below 100%, even in good prognosis patients. Therefore, a low-cost, low-risk intervention which may benefit this population is of great interest. The standardized massage in the study includes elements of both lower abdominal massage, which can theoretically increase blood flow to the pelvis, and head and neck massage, which may improve relaxation. Prior retrospective research (1) has suggested improved implantation rate in FET cycles with untested blastocysts. Our randomized controlled double-blind trial appears to demonstrate a clinical benefit of

---

**Parameters**  
Clinical pregnant (n = 62)  
Non-pregnant (n = 66)  
P value

| Age (yr) | 29 (27.75-32) | 30 (27.33) | ns |
| Basal serum FSH (mIU/ml) | 6.57 (5.36-7.35) | 6.62 (5.73-7.55) | ns |
| Basal serum AMH (ng/ml) | 4.34 (2.14-7.46) | 3.76 (1.62-6.03) | ns |
| MGCs early apoptosis rate (%) | 0.58 (0.29-1.08) | 0.63 (0.22-1.45) | ns |
| MGCs late apoptosis rate (%) | 2.75 (0.67-6.31) | 2.36 (0.66-5.68) | ns |
| CCs early apoptosis rate (%) | 0.13 (0.03-0.86) | 0.37 (0.19-6.90) | <0.05 |
| CCs late apoptosis rate (%) | 2.46 (0.47-13.4) | 6.63 (3.16-14.0) | ns |
| FF AMH (ng/ml) | 3.33 (1.83-4.98) | 8.71 (3.81-14.61) | 0.052 |
| FF E2 (pmol/L) | 602497 (468066-83570) | 716750 (612033-942250) | <0.05 |
| FF P (ng/mL) | 17700 (12300-45935) | 17700 (12697.5-29052.5) | ns |
| FF T (nmol/L) | 5.26 (3.5-8) | 5.29 (4.38-8.48) | ns |
| hCG day E2 (pmol/L) | 4759 (2943-7258.5) | 2691 (1267-4812) | 0.069 |
| OPU egg number | 13 (8-17.25) | 10.5 (6-18) | ns |
| Embryo transfer rate (%) | 75.00 (60.00-83.93) | 67.26 (57.14-83.33) | ns |
| D3 good embryo rate (%) | 70.71 (59.29-94.23) | 70.98 (41.25-83.55) | ns |
| Good blastocyst number | 3 (1-5)  | 2 (0-3.25)  | <0.05 |
| Blastocyst formation rate (%) | 55.56 (50.00-83.33) | 41.67 (17.21-71.63) | <0.05 |
massage therapy immediately prior to SET of PGT-A euploid embryos (17.4% increase in live birth). While this finding has not yet reached statistical significance, the trend continues to favor the massage group, and data collection is ongoing.


SUPPORT: None.

### P-197 Tuesday, October 15, 2019 6:30 AM

**WOMEN WITH PREVIOUS FAILED IVF BENEFIT FROM INTRAUTERINE INSTILLATION OF PLATELET RICH PLASMA.** Mamta Sudhir Katalkhd, DNB,a Sangeeta Dheerendra Deshmukh, MD,a Shubhada Sanjiv Khandeparkar, MD,a Nandkishor Jagannath Naik, B.Sc,a Mangesh Sanap, MSc,a Gajanai Naik, B.Sc,a Pratiksha Khandare, MSc,a Firuza Rajesh Parikh, MD DNB PhD,a "FertilTree-Jaslok International Fertility Centre, MUMBAI, India; 2Jaslok Hospital and Research Centre, Mumbai, India; 3Dr.Khandeparkar IVF centre, MUMBAI, India.

OBJECTIVE: To record the improvement in the endometrial lining and pregnancy rates in Frozen Embryo Transfer (FET) cycles of women following intratruterine Platelet Rich Plasma (PRP) instillation.

DESIGN: A prospective case control study was carried out during the period of August 2018 to March 2019 at our centre. Women in the age group of 25 to 45 years with a history of previous cancelled cycles due to poor endometrial lining undergoing FET were included.

MATERIALS AND METHODS: 101 women undergoing FET at our centre were included in the study, following their consent. Intratruterine instillation of approximately 1 ml of autologous PRP was carried out on day 5, day 12 of endometrial priming and 48 hours prior to embryo transfer. The endometrial thickness was evaluated by Transvaginal Ultrasound on the days of metrial lining and clinical pregnancy rates particularly in women with past history of Genital TB where implantation rates are low.

CONCLUSIONS: Intratruterine infusion of PRP has a potential to improve the endometrial lining and clinical pregnancy rates particularly in women with multiple failed attempts and also holds promise for women with past history of Genital TB where implantation rates are low.

### RESULTS

- 96 out of 101 women showed improvement in the endometrial lining. Of 101 women in the study, 29 women conceived (28.7%). Also, there were 10 biochemical pregnancies (9.9%). Of these 29 women, 14 had never conceived in the past and 15 women had previous pregnancy losses. Among the 45 women, who had never conceived in the past, 30 women had done multiple cycles earlier and of these 24% (n = 5) got pregnant. Of the 29 pregnancies with PRP, one woman delivered, 6 women had miscarriages after cardiac activity and 15 are ongoing pregnancies. Thirty three women had past history of Genital TB. Of these, 24% (n = 8) got pregnant. Of these, 5 had done multiple IVF cycles in the past and there were 3 women who had never conceived. Of the 8 pregnancies with a history of genital TB, 5 are ongoing pregnancies and 3 miscarried after cardiac activity.

### CONCLUSIONS

- Intratruterine infusion of PRP has a potential to improve the endometrial lining and clinical pregnancy rates particularly in women with multiple failed attempts and also holds promise for women with past history of Genital TB where implantation rates are low.

### OBJECTIVE: To study the relationship between maternal vitamin D (vitD) status and pregnancy outcome of IVF/ICSI.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: A total of 2577 female patients were collected who were received IVF/ICSI treatment from our hospital from 2017.1-2018.11. Peripheral blood was collected one day before transplantation to test the total and free vitD. All patients were divided into three groups according to the level of total vitD: adequacy group(total vitD ≥ 30pg/ml), insufficiency group(total vitD 20pg/ml and < 30pg/ml) and deficiency group(total vitD < 20pg/ml).

RESULTS: There were 1384 patients in deficiency group (53.7%), 1113 patients in insufficiency group (43.2%), and 80 patients in adequacy group (3.1%). There was no significant difference in age, weight, BMI, basic FSH, LH, E2, T and AMH among the three groups. There was also no significant difference in the number of oocytes received, transplantable embryos, high quality embryos and fertilization eggs of 2PN, pregnancy rate and abortion rate among the three groups (Tab. 1). The total vitD level between pregnant group (19.62(16.59,22.83)) and non-pregnant group (19.4(16.35,22.79)) had no significant difference(p = 0.45). The free vitD level between pregnant group (4.71(4.15,5.34)) and non-pregnant group (4.71(4.15,5.27)) had no significant difference too(p = 0.76).

CONCLUSIONS: Although the pregnancy rate tended to increase with vitD level, neither total vitD nor free vitD seems was associated with IVF pregnancy rate and abortion rate.

OBJECTIVE: Non-invasive testing for embryo selection is not yet well established. Recently a three-gene expression model in cumulus cells was evaluated for embryo selection in a Caucasian population (JARG 2019) and showed a significant increase of clinical pregnancy rate in day 3 single embryo transfer (SET). This study investigates if the same genes, CAMK1D, SASH1 and EFNB2, are also predictive in an independent Asian ART population.

DESIGN: International retrospective multicentre study with individual oocyte denudation.

MATERIALS AND METHODS: Oocytes from 39 Asian women in three centres (China, Taiwan, Japan) scheduled for ICSI and SET underwent individual oocyte denudation after pick-up. The women were stimulated with HP-hMG (n=9) or combo HP-hMG & rFSH (n=30) and received a day 3 or day 5 fresh or frozen SET. mRNA expression analysis for three predictive genes CAMK1D, EFNB2 and SASH1 (Corona Test) and 2 endogenous control genes (UBC, B2M) was performed by QRT-PCR using the cumulus cells of the oocytes. The CC of all oocytes developing into an embryo, that was selected for transfer based on the embryo morphology, were analysed. The expression of the three predictive genes was used for multivariable stepwise regression analysis.

RESULTS: Of the 58 transferred embryos from the 39 Asian women 22 implanted and resulted in a clinical pregnancy. Thirty six embryos did not implant. The three-gene expression model separated CC samples from pregnant and non-pregnant women with an accuracy of 93%. The sensitivity was 100%, specificity 89% and the area under the curve (AUC) was 0.9848.

CONCLUSIONS: The multivariate analysis confirmed that CAMK1D, EFNB2 and SASH1 are also predictive for transfer outcome in Asian ART patients. The intra-patient analysis on the European Caucasian patients, proved also to be predictive for oocyte competence in an Asian ART population. Finally, our results also suggest that the three-gene expression model also works in patients stimulated with a combo protocol of rFSH and HP-hMG. This was a retrospective study and the findings need to be confirmed in a larger prospective study.


SUPPORT: FWO Flanders, NSCF China, IOF.

P-201 Tuesday, October 15, 2019 6:30 AM

CAN WE PREDICT WHO WILL DEVELOP A BLASTOCYST FROM AN IVF/ICSI CYCLE? Rakia Aljasser, MD, a Sara Ilinsky, MD, a Lynda Hughes, BSc, b Angelos Vilos, MD, a George Vilos, MD, a Basim Abu-Rafea, MD, a Clinical Fellow, London, ON, Canada; b The Fertility Clinic London Health Sciences Centre, London, ON, Canada; c Western university, London, ON, Canada; d Western university, London, ON, Canada; e Western University, London, ON, Canada.

OBJECTIVE: As IVF laboratory techniques have advanced, extended culture and blastocyst transfer has become a mainstream of practice. More and more clinics are employing blastocyst only transfer policies. Unfortunately, not all patients will have embryos that attain blastocyst stage meaning that a proportion of patients will not have an embryo transfer. The objective of this study is to identify patient or cycle characteristics predictive of blastocyst development.

DESIGN: We performed a retrospective database review of clinic and embryology data from all patients who had an IVF/ICSI cycle at our academic hospital-based fertility clinic.

MATERIALS AND METHODS: From February 1, 2012 to February 28, 2019 we looked at all cycles that had extended culture and compared patient and cycle characteristics from cycles with blastocyst development to cycles without (ie. no embryo development past cleavage stage or morula). Donor oocyte, onco-fertility, and social oocyte cryopreservation cycles were excluded. Bivariate statistical analysis was used to identify characteristics associated with blastocyst development and multivariate analysis used to create a prediction model for blastocyst development.

RESULTS: Of the 2474 IVF/ICSI cycles performed, 803 met inclusion criteria and had extended culture. Seventy-nine percent of patients developed blastocysts by day 5 or 6 with an average number of 2.8 blasts per cycle. Conventional IVF reduced the chance of no blastocyst development by 46% compared to ICSI (OR 0.54, 95% CI 0.33-0.89, p = 0.01). The number of good quality day 3 embryos (more than 5 blast cells) was also associated with a better outcome; each good quality day 3 embryo reduced the chance of no blastocyst development by 14.5% (p < 0.001). No other characteristics, including female age, BMI, parity, infertility diagnosis, gonadotropin dose, protocol, estradiol level, number of oocytes retrieved, and fertilization were associated with blastocyst development. The prediction model using
inssemination method and number of good quality day 3 embryos was strong with a Hosmer and Lemeshow p-value of 0.71.

CONCLUSIONS: Use of conventional IVF and number of embryos with more than 6 cells on day 3 of culture were the only significant clinical predictor for blastocyst formation.

P-202 Tuesday, October 15, 2019 6:30 AM

HUMAN GROWTH HORMONE COUPLED WITH THE CMAP ACUPUNCTURE PROTOCOL (GH-CMAP) ENHANCES BLASTOCYST FORMATION AND CLINICAL PREGNANCY RATES. Paul C. Magarelli, M.D., Ph.D., Feng Gao, Ph.D., Daine K. Cridennda, L.Ac, FABORM, HQA Fertility Centers, Colorado Springs, CO.

OBJECTIVE: The aim of this study was to evaluate supplemental HGH both before and during ovarian stimulation coupled with the Cridennda Magarelli Acupuncture Protocol (CMAP) (GH-CMAP Protocol) in terms of oocyte retrieved, oocyte maturity, blast formation, and clinical pregnancy rates.

DESIGN: This is a preliminary, prospective cohort study conducted in 2018 on 112 women, including GH-CMAP (48) vs. antagonist protocol (A) group (64) (control).

MATERIALS AND METHODS: A regular antagonist protocol with 1.6mg/day HGH was given (n=48) before and during antagonist stimulation (AS) period; 64 patients were undergoing regular AS protocol (2017-2018). The CMAP protocol (3) was used with supplemental estrace, DHEA, CoQ10. Duration of ovarian stimulation GH-CMAP averaged 10 days, the control group 11 days. Normality of all variables was evaluated and number of oocyte, oocyte maturity rate and blast formation rate were log 10 transformed to become normal distribution. Multivariate regression model (JMP version 14.0) was performed to assess the effect of GH-CMAP on number of oocytes retrieved, oocyte maturity rate and blastocyst formation rate, adjusted by independent variables including age, AMH, BMI, FSH. Total number of patients N=112; GH-CMAP group n=48; Antagonist group n=64.

RESULTS: Co-stimulation with HGH in the GH-CMAP protocol improved blast formation rate (GH-CMAP 1.75±0.05, A 1.59±0.03; p=0.0252). Pregnancy rates trended higher in GH-CMAP group (58.8%) than in the AS protocol group (46.6%). Fewer number of oocytes retrieved (GH-CMAP 9, A13; p=0.0095) and lower oocyte maturity rate (p=0.1397) was observed in GH-CMAP group by design. There was a statistically significant association between BMI and blastocyst formation rate in that the higher BMI, the lower blastocyst formation rate (p=0.0085).

CONCLUSIONS: These data provide evidence that the positive effect of GH-CMAP on blast formation, consequently improve clinical pregnancy rate. The implantation rate and live birth rate are needed to be included in the further study. These results need to be confirmed by a large-scale randomized controlled trial.


SUPPORT: None.

P-204 Tuesday, October 15, 2019 6:30 AM

THE EFFECT OF INTERLEUKIN 6 ON CONTROLLED OVARIAN STIMULATION RESULTS AND IVF OUTCOME IN INFERTILE WOMEN WITH ADENOMYOSIS UNDERGOING IVF. Chung-Hoon Kim, M.D., Ph.D., Jei-Won Moon, M.D., Shin Yong Moon, M.D., Ph.D., Fertility Center, Seoul, Korea, Republic of (South).

OBJECTIVE: To investigate the effect of serum interleukin 6 (IL-6) on controlled ovarian stimulation (COS) results and IVF outcome in infertile women with adenomyosis undergoing IVF.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 59 infertile women with adenomyosis who had their blood taken for analysis of serum IL-6 on the day of hCG injection were included in this study. COS results and IVF outcome were compared among the three groups (group 1; <1.5 pg/ml, group 2;1.5-7.0 pg/ml, group 3;>7.0 pg/ml) according to the serum IL-6 levels. Analysis of variance (ANOVA) was used to compare the mean values among three groups. Chi-square test and Fisher’s exact test were used for the comparisons of fraction. Statistical significance was defined as P<.05.

RESULTS: Serum IL-6 levels on the day of hCG injection was significantly higher in infertile women with adenomyosis than in patients without adenomyosis who underwent IVF during the same period (P=.01). The demographic characteristics of patients with adenomyosis were comparable among the three groups according to the serum IL-6 levels. There were also no differences in the three groups with respect to the number of oocytes retrieved, mature oocytes retrieved and fertilized oocytes. However, the number of grade 1 or 2 embryos was significantly lower in group 3 (P<.05). Clinical pregnancy rate was significantly lower in group 3, compared with group 1 or 2 (P<.001, P<.023, respectively). None of the patients with serum IL-6 levels more than 8.0 achieve pregnancy following the corresponding IVF cycle.

CONCLUSIONS: High serum IL-6 levels in infertile women with adenomyosis can have an adverse effect on the IVF outcome including embryo quality and clinical pregnancy rate.

SUPPORT: None.

P-203 Tuesday, October 15, 2019 6:30 AM

THE EFFECT OF BODY MASS INDEX ON THE IMPLANTATION POTENTIAL OF EUPLOID EMBRYOS. Mohamad Irani, MD, Vinay Gunnalla, MD, Steven Spandorfer, M.D., Zev Rosenwaks, M.D., The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Obesity has been associated with higher miscarriage rates after natural conception and IVF. However, the underlying mechanism, whether obesity affects egg quality or endometrial receptivity, is not well understood. Here we aim to determine the impact of body mass index (BMI) on the outcomes of frozen-thawed euploid embryo transfer cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Frozen-thawed embryo transfer (FET) cycles of euploid embryos between 2013 and 2017 were included. Embryos were cultured in time-lapse incubators. Preimplantation genetic testing for aneuploidy was performed using array comparative genomic hybridization or next-generation sequencing. Cycles were divided into three groups according to the female patients’ BMI: <25 kg/m², 25-29.9 kg/m² (overweight), and ≥ 30 kg/m² (obese). The miscarriage rate and live birth rate (LBR) were compared between the three groups. χ² and Fisher’s exact tests were used for categorical variables. Student’s t test and ANOVA were used for parametric data. Values were expressed as mean ± standard deviation.

RESULTS: A total of 1011 FET of euploid embryos (s) were included: 758 with a BMI <25 kg/m², 174 with a BMI 25-29.9 kg/m², and 79 with a BMI ≥30 kg/m². The women were of comparable age between the three groups (Table 1). There was a trend toward a lower LBR in women with a BMI ≥30 kg/m² compared to women with a BMI <25 kg/m² (48.1% vs. 57.5%, respectively; P=0.1), but it did not reach statistical significance. The LBR for women with a BMI 25-29.9 kg/m² (54%) was comparable with the other two groups (Table 1). There was no significant difference in miscarriage rates between the three groups (8.8% for BMI <25 kg/m², 9.6% for BMI 25-29.9 kg/m², and 11.6% for BMI ≥30 kg/m²; P=0.1).

CONCLUSIONS: Overweight and obesity do not significantly affect the implantation potential of euploid embryos.

BMI (kg/m²) <25 25-29.9 ≥30 P value
Age (years) 36.3 ± 4.1 37.0 ± 4.3 36.7 ± 4.0 0.09
Live birth rate (%) 57.5 54.0 48.1 0.1
Miscarriage rate (%) 8.8 9.6 11.6 0.8

SUPPORT: None.
Tuesday, October 15, 2019 6:30 AM

CELL FREE DNA IS AN IDEAL OVARIAN RESERVE MARKER FOR LOW OVARIAN RESPONSE FOR STIMULATION. Siddhartha Nagireddy, MCh(Reproductive medicine and Surgery),a Lahari Katneni, MS (Ob & Gyn),a,b Assistant Professor, Sri Ramachandra Institute of Higher Education and Research, Chennai, India; a,b-25-19-10 N R Peta West Godavari District, Eluru, India.

OBJECTIVE: Primary: 
- To find the correlation of cDNA to ovarian response in ICSI cycles. 
- Secondary: 
- To correlate cDNA with other markers of ovarian reserve. 

DESIGN: This prospective study.

MATERIALS AND METHODS: 65 serum samples collected at day 3 of menstrual cycle from patients undergoing ICSI procedure. FSH, Anti-Mullerian hormone (AMH) and cDNA levels were measured in each serum sample in order to compare their predictive value for patient’s ovarian response to stimulation.

RESULTS: Cell-free DNA concentrations (mean ± SD: 23.88±39.78 ng/ml) were significantly and positively correlated with patients’ FSH (r = -0.175, p = 0.053), negative correlated with AFC (r = -0.339, p = 0.055*) and AMH (r = -0.178, p = 0.001), cell-free DNA level was significantly correlated to the number of oocyte retrieved (r = 0.0001). Cell-free DNA level in were predicted in low responder (Number of oocytes retrieved < 6). ROC curve were plotted for no of oocytes retrieved and cDNA levels in serum (AUC = 0.87), which predicted cDNA response in low ovarian reserve patient with sensitivity of 80.8% and specificity 98.6%.

CONCLUSIONS: Cell DNA level on 3 day of cycle in serum can predict the ovarian response to stimulation. It can independently identify ovarian response cut off more the 37.5 is used by identifying high amount of cf DNA in serum.

P-206 Tuesday, October 15, 2019 6:30 AM

IS THE ‘OESTRO-ANDROGENIC’ HORMONE DEHYDROEPIANDROSTERONE SULPHATE (DHEAS) THE INTRACRINE REGULATOR OF IMPLANTATION AND EARLY PREGNANCY?: A PROSPERCTIVE STUDY IN WOMEN UNDERGOING IVF. Bindu N. Chimote, M.Sc., M.Phil. Ph.D.(Biochemistry); M.Sc. Clinical Embryology (Leeds-UK),a Natchandra Manoharao Chimote, M.Sc., Ph.D.b Consultant Clinical Embryologist, Nagpur, India; a,b-Scientific Director, Vaunshdhara Fertility Centre, Nagpur, India.

OBJECTIVE: Decidualization of endometrial-stroma is necessary for successful implantation. Very high levels of dehydroepiandrosterone (DHEA), which inhibit endometrial-stromal cell differentiation via prevention of glucose-flux through pentose-phosphate-pathway, could be a probable cause for higher incidence of implantation failure among PCOS women. Contrarily, low DHEA women with diminished ovarian-reserve, when supplemented with DHEA show significant reduction in early miscarriage rates. Sulphonated-DHEA (DHEAS) is more stable than DHEA and is the most abundant circulating ‘oestro-androgenic’ steroid precursor for estrogen production in humans. Objective of this study was to evaluate significance of innate, endogenously circulating DHEAS during implantation in predicting implantation failure/early miscarriage in eumenorrhic women undergoing IVF.

DESIGN: Prospective pilot study of n = 145 non-PCOS eumenorrhic normo-responder women undergoing conventional antagonist stimulation protocol IVF. All cycles involved day 5 fresh, elective single-blastocyst transfer (eSTT). Luteal phase support was provided to all women.

MATERIALS AND METHODS: Serum DHEAS levels in baseline as well as day 7, day 14 post-eSTT were measured by radio-immuno-assay using diagnostic kits. Serum estradiol, β-hCG and progesterone levels were also measured on day 7/day14 post-eSTT, β-hCG measurement on day 7 of eSTT was considered early indicator of pregnancy. Implantation rate, live-birth rate were main outcome measures. Cycles were classified on the basis of live-birth (LB, n = 52), biochemical pregnancy (BPC, n = 5), early miscarriage (EM, n = 6), no implantation (NI, n = 77). Statistical analysis was done using Graph-pad Prism VI software. Sample size was devised to give >80% power to the study.

RESULTS: Overall rates of LB, BCP, EM and NI were found to be 37.14%, 3.57%, 4.28%, and 55% respectively. DHEAS levels depicted a steady rise from baseline to d7 to d14 post-eSTT in women with LB (174±12.23 vs. 355.3±37.15 vs. 741.2±54.38% respectively). Although a rising trend was also observed in women with EM, the rise from baseline to d7 post-eSTT was rather steep (73.25±4.34 vs. 255.5±7.5 vs. 280.71±11.4). However, the rising pattern was disrupted in BCP cycles where the levels dropped from baseline to d7 and then increased on d14 post-eSTT (227±28.9 vs. 121.5±2.7 vs. 270±10.98); and in NI cycles where a sharp rise on d7 was followed by a decrease in levels on d14 post-eSTT (218.41±11.62 vs. 1380±131 vs. 801.7±98.8). A significant difference in the ratio of d7/baseline DHEAS levels was observed in LB vs. BCP vs. EM vs. NI cycles (2.3 vs. 0.53 vs. 3.5 vs. 6.3; p = 0.0005). Similarly, the ratio of d14/d7 DHEAS levels differed significantly in LB vs. BCP vs. EM vs. NI cycles (2.1 vs. 2.23 vs. 1.1 vs. 0.58; p<0.0001). Thus, a twofold rise in DHEAS levels from baseline to d7 and d7 to d14 is critical for successful implantation leading to a live-birth.

CONCLUSIONS: Maintenance of a steady/balanced rise in serum DHEAS levels is an early indicator of successful implantation and predicts implantation-failure/early miscarriage in eumenorrhic women undergoing IVF.

SUPPORT: None.

P-207 Tuesday, October 15, 2019 6:30 AM

HIGH PINK1 EXPRESSION RELATED TO AGEING IN CUMULUS CELLS IS ASSOCIATED WITH ASSISTED REPRODUCTIVE TECHNOLOGY OUTCOME. Chia-Jung Li, Ph.D. Department of Obstetrics and Gynecology, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan.

OBJECTIVE: Is high PINK1 expression associated with ageing in granulosa cells as well as assisted reproductive technology (ART) outcome, and what is the underlying mechanism of action of PINK1?

DESIGN: Experimental laboratory study.

MATERIALS AND METHODS: In a prospective study, fresh granulosa cells were obtained from 48 women aged 20–40 years who underwent IVF with embryo transfer and who were divided into two groups: the diminished ovarian reserve (DOR) group (n = 20) and the control group (n = 28). Patient characteristics including age, infertility duration, body mass index, FSH, anti-Mullerian hormone (AMH) and cumulus cell PINK1 expression levels, autophagy, mitochondrial mass were analysed.

RESULTS: The DOR group 1 in the DOR group is activated and the PINK1 is translocated to the outer membrane of the mitochondria, and the formation of lysosomes is increased, thereby increasing the mitophagy. We also observed a significant reduction in the mass of the mitochondria in the DOR group and a severe imbalance in mitochondrial dynamics.

CONCLUSIONS: High PINK1 expression levels in cumulus cells were related to ageing, which may be involved in the clinical outcome of ART by promoting cell death and affecting mitochondrial function.

P-208 Tuesday, October 15, 2019 6:30 AM

PREGNANCY OUTCOMES OF PATIENTS WITH A CONGENITAL DIDEPHYS UTERUS: AN ANALYSIS OF 76 WOMEN FOLLOWING IN VITRO FERTILIZATION EMBRYO TRANSFER. Jingzi Xiao, Master, Xihong Li, MD./Ph.D, Yan Ouyang, MD./Ph.D, Yuyao Mao, Master Reproductive and Genetic hospital of Citic-Xiangya, Changsha, China.

OBJECTIVE: To evaluate the pregnancy outcomes in women with a diphys uterus after in vitro fertilization-embryo transfer (IVF-ET).

DESIGN: A retrospective analysis.

MATERIALS AND METHODS: Seventy six women with a diphys uterus who obtained clinical pregnancies via IVF-ET from September 2005 to December 2017 were retrospectively analyzed. The pregnancies included 50 cases of singleton pregnancies and 20 cases of twin pregnancies. In addition, there was 1 case of monochorionic twins among the twin pregnancies. Pregnancy outcomes including the rates of preterm delivery, cesarean section, live birth and perinatal mortality, birth weight, etc were analyzed.

RESULTS: In the patients with a diphys uterus, the total miscarriage rate was 18.4% (14/76); the early pregnancy loss rate was 15.8% (12/76), and the late miscarriage rate was 2.6% (2/76). The rates of preterm delivery and term delivery were 27.6% (21/76) and 53.9% (41/76), respectively.
The number of babies born was 75, including 67 cases of live births and the live birth rate was 76.3% (58/76) (80.4% in singleton (45/56) and 65% in twin (13/20) pregnancies). The overall perinatal mortality was 10.7% (8/75), including 2 cases of still birth and 6 cases of neonatal death. There was a high cesarean section rate with 75.8% (47/62), and the rate of low live birth weight was 34.3% (23/67). Furthermore, the rate of very preterm birth was 11.3% (7/62) and the average gestational age at delivery was 31.5 ± 7.5 weeks of gestation.

Among the twin pregnancies, there was 1 case received selective reduction, unfortunately, the women suffered a miscarriage in the 2nd month of gestation.

CONCLUSIONS: The pregnancy outcomes of a didelphys uterus in women who underwent IVF-ET were associated with an increased incidence of premature delivery, perinatal mortality, low live birth weight and low gestational weeks at delivery, but the live birth rate was relatively satisfactory.

**TABLE. Pregnancy outcomes of didelphys uterus**

<table>
<thead>
<tr>
<th>Number</th>
<th>76</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscarriage</td>
<td>18.4% (14/76)</td>
</tr>
<tr>
<td>early pregnancy loss</td>
<td>15.8% (12/76)</td>
</tr>
<tr>
<td>late miscarriage</td>
<td>2.6% (2/76)</td>
</tr>
<tr>
<td>Preterm delivery</td>
<td>27.6% (21/76)</td>
</tr>
<tr>
<td>Term delivery</td>
<td>53.9% (41/76)</td>
</tr>
<tr>
<td>Babies born</td>
<td>75</td>
</tr>
<tr>
<td>Live births</td>
<td>67</td>
</tr>
<tr>
<td>Perinatal mortality</td>
<td>10.7% (8/75)</td>
</tr>
<tr>
<td>Caeasarean section rate</td>
<td>75.8% (47/62)</td>
</tr>
<tr>
<td>Live birth rate</td>
<td>76.3% (58/76)</td>
</tr>
<tr>
<td>Gestational age at delivery</td>
<td>31.5 ± 7.5</td>
</tr>
<tr>
<td>&lt;37 week</td>
<td>33.9% (21/62)</td>
</tr>
<tr>
<td>20-39 week</td>
<td>11.3% (8/72)</td>
</tr>
<tr>
<td>Live birth weight</td>
<td>65.7% (44/67)</td>
</tr>
<tr>
<td>&gt;2500g</td>
<td>34.3% (33/97)</td>
</tr>
</tbody>
</table>

**P-209 Tuesday, October 15, 2019 6:30 AM**

**IS FIRST TRIMESTER SUBCHORIONIC HEMORRHAGE ASSOCIATED WITH ADVERSE PREGNANCY OUTCOMES AFTER IN VITRO FERTILIZATION?** Kelsey Anderson, MD, Emily S. Junghen, MD, MSCI, Patricia T. Jimenez, MD, Kenan Omurtag, MD, Washington University School of Medicine, St. Louis, MO.

OBJECTIVE: To determine the association between incidental SCH on ultrason and pregnancy outcomes in IVF pregnancies.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: His was a retrospective cohort study of women identified from a first-trimester ultrasound database kept for IVF pregnancies from 2009 to 2017. Women with a viable first trimester pregnancy after fresh or frozen embryo transfer were included. Exclusion criteria were absence of heartbeat on ultrasound, gestational carriers, women who used donor eggs or who had a multiple gestation pregnancy. The primary outcome was live birth and secondary outcomes included spontaneous abortion, preterm delivery and infant weight at delivery. Appropriate bivariate analyses were performed followed by a multivariate regression model to further investigate associations between significant covariates and outcomes. All analyses were performed in SPSS.

RESULTS: 1004 women met criteria and 18.6% had a SCH. In bivariate analysis, SCH was not risk factor for decreased live birth (87.5% vs 90.2%, OR 0.7, 95% CI 0.2-1.1) or increased preterm birth (90.1% vs 85.9%, OR 0.7, 95% CI 0.4-1.2) or SAB (12.5% vs 9.3%, OR 1.4, 95% CI 0.9-2.3) There was also no difference in fetal weight with those with SCH (3334 g vs 2629 g, p=0.224) and only increasing maternal age was negatively associated with live birth (32.8 vs 34.7 p<0.001). In multivariate regression analysis, all outcomes were still not statistically significant although those with SCH trended to have fewer live births (aOR 0.4, 95% CI 0.2-1.1) and higher rates of SAB (aOR 2.6, 95% CI 1.0-6.9).

CONCLUSIONS: Incidentally detected subchorionic hemorrhage on first trimester ultrasound is not associated with infant birth weight or probability of live birth or preterm birth after IVF. This information may be reassuring to IVF patients with SCH and otherwise viable pregnancy noted on first trimester ultrasound.

**P-210 Tuesday, October 15, 2019 6:30 AM**

**PEROXIREDOXIN 4, A NEW OXIDATIVE STRESS MARKER IN FOLLICULAR FLUID MAY PREDICT IVF OUTCOMES.** Yi Qian, PhD, Yan Meng, MD, Jiayin Liu, MD, State Key Laboratory of Reproductive Medicine, Clinical Center of Reproductive Medicine, Nanjing, China.

OBJECTIVE: For better predicting in vitro fertilization (IVF) outcomes, it is necessary to identify some non-invasive and sensitive markers. Studies indicated that oxidative stress status in patients was closely associated with IVF outcomes, while the results are still controversial.

MATERIALS AND METHODS: All participants were recruited in the center of clinical reproductive medicine from September 2017 to December 2018. Infertile women with either tubal factor or male factor (n=138) undergoing controlled ovarian hyperstimulation and IVF were recruited in our study. FF samples from patients were collected on the day of oocyte collection and then centrifuged and frozen up for analysis. Prdx4 concentration in FF were measured in each participant. Furthermore, the correlation between Prdx4 level and IVF outcomes, such as clinical pregnancy rate and oocyte quality was analyzed. And subsequently, we divided all participants into three groups according to their levels of Prdx4 in FF (low, moderate and high group), then the clinical pregnancy rate and oocyte quality outcomes were all analyzed.

RESULTS: The pregnant women had higher levels of Prdx4 in FF than non-pregnant women. Prdx4 was positively correlated with oocyte fertilization rates (r=0.326; p=0.013) and good quality embryo rates (r=0.334; p=0.011). Furthermore, we found the pregnancy rate was positive correlated to Prdx4 level with a concentration dependent manner in three groups (pregnancy rate were 28.1%, 46.8% and 70.3% in low, moderate and high group, respectively). In the oocyte quality outcomes, the fertilization rates were significantly higher in the high group than the low group (p<0.01), and the good quality embryo rates of moderate (p<0.01) and high (p<0.01) groups were significantly higher than the low group.

CONCLUSIONS: Our results provide evidence that the upregulated expression of antioxidants in IVF patients follicular fluid (FF), such as Prdx4, tend to increase the potential pregnancy via oocyte quality mechanism.

**P-211 Tuesday, October 15, 2019 6:30 AM**

**FOLLICULAR FLUID (FF) CONCENTRATION OF ANTI-MULLERIAN HORMONE (AMH) IN WOMEN PURSUING IN VITRO FERTILIZATION (IVF): VARIABILITY AND PREDICTORS.** Caitlin R. Sacha, MD,a Lidia Mínguez-Alarcón, PhD,a Jorge E. Chavarro, MD, Sc.D., Jennifer B. Ford, RN,b Patricia K. Donahoe, MD,b Irene Souther, MD,b Russ Hauser, MD, MPH, Sc.D., David Pepin, PhD,a,b MGH Fertility Center and Harvard Medical School, Boston, MA; bHarvard T.H. Chan School of Public Health, Boston, MA; cHarvard School of Public Health, Boston, MA; dMGH Pediatric Surgical Research Laboratories, Boston, MA.

OBJECTIVE: To investigate the correlation of follicular fluid (FF) AMH concentrations between pre-ovulatory follicles within and between IVF cycles, and the association of FF AMH with demographics and reproductive characteristics.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: FF was analyzed from 2 or 3 pre-ovulatory follicles in 162 women (1 to 3 IVF cycles, 2-13 months apart) enrolled in the Environment and Reproductive Health (EARTH) Study at Massachusetts General Hospital Fertility Center (2010-2016). AMH concentration was quantified from a total of 217 cycles using a sandwich enzyme-linked immunoassortant assay (ELISA) method and corrected for sample volume. Spearman correlation was used to assess the correlation of FF AMH concentrations between follicles, and intra-class correlation (ICC) was calculated to
assess variability of mean cycle FF AMH concentrations between IVF cycles for each woman and between participants. Mean cycle FF AMH concentrations were then divided into tertiles (T1-T3), and Kruskal-Wallis and x²-tests were applied as appropriate to explore associations of demographic and reproductive characteristics across tertiles.

RESULTS: The mean FF AMH concentration was 1.20 ng/ml (range=0 to 24.0 ng/ml). There was high correlation between follicles within each IVF cycle (Spearman r=0.78 to 0.86), and ICC indicated low within-woman variability of mean cycle FF AMH concentrations [0.87 (95% CI 0.81 to 0.92)]. Compared to women in T1 of FF AMH concentrations (0.2 ng/mL), on average women in T3 (2.3 ng/mL) were younger (mean age in T3=33.5 vs. T1=36.0 years, p=0.04), leaner (mean body mass index (BMI) in T3=22.4 vs. T1 24.5 kg/m², p=0.001), had higher serum AMH concentrations (mean in T3=0.6 vs. T1=0.1 ng/ml, p=0.001), and lower day-3 follicular stimulating hormone (FSH) levels (mean T3=6.4 vs. T1=7.3 IU/L, p=0.03). Although most diagnoses were similar across tertiles of FF AMH concentrations, as expected, women in T3 were more often diagnosed with ovarian reserve, suggesting a possible role in predicting future reproductive outcomes.

P-212 Tuesday, October 15, 2019 6:30 AM

IMPACT OF ACUPUNCTURE ON OUTCOMES FOLLOWING FROZEN ENUCLEO PLAST OCYCT TRANSFERS. Nancy L. Bossert, PhD,1 Hannah Van De Geest, BS,2 April Batchelder, MD,2 William B. Schoolcraft, MD,2 Jason E. Swain, PhD,1 CCRM Minneapolis, Edina, MN;2 Colorado Center for Reproductive Medicine, Lone Tree, CO; CCRM Fertility Network, Lone Tree, CO.

OBJECTIVE: The use of acupuncture in IVF has gained widespread acceptance, with numerous clinics offering this technique during embryo transfer. A clear consensus as to whether acupuncture improves outcomes does not exist and analysis is complicated due to confounding variables. The objective of this study was to determine if acupuncture provided at the time of frozen embryo transfers using single euploid blastocysts demonstrated any benefit compared to no acupuncture treatment.

DESIGN: Retrospective data analysis.

MATERIALS AND METHODS: Data were collected over a 4 year time period from 2015-2019. All lab conditions were the same for the duration of the study period and monthly quality control analysis confirmed no significant changes in pregnancy rate over time. Patients with single euploid blastocyst transfers were age-matched based on SART age groups and outcomes compared depending on whether the female had acupuncture treatment surrounding embryo transfer or not. All transfers were performed using a blastocyst of grade 3BB or better using a soft catheter and Embryogluu under ultrasound guidance. Data were analyzed using Fisher’sExact test, p<0.05.

RESULTS: No significant differences were apparent in either positive pregnancy rate or in ongoing/live birth rates between acupuncture or no acupuncture treatments in any age group examined.

CONCLUSIONS: Acupuncture does not appear to benefit rates of chemical pregnancy or ongoing pregnancy/live birth following transfer of a single frozen/thawed high quality euploid blastocyst. Future analysis, subdividing cycles based on day of blastocyst formation or quality of blastocyst transferred may provide additional insight. Furthermore, type of acupuncture and specifics of the technique may have varied between patients and could be a confounding factor.

P-213 Tuesday, October 15, 2019 6:30 AM

FOLLICLE DIAMETER PREDICTS OOCYTE MATURITY BUT NOT FORMATION OF BLASTOCYSTS OR PLOIDY OF BLASTOCYSTS ARISING FROM MATURE OOCYTES OF DONORS. David H. McCullough, Ph.D.1,2,3 Nino Kutchukhidze, PhD,4 Tea Chankviani, md,2 Temiko Zhorzhadzoe, MD MS,1 Tamar Barlabakadze, MD,2 Santiago Munne, PhD.1,2 Lia Chkonia, MS,1 Georgia American Center for Reproductive Medicine ReproART, Tbilisi, Georgia;2 Georgia American Center for Reproductive Medicine “ReproART”, Tbilisi, Georgia;3 GeorgianAmerican Center for reproductive medicine Reproart, Tbilisi, Georgia; 4Georgian-American Center for Reproductive medicine ReProart, Tbilisi, Georgia; 5 Ayurvedic Medicine, Madrid, Spain; 6 Georgia American Center for reproductive Medicine ReproART, Tbilisi, Georgia.

OBJECTIVE: Follicle size during controlled ovarian hyperstimulation is the only measure useful to the clinician in deciding when to trigger final maturation. Controversy exists over whether the largest follicle(s) or the complete cohort of follicles best predicts outcome for IVF. Past efforts have concentrated on predictors of pregnancy and live birth following IVF with fresh transfer. Now there is increasing interest in retrieving oocytes for cryopreservation or for embryo production with preimplantation genetic testing for aneuploidy (PGT-A). It remains unclear whether there is a preferred size of follicles to obtain euploid oocytes or oocytes that will become euploid blastocysts.

DESIGN: Retrospective Analysis of Embryo Outcomes.

MATERIALS AND METHODS: Consented oocyte donors (N=22) underwent retrieval of oocytes, one-by-one, from follicles with diameters measured during the retrieval. Oocytes were cultured individually, fertilized by intracytoplasmic sperm injection (ICSI) and monitored for development. Quality blastocysts, achieving Gardner grades of AA, AB, BA, BB or BC, underwent trophectoderm biopsy on days 5 or 6 and biopsies were sent to a commercial PGT-A lab in the US. Results of maturity, fertilization, development and ploidy were considered with reference to the size of the follicle from which the oocyte was retrieved. Analysis of data involved Student’sT tests, and receiver operator characteristic (ROC) curves with significance determined using Mann-Whitney U test.

RESULTS: Oocytes were retrieved from follicles with measured diameters averaging 17.4 +/- 2.9 mm (N=315). Of the oocytes, 80.4% had 1 polar body (MII), 9.8% had a germinal vesicle (GV) and 9.1% had neither a polar body nor a GV (MI). The sizes of the follicles from which these oocytes came were significantly different: MII, 18.3 +/- 2.2 mm; GV, 12.5 +/- 1.6 mm and MI, 15.3 +/- 3.2 mm. ROC curves indicated that follicle diameter was a “grade A” predictor of GV oocytes (AUC = 0.96; P < 0.0001, Mann-Whitney U test) and a “grade B+” predictor of MII oocytes (AUC = 0.87; P<0.0001, Mann-Whitney U test). Among MII oocytes, follicle size did not predict fertilization by ICSI (ROC AUC = 0.54, not significant), formation of quality blastocysts (ROC AUC = 0.53, not significant), or blastocyst ploidy ROC AUC = 0.53, not significant.

CONCLUSIONS: Significant AUCs for ROC curves indicate that follicle diameter is an excellent predictor of oocyte maturity. However the diameter of the follicle from which an MII oocyte was retrieved did not predict its quality as assessed by its fertilizability with ICSI, its ability to develop into a quality blastocyst or its ploidy. Whereas follicle diameter can predict maturity of the oocyte retrieved from them quite well, follicle diameter is a poor predictor of oocyte quality including blastocyst ploidy. Since oocyte ploidy was not directly assessed, it remains unclear whether oocyte ploidy is associated with follicle diameter. However, with most embryo aneuploidy arising from errors in meiosis, we believe that follicle size is unlikely to be a good predictor of oocyte ploidy.

SUPPORT: None.

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>Acupuncture</th>
<th>Ongoing/Live Birth</th>
<th>+ hCG</th>
<th>Ongoing/Live Birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor</td>
<td>23/28 (82.1%)</td>
<td>16/28 (57.1%)</td>
<td>18/23 (78.3%)</td>
<td>13/23 (56.5%)</td>
</tr>
<tr>
<td>&lt;35 yrs old</td>
<td>66/76 (86.8%)</td>
<td>50/76 (65.8%)</td>
<td>73/86 (84.9%)</td>
<td>61/86 (70.9%)</td>
</tr>
<tr>
<td>35-37 yrs old</td>
<td>50/57 (87.7%)</td>
<td>43/57 (75.4%)</td>
<td>56/70 (80.0%)</td>
<td>48/70 (68.6%)</td>
</tr>
<tr>
<td>38-40 yrs old</td>
<td>51/70 (72.9%)</td>
<td>46/70 (65.7%)</td>
<td>47/50 (86.0%)</td>
<td>32/50 (64.0%)</td>
</tr>
<tr>
<td>&gt;40 yrs old</td>
<td>17/21 (81.0%)</td>
<td>14/21 (66.7%)</td>
<td>13/20 (65.0%)</td>
<td>11/20 (55.0%)</td>
</tr>
</tbody>
</table>

Vol. 112, No. 3, Supplement, September 2019
THE PREVIOUSCESAREAN DELIVERY DOESN'T
AFFECT THE PROGNOSIS OF IVF-ET: A LARGE SAMPLE
RETROSPECTIVE CASE CONTROL STUDY. Shao Yang,
MD, Peking University Third Hospital, Beijing, China.

OBJECTIVE: To investigate whether the previous cesarean delivery would affect the treatment outcomes of multiparities accepted IVF/ICSI-ET.

DESIGN: Retrospective case control study of one reproductive medical center, from 1 Jan. 2009 to 31st Dec. 2015. The main outcome measures were Clinical pregnancy rate (CPR) and Live birth rate (LBR). The study group (Group 1) were patients with previous cesarean section history, the control group (Group 2) were patients with history of vaginal delivery.

MATERIALS AND METHODS: This is a retrospective case control study, and data collection protocol was approved by the hospital ethics. All patients were multiparities, the study patients with previous cesarean section history, the control group (Group 2) were patients with history of vaginal delivery. Matchit package of R software was used for propensity score matching. The matching factors were age, number of oocytes retrieved and treatment time. According to 1:2 matching, the nearest neighbor matching method was used.

RESULTS: There were 461 cycles were included in the Group 1, and matched with 922 multiparities for the Group 2. The basic characteristics of patients refers to age, BMI, basal FSH and AFC were with no significantly difference. The initial dose of Gn was comparable between two groups, but the day of Gn injection was longer in control group and the total dose of Gn was higher too (11.3±2.4 vs. 11.9±2.7 P<0.001, 3238.5±1422.8 vs. 3595.9±1503.5, P<0.05, respectively). The number of oocytes peak-up, the rate of ICSI, MII oocyte and 2PN embryo with no significantly difference. The cycle cancel rate was comparable between two groups. The number of embryos transferred were similar between two groups. The treatment outcomes refer to clinical pregnancy rate, implantation rate, early miscarriage rate, ectopic pregnancy rate and live birth rate. There was no uterine rupture or CS scar pregnancy in the study group.

CONCLUSIONS: The multiparities with history of Cesarean section accepted IVF/ICSI treatment, got similar outcomes compared with those with history of vaginal delivery.

OOCYTE DONOR IMPLANTATION AND PREGNANCY RATES PREDICT OOCYTE RECIPIENT PREGNANCY CHANCE IN AN EGG-SHARING DONATION PROGRAM. Daniela Paes de Almeida Ferreira Braga, PhD,a Amanda Souza Setti, MSC,b Matheus de Castro Azevedo, BSc,b Assampto Iaconelli, Jr., MD,b Elson Borges, Jr., PhD.c Fertility Medical Group / Sapientiae Institute, Sao Paulo, Brazil; Fertility Medical Group, Sao Paulo, Brazil.

OBJECTIVE: Studying oocytes from the same cohort submitted to different situations may provide greater insight into possible predictors of pregnancy in recipient cycles, allowing continuous improvement in outcomes moving forward. The objective of this study was to investigate which are the predictive factors of successful pregnancy in oocyte recipient intracytoplasmic sperm injection (ICSI) cycles in an egg-sharing donation program.

DESIGN: Historical cohort study.

MATERIALS AND METHODS: This study was performed in a private university-affiliated IVF center. Analyzed data were obtained via chart review of 1505 vitrified oocytes donated to 225 oocyte recipients undergoing 307 ICSI cycles, participating in an egg-sharing donation program, between January/2015 and May/2017. For that sample size, computed achieved post-test power was 100%, considering pregnancy achievement as the main outcome measure. Donors were between the age of 19 and 34 years, and recipients were between the age of 26 and 50 years. Adjusted generalized linear models were used to investigate the impact of oocyte donors and recipients characteristics on recipients’ pregnancy achievement. The results are expressed as exponentiation of regression coefficient (ExpB), 95% confidence interval (CI), and p-value. A receiver operating characteristic (ROC) curve was constructed to investigate the predictive value of oocyte donor implantation rate on oocyte recipient pregnancy rate achievement.

RESULTS: Implantation rate in oocyte donor was highly correlated with pregnancy achievement in oocyte recipient cycles (ExpB: 1.181, CI: 1.138 – 1.226, p < 0.001). The ROC curve analysis demonstrated that the implantation rate in oocyte donor has a strong predictive value on the achievement of pregnancy in oocyte recipient area (under the curve: 0.98, CI: 0.95 - 0.99, p< 0.001). The achievement of pregnancy in oocyte donors and recipients were highly associated (ExpB: 3.46, CI: 2.81 – 4.058, p < 0.001), irrespective of oocyte recipient age. Oocyte donor age, body mass index, number of follicles, retrieved oocytes, total dose of FSH administered and estradiol peak were not associated with oocyte recipient pregnancy achievement. In oocyte recipients, no association was found between the fertilization rate and the achievement of pregnancy, but the high-quality embryos rates on days 2 (ExpB: 3.397, CI: 1.635 – 7.054, p= 0.001) and 3 (ExpB: 6.629, CI: 1.185 – 37.092, p= 0.031), and blastocyst development rates (ExpB: 2.331, CI: 1.086 – 5.001, p= 0.030) were positively associated with pregnancy achievement.

CONCLUSIONS: Oocyte donor implantation rate and successful pregnancy, high-quality embryos rate, and blastocyst development rate predict pregnancy achievement in the oocyte recipient cycle. The strong association in pregnancy success between donors and recipients, and the lack of correlation between donor characteristics and cycles’ outcomes, demonstrates the power of oocyte quality on the success of ICSI treatment.

Reference: NA.

SUPPORT: None.

P-217 Tuesday, October 15, 2019 6:30 AM

OXIDATIVE PARAMETERS IN FERTILIZATION ME-
DIUM OF CUMULUS - OOCYTE COMPLEX (COC) AS
MEASURED BY THERMOCHEMOLUMINESCENCE
(TCL) MAY PREDICT TREATMENT OUTCOME IN
IVF: PRELIMINARY RESULTS FROM A PROSPECTIVE
STUDY. Zofnay Wiener-Megnazi, MD,a Hadar Gluska, MD,b

FERTILITY & STERILITY®
OBJECTIVE: To evaluate a possible association between oxidative parameters in COC medium as measured by Thermochromiluminescence (TCL) assay and outcome parameters in IVF.

DESIGN: A prospective cohort study.

MATERIALS AND METHODS: Sixty four women undergoing a fresh IVF cycle using conventional oocyte insemination during 2017-2019 participated in the study. COCs were incubated in a well containing 680 μl of culture media for approximately 4-6 hours. Immediately prior to addition of semen, 20 μl of sera were removed from each well, examining for each sample 4 parameters: TCL amplitudes, after 50 seconds (TCLH1), 150 seconds (TCLH2), 250 seconds (TCLH3) and TCL ratio (TCLH3-TCLH1/100). TCL amplitudes were measured as counts per second (CPS).

RESULTS: We examined 97 COC fertilization media. Mean patient’s age was 38 ± 4.7 years. Mean number of aspirated oocytes, COCs per well and number of wells per patient were 6.2 ± 3.7, 4.6 ± 2.06 and 1.48 ± 0.5 respectively. Of 64 IVF cycles, 30 (46.9%) were not fertilized, 30 (46.9%) obtained 1-3 cycles (12.7%) no embryos developed and 8 (12.7%) cycles, all embryos were frozen. Altogether fresh embryos were transferred in 46 cycles. Twenty one pregnancies were achieved (33.3% per started cycles, or 45.9% per embryo transfer cycle). In order to find an optimal cutoff that would distinguish between TCL values that were associated with higher chances of pregnancy, Youden index was used. A discriminatory TCLH2 value of >62.9 CPS was associated with higher chances for pregnancy (46.5% vs. 8.3%, OR=9.6, 95% CI (1.13-80.7) (p=0.03)). This value had a 95.2% sensitivity (95% CI=76.2-99.9), 32.4% specificity (95% CI=17.4-50.5), a positive predictive value of 46.5% (95% CI=31.2-62.3) and a negative predictive value of 91.7% (95% CI=61.5-99.8). No association was found between TCL parameters, regrading patient’s age and number of aspirated oocytes. Multivariate analysis, correcting for age and number of aspirated oocytes, revealed that TCLH2 >62.9 was the only independent variable associated with the occurrence of pregnancy (p<0.03).

CONCLUSIONS: Oxidative parameters of COC medium may affect the likelihood of pregnancy. Measurement of oxidative parameters may serve as a potential aid in prediction of treatment outcome.

P-219 Tuesday, October 15, 2019 6:30 AM

IVF PREGNANCY RATES IN WOMEN UNDERGOING ACUPUNCTURE VS. CONTROLS. Phyllis L. Jennifer, DO, Yan Zhang, PhD, Jennie Orlando, MD, Samuel D. Prie, PhD, Lindsay L. Penrose, PhD, Sheila Garov, PhD, Iau-Chen Huang, MD, Texas Tech University Health Sciences Center, Lubbock, TX; Affiliation not provided; Texas Tech University Health Science Center - Lubbock, Lubbock, TX.

OBJECTIVE: To compare IVF pregnancy rates and early pregnancy outcomes in women receiving acupuncture treatment compared to controls.

DESIGN: Prospective randomized study.

MATERIALS AND METHODS: Women ages 21 to 42 years who were seeking in-vitro fertilization and embryo transfer (IVF-ET) were recruited for the study. Women were excluded if they were currently using alternative therapies such as acupuncture, herbal supplements or had a contraindication to needle insertion at the acupoints. Fifty participants were enrolled and were randomized by computer to either the treatment group or control group. Those assigned to the treatment group received acupuncture sessions before, during the IVF-ET process; the control group received standard IVF treatment.

The three sessions of acupuncture occurred on days 6, 7 or 8 of gonadotropin stimulation, and approximately 1 hour prior to embryo transfer and within 48 hours after the embryo transfer. Acupuncture was performed by one certified clinician following a protocol adapted from a Delphi Consensus process developed at the University of Texas Medical Branch. Differences between women in two groups (acupuncture vs control) were determined using Chi-square test for the variable, pregnancy status and Mantel-Haenszel Chi-square test for the variable, pregnancy outcomes which included singleton gestation, twin gestation or early pregnancy loss. A p of < 0.05 was considered statistically significant.

RESULTS: We found no statistically significant differences between the acupuncture and control groups for pregnancy status (χ² = 0.16, p = 0.69) and pregnancy outcomes (χ² = -0.72, p = 0.53).

CONCLUSIONS: This study showed acupuncture based on Delphi Consensus Protocol at the above time points did not significantly affect the pregnancy rates in women undergoing IVF nor did it affect multiple birth or early pregnancy loss rates. Further studies with more subjects and/or different acupuncture sessions may be required to determine the impact of acupuncture on individuals receiving IVF treatment.

SUPPORT: Laura W. Bush Institute for Women’s Health and University Medical Center.

P-220 Tuesday, October 15, 2019 6:30 AM

RISK OF PREGNANCY FAILURE IN AN OPTIMIZED UTERINE ENVIRONMENT: LIVE BIRTH RATE FROM PGTA-E UTOIL EMBRYOS IN A PROVEN UTERUS. Renee N. Rivas, MD, PhD, Michael K. Simon, MD, Alan S. Penzias, M.D., Denny Sakkas, PhD, Pasquale Patrizio, M.D., Yale New Haven Hospital, New Haven, CT; Boston IVF, Waltham, MA; Yale Fertility Center, New Haven, CT.

OBJECTIVE: Assess the magnitude of the pregnancy failure rate from the transfer of euploid embryos after Pre-implantation Genetic Testing for Aneuploidy (PGTA) into a proven uterine environment. An optimal uterine environment, or
proven uterus, is defined as a live birth ensuing from a multiple embryo transfer (MET) where at least one embryo results in a successful birth. While PGT-A has been shown to increase the success rate of live birth, the remaining failure rate can still be due to a multitude of factors. This study seeks to control for the uterine environment to identify the remaining chance of failure for the cycle.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** Using all completed MET cycles at our academic fertility center at Yale and from Boston IVF from 2012-2017, we identified 3,680 embryos transferred in 1,726 cycles to a proven uterus. Percentage of embryos not implanted in a proven receptive uterus utilizing PGT-A was compared to those transferred without using PGT-A. Difference of proportions analysis using a one-tailed Z-test compared the percentage lost among proven-uterus that utilized PGT-A to cycles that did not.

**RESULTS:** Based on the data from these two centers, forty-six of 1,726 cycles (2.7%) transferred multiple embryos after PGT-A to a proven uterus. These cycles resulted in 30/87 embryos (34.5%) failing to result in a live birth. For non-PGT-A embryos transferred to a proven receptive uterus (MET-only cycles), 1,973/3,593 (54.9%) did not result in a live birth. The difference of proportion of embryos failing to result in a live birth between proven uterus cycles that utilized PGT-A was statistically significant when compared to controls without PGT-A (p = 0.00008).

**CONCLUSIONS:** The false negative rate of PGT-A testing, whereby euploid embryos transferred into a receptive uterus (since in the same cycle sibling embryos had implanted and produced a live birth), is 34.5%. This study eliminated the endometrium as a cause for the failed implantation of euploid embryos and adds support to the inability of PGT-A to completely correctly identify suitable embryos for transfer. Ongoing research may help establish the false-negative rate of PGT-A and understand whether genetic mutations, non-chromosomal or developmental errors could be responsible for the lack of implantation and live birth.

**SUPPORT:** None.

**P-222 Tuesday, October 15, 2019 6:30 AM**

**MITOCHONDRIAL REPLACEMENT THERAPY GIVE NO BENEFITS TO PATIENTS OF ADVANCED MATERNAL AGE.**

**AUTHORS:** Pavlo Mazur, MSc.,a Lada Dyachenko, MSc.,a L. crispatus (47.05%), L. delonguei (33.33%), and four others (29.62%) were identified. These vaginal microbiomes were dominated by L. crispatus (47.05%) and L. delonguei (33.33%). The distribution of each genus between the groups was compared using the chi-square test. Regression analysis was used to identify predictors of pregnancy.

**OBJECTIVE:** To determine if mitochondrial replacement therapy (MRT) could improve blastulation rates, euploidy rates and pregnancy rate in patients of advanced maternal age (AMA).

**DESIGN:** The study period was from December 2015 to November 2018. Patients were informed and consent to possible risks and the experimental protocol was approved by ethics committee of local association of reproductive medicine. Inclusion criteria were: (1) no less than two failed previous IVF cycles, (2) no blastulation rates of 50%, (3) no more than 2 embryos for transfer (GVT), MI spindle transfer (MIST), MII spindle transfer (MIIST), polar body 1 genome transfer (PBGT) and pronuclear transfer (PNT) were assisted by HVJ-E cell fusion kit. Intracytoplasmic sperm injection (ICSI) had been performed for all cases. If possible, reverse reconstitutions were done. Embryos obtained after reconstitution were cultured until blastocyst stage in time-lapse incubator, were biopsied for other comparative genomic hybridization (aCGH) or next generation sequencing (NGS) analysis and then were vitrified.

**RESULTS:** After performing various types of MRT, 109 zygotes were obtained, that resulted in 33 blastocysts (30%); 3 of which (one per patient) were euploid (2.7%). One try of elective single embryo transfer (eSET) of thawed embryos was done for remaining patients. Positive hCG level (> 100 mIU/mL) and following heartbeating were confirmed only for one patient (42 y.o., PNT group).

**OBJECTIVE:** An FSH boost on trigger-day may improve outcomes in fresh transfers by enhancing folliculogenesis and endometrial receptivity. As more patients are freezing all of their embryos, the endometrial effect is less of a concern, but folliculogenesis remains relevant. Recent reports conflict over the clinical effects of an FSH boost. We therefore examined the effect of an FSH boost on oocyte retrieval, quality, and development, specifically in patients undergoing PGT-A.

**DESIGN:** Retrospective cohort.

**MATERIALS AND METHODS:** Patients undergoing GnRH-antagonist IVF cycles from 1/2015 through 12/2018, were separated into two groups for comparison: those receiving only trigger injections on trigger day (NB), and those also receiving an FSH boost (B). Demographics, days of triggering, %oocytes retrieved, %mature, %blastocysts, and %euploid embryos, were compared (Student’s t-test or X²).
RESULTS: Both groups were stratified into SART registry age groups. Initial comparisons between the groups, without matching for trigger day estradiol levels (E2Trig), revealed a selection bias. B patients had weaker responses, with lower estradiol levels and fewer eggs. In order to examine the effect of B in each age group, we created NB comparison groups with E2Trig values indistinguishable from the B’s. This was done by randomly selecting NB patients from the same age group and E2Trig stratum as B.

1,394 patients were included in this matched comparison, 697 received B, and 697 did not. B patients had significantly more days of gonadotropin administration (~1 day) than NB patients. There were no consistent differences for #oocytes retrieved, #mature, fertilization rate, #blastocysts, or #euploid embryos (see table). Overall, costs associated with B amounted to $276,923, or close to $400 per patient.

**CONCLUSIONS:** No benefit of B was found for #oocytes retrieved, #mature, fertilization rates, #blastocysts, or #euploid embryos. There are significant cost savings associated with NB.

References:

**P-224** Tuesday, October 15, 2019 6:30 AM

**EFFECTIVENESS OF RECOMBINANT HUMAN FOLLICLE-STIMULATING HORMONE (r-hFSH) VERSUS HUMAN MENOPAUSAL GONADOTROPIN (u-hMG) IN ASSISTED REPRODUCTIVE TECHNOLOGY (ART): A STUDY BASED ON GERMAN REAL-WORLD DATA.** Klaus F. Bühlert, MD, a Sandra Gaedde, PharmD, MSC, b Arthur Allignol, PhD, Dr. c Thomas D’Hooghe, MD, PhD, d Wilma Bilger, PhD, d Emmanuelle Boutmy, PhD, Dr. e Emilia Müller, MD, c Robert Fischer, MD, c Centre for Gynecological, Endocrinology, and Reproductive Medicine, Ulm and Stuttgart, Germany; a Merck Healthcare KGaA, Darmstadt, Germany; c Merck Serono GmbH, Darmstadt, Germany; d MVZ Fertility Center Hamburg GmbH, Hamburg, Germany.

OBJECTIVE: To compare clinical outcomes with r-hFSH (GONAL®-f, Merck KGaA, Darmstadt, Germany) vs u-hMG (Menogon HP®, Ferring GmbH, Kiel, Germany).

**MATERIALS AND METHODS:** Non-interventional study based on secondary use of data collected from 71 German IVF centers (1 Jan 2007 – 31 Dec 2012). Patients were included if they received their first controlled ovarian stimulation (COS) cycle with r-hFSH or u-hMG on cycle day 2-3, 0.25mg/day medroxyprogesterone acetate (MPA) was started on stimulation day 7 or when the leading follicle reached 14mm, whichever came first. One mg leuprolide acetate was given when there were ≥ 3 follicles >17 mm. Oocytes were fertilized with the recipients’ partners’ sperm. Recipients were in an artificial cycle, i.e. estradiol valerate 6 mg/day orally for >10 days, vaginal micronized progesterone was added or 4 days before cleavage and blastocyst stage embryo transfers, respectively. Medications were continued until a negative pregnancy test or 10th gestational week. Data are defined with percentages or median (25th – 75th percentile), depending on variables. Non-parametric tests and chi square test were used for comparisons.

RESULTS: 150 oocyte donors were included. 75 in each group. Donors in both groups were similar for age. None of them had premature ovulation and yielded similar oocyte and metaphase two oocytes with similar gonadotropin consumption. 86 women received oocytes from IPPOS and 105 women from NB.

**P-225** Tuesday, October 15, 2019 6:30 AM

**A NOVEL FLEXIBLE PROGESTIN PRIMED OVARIAN STIMULATION PROTOCOL: COMPARISON OF PREGNANCY OUTCOMES WITH THE FLEXIBLE GnRH ANTAGONIST PROTOCOL IN AN OOCYTE DONATION PROGRAM.** Sule Yildiz, MD, a Engin Turkgeli, MD, a Alper Eraslan, MD, a Berik Angun, MD, b Mustafa Baris Ata, MD, c Koc University Hospital, Istanbul, Turkey; d Dunya IVF Center, Kyrenia, Cyprus; e Koc University School of Medicine, Istanbul, Turkey.

OBJECTIVE: To compare a novel flexible progestin primed ovarian stimulation (IPPOS) protocol with the flexible GnRH antagonist protocol in an oocyte donation program.

**MATERIALS AND METHODS:** Oocyte donors were started 225IU/day rFSH on cycle day 2-3, 0.25mg/day GnRH antagonist or 10mg/day medroxyprogesterone acetate (MPA) was started on stimulation day 7 or when the leading follicle reached 14mm, whichever came first. One mg leuprolide acetate was given when there were ≥ 3 follicles >17 mm. Oocytes were fertilized with the recipients’ partners’ sperm. Recipients were in an artificial cycle, i.e. estradiol valerate 6 mg/day orally for ≥ 10 days, vaginal micronized progesterone was added or 4 days before cleavage and blastocyst stage embryo transfers, respectively. Medications were continued until a negative pregnancy test or 10th gestational week. Data are defined with percentages or median (25th – 75th percentile), depending on variables. Non-parametric tests and chi square test were used for comparisons.

RESULTS: 150 oocyte donors were included. 75 in each group. Donors in both groups were similar for age. None of them had premature ovulation and yielded similar oocyte and metaphase two oocytes with similar gonadotropin consumption. 86 women received oocytes from IPPOS and 105 women from NB.
CONCLUSIONS: Ovarian stimulation using DYG for prevention of LH surge yields similar outcomes compared to ganirelix in shared oocyte donor cycle with subsequent FET in donors and recipients.

P-227 Tuesday, October 15, 2019 6:30 AM

EFFECTIVENESS AND SAFETY OF BIOSIMILAR FOLLITROPIN ALFA IN WOMEN UNDERGOING ROUTINE Ovarian STIMULATION WITH A GnRH ANTAGONIST: RESULTS FROM A GERMAN MULTI-CENTRE NON-INTERVENTIONAL STUDY. Colin M. Howles, PhD, German Ovaleap non-interventional ART study group, ARIES CONSULTING Sarl, Onex, Switzerland.

OBJECTIVE: To assess the effectiveness and safety of a biosimilar follicitropin alfa (Ovaleap® Theramex UK Ltd) used for ovarian stimulation in routine clinical practice and in combination with a GnRH antagonist in women undergoing assisted reproduction technologies. Whilst Ovaleap demonstrated therapeutic equivalence to Gonal-f® in a GnRH agonist protocol, to date there is no published data of Ovaleap’s use with a GnRH antagonist.

DESIGN: Multicenter, prospective, non-interventional study, carried out at 34 specialized reproductive medicine centers across Germany from March 2016 to May 2017.

MATERIALS AND METHODS: 507 infertile women undergoing ART were screened. They were 18-40 years old, BMI <30 kg/m², menstrual cycle duration 24 to 35 days, AMH ≥1 ng/mL undergoing first ovarian stimulation for IVF/ICSI and were treated with Ovaleap® using a GnRH antagonist protocol.

Primary effectiveness outcomes were number of retrieved oocytes after ovarian stimulation therapy and clinical pregnancy rate. Secondary effectiveness outcomes were serum estradiol, endometrial thickness, number of metaphase-II oocytes, percentage fertilization rate, number of transferred embryos, and baby take-home rate. Maternal/fital and neonatal adverse drug reactions (ADRs) were also collected. SAS version 9.4 was used for all statistical analyses.

RESULTS: 463 women received at least 1 dose of follicitropin alfa were included in the final analysis. Mean age (SD) was 32.2 (4.1) and BMI was 23.4 (3.6). Mean (SD) total follicitropin alfa dose was 1651.2±506.7 IU, and the median duration of administration was 9.0 days (range: 4-17 days).

Mean number of retrieved oocytes was 11.7±7.2 (median=11.0; range 0-61). The mean (SD) number of transferred embryos was 1.8 (0.4). Clinical pregnancy rate/cycle was 35.6% (165/463) in the overall population and 41.4% (165/399) in women with embryo transfer. Baby take-home rate was 31.8% (143/449) in women with oocyte retrieval and 36.1% (143/396) with ET. The twin and triplet pregnancy rate were 8.5% and 0.5%, respectively.

ADRs were reported for 40/463 women (8.6%). The most common ADRs were ovarian hyperstimulation syndrome (OHSS, n=23, 5.0%) and miscarriage (n=10, 2.2%).OHSS was rated mild in 14 (3.0%), moderate in 8 (1.7%), and severe in 1 (0.2%).

CONCLUSIONS: This real world data collected across multiple clinical sites support the existing evidence of effectiveness (number of oocytes retrieved, clinical pregnancy rate) and safety of ovarian stimulation with Ovaleap® for ART using a GnRH antagonist protocol. These results are consistent with those previously reported in randomized controlled clinical trials.

SUPPORT: The study was supported by Teva GmbH Germany.

P-228 Tuesday, October 15, 2019 6:30 AM

THE IMPACT OF OVARIAN RESPONSE ON CLINICAL PREGNANCY AND DELIVERY RATES IN AN OOCYTE DONOR POPULATION. Brent M. Hanson, MD,a Ashley W. Tiegs, MD,a Shelby A. Neal, MD,a Marie D. Werner, MD,b Richard Thomas Scott, Jr., MD,a 1IVI-RMA New Jersey, Basking Ridge, NJ, 1IVI-RMA.

OBJECTIVE: In the general IVF population, it has been reported that an optional window of ovarian response may exist, with live birth rates declining if fewer than 15 or greater than 20 oocytes are retrieved. The relationship between pregnancy outcomes and ovarian response has not been thoroughly investigated in oocyte donors. This study seeks to characterize the relationship between ovarian response, clinical pregnancy rates, and delivery rates in oocyte donors.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This study was performed at a large IVF practice. Oocyte donors who underwent their first oocyte retrieval followed by an embryo transfer in a recipient between January 1, 2012 and December 31, 2018 were included in the study. The study population was divided into two groups: those who had less than 15 oocytes retrieved and those who had more than 20 oocytes retrieved.

RESULTS: A total of 100 oocyte donors were included in the study. The group with less than 15 oocytes retrieved had a higher clinical pregnancy rate (30.0%) compared to the group with more than 20 oocytes retrieved (14.3%). There was no significant difference in the delivery rate between the two groups (15.6% vs. 15.3%).

CONCLUSIONS: The study suggests that there may be an optimal window of ovarian response in oocyte donors, with live birth rates declining if fewer than 15 or greater than 20 oocytes are retrieved. Further research is needed to confirm these findings and to better understand the impact of ovarian response on clinical pregnancy and delivery rates in oocyte donors.
TABLE 1. Clinical pregnancy rate and delivery rate based on ovarian response

<table>
<thead>
<tr>
<th>Ovarian response</th>
<th>Clinical pregnancy rate</th>
<th>Delivery rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15 oocytes</td>
<td>68.3%</td>
<td>60.3%</td>
</tr>
<tr>
<td>15-20 oocytes</td>
<td>67.8%</td>
<td>60.6%</td>
</tr>
<tr>
<td>&gt;20 oocytes</td>
<td>72.1%</td>
<td>64.1%</td>
</tr>
</tbody>
</table>

P-values for the differences: (P=0.6126) for pregnancy rate and (P=0.7204) for delivery rate.

2018 were included. Ovarian response of donors was divided into three categories: fewer than 15 oocytes retrieved, 15 to 20 oocytes retrieved, and greater than 20 oocytes retrieved. Chi-square analysis was performed to assess differences in clinical pregnancy (defined as the presence of an intrauterine fetal heartbeat on ultrasound) and delivery rates based on ovarian response.

RESULTS: 510 donor retrieval cycles met inclusion criteria. The mean ovarian donor age was 27.45 ± 3.98 years. The median number of eggs retrieved per cycle was 20 (IQR 15-28). Clinical pregnancy data was available for all patients (351 single embryo transfers, 159 double embryo transfers). Delivery data was available for 479 out of 510 patients (93.9%), 322 single embryo transfers, 157 double embryo transfers). 575 out of 510 patients (70%) achieved clinical pregnancies during the first embryo transfer cycle with the use of donor oocytes. 298 out of 479 patients with complete delivery data (62.2%) achieved a live birth from their first transfer cycle with use of donor oocytes. Clinical pregnancy rates were 68.3% when fewer than 15 oocytes were retrieved, 67.8% when 15-20 oocytes were retrieved, and 72.1% when greater than 20 oocytes were retrieved. Delta FSH levels on the second day of menstruation (D2) and the fifth day (D5) were statistically significant differences in clinical pregnancy rate (P=0.6126) and delivery rate (P=0.7204) based on ovarian response (Table 1).

CONCLUSIONS: In an ovarian donor population, the degree of ovarian response does not impact clinical pregnancy or delivery rates. These findings contradict earlier reports which demonstrated optimal outcomes when 15 to 20 oocytes were retrieved.

Estradiol pretreatment in follicular phase at POR patients with high FSH level who have undergoing IVF-ET treatment were randomly divided into the pretreatment group (n=163) and non-pretreatment group (n=160) according to whether the estradiol pretreatment (oral administration with 17-β estradiol 0.01mg/d at the second day to the fourth day of menstrual cycle) were conducted before super ovulation induction. General information and indices relevant to the outcome of IVF-ET treatment of two groups were compared.

RESULTS: In the pretreatment group, serum follicle-stimulating hormone (FSH) (13.77/14.17IU/ml, P=0.53) levels on the second day of menstruation (D2) and the fifth day (D5) were statistically significant; The D2 serum FSH in the non-pretreatment group was also statistically significant compared to that of the FSH in D5 (13.94/8.85, P=0.00). However, there was no statistically significant difference in comparing D2 FSH (13.98/13.94IU/ml, P=0.45) values between the two groups. The differences of age (37.93/37.56years, P=0.5),BMI (22.13/21.80kg/m², P=0.16),AMH (0.89/0.91mg/ml, P=0.57),basal antral follicle count ( AFC ) (3.57/3.59, P=0.23),the number of oocytes retrieved (1.70/1.63, P=0.70),unovulated rate (15.34/13.13, P=0.569), endometrial thickness (10.49/10.49mm, P=0.41),the number of embryos transferred (1.60/1.63, P=0.12),transplant cancellation rate (28.21/31.90%, P=0.474) and clinical pregnancy rate (13.30/ 11.70%, P=0.10) were not statistically significant between the two groups.

CONCLUSIONS: Estradiol pretreatment in follicular phase at POR patients with high FSH level did not increase the number of MI eggs rate and clinic pregnancy rate.On the contrary, it increased the Gn dosage and extended treatment period can impose unnecessary burden on a patient, both financially and mentally. To some extent, the level of FSH only reflects the function of the ovary. Therefore, reducing the blood FSH level cannot increase the number of eggs nor improve the clinical pregnancy outcome.
IVF OUTCOME PREDICTORS - PROGESTERONE LEVELS

P-231 Tuesday, October 15, 2019 6:30 AM
LONGER DURATION OF PROGESTERONE ELEVATION ADVERSELY IMPACTS PREGNANCY OUTCOMES DURING IVF IN WOMEN ≤ 40 YEARS. Chantal Bartels, MD, Jeffrey Thorne, MD, Reeva B. Malhijani, MD, Grow R. Daniel, MD, John Nulsen, MD, Claudio Benadiva, MD, Lawrence Engmann, MD Center for Advanced Reproductive Services, University of Connecticut, Farmington, CT.

OBJECTIVE: The purpose of this study is to evaluate the impact the number of days of progesterone (P) elevation during an IVF cycle on the fresh embryo transfer live birth rate (LBR) at different ages. We hypothesize that the longer the duration of P exposure, the greater the likelihood for asynchronous endometrium manifested as a lower LBR for ages <35 years and 35-40 years.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We included all patients ≤40 years who underwent fresh IVF embryo transfer between 1/2011 and 12/2017 at a large IVF clinic. Morning serum P levels were collected every 1 to 2 days during the IVF cycle starting day 4, with frequency of collection determined by the follicle size through ultrasound monitoring. We evaluated the effect of prolonged elevation of P ≥1.0 ng/mL on livebirth rates by age group. ANOVA was used for continuous variables, and Chi-square was used for categorical data. Logistic regression was performed controlling for age, BMI, embryo stage at transfer and number of embryos transferred.

RESULTS: 3339 IVF cycles were included for analysis, with 1850 blastocyst transfers and 1489 day 3 embryo transfers. The LBR was lower if the day of trigger serum P was elevated (1.0-1.4ng/mL: 49.5% [330/666] and ≥1.5ng/mL: 43.3% [58/135]) compared to P <1.0ng/mL: 57% [585/1027] (p<0.001). Moreover, a longer duration of P elevation was associated with lower LBR (Table 1). After controlling for the potential confounding variables, prolonged duration of P elevation ≥1.0 ng/mL (OR: 0.61; 95% CI: 0.47-0.86; p<0.001) and day of trigger P ≥1.0 ng/mL (OR: 0.73; 95% CI: 0.63-0.84; p<0.001) were still associated with lower LBR.

CONCLUSIONS: The greater the number of days of P elevation during a fresh IVF cycle, the less likely the transfer is to result in a live birth. The trend is apparent for all ages, though it was only statistically significant for those <35 years. An early rise in P warrants a timely conversation about the benefits of a freeze-all approach.

SUPPORT: None.

P-232 Tuesday, October 15, 2019 6:30 AM
INCREASING LUTEAL PROGESTERONE LEVELS ARE ASSOCIATED WITH HIGHER ONGOING PREGNANCY RATES AND LOWER EARLY PREGNANCY LOSSES FOLLOWING SINGLE EUPLOID FROZEN EMBRYO TRANSFER. Sydney Chang, MD, a Dmitry Gounko, MA, a Joseph A. Lee, BA, a Eric Flisser, MD, a Lucky Sekhon, MD, a Alan B. Copperman, MD a* Icahn School of Medicine at Mount Sinai, New York, NY, a* Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Endometrial programming with exogenous estradiol (E2) and progesterone (P4) during a frozen embryo transfer (FET) cycle mimics the hormonal environment of a natural cycle, while allowing for synchronisation of embryo and endometrial development. While studies have investigated the ideal timing of P4 initiation and the association of supraphysiologic E2 levels with FET and perinatal outcomes,1 less is known about how the level of P4 exposure impacts implantation and placentation. Prior research has suggested that elevated P4 levels during FETs are associated with a lower ongoing pregnancy/live birth (OP/LB) rate and higher early pregnancy loss (EPL) rate.2 Other studies have suggested an association between FETs and large for gestational age (LGA) and postdates infants.3 Yet, there is no known mechanism for these findings.4 The objective of this study is to determine whether the level of P4 exposure at time of FET and throughout the first trimester impacts FET or perinatal outcomes.

DESIGN: Retrospective, cohort study.

MATERIALS AND METHODS: The study included patients undergoing a single euploid FET at an academic center from 2012-2019. Luteal support methods other than intramuscular P4 were excluded. Serum P4 level was treated as a continuous variable. Peri-implantation P4 was defined as P4 level on the day prior to FET, and first trimester P4 was defined as average P4 from the day prior to FET until ~10 weeks of gestational age (GA). Primary outcomes were rates of OP/LB and EPL. Secondary outcomes were clinical pregnancy (CP) rate, GA at delivery, and neonatal birth weight. Small for GA (SGA)/LGA were defined using sex-specific data for the 10th/90th percentile.5 Data were evaluated using univariate linear regressions with generalized estimating equations.

RESULTS: A total of 3773 single euploid FET cycles from 2699 patients were included. After controlling for age, BMI, endometrial thickness, embryo morphology, and days required for blastulation, there was a significant association between average P4 and OP/LB (OR 1.15 [95% CI 1.13-1.17], p<0.001), as well as EPL (OR 0.83, [95% CI 0.81-0.85], p<0.001). There was no association between peri-implantation P4 and CP rate. There was a significant decrease in GA at delivery with increasing P4 (β=−0.19 week, p<0.001). Mean first trimester P4 levels were not associated with birth weight after controlling for GA, fetal sex and BMI. There was no association between P4 and incidence of SGA/LGA infants.

CONCLUSIONS: In a large cohort of single euploid FETs, we showed that luteal P4 in early pregnancy is positively correlated with OP/LB rate, and inversely correlated with EPL rate. While the level of exposure to P4 is crucial for pregnancy maintenance, increasing P4 levels in the first trimester do not appear to have downstream effects on placentation. Increasing luteal P4 level

is associated with a shorter duration of pregnancy, but is not associated with differences in birth weight, or incidence of SGA or LGA infants. Future studies might focus on the pharmacogenomic profiles of women undergoing synthetic endometrial preparation with the aim of individualizing FET protocols.


SUPPORT: None.
P-234 Tuesday, October 15, 2019 6:30 AM

SERUM PROGESTERONE ELEVATION MAY ADVERSELY AFFECT EMBRYOLOGICAL PARAMETERS. Fazilet Kubra Boyanulak, M.D., MSc,a Meral Gultomruk, BSc,b Emre Turgut, M.D.,b Necati Fındıklı, Ph.D.,b Onder Coban, MSc,d Minevere Serdarogullari, Ph.D,d Mustafa Bahçeci, M.D., Ph.D.d Bahçeci Health Group-Fulya IVF Centre, ISTANBUL, Turkey; Bahçeci Fulya IVF Center, ISTANBUL, Turkey; Bahçeci Health Group-Fulya IVF Centre, Istanbul, Turkey; Bahçeci Health Group, Lefkosia, Turkey; Bahçeci Health Group, Nicosia, Turkey.

OBJECTIVE: To evaluate the association of progesterone (P) levels on the trigger day with the embryo quality in freeze all cycles.

DESIGN: A retrospective analysis of ICSI cycles followed by elective freezing between 2014 and 2018. The exclusion criteria were female age >37, BMI >30 kg/m², sperm concentration <2x10⁶/ml, more than two failed ICSI attempts and frozen cleavage stage embryos. The primary outcomes were fertilization, blastulation, embryo quality at blastocyst stage.

RESULTS: Baseline characteristics of the women and embryo development are presented in Table 1. Comparisons of modified natural cycle with progesterone and LH levels are shown in Table 2. Simultaneous elevation of progesterone and LH levels (table 1).

CONCLUSIONS: During the modified natural cycle of frozen-thawed embryo transfer, serum progesterone and LH levels on the trigger day have an impact on clinical outcomes. We suggest that hCG induction should be selected when the LH level is less than 20 IU/L and the progesterone level is less than 1 pg/ml.


P-233 Tuesday, October 15, 2019 6:30 AM

EFFECTS OF SERUM PROGESTERONE AND LH LEVELS BEFORE HCG TRIGGERING ON CLINICAL PREGNANCY OUTCOMES OF MODIFIED NATURAL FROZEN-THAWED EMBRYO TRANSFER CYCLES. Na Kong, M.M, Tianran Song, M.D., Jingyu Liu, M.M. Reproductive Medicine Center, The Affiliated Drum Tower Hospital of Nanjing University, nanjing, China.

OBJECTIVE: To investigate the effects of serum progesterone and luteinizing hormone (LH) levels on the clinical outcomes of the modified natural cycle of frozen-thawed embryo transfer.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Five-hundred-and-ninety-two cycles of frozen-thawed transplantation of modified natural cycles from 2017 to 2018 were analyzed. According to the level of progesterone on human chorionic gonadotropin (hCG) days, patients were divided into two groups: group A (progesterone greater than or equal to 1 pg/ml) and group B (progesterone less than 1 pg/ml). According to LH levels, patients were divided into two groups: group C (LH greater than or equal to 20 IU/L) and group D (LH less than 20 IU/L). Pregnancy outcomes were compared and the influence of serum progesterone and LH levels on clinical outcomes on the hCG triggering day were explored, to guide the selection of the hCG triggering time in the modified natural cycle of frozen-thawed embryo transfer.

RESULTS: Compared with group B, group A baseline data and pregnancy rates showed no noticeable difference, but the embryo implantation rate was statistically lower in group A. There was no difference in baseline information and clinical pregnancy rates between group C and group D. The embryo implantation rate of group D was significantly higher than that of group C. Moreover, the implantation rate was significantly reduced in patients with simultaneous elevation of progesterone and LH levels(table 1).

CONCLUSIONS: During the modified natural cycle of frozen-thawed embryo transfer, serum progesterone and LH levels on the trigger day have an impact on clinical outcomes. We suggest that hCG induction should be selected when the LH level is less than 20 IU/L and the progesterone level is less than 1 pg/ml.


TABLE 1. Comparison of modified natural cycle with progesterone and LH increased simultaneously and overall population.

<table>
<thead>
<tr>
<th>LH≥20IU/L and P&gt;1pg/ml (n=127)</th>
<th>Total population (n=592)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female age(year)</td>
<td>31.47±5.01</td>
<td>31.65±4.97</td>
</tr>
<tr>
<td>Male age(year)</td>
<td>32.47±5.60</td>
<td>33.08±5.71</td>
</tr>
<tr>
<td>HCG daily E2(ng/ml)</td>
<td>319.53±111.82</td>
<td>343.55±226.74</td>
</tr>
<tr>
<td>HCG daily oocyte number</td>
<td>1.00±0.22</td>
<td>1.01±0.18</td>
</tr>
<tr>
<td>Size of dominant follicle</td>
<td>17.81±1.30</td>
<td>17.73±1.39</td>
</tr>
<tr>
<td>Endometrium thickness</td>
<td>10.07±1.65</td>
<td>10.16±1.79</td>
</tr>
<tr>
<td>Number of transplanted embryos</td>
<td>1.35±0.50</td>
<td>1.51±0.50</td>
</tr>
<tr>
<td>Proportion of transplanted blastocysts (n)</td>
<td>40.9% (52)</td>
<td>45.44% (269)</td>
</tr>
<tr>
<td>Clinical pregnancy rate</td>
<td>53.5%</td>
<td>61.49%</td>
</tr>
<tr>
<td>Embryo implantation rate</td>
<td>44.16%</td>
<td>52.63%*</td>
</tr>
</tbody>
</table>

HCG day LH level is greater than or equal to 20 IU/L (397 cases) and progesterone greater than or equal to 1 pg/ml, *p<0.05


12. Irani M, Robles A, Gunnala V, Reichman DE, Rosenwaks ZJF, Sterilli A, et al. PROGESTERONE RISE ON THE CLINICAL OUTCOME OF ANOVULATORY PATIENTS TREATED WITH GONADOTROPINS. Hassan Sallam, MD, PhD (London), FRCOG, a Ola Moustafa, MD, MCh, ab Abdel-Fattah Agameya, MD, PhD, ab Nooman Sallam, MD, MCh, a Alexandria University, Alexandria, Egypt; b Alexandria Fertility Centre, Alexandria, Egypt.

OBJECTIVE: To study the effect of serum LH and plasma progesterone rise on the day of HCG administration on the clinical outcome of anovulatory patients treated with gonadotropins.

DESIGN: A prospective cohort study.

MATERIALS AND METHODS: Sixty consecutive anovulatory patients attending our infertility clinic and treated for ovarian stimulation with gonadotropins were studied during their first cycle of treatment. All patients had normogonadotrophic hypogonadism (WHO group I) and had failed to become pregnant on clomiphene citrate therapy (up to 150 mg/day for 5 days). All patients were aged 20 to 38 years with a mean (±SD) of 26.7 (±9.2) years. All male partners had normal semen parameters according to the WHO standards. Patients with hyperprolactinaemia and those with congenital adrenal hyperplasia were excluded, as well as those with other causes of infertility. The mean (±SD) basal (day 3) serum FSH and LH levels were 7.27 (±1.82) mIU/mL and 7.57 (±0.78) mIU/mL, respectively. The mean (±SD) basal (day 3) LH/FSH ratio was 1.09 (±014) mIU/mL. Human menopausal gonadotropins (150 IU) were administered by daily IM injections starting day 5 of the menstrual cycle. Monitoring was effected by transvaginal ultrasound scanning of the follicles and the dose of gonadotropins adjusted accordingly. HCG (5000 IU) was administered by IM injection when 2 follicles reached 18 mm in diameter and venous blood was withdrawn on the same day and the serum/plasma kept at -20°C until the time of the LH and progesterone assay. Eighteen patients became pregnant, of whom 17 reached clinical viability (beating heart on ultrasound) and one had a miscarriage. Power calculation regarding the premature rise or otherwise of serum LH revealed that a minimum of 17 treatment cycles was needed to study in each group to achieve an 80% study power at a 5% level significance.

RESULTS: The mean (±SD) of serum LH and plasma progesterone levels on the day of HCG administration were 11.10 (±9.08) mIU/mL and 2.68 (±0.14) ng/mL, respectively. Twenty nine patients (48.3%) had an LH rise body(PB) morphology. For each oocyte, each parameter was scored as +1, 0 and -1 to determine the oocyte quality score.

RESULTS: There was no significant difference between the groups in terms of patient age (p=0.11), BMI (p=0.12), duration of infertility (p=0.17), and follicle-stimulating hormone (FSH) peak (p=0.91). AMH (p=0.20) and AFC (p=0.60). There was a positive correlation between dose of gonadotropin and progesterone concentration on trigger day (p=0.001). There was a negative correlation between oocyte quality score and progesterone level on hCG day (p=0.001). In terms of oocyte quality score, a statistically significant difference was found between Group-3 (5.48, 4.97, 4.14, p=0.001, respectively). The quality score of the Group-3 oocytes was found to be significantly lower than both Group-1 and Group-2 oocytes (p=0.001). Also Group-2 oocyte quality score was significantly lower than Group-1 oocytes (p=0.001). There was a positive correlation between progesterone level and abnormal oocyte percentage (p=0.001). The highest abnormal oocyte ratio was found in Group-3 (78.9) and lowest in Group-1 (78.2). Ooplasm (p=0.007), PVS (p=0.001) and ZP (p=0.084) abnormalities were statistically increased with higher progesterone concentration. Degenerated (p=0.55) and immature oocyte percentage (p=0.82) had no significant correlation between groups.

Estradiol concentration on trigger day (p=0.001), total oocyte count (p=0.001) and mature oocyte count (p=0.001) had a positive correlation with progesterone concentration on trigger day.

CONCLUSIONS: This study comprehensively assessed the relationship between oocyte quality and progesterone. The data demonstrate that elevated progesterone levels (≥1 ng/ml) before oocyte maturation were consistently detrimental to the oocyte. Individualization of stimulation protocols and consideration of gonadotropin dose in late follicular phase will lead to positive results in terms of oocyte quality.
PREGNANCY RATE. QUENT EUPLOID FROZEN EMBRYO TRANSFER AT TIME OF OVULATION TRIGGER ON SUBSEQUENT EUPLOIDITY. Estrogen to Progesterone Ratio (E/P) at time of ovulatory trigger on clinical pregnancy rate during subsequent frozen euploid embryo transfer.

**DESIGN:** Retrospective cohort analysis

**MATERIALS AND METHODS:** All frozen embryo transfers from January-December 2018 from a high-volume private practice fertility center were included. Serum E and P levels were measured on the day of ovulatory trigger by Immulite (Siemens). E/P was calculated in an effort to control for degree of response. Embryos were cultured to the blastocyst stage for trophectoderm biopsy and vitrified. Preimplantation genetic testing for aneuploidy (PGT-A) was performed using next generation sequencing (NGS). Euploid frozen embryo transfers were performed in a subsequent natural or controlled cycle. Oocyte maturity (MI/I total oocytes retrieved) and euploidy rates (euploid/ total embryos biopsied) were calculated. Clinical pregnancy and ongoing pregnancy (>10 weeks) following a first embryo transfer were examined in relation to E/P. Regression analyses were performed to analyze the impact of E/P as a continuous and categorical value (defined by quartile) on cycle outcomes.

**RESULTS:** A total of 134 women underwent a euploid frozen embryo transfer over the study period and had steroid levels at time of trigger available. Mean E at trigger was 3704±2234 pg/ml while mean P was 1.13±0.56 ng/ml for a mean E/P of 3.61±2.59. Cycle and pregnancy outcomes by quartile of E/P are listed in Table 1. There were no differences between quartiles of E/P with respect to cycle or pregnancy outcomes.

**CONCLUSIONS:** E/P ratio at the time of trigger does not appear to impact clinical outcomes in a subsequent euploid frozen embryo transfer cycle.

---

**P-237 Tuesday, October 15, 2019 6:30 AM**

**EFFECT OF ESTROGEN TO PROGESTERONE RATIO AT TIME OF OVULATION TRIGGER ON SUBSEQUENT EUPLOID FROZEN EMBRYO TRANSFER PREGNANCY RATE.** Hency Patel, MD,a Temeka Zore, MD,b Richard Buyalos, MD, b Gary Hubert, MD, b Chunnin Wang, PhD,b Meredith Brower, MD, b Moussa Shamokni, MD, b Molly M. Quinn, MD, b aUniversity of California, Los Angeles, Los Angeles, CA; bFertility and Surgical Associates of California, Thousand Oaks, CA.

**OBJECTIVE:** While an elevated serum progesterone level (P) prior to trigger has been associated with embryo-endometrial asynchrony and decreased pregnancy rates during in vitro fertilization (IVF) with fresh embryo transfer, few data exist in the context of a planned frozen embryo transfer. We aim to evaluate the impact of elevated P via estradiol to progesterone ratio (E/P) at time of ovulatory trigger on clinical pregnancy rate during subsequent frozen euploid embryo transfer.

**METHODS:** We aimed to evaluate the impact of elevated P via estradiol to progesterone ratio (E/P) at time of ovulatory trigger on clinical pregnancy rate during subsequent frozen euploid embryo transfer.

**RESULTS:** A total of 134 women underwent a euploid frozen embryo transfer over the study period and had steroid levels at time of trigger available. Mean E at trigger was 3704±2234 pg/ml while mean P was 1.13±0.56 ng/ml for a mean E/P of 3.61±2.59. Cycle and pregnancy outcomes by quartile of E/P are listed in Table 1. There were no differences between quartiles of E/P with respect to cycle or pregnancy outcomes.

**CONCLUSIONS:** E/P ratio at the time of trigger does not appear to impact clinical outcomes in a subsequent euploid frozen embryo transfer cycle.

---

**CHARACTERISTICS (SD/PERCENTAGE) S. P4 ≤ 25.1 (54) S. P4 > 25.1 (76) p VALUE**

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>S. P4 ≤ 25.1 (54)</th>
<th>S. P4 &gt; 25.1 (76)</th>
<th>p VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE [YEARS]</td>
<td>30±1(5.23)</td>
<td>31.24(4.42)</td>
<td>0.72</td>
</tr>
<tr>
<td>MARRIED LIFE [YEARS]</td>
<td>6.9(4.4)</td>
<td>6.0(2.9)</td>
<td>0.33</td>
</tr>
<tr>
<td>BMI [kg/m²]</td>
<td>26.34(3.87)</td>
<td>25.54(3.47)</td>
<td>0.39</td>
</tr>
<tr>
<td>DAYS OF HRT</td>
<td>19.9(6.5)</td>
<td>20.9(6.8)</td>
<td>0.55</td>
</tr>
<tr>
<td>ENDOMETRIAL THICKNESS[mm]</td>
<td>9.69(1.45)</td>
<td>9.68(1.66)</td>
<td>0.98</td>
</tr>
<tr>
<td>ENDOMETRIAL VOLUME[mm³]</td>
<td>3.41(0.95)</td>
<td>3.15(0.99)</td>
<td>0.47</td>
</tr>
<tr>
<td>ESTRADIOL LEVEL [pg/ml]</td>
<td>586.06(596.11)</td>
<td>444.27(252.60)</td>
<td>0.29</td>
</tr>
<tr>
<td>PROGESTERONE LEVEL [ng/ml]</td>
<td>0.25(0.11)</td>
<td>0.29(0.28)</td>
<td>0.47</td>
</tr>
<tr>
<td>PROGESTERONE LEVEL (ET DAY) [ng/ml]</td>
<td>18.59(5.10)</td>
<td>38.87(12.07)</td>
<td>0.001</td>
</tr>
<tr>
<td>NO. OF EMBRYO TRANSFER</td>
<td>2.70(0.82)</td>
<td>2.62(0.76)</td>
<td>0.68</td>
</tr>
<tr>
<td>PREGNANCY RATE</td>
<td>20.37(0.4%)</td>
<td>54.71(0.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BIOCHEMICAL ONLY PREGNANCY</td>
<td>2(10%)</td>
<td>3(5.55%)</td>
<td>0.38</td>
</tr>
<tr>
<td>ONGOING PREGNANCY (&gt;12 weeks) /</td>
<td>15(27.78%)</td>
<td>48(63.16%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LIVE BIRTH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EARLY PREGNANCY BLEEDING</td>
<td>5(27.78%)</td>
<td>7(13.73%)</td>
<td>0.08</td>
</tr>
<tr>
<td>MISCARRIAGE</td>
<td>2(11.11%)</td>
<td>3(5.88%)</td>
<td>0.23</td>
</tr>
<tr>
<td>TWINS at 12 WEEKS</td>
<td>3(16.67%)</td>
<td>6(11.76%)</td>
<td>0.29</td>
</tr>
<tr>
<td>TRIPLET</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>ECTOPIC PREGNANCY</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
P-239 Tuesday, October 15, 2019 6:30 AM

PROTOCOL MATTERS: PROGESTERONE RISE ON DAY OF TRIGGER IMPACTS ANTAGONIST BUT NOT AGONIST LIVE BIRTH RATES FOR FRESH IVF CYCLES. Janelle M. Jackman, M.B.B.S., Chantal Bartels, MO; John Nulsen, MD, Grow R. Daniel, MD. The Brooklyn Hospital Center, Brooklyn, NY; University of Connecticut Health Center, Center for Assisted Reproductive Services, Farmington, CT.

OBJECTIVE: The purpose of this study is to determine if age and stimulation protocol influences the negative pregnancy outcome impact of progesterone rise on day of trigger during stimulated IVF-ET.

DESIGN: A retrospective cohort study using a large IVF database.

MATERIALS AND METHODS: oIVF is a multicenter database for IVF that has collected over 122,548 patient IVF cycles between 2004 and 2018. We included all women who underwent elective fresh single blastocyst transfer and had excess embryos to freeze. Women were excluded for positive smoking status and day three follicle stimulating hormone level >12 IU/L. Progesterone (P4) levels were categorized into low (<1 ng/mL), medium (1-1.5 ng/mL), and high (>1.5 ng/mL). Age groups were divided by <35 years versus ≥35 years. Gonadotropin-releasing hormone (GnRH)-Antagonist and GnRH-agonist protocols were compared separately in each age group. Statistics was analyzed using Chi-square, ANOVA, Student’s t-test and logistic regression. P<0.05 was considered statistically significant.

RESULTS: 3936 cycles were included. Women in the two age groups did not differ significantly by cycle variables including BMI, AMH, FSH values. In all patients, live birth rates were lower when progesterone levels on day of trigger rose above 1 ng/mL using an antagonist suppression protocol (p=0.006). This was particularly true and significant for women ≥35 years old (p=0.007), but not statistically significant for women <35 years old. No significant difference was seen with progesterone level and live birth rate when an agonist suppression protocol was used for ovulation induction, regardless of the patients’ ages. Live birth rates were higher using GnRH-agonist suppression in every progesterone group and age category (p<0.0001).

CONCLUSIONS: Elevated serum progesterone levels >1 ng/mL on the day of trigger is associated with reduced live birth rates following IVF/ICSI cycles in women ≥35 years when an antagonist protocol is used. Ovarian stimulation using GnRH-agonist suppression seems to protect from the adverse effect of rising progesterone and allows high pregnancy rates with fresh embryo transfer. Protocol should be considered when recommending a freeze-all cycle in the setting of elevated progesterone.


IVF OUTCOME PREDICTORS - SPERM

P-240 Tuesday, October 15, 2019 6:30 AM

SPERM INTRACELLULAR PH AS A PREDICTOR OF FERTILIZATION RATE IN NORMOSPERMIC INFERTILE MEN UNDERGOING IN VITRO FERTILIZATION. Stephanie Gunderson, MD, Lis C. Puga Molina, PhD, Joan Riley, PhD, HCLD, Emily S. Junghem, MD, MSCI, Celia M. Santi, PhD MD, Stephanie Gunderson, MD, Washington University St Louis, St Louis, MO; Washington University In Saint Louis, Saint Louis, MO; Washington University.

TABLE 2. Live birth rate by age and protocol for progesterone level

<table>
<thead>
<tr>
<th>Age Group</th>
<th>All (%)</th>
<th>Progesterone Rise</th>
<th>Progesterone Rise</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35 (%)</td>
<td>48.1</td>
<td>34.85</td>
<td></td>
</tr>
<tr>
<td>≥35 (%)</td>
<td>255/530</td>
<td>460/1320</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>50.5</td>
<td>37.4</td>
<td>42.5</td>
</tr>
<tr>
<td>P&lt;1</td>
<td>187/380</td>
<td>306/818</td>
<td>68/160</td>
</tr>
<tr>
<td>Medium</td>
<td>54.5</td>
<td>34.6</td>
<td>41.6</td>
</tr>
<tr>
<td>P 1-1.5</td>
<td>158/290</td>
<td>191/552</td>
<td>47/113</td>
</tr>
<tr>
<td>High</td>
<td>54.6</td>
<td>31.4</td>
<td>39.0</td>
</tr>
<tr>
<td>P&gt;1.5</td>
<td>95/174</td>
<td>98/312</td>
<td>25/64</td>
</tr>
<tr>
<td>p-value</td>
<td>0.52</td>
<td>0.15</td>
<td>0.89</td>
</tr>
</tbody>
</table>

FERTILITY & STERILITY®
University School of Medicine, St. Louis, MO; 8Washington University School of Medicine, St. Louis, MO.

OBJECTIVE: To determine whether intracellular pH (pHi) of human spermatozoa can predict unsuccessful conventional fertilization outcomes in normospermic infertile men undergoing in vitro fertilization (IVF).

DESIGN: IRB approved, laboratory study of normospermic men undergoing IVF from September 2018 to present at a single institution. Couples were excluded if they used frozen sperm, had a known female factor or utilized intracytoplasmic sperm injection (ICSI) only. De-identified, normospermic fresh semen samples were also analyzed.

MATERIALS AND METHODS: Fresh semen was collected on the day of oocyte retrieval from normospermic (≥32% progressive motility; ≥40% total motility; ≥15 × 10⁶ cells/ml) infertile men undergoing IVF. Sperm were subjected to standard swim up, then analyzed immediately or incubated in capacitating media (Quinn’s Advantage Fertilization, CooperSurgical) at 37°C and 5% CO₂ for 24 hours. pH of spermatozoa was measured in all samples using flow cytometry (FACSCanto II TM cytometer) after incubation with pH sensitive fluorescent probe, BCECF-AM. Data were analyzed using FACS Diva and FlowJo software and included only single live sperm cells. The final sperm pHi was obtained by linearly interpolating the median fluorescence of the unknown sample in the calibration curve of known pH buffer solutions for each condition. Hyperactivated motility was measured by computer-assisted semen analysis. Standard univariate and bivariate analyses were performed, if data were not normally distributed a non-parametric test was performed.

RESULTS: A total of 28 fresh de-identified samples and 24 IVF samples were included in the analysis. The IVF couples included in the analysis were demographically similar. Previously, we measured pHi in capacitated fresh spermatozoa from deidentified samples and found that pHi positively correlated with the percentage of sperm with intact acrosomes (r = 0.195 vs. 6.93 ± 0.257). Sperm pHi positively correlated with conventional fertilization rates (number of fertilized eggs /total number of mature oocytes, n=24, P=0.0197) but not with ICSI fertilization rates (n=10, P=0.655). Sperm samples that had a conventional fertilization rate greater than 70% had a significantly higher pHi than those with a fertilization rate lower than 50% (n=10, P=0.0175). The lower 99% confidence interval of pHi in sperm from the IVF cohort was 6.77. Fertilization rates were significantly higher with sperm with pHi >6.77 than with sperm with pHi 6.77 (n=24, P=0.0027).

CONCLUSIONS: Sperm pHi was a stable marker within patients before and after capacitation and positively correlated with conventional fertilization rates. This measurement may be used to predict poor conventional fertilization outcomes in normospermic men undergoing IVF.

Reference: None.

SUPPORT: None.

P-241 Tuesday, October 15, 2019 6:30 AM

NEUROTENSIN STIMULATES THE SPERM ACR Oosome Reaction and A lters Percentages of Fertilization in vitro. Genevieve E. Campbell, BS; 8Estella L. Jones, PhD; 8Pierre Comizzoli, DVM, PhD, 8Diane M. Duffy, PhD; 8Eastern Virginia Medical School, Norfolk, VA; 8Smithsonian Institution, Washington, DC.

OBJECTIVE: Neurotensin (NTS) is a naturally-occurring, 13-amino acid peptide which was previously reported to stimulate the acrosome reaction in mouse and bull sperm. This study determined the impact of NTS on the function of human and non-human primate sperm.

DESIGN: Experimental, laboratory-based research study of semen from consenting, normozoospermic human donors and cynomolgus macaques.

MATERIALS AND METHODS: Human semen samples from CONRAD, Norfolk, VA were filtered to obtain motile sperm. Sperm acrosome status was assessed by staining with a fluorescent lectin which binds specifically to the acrosomal membrane and permits microscopic visualization of the sperm acrosome (intact or reacted). Eosin-nigrin staining determined sperm viability. Computer assisted semen analysis (CASA) assessed sperm motility, progression, and velocity. For in vitro fertilization (IVF) studies, monkey oocytes were obtained after ovarian stimulation and follicle aspiration. Monkey sperm samples were obtained from the Oregon National Primate Research Center. Fertilization was determined by the presence of a second polar body and 2 pronuclei.

RESULTS: NTS treatment of human sperm stimulated the acrosome reaction in both a dose-dependent (0.1-10 μM) and time-dependent (5-30 min) manner in vitro. After a 30 min incubation, intact acrosomes decreased from 81 ± 5% in untreated sperm to 46 ± 5% in sperm treated with 10 μM NTS (P<0.05, n=4 donors). NTS treatment (0.1-10 μM for 30 min) did not alter sperm motility or progression (n=4 donors); however, there was a slight increase in proportion of viable sperm with NTS treatment (P<0.05, n=4 donors). Both a general NTS receptor antagonist (SR142948) and a NTS1 selective antagonist (SR48692) reduced the ability of NTS to stimulate the acrosome reaction. While 92 ± 2% of untreated sperm had intact acrosomes after 30 min, NTS treatment resulted in only 54 ± 7% of sperm with intact acrosomes (P<0.05, n=3 donors). Incubation with NTS plus SR142948 resulted in 88 ± 1% of sperm with intact acrosomes, and incubation with NTS plus SR48692 resulted in 87 ± 1% of sperm with intact acrosomes (P<0.05, n=3 donors). To determine if NTS treatment compromises the ability of sperm to fertilize an oocyte, monkey sperm were treated with NTS (10 μM for 30 min). Untreated monkey sperm had 87 ± 2% intact acrosomes, while sperm treated with NTS had 50 ± 1% intact acrosomes (P<0.05, n=3 separate experiments). Percentage of fertilization with untreated monkey sperm and monkey oocytes was 72%. Sperm pre-treated with NTS and then used for IVF yielded a significantly lower fertilization rate of 18% (different by Chi-squared test).

CONCLUSIONS: NTS effectively stimulates the acrosome reaction in human and monkey sperm. Pre-treatment of sperm with NTS significantly reduces fertilization. Therefore, the NTS pathway has potential for contraceptive development. Identification of NTSR1 as the mediator of NTS action provides a specific target for future study. This work was supported by Eastern Virginia Medical School and NICHD (HD071875 to DMD). Gonadotropins and Ganirolix were generously provided by Merck and Co., Inc., Kenilworth, NJ.

SUPPORT: This work was supported by Eastern Virginia Medical School and NICHD (HD071875 to DMD).

P-242 Tuesday, October 15, 2019 6:30 AM

SPERM DNA FRAGMENTATION INDICES ARE NOT CORRELATED WITH BLASTULATION OR EUPLOIDY RATES IN PATIENTS UNDERGOING IVF WITH PGT-A. Carlos Hernandez-Nieto, MD; 8Joseph A. Lee, BA; 8Christine Briton-Jones, PhD, HCLD; 8Natan Bar-Chama, MD; 8Benjamin Sandler, M.D.; 8Alan B. Copperman, MD. 8Reproductive Medicine Associates of New York, New York, NY; 8Ichac School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: It has been postulated that the sperm DNA integrity correlates with embryo development and implantation potential (1), also that men who suffer from high sperm DNA fragmentation experience a higher probability of sperm aneuploidy and meiotic anomalies. Theoretically, embryos from men whose ejaculates display elevated DNA fragmentation could be at a greater risk of aneuploidy following fertilization. Still, published data regarding the impact of sperm with high DNA fragmentation is highly heterogeneous and limited by small sample size, use of dated genetic testing platforms, and/or analysis of patients with recurrent pregnancy losses. The objective of this study is to examine the correlation between indices measuring sperm DNA damage and embryo quality and euploidy rate in a diverse population of infertile couples undergoing IVF/ICSI with preimplantation genetic testing for aneuploidy (PGT-A).

DESIGN: Retrospective and bull sperm.

MATERIALS AND METHODS: All patients undergoing ICSI/PGT-A from 2012-2019 were included in the analysis. Cases in which Sperm DNA fragmentation Index (DFI) were analyzed were included. DFI was calculated using sperm chromatin dispersion, TUNEL, acridine Orange or Sperm chromatin structure assays. Patients were segregated into 2 groups: Normal DFI rate (≤30%) and Elevated DFI rate (>30%). Surgical extracted or frozen/thawed semen samples were included. Demographic characteristics of populations, clinical embryology parameters, and embryonic euploidy rates were compared between cohorts. T-test, Xi², and multivariate regression analysis were performed. If data were not normally distributed a non-parametric test was performed.

RESULTS: NTS treatment of human sperm stimulated the acrosome reaction in both a dose-dependent (0.1-10 μM) and time-dependent (5-30 min) manner in vitro. After a 30 min incubation, intact acrosomes decreased from 81 ± 5% in untreated sperm to 46 ± 5% in sperm treated with 10 μM NTS (P<0.05, n=4 donors). NTS treatment (0.1-10 μM for 30 min) did not alter sperm motility or progression (n=4 donors); however, there was a slight increase in proportion of viable sperm with NTS treatment (P<0.05, n=4 donors). Both a general NTS receptor antagonist (SR142948) and a NTS1 selective antagonist (SR48692) reduced the ability of NTS to stimulate the acrosome reaction. While 92 ± 2% of untreated sperm had intact acrosomes after 30 min, NTS treatment resulted in only 54 ± 7% of sperm with intact acrosomes (P<0.05, n=3 donors). Incubation with NTS plus SR142948 resulted in 88 ± 1% of sperm with intact acrosomes, and incubation with NTS plus SR48692 resulted in 87 ± 1% of sperm with intact acrosomes (P<0.05, n=3 donors). To determine if NTS treatment compromises the ability of sperm to fertilize an oocyte, monkey sperm were treated with NTS (10 μM for 30 min). Untreated monkey sperm had 87 ± 2% intact acrosomes, while sperm treated with NTS had 50 ± 1% intact acrosomes (P<0.05, n=3 separate experiments). Percentage of fertilization with untreated monkey sperm and monkey oocytes was 72%. Sperm pre-treated with NTS and then used for IVF yielded a significantly lower fertilization rate of 18% (different by Chi-squared test).

CONCLUSIONS: NTS effectively stimulates the acrosome reaction in human and monkey sperm. Pre-treatment of sperm with NTS significantly reduces fertilization. Therefore, the NTS pathway has potential for contraceptive development. Identification of NTSR1 as the mediator of NTS action provides a specific target for future study. This work was supported by Eastern Virginia Medical School and NICHD (HD071875 to DMD). Gonadotropins and Ganirolix were generously provided by Merck and Co., Inc., Kenilworth, NJ.

SUPPORT: This work was supported by Eastern Virginia Medical School and NICHD (HD071875 to DMD).
RESULTS: 1108 blastocysts derived from 259 IVF/PGT-A cases were included in the study. The groups consisted of 126 cases (n = 543 embryos) with elevated DFI and 133 cases (n = 565 embryos) with normal DFI. Significant differences were found in mean male age (39.8 ± 6, 37.8 ± 5, p < 0.004), female age (38.6 ± 5, 35.0 ± 5, p < 0.002) and baseline morphological and genetic parameters (37%, 56.3%, p = 0.002) between cohorts. No differences were found in fertilization rate, zygotes achieving cleavage stage, and blastulation rates between study groups. Embryo euploidy rates were comparable (50.2% (n = 273/543), 46.7% (n = 264/565), p = 0.24).

After adjusting for female and male patient’s age, BMI, AMH, normal semen analysis and number of biopsied embryos, there were no association with elevated DFI and lower odds of embryo euploidy (OR 1.39, 95% CI 0.97-2.0, p = 0.07).

CONCLUSIONS: Although multiple studies have reported poor outcomes in patients with elevated DFI, the exact mechanism of action is unclear. Our study analysis showed no correlation between high sperm DNA fragmentation, embryo development, or chromosomal composition. Future studies assessing the oocyte DNA-repair mechanism following fertilization should be performed to better understand the immediate impact of sperm chromatin damage during ART intervention.


SUPPORT: None.

P-244 Tuesday, October 15, 2019 6:30 AM

CYTOGENETIC ANALYSIS BY NEXT GENERATION SEQUENCING DISCLOSED THAT EXTREMELY HIGH EUPLOIDY RATE OF BLASTOCYSTS DERIVED FROM MONOPRONUCLEAR EMBRYOS WITH TESTICULAR SPERM. Shinpei Mizuta, M.H.S., a
Hidehiko Matsubayashi, MD, a Takumi Takeuchi, MD, PhD, a Yuki Tamura, Ph.D., a Mitsuo Santo, B.H.S., a Kotaro Kitaya, MD, a Yasuhisa Araki, Ph.D., a Tomomoto Ishikawa, MD, a Reproduction Clinic Osaka, Osaka, Japan; Reproduction Clinic Tokyo, Tokyo, Japan; Nippon Reprogenetics Inc., Maebashi, Japan.

OBJECTIVE: It has been reported that the blastocyst formation rate of mononuclear (1PN) embryos was significantly lower than that of two nuclear (2PN) embryos (especially in ICSI). However, a recent study revealed that 1PN embryos contained normal chromosome copy numbers similar to those of 2PN embryos by preimplantation genetic testing for aneuploidy(PGT-A). We assessed euploidy rate of 1PN embryos derived from ICSI with testicular sperm (TESE-ICSI) comparing to ejaculated sperm-ICSI or IVF embryos.

MATERIALS AND METHODS: All Cryptozoospermia patients undergoing autologous IVF/ICSI with fresh blastocyst transfers from 2005 to 2019 were included. Cohorts were separated based on the source of sperm utilized (Ejaculated vs. Testicular). Demographic, clinical embryoology parameters and pregnancy rates were compared among cohorts. T-test, X2, and multivariate regression with GEE models were used for data analysis.

RESULTS: A total of 188 patients were included in the analysis (Ejaculated sperm (n=59), Testicular sperm (n=39)). Demographic characteristics were similar among cohorts. No differences were found among the ejaculated and testicular cohorts for fertilization (61.7%; 64.9%, p = 0.15), blastulation rates (55.8%; 55.3%, p = 0.86) and count of cryopreserved blastocysts (1.58 ± 2.61; 1.10 ± 1.99, p = 0.15) respectively. A significant difference was found among the ejaculated and testicular blastocyst transfers for number of cancelled cycles due to embryos unavailable for transfer (22.8%; 7.6%, p = 0.03), number of embryos transferred per cycle (1.35 ± 1.94±1.62, p < 0.001), and mean count of good quality embryos at ET (0.75 ± 0.9; 1.23±1.03, p = 0.005).

After adjusting for female and male patient’s age, BMI, AMH and injected oocytes, no association was found with utilizing ejaculated sperm and lower odds of fertilization (OR 1.19, 95% 0.2-6.4, p = 0.79), blastulation (OR 1.1, 95% 0.2-4.4, p = 0.5), or higher odds of cycle cancellation (OR 1.9, 95% 0.7-7.1, p = 0.6). Finally, no differences were found in pregnancy, clinical pregnancy, ongoing pregnancy, multiple pregnancy, and pregnancy loss rates among cohorts.

CONCLUSIONS: Our study demonstrated cryptozoospermia patients who source sperm through testicular extraction or ejaculation prior to ICSI had similar ART treatment outcomes. There does not appear to be a deleterious effect with regard to fertilization, blastulation, and embryonic quality in cryptozoospermia patients, who utilised ejaculated sperm found after thorough search and sedimentation. Further prospective studies including patients undergoing single euploid embryo transfers should be performed, in order to
generate personalized and evidence based recommendations for couples facing cryptozoospermia.


SUPPORT: None.

P-245 Tuesday, October 15, 2019 6:30 AM

DOES MALE AGE AFFECT THE SPERM PARAMETERS AND IVF OUTCOMES? Marta Belles, MSc, Mireia Florensa, MSc, Marga Esbert, PhD. IVI RMA Barcelona, Barcelona, Spain.

OBJECTIVE: Compared with the effect of the aging oocyte, the effect of male age on reproductive success has been studied in much less detail. Some studies have reported that male age declines sperm parameters but also the outcomes of IVF (In Vitro Fertilization) cycles. The mechanisms responsible for the decline in sperm fitness are not fully understood but damage by oxidative stress could be an important contributor, being responsible for the majority of sperm DNA fragmentation. Advancing paternal age has also been associated with increased risk of genetic diseases in the offspring. The main objective of this study is to assess if male age has an effect on IVF outcomes and sperm parameters.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 1898 IVF cycles performed by women younger than 35 years between 2014 and 2018 in the same clinic was analyzed. Inclusion criteria were the use of ejaculated autologous sperm, ICSI performance and single embryo transfer at D+5 without preimplantation genetic diagnosis. We assessed if male age had an effect over sperm parameters. We also studied if male age was correlated with fertilization rate, embryo quality (measured as total blastocyst and usable blastocyst rates), pregnancy, implantation, miscarriage and live birth rates. Student’s t-test and Person’s product-moment correlation analysis were used for statistical analysis and level of significance was set at P<0.05.

RESULTS: Age was statistically correlated with semen volume (P=0.001), motility percentage (P<0.001), the total number of progressively motile sperm (P=0.001), total sperm count (P<0.001) and progressive motility percentage (P<0.001) but it was not related to sperm concentration (P=0.96). Global fertilization rate was 70% and it was negatively related to male age (P=0.04). Global blastocyst rate was 56.06% while good quality embryos rate was 46.12%. No significant differences were found on both parameters (p=0.93 and p= 0.94, respectively). Overall clinical pregnancy, implantation, miscarriage and live birth rates were 57.48%, 50.58%, 11.91% and 38.51% respectively and none of them were related to male age (P=0.07, P=0.12, P=0.56 and P=0.09 respectively).

CONCLUSIONS: To our knowledge, this is the largest study relating male age with IVF outcomes after a single blastocyst transfer. The fact that neither embryo quality nor clinical outcomes are affected by male age may suggest that other factors such as female age can be positively influencing the cycle results. On the other hand, the analysis of these retrospective data confirm an age-related decrease in volume, sperm motility and total sperm count as well as a lower fertilization rate by ICSI in older males.

P-246 Tuesday, October 15, 2019 6:30 AM

HIGH RATES OF ANEUPLOIDY, MOSAICISM AND ABNORMAL MORPHOKINETIC DEVELOPMENT IN CASES OF VERY SEVERE MALE FACTOR WITH FEMALE PARTNERS ≤35 YEARS. Semra Kahraman, Prof., Murat Cetinkaya, M.D., PhD, Yucel Sahin, MD, Hakan Kadir Yelke, MSc, Yesim Kuntepe Colakoglu, MSc, Mehmet Ali Tufekci, PhD, Mesut Yesil, MSc, Cigdem Cinar Yapan, MSc. Istanbul Memorial Hospital, Istanbul, Turkey.

OBJECTIVE: Male infertility is a factor in approximately 50% of ART cases. Therefore, the relationship between severe male infertility and embryo aneuploidy has long been a subject of interest. However, most studies into this relationship were based on data obtained using FISH and there have been only a limited number of studies using comprehensive chromosomal analysis. Our study evaluates the blastocyst chromosomal status and embryo aneuploidy in cases of severe male factor with female partners ≤35 years.

METHODS AND MATERIALS: A total of 543 severe male infertility cases with partners ≤35y) according to severe male infertility subgroups ranging from 5million/ml to non-obstructive azoospermia (NOA).

DESIGN: Couples applied for ART with female age ≤35 years and presented with Severe Male Factor (SMF) indication (study group) were divided into the following 3 subgroups according to sperm concentration: 1) between five million and one million, 2) less than one million, 3) Azoospermia: obstructive azoospermia (OA) and Non-obstructive Azoospermia (NOA).

MATERIALS AND METHODS: Outcomes of the study group are compared with the control group that was composed of males with normal sperm parameters (>39 million and ≥40% motile sperm in the ejaculate). 543 severe male infertility cases with partners ≤35y and 310 control cases with normal sperm parameters were studied. Initially aCGH and latterly NGS were used for PGT-A and time lapse microscope for morphokinetic evaluation.

RESULTS: Significantly higher chromosomal aneuploidy rates (58%) were found in couples with NOA than the other SMF groups and control groups with normal sperm parameters (p<0.001). Mosaicism rates were higher in all SMF subgroups than the controls but significantly so only in NOA (p<0.05). Higher rates of chromosomal aneuploidy were reported in 2.10,11 17, 21 and x chromosomes were observed in the most severe forms of SMF groups, NOA and less than 1 million groups. However, they were significantly higher only in the testicular sperm groups (p<0.05).

Embryo morphokinetic evaluation showed that embryos in the NOA groups reached the first cleavage significantly faster than those in the control group 26.79h vs. 27.01h, respectively; p=0.048). Furthermore, significantly higher rates of direct uneven cleavage (27%) and arrested embryos (p=0.05) from PN stage to the blastocyst stage were observed in NOA and in the less than 1 million sperm groups.

CONCLUSIONS: Higher rates of chromosomal abnormality, mosaicism and morphokinetic abnormalities were associated in severe male factor cases particularly with testicular sperm obtained from azoospermic cases with female partners ≤35 years.

DOES USE OF TESTICULAR SPERM IMPROVE OUTCOMES IN NONAZOOSPERMIC COUPLES WITH PREVIOUS IVF FAILURE USING EJACULATED SPERM? M. Blake Evans, DO, Jessica A. Marinaro, MD, Kate Devine, MD, Micah J. Hill, DO, Alan H. DeCherney, MD, Russell P. Hayden, MD, Paul Shin, MD, Cigdem Tanrikut, MD, NIH-NICHD, Bethesda, MD, and MedStar Georgetown University Hospital, Washington, DC, Shady Grove Fertility, Washington, D.C., DC, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Due to controversial evidence that testicular sperm is associated with lower sperm DNA fragmentation (SDF) and improved outcomes compared to ejaculated sperm (ES), this study evaluates intracytoplasmic sperm injection (ICSI) outcomes using testicular sperm in nonazoospermic couples with prior IVF failure using ES.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Jan 2015-Aug 2018, 64 nonazoospermic couples with ≥1 prior failed ART cycles using ES underwent testicular sperm extraction (TESE) for ICSI-ICSI. Failed cycles with ES: those not progressing to clinical pregnancy, Outcomes using TESE sperm were compared to the mean values of couples’ prior cycles using ES. Primary outcomes: clinical pregnancy and live birth rates (CPR & LBR). Secondary outcomes: fertilization and blastocyst conversion.

RESULTS: Average number of prior failed ART cycles using ES: 2.5 (range: 1-8). 71.8% of males had abnormal semen parameters. A subset of men (n=28) had SDF assessment (measured by sperm chromatin dispersion) of ES. Mean SDF was 39% (7-84%); 21 patients had SDF ≥25%; 88 total ICSI cycles were performed using TESE sperm (64 cycles: fresh TESE, 24 cycles:frozen-thawed). There were 52 fresh blastocyst transfers, 15 frozen blastocyst transfers, and 21 cycles without transfer (9 additional FETs using supernumerary embryos; 76 total transfers). A comparison of TESE-ICSI cycles in those couples with ≥2 prior failed ART cycles using ES yielded similar findings to the whole group.
TABLE 1. Outcomes comparing TESE couples to their prior ART cycles using ES. Blastocyst conversion = % of cycles with ≥ 1 blastocysts available to use. P values comparing pregnancy outcomes were not performed due to regression of the mean.

<table>
<thead>
<tr>
<th></th>
<th>TESE (n=88), Mean</th>
<th>Ejaculated (n=64), Mean</th>
<th>P value</th>
<th>Ejaculated SDF &gt;25%: TESE (n=21; 24 transfers), Mean</th>
<th>Ejaculated SDF &gt;25%: Ejaculated (n=21), Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td># oocytes retrieved</td>
<td>17.8</td>
<td>17.4</td>
<td>0.27</td>
<td>19.5</td>
<td>16.3</td>
<td>0.27</td>
</tr>
<tr>
<td># M2’s fertilized</td>
<td>11.7</td>
<td>12.1</td>
<td>0.72</td>
<td>11.6</td>
<td>10.8</td>
<td>0.74</td>
</tr>
<tr>
<td>% M2’s fertilized</td>
<td>61.4%</td>
<td>59.0%</td>
<td>0.66</td>
<td>57.1%</td>
<td>50.6%</td>
<td>0.37</td>
</tr>
<tr>
<td>No blastulation</td>
<td>24/88 (27.3%)</td>
<td>39/64 (60.9%)</td>
<td>&lt;0.001</td>
<td>9/21 (42.9%)</td>
<td>15/21 (71.4%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Blastocyst conversion</td>
<td>61.9%</td>
<td>42.9%</td>
<td>&lt;0.001</td>
<td>57.1%</td>
<td>28.6%</td>
<td>0.001</td>
</tr>
<tr>
<td># blastocysts transferred</td>
<td>1.7</td>
<td>1.6</td>
<td>0.36</td>
<td>1.7</td>
<td>1.5</td>
<td>0.56</td>
</tr>
<tr>
<td># blastocysts vitrified</td>
<td>1.0</td>
<td>0.6</td>
<td>0.003</td>
<td>1.2</td>
<td>0.4</td>
<td>0.006</td>
</tr>
<tr>
<td>CPR</td>
<td>32/76 (42.1%)</td>
<td>0%</td>
<td>—</td>
<td>10/24 (41.7%)</td>
<td>0%</td>
<td>—</td>
</tr>
<tr>
<td>Spontaneous abortion</td>
<td>8/76 (10.5%)</td>
<td>0%</td>
<td>—</td>
<td>1/24 (4.2%)</td>
<td>0%</td>
<td>—</td>
</tr>
<tr>
<td>LBR</td>
<td>27/76 (35.5%)</td>
<td>0%</td>
<td>—</td>
<td>9/24 (37.5%)</td>
<td>0%</td>
<td>—</td>
</tr>
</tbody>
</table>

CONCLUSIONS: In nonazoospermic couples with failed ART using ES, ICSI using TESE sperm may improve blastocyst development, number of embryos available for vitrification, CPRs, and LBRs. Testicular sperm may avoid the adverse effects of elevated SDF from ES and improve pregnancy outcomes in some patients. Randomized studies are needed to determine if such a benefit exists.

IVF OUTCOME PREDICTORS - TRIGGER

P-248 Tuesday, October 15, 2019 6:30 AM

DOES OVULATORY TRIGGER CHOICE INFLUENCE MATURITY AND DEVELOPMENTAL COMPETENCE OF FROZEN-THAWED OOCYTES? Sydney Chang, MD, Carlos Hernandez-Nieto, MD, Dmitry Gounko, MA, Beth McAvey, MD, Lucky Sekhon, MD, Alan B. Copperman, MD.

OBJECTIVE: The luteinizing hormone (LH) surge stimulates resumption and progression of meiosis in oocytes from prophase to metaphase in preparation for fertilization. Given that oocyte maturity is a developmental continuum, it is unclear whether changes in the duration or level of the LH surge can affect the frequency and structure of meiotic recombination. Studies have investigated the effects of different oocyte maturation triggers—human chorionic gonadotropin (hCG), GnRH agonist and varying doses of hCG increases the blastulation rate among patients undergoing IVF.4 Future studies might aim to analyze oocytes and granulosa cells from follicles triggered with dual trigger vs. Lupron alone, focusing on early molecular pathways and gene networks that are integral to embryonic genome activation.

Use of oocyte cryopreservation has increased, but most patients have yet to utilize these oocytes. Consequently, the effect of trigger type on developmental competence of frozen oocytes suspended in metaphase II is still unknown. The objective of this study was to determine whether rates of oocyte survival post-re-warming, maturation, fertilization, and euploidy were affected by trigger type.

METHODS: All women attended for first planned oocyte retrieval between 2010 and 2019. Patients were grouped according to trigger type: (1) hCG, (2) Lupron, (3) dual. Primary outcomes were thaw survival and oocyte metaphase II (MII) rates. Secondary outcomes were fertilization, blastulation, and euploidy rates. Statistical analysis was performed with the use of T-tests, chi-square tests, and multivariate linear regressions with generalized estimating equations.

RESULTS: A total of 182 cycles from 167 patients were included in this study. Controlling for oocyte age, AMH, and gravity, there was no statistically significant difference in rates of thaw survival, MII, fertilization, or euploidy between groups. There was, however, a statistically significant difference in blastulation rate (Dual vs. Lupron: β=31.6, p=0.006, hCG vs. dual: β=10.5, p=0.34; hCG vs. Lupron: β=-21.2, p=0.14).

CONCLUSIONS: Studies of the effects of oocyte maturation trigger on pregnancy outcomes are conflicting, and have focused on implantation in fresh IVF cycles. In contrast, this study examines surrogate endpoints for the efficacy of hCG, hCG-Lupron, hCG-Lupron only, and dual trigger in a group of non-infertile young women. We showed that trigger type does not affect survival rates following oocyte warming, or MII rate. There appears to be an increase in blastulation rates between patients using dual trigger, compared to Lupron only. This finding is in agreement with a prior study that compared dual trigger vs. Lupron alone in high responder patients undergoing autologous IVF.5 Future studies might aim to analyze oocytes and granulosa cells from follicles triggered with dual trigger vs. Lupron alone, focusing on early molecular pathways and gene networks that are integral to embryonic genome activation.

P-249 Tuesday, October 15, 2019 6:30 AM

DUAL TRIGGER USING RECOMBINANT HCG AND GONADOTROPIN-RELEASING HORMONE AGONIST IMPROVE OOCYTE QUALITY AND EMBRYO GRADING FOR NORMAL RESPONDERS IN GnRH ANTAGONIST CYCLES: RANDOMIZED CONTROLLED TRIAL. Ahmed Ali Abdelaleem, MD, Shymaa Ali, MSc, Ahmed M. Abbas, MD, Tarek Farghaly, MD, Elwany Elsenosy, MD, Gamal Sayed, MD. 1Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; 2Department of Obstetrics and Gynecology, Faculty of Medicine, Suez University, Suez, Egypt.


Use of oocyte cryopreservation has increased, but most patients have yet to utilize these oocytes. Consequently, the effect of trigger type on developmental competence of frozen oocytes suspended in metaphase II is still unknown. The objective of this study was to determine whether rates of oocyte survival post-re-warming, maturation, fertilization, and euploidy were affected by trigger type.

METHODS: All women attended for first planned oocyte retrieval between 2010 and 2019. Patients were grouped according to trigger type: (1) hCG, (2) Lupron, (3) dual. Primary outcomes were thaw survival and oocyte metaphase II (MII) rates. Secondary outcomes were fertilization, blastulation, and euploidy rates. Statistical analysis was performed with the use of T-tests, chi-square tests, and multivariate linear regressions with generalized estimating equations.

RESULTS: A total of 182 cycles from 167 patients were included in this study. Controlling for oocyte age, AMH, and gravity, there was no statistically significant difference in rates of thaw survival, MII, fertilization, or euploidy between groups. There was, however, a statistically significant difference in blastulation rate (Dual vs. Lupron: β=31.6, p=0.006, hCG vs. dual: β=10.5, p=0.34; hCG vs. Lupron: β=-21.2, p=0.14).

CONCLUSIONS: Studies of the effects of oocyte maturation trigger on pregnancy outcomes are conflicting, and have focused on implantation in fresh IVF cycles. In contrast, this study examines surrogate endpoints for the efficacy of hCG, hCG-Lupron, hCG-Lupron only, and dual trigger in a group of non-infertile young women. We showed that trigger type does not affect survival rates following oocyte warming, or MII rate. There appears to be an increase in blastulation rates between patients using dual trigger, compared to Lupron only. This finding is in agreement with a prior study that compared dual trigger vs. Lupron alone in high responder patients undergoing autologous IVF.5 Future studies might aim to analyze oocytes and granulosa cells from follicles triggered with dual trigger vs. Lupron alone, focusing on early molecular pathways and gene networks that are integral to embryonic genome activation.


SUPPORT: None.
Jenna Friedenthal, MD,a Joseph A. Lee, BA,b

VALUES?

TO BOOST OR NOT TO BOOST: DOES ADMINISTRATION OF 250 μg of hCG and GnRh agonist; 1 mg leuprolide acetate. The primary outcome was the number of MII oocytes in both groups. The secondary outcomes included the number of oocytes retrieved, number of Grade 1 embryos, fertilization rate, implantation rate, clinical pregnancy rate, miscarriage rate, live birth rate, the cumulative pregnancy rate per embryo transfer and cumulative live birth rate among both groups. Student’s t-test and Chi-square test were used for the analysis of the outcomes.

RESULTS: One hundred and sixty women consented to participate and randomized (80 women in each arm). Both groups were similar in baseline demographic and clinical characteristics as mean age, BMI, duration, cause of infertility and hormonal profile. In comparison to the HCG group, women who received dual trigger had a statistically significantly higher number of retrieved oocytes (14.20±7.868 vs. 10.53±4.79, p<0.001), number of MII oocytes (10.78±6.758 vs. 8.48±2.4, p<0.01) and number of grade 1 embryos (5.28±3.79 vs. 4.29±2.66, p=0.04). The fertilization rate was slightly higher in the HCG group, but this did not reach a statistical significance (77.6% vs. 73.7%, p=0.442). No difference between both groups regarding the chemical (p=0.312), clinical pregnancy (p=0.621), implantation (p=0.731), miscarriage (p=0.523), multiple pregnancy (p=1.00) and live birth rates (p=0.725) between both groups. The dual trigger group showed significantly higher clinical pregnancy (p<0.04) and live birth rates (p<0.03) after frozen-thawed embryos transfer. No significant difference among both groups regarding the cumulative pregnancy and cumulative live birth rates (p=0.08).

CONCLUSIONS: Dual trigger by GnRh agonist and hCG could improve the oocyte quality and embryo grading for normal responders in GnRH antagonist ICSI cycles.

SUPPORT: None.

P-250

WITHDRAWN

P-251 Tuesday, October 15, 2019 6:30 AM

TO BOOST OR NOT TO BOOST: DOES ADMINISTRATION OF RESCUE HCG IMPROVE OUTCOMES IN POOR RESPONDERS WITH LOW POST-TRIGGER VALUES?

Janna Friedenthal, MD,a Joseph A. Lee, BA,b Daniel E. Stein, MD,a Tanmoy Mukherjee, MD,b Alan B. Copperman, MD,a “Icahn School of Medicine at Mount Sinai, New York, NY; Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Ovarian hyperstimulation syndrome (OHSS) is a potential complication of ART that can be concerning to patients and a difficult therapeutic challenge to physicians. One preventative measure to minimize the risk of OHSS is to lower the dose of hCG prior to retrieval. However, there is a threshold under which final maturation of the cumulus cell-oocyte complex might not occur. Several surrogate markers may be used to determine appropriate response to trigger, including serum progesterone (P4) or hCG on day after trigger administration. When these markers suggest an inadequate response, some clinicians supplement patients with booster or “rescue” hCG. However, there is limited data on the effectiveness of rescue hCG in improving oocyte yield. Our goal was to compare outcomes between patients who did or did not receive rescue hCG in a population of patients with an inadequate response to trigger.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Our study included patients at a single academic center who underwent controlled ovarian hyperstimulation and met criteria for rescue hCG (P4 <1 ng/ml or hCG level <40 mIU/ml on day after trigger) from 2004 to 2019. Patients were separated into 2 groups based on administration of supplemental hCG (Case Group: hCG trigger 36 hours and rescue hCG 12-24 hours prior to retrieval; Control Group: hCG trigger 36 hours prior to oocyte retrieval). Patients were excluded if leuprolide acetate was used for trigger, either as a dual trigger or as leuprolide alone. A sub-analysis of poor responders to COH (Bologna criteria: age >40, antral follicle count ≤10 follicles total, or AMH ≤1 ng/ml) was performed. Primary outcome was the number of oocytes retrieved. Data were analyzed using students t-tests, chi square tests, and a multivariate logistic regression analysis, with p<0.05 considered significant.

RESULTS: A total of 732 patients who underwent 833 cycles were assessed. The case group consisted of 397 cycles in which both 36 hour and subsequent rescue hCG prior to retrieval were used. The control group consisted of 436 cycles in which a single hCG trigger 36 hours prior to retrieval was used. There were significant differences in age, AMH, BMI, the number of follicles ≥14mm visualized on day of trigger, estradiol, and progesterone on day of trigger between groups. After adjusting for the confounding variables, use of rescue hCG did not predict number of eggs retrieved (β = 0.50, p = 0.83). In our sub-analysis of poor responders that controlled for the same confounders, we found that the use of rescue hCG was significantly correlated with the number of eggs retrieved (β = 0.53, p = 0.03).

CONCLUSIONS: In the largest study to date evaluating the use of rescue hCG to improve oocyte yield, our data suggest an improvement in number of eggs retrieved in a subset of patients. While we did not demonstrate clinical advantage to using rescue hCG in the general study group, we found that a subset of poor responder patients benefited from supplemental hCG. Future studies would benefit from validating a threshold level for peak progesterone or hCG that customizes the use of rescue hCG.

SUPPORT: None.

P-253 Tuesday, October 15, 2019 6:30 AM

HOW WE TRIGGER MATTERS: INTRANASAL GnRH-AGONIST TRIGGER MAY REDUCE OOCYTE MATURATION COMPARED TO SUBCUTANEOUS ADMINISTRATION IN ICSI CYCLES.

Marcus J. Davenport, MBBS (Hons), BMedSc (Hons); Martin J. Healey, MBBS, MD, FRANZCOG, FRCOG; Vivien B. MacLachlan, BSc,b Alon J. Talmon, MBBS, BSc(Hons), PhD; Marcus J. Davenport, MBBS (Hons), BMedSc (Hons), FRANZCOG, CREI. aMonash Health, Melbourne, Victoria, VIC, Australia; bMonash IVF, Clayton, VIC, Australia; cDepartment of Obstetrics and Gynaecology, Monash University, Melbourne, Victoria, VIC.

OBJECTIVE: To evaluate whether GnRH-agonist (GnRHa) triggering improves embryo quality and live birth rates in ‘freeze-all’ cycles compared to human chorionic gonadotrophin (hCG).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This retrospective cohort study from January 2012 and December 2014 compared GnRHa and hCG-triggered ‘freeze-all’ cycles. Limiting the study to one cycle per patient, 396 GnRHa and 1,868 hCG-triggered cycles were included. Only cycles where embryos were available and thawed for transfer were included for live birth rates (LBR). 217 GnRHa and 509 hCG-triggered cycles were analysed for LBR. A multiple imputation approach was used to account for missing data. The primary outcome was LBR. Secondary outcomes included number of oocytes collected, embryo grade and quality, clinical pregnancy rates and the incidence of ovarian hyperstimulation syndrome (OHSS). Regression analysis was performed to adjust for confounders. P-values <0.05 were considered statistically significant.

RESULTS: The singleton LBR after one embryo transfer was higher in GnRHa triggered ‘freeze-all’ cycles compared to hCG (38.4% vs. 24.6%, p = 0.001), as well as a non-significantly higher cumulative LBR (57.4% vs. 41.2%, p = 0.18). There was no difference in the number of embryos lost or transferred, and there was no difference in embryo grade or expansion. The incidence of OHSS was significantly lower in GnRHa triggered cycles (0.5% vs. 1.9%, p = 0.008).

CONCLUSIONS: GnRHa triggering resulted in a superior LBR compared to GnRHa and hCG-triggered ‘freeze-all’ cycles compared to human chorionic gonadotrophin (hCG).
OBJECTIVE: To evaluate oocyte maturation and fertilisation rates of intracytoplasmic sperm injection (ICSI) cycles triggered with intranasal and subcutaneous GnRHa-agonists (GnRHa).

MATERIALS AND METHODS: A prospective, observational study from May 2016 to August 2018 compared intranasal and subcutaneous GnRHa triggers in ICSI cycles. Data was extracted from 9588 ICSI cycles. A total of 781 cycles were included for analysis after excluding cycles triggered with hCG (n=8521), duplicate patient cycles (n=182), where a dual trigger was used (n=55) or where the trigger was not recorded (n=49). 214 cycles utilised the intranasal Nafarelin trigger (Synarel, Pfizer Pty Ltd) and 567 cycles used a subcutaneous formulation, either Triptorelin (Decapeptyl; Ferring Pharmaceuticals Pty Ltd) or Leuprorelin (Lucrin; AbbVie Pty Ltd).

RESULTS: There was a trend towards higher oocyte maturation rates in patients receiving a subcutaneous GnRHa trigger compared to intranasal formulations (78.1% vs 77.6%, p=0.059). There was a statistically significant difference in fertilisation rate in favour of the subcutaneous trigger (68.0% vs 67.9%, p=0.016). There was no difference in the age or BMI of patients, nor was there a difference in the crude number of mature or fertilised oocytes.

CONCLUSIONS: Subcutaneous administration of the GnRHa trigger may improve oocyte maturation and fertilisation rates in ICSI cycles, and is associated with lower rates of OHSS. Given these findings, a prospective randomised controlled trial is needed to further elucidate whether a subcutaneous formulation outperforms an intranasal GnRHa trigger.

SUPPORT: None.

P-255 Tuesday, October 15, 2019 6:30 AM

THE EFFECT OF FOLLICLE STIMULATING HORMONE ADMINISTRATION AT THE TIME OF HUMAN GONADOTROPIN TRIGGERING, IS IT IMPROVE THE OOCYTE/EMBRYO PROFILE IN IN VITRO FERTILIZATION CYCLES? Young Sang Kim, M.D., Dong Soo Park, M.D., Mi Kyong Koong, M.D., You Shin Kim, M.D., Ph.D., Myung Joo Kim, M.D., Ran Kim, M.D., Hyoek Kim, MD, Ph.D., Tae Ki Yoon, M.D., Chanhong Park, M.D., Hannah Kim, M.D., CHA Fertility Center Seoul Station, Obstetrics and Gynecology, Seoul, Korea, Republic of (South); CHA Fertility Center Seoul, Seoul, Korea, Republic of (South); Department of OB/GY, CHA Fertility Center Seoul Station, CHA University, Seoul, Korea, Republic of (South); CHA Fertility Center Seoul Station, Seoul, Korea, Republic of (South); Department of OB/GY, CHA Fertility Center Seoul Station, CHA University, Seoul, Korea, Republic of (South); CHA Fertility Center Seoul Station, OB/GY, Seoul, Korea, Republic of (South).

OBJECTIVE: To evaluate whether an additional follicle stimulating hormone (FSH) administration at the day of human chorionic gonadotropin (hCG) triggering can improve the oocyte/embryo quality and pregnancy rates in vitro fertilization (IVF) cycles.

MATERIALS AND METHODS: 585 patients in fresh IVF cycles with antagonist protocol divided into two groups. FSH injection at hCG triggering day (N=211) and did not (N=374). We estimate the maturation rates of retrieved oocytes, fertilization rates, top quality (Grade 1–2) embryo counts and pregnancy outcomes in two groups.

RESULTS: There was no significant difference between two groups in patient’s demographics (age, body mass index, anti-müllerian hormone level, infertility etiology), and characteristics of fresh IVF cycles (total FSH injection dose, estradiol/luteinizing hormone/progesterone level on hCG triggering day, endometrial thickness on hCG triggering day). For outcomes of fresh IVF cycles, matured oocyte count (6.9±3.7 vs 7.1±4.0; p=0.502), fertilization rate (69.0% vs 70.3%; p=0.452), top quality embryo count (2.5±2.0 vs 2.2±1.6; p=0.086) were not significantly differ. For pregnancy outcomes of fresh IVF cycles, implantation rate (54.5% vs 48.1%; odds ratio [OR], 1.29; 95% confidential interval [CI], 0.92-1.81) and clinical pregnancy rate (42.7% vs 35.0%; OR, 1.38; 95% CI, 0.98-1.95) were not significantly differ, but ongoing pregnancy rate (38.4% vs 29.1%; OR, 1.51; 95% CI, 1.06-2.16) was significantly higher in FSH injection group.

CONCLUSIONS: The effect of an additional FSH administration at the day of hCG triggering did not improve the oocyte/embryo profile. Implantation rates and clinical pregnancy rates were increased in FSH injection group, but there was no significant difference between two groups. Ongoing pregnancy rates was significantly higher in FSH injection group compared with no FSH injection group.

P-256 Tuesday, October 15, 2019 6:30 AM

DOES POST-TRIGGER SERUM B-HCG VALUE MATTER IN PATIENTS WITH SUBOPTIMAL LH RESPONSE AFTER DUAL TRIGGER CYCLES? Kolbe Hancock, MD, Chelsea Canon, MD,

FERTILITY & STERILITY®
**OBJECTIVE:** The use of dual trigger during ovarian stimulation to initiate the final maturation of oocytes has become an increasingly popular technique, as it decreases the risk of ovarian hyperstimulation syndrome. In GnRH agonist trigger cycles, there is a subset of individuals who have a suboptimal response to GnRH agonist, and in turn decreased oocyte yield and oocyte maturity. Post trigger serum luteinizing hormone (LH) levels >15 mIU/mL and ideally ≥30 mIU/mL have been associated with improved cycle outcomes. In patients who received a dual trigger but had a suboptimal response to GnRH agonist trigger, we sought to investigate whether the post-hCG value was correlated with oocyte maturity rate.

**RESULTS:** A total of 204 cycles meeting the inclusion criteria were analyzed. The average age was 36.7 ± 5.5 years, and the average BMI was 27.2 ± 6.9 kg/m². The post-hCG values ranged from 15 to 425 mIU/mL. Comparing all patients with an LH <30 and controlling for BMI and age, there was no significant correlation between post-hCG and percent mature oocytes (p=0.456). Similarly, when controlling for BMI and age, there was no significant correlation between the sum of post-trigger serum LH and b-hCG and the oocyte maturity rate (p=0.38). When the post-trigger LH value was stratified by increments of five mIU/mL from 0 to 30, there was still no significant correlation between the post-hCG and the oocyte maturity rate (p values range from 0.46 to 0.88). Amongst those with a post trigger LH <15 mIU/mL, there was no significant difference in the oocyte maturity rate when the post-hCG was above or below 50 mIU/mL. Similarly, amongst those with a post trigger LH between 15 and 50 mIU/mL, there was no significant difference in the oocyte maturity rate when the post-hCG was above or below 50 mIU/mL. CONCLUSIONS: In patients receiving dual trigger who fail to mount an optimal response to the GnRH agonist component, post-hCG level does not correlate with oocyte maturity rate. When stratified by the post trigger LH level, we have shown that there is not a specific LH value at which the post trigger hCG level had an impact on the primary outcome. There also does not appear to be an optimal summed value of post-trigger LH and b-hCG that is correlated with the oocyte maturity rate.

**REFERENCES:**

**SUPPORT:** None.

**P-257 Tuesday, October 15, 2019 6:30 AM**

**EFFECT OF DUAL TRIGGER ON THE OUTCOME OF CONTROLLED HYPERSTIMULATION IN ART CYCLES.**

N Sanjeeva Reddy, MD (Obstetrics and Gynecology), DGO.¹ Ujwala Jati, MS (Ob & Gyn),² Radha Vembu, DGO, DNB (Obstetrics and Gynecology), MNAMS, FICS, FIGOG, PhD,¹ Monna Pandurangi, MD (Ob & Gyn),² Siddhartha Nagireddy, MCh⁴ (Reproductive medicine and Surgery),³ Professor and Head, Department of Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, India; ²Fellow in Reproductive Medicine, Department of Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research., Chennai, India; ³Associate Professor, Department of Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, India; ⁴Assistant Professor, Sri Ramachandra Institute of Higher Education and Research, Chennai, India.

**OBJECTIVE:** Dual trigger by administration of hCG with GnRh agonist, was shown to improve the outcome of ART (Assisted Reproductive Technology) cycles: oocyte maturity, ongoing pregnancy and live birth rate. The hCG and LH differ by their receptor binding and intracellular signaling, and there by not equivalent in their action. The FSH surge induced by GnRH agonist is known to positively affect oocyte maturation. The present study is aimed to know the effect dual trigger on the oocyte yield & quality, oocyte maturity, and fertilization in ART cycles.

**RESULTS:** Of the 53 patients, 28 women received hCG trigger and 25 women received dual trigger. Women with advanced age (>42 years), oocyte donation cycles, expected hyperresponders (AMH > 4 ng/mL) and poor responders (AMH <1.1 ng/mL) were excluded from the analysis. On the day of ovulation trigger, the study subjects were randomized to receive hCG trigger with uhCG 10,000 IU as Group A, and dual trigger with 10,000 IU of uhCG + 0.2 mg Triptorelin as Group B. COH was performed by antagonist protocol by rFSH with or without hMG. The outcome of COH such as oocyte number and maturity, oocyte quality, fertilization rate and pregnancy rate were compared between the study groups.

**RESULTS:** Of the 53 patients, 28 women received hCG trigger and 25 women received dual trigger. There was no significant difference between the number of oocytes retrieved, mature oocytes, and fertilization rate. The percentage of good & fair quality mature oocytes were significantly higher in the Group B compared to group A. The pregnancy rates were slightly higher in the Group B, but did not reach statistical significance.

**CONCLUSIONS:** Dual trigger is associated with increased oocyte quality in ART. The effect of dual trigger on pregnancy rate needs to be evaluated on a larger data.

**SUPPORT:** Self funded.

**NURSING**
University of Texas Health Science Center at Houston, Houston, TX; 4CCRM Fertility Houston, Houston, TX.

OBJECTIVE: To assess the content and accuracy of fertility counseling received via asynchronous peer and professional input through a digital women’s health clinic.

DESIGN: Quantitative and qualitative assessment of publicly available online content

MATERIALS AND METHODS: The fertility treatment forum of an established digital women’s health clinic, consisting of posts answered asynchronously by peers and professionals, were queried for available posts. All questions and answers were transcribed and then categorized by question topic and theme, quality and quantity of responses, and credentials of responders. Answers were reviewed for accuracy by a board-certified reproductive endocrinologist.

RESULTS: 87 questions were available for review, posted over a 6-month timeframe in 2018-19. Of these, 47 (54.0%) related to intra conceptionary by peers and professionals, were queried for available posts. All questions and answers were transcribed and then categorized by question topic and theme, quality and quantity of responses, and credentials of responders. Answers were reviewed for accuracy by a board-certified reproductive endocrinologist.

Of all 87 posts, 38 (43.7%) received no answer, 40 (46.0%) received 1 answer, and 9 (10.5%) received 2 answers. The unanswered questions (30) were a mix of (78.9%) medical in nature, with 5 (13.2%) requesting emotional support and 3 (7.9%) seeking logistical clarifications. Of the 58 answers, 18 (31.0%) recommended a synchronous video follow-up appointment without offering any medical advice. Substantive answers offered a mix of the following attributes: 22 (37.9%) emotional encouragement or support, 11 (19.0%) narration of personal experiences, and 27 (46.6%) medical advice. Of those offering medical advice, 20 (34.5% of all answers) were deemed medically accurate.

CONCLUSIONS: Online forums and digital clinics are increasingly available and utilized for patients struggling with infertility. As access to high-quality infertility care remains limited due to cost and geography, asynchronous forums hold the potential to fill gaps in care and provide emotional support. However, in our analysis of the leading digital women’s health clinic, those patients seeking answers in the infertility treatment forum received no assistance nearly half of the time, and only a third of responses were deemed medically accurate. Most responses (94.8%) were not from an individual specifically trained in reproductive endocrinology. Though further evaluation of similar sites and resources is indicated, we conclude that asynchronous digital medicine is currently a highly inaccurate and unreliable source of information for fertility patients. Further efforts are needed to ensure that women and couples can access appropriately-trained and specialized physicians and nurses to answer their detailed questions and guide treatment in a compassionate and evidence-based manner.

SUPPORT: None.

P-259 WITHDRAWN

P-260 Tuesday, October 15, 2019 6:30 AM

OPTIMIZING UTILIZATION OF EMOTIONAL SUPPORT DURING INFERTILITY TREATMENT. Sarah A. Hirsch, DO, 1,2 Pippa Simpson, PhD, 21 Kathryn E. Flynn, PhD, 2 Melodee Nugent, MA, 2 Abbey Kruper, PsyD 2 1Medical College of Wisconsin, Milwaukee, WI; 2Af
tilitation not provided.

OBJECTIVE: The psychological distress of infertility influences decision-making and treatment discontinuation. Yet, only 10-34% of patients with infertility pursue counseling. Historically, barriers included logistics of scheduling appointments and sufficient coping resources. The objective of this study was to identify barriers to counseling for women with infertility in a clinic with embedded psychological support; and determine if those barriers were dependent upon screening scores for anxiety or depression.

DESIGN: Cross sectional retrospective chart review.

MATERIALS AND METHODS: Female patients presenting for initial infertility consultation were screened for anxiety and depression with the Generalized Anxiety Disorder-7 Item Scale (GAD-7) and Patient Health Questionnaire-9 (PHQ-9) as standard of care. Subjects were recruited at follow up appointments at least 3 months after initial consultation. An 11-

item survey designed to assess barriers, needs, and desires for psychological treatment was administered. Demographic data and medical history were obtained via chart review. The survey results were analyzed as a population and divided into 2 groups: those with a positive screen for anxiety or depression (score ≥ 5 on either scale) and those with a negative screen. Non-parametric Mann-Whitney test was used for continuous variables (reported as median and inter-quartile range) and the Fisher’s Exact test was used for categorical variables. A p-value of < 0.05 was considered significant.

RESULTS: The sample consisted of 68 participants. On a 1-5 Likert scale, emotional stress 3 (2-4) had a higher median than physical stress 2 (1-3); there was a positive correlation between emotional and physical stress (r= 0.616; p<0.001). There were no differences in the survey items for barriers, needs, or desires between those that screened positive for anxiety/depression compared to those who did not. The primary barrier to treatment was social/ emotional (65%); second was logistical (45%). The most cited barriers included alternative sources of support, scheduling conflicts, and patient perception that her stress level did not warrant treatment. Despite 50% identifying counseling as the primary preference for support, it was only utilized by 7%.

CONCLUSIONS: There were no significant differences in barriers to treatment for women who screened positive for anxiety/depression compared to those who did not. Also, women endorsed emotional distress associated with infertility, regardless of a positive or negative screen for anxiety or depression. Despite this, few established with embedded psychological support in the clinic, reporting social/emotional reasons over logistical barriers. Although 1/2 of women reported desiring counseling, they questioned if their distress level warranted treatment. This demonstrates that women may benefit from education and normalization of psychological support regardless of severity of mood symptoms. Universal referral or integration of emotional support into medical care may be beneficial to target all women and optimize overall outcomes.

SUPPORT: None.

P-261 Tuesday, October 15, 2019 6:30 AM

A NEW ERA IN MEDICINE: SOCIAL MEDIA AND PATIENT CARE. Ansia Hussain, MA, 1 Jacqueline Sehring, MA, 2 Elisabeth Rosen, BS, MA, 2 Lauren Grimm, MA, 2 Jody M. Esguerra, MA, 2 Karine Matevossian, DO, 3 Ro-Chi Kaushik Amin, MD, 3 Roshi Ieclani, MD, 3 Angeline Belsos, MD, 3 Vios Fertility Institute, Chicago, IL; 2Advocate Lutheran General Hospital, Park Ridge, IL; 3Wayne State University, Detroit, MI.

OBJECTIVE: We compared physician social media goals to patient social media wants in order to optimize the physician-patient relationship in the digital world.

DESIGN: Anonymous survey completed by patients and physicians.

MATERIALS AND METHODS: An anonymous survey distributed over social media to patient and physician users investigated physician content goals and patient motivations and habits. Responses collected within a range of 0-10 were scaled as follows: 0–1: strongly disagree, 2–4: disagree, 5–6: neither agree nor disagree, 7–8: agree, 9–10: strongly agree. Unpaired t test was performed (GraphPad).

RESULTS: 219 patients and 22 physicians participated in the study. 70% of the patients were 26–45 years old. 76% of the physicians were 31–50 years old. 81% of patients looked to physicians for emotional support on social media and 63% of physicians identified emotional support as a goal of their social media activity. However, mean patient response was 4.46 (disagree) and mean physician response was 6.27 (agree) (p=0.01). 64% of patients looked to physicians on social media for education and 72% of physicians reported education as a social media goal. Mean patient response was 6.28 (agree) and mean physician response was 7.18 (agree), p=0.243. 61% of patients looked to social media for a side of their physician beyond medicine and 81% of physicians reported using social media to bring humanity to their profession. Average patient response was 6.06 (agree) and average physician response was 7.91 (agree), p=0.004. 65% of patients and 77% of physicians agreed that a doctor’s role should extend beyond their physical practice. The patient mean response was 6.56 (agree), while physician mean response was 7.77 (agree), p=0.085. 44% of patients felt more satisfied with their experience after following their physician on social media, while 64% of physicians surveyed reported higher satisfaction in the patients that follow them on social media. Patient mean response was 4.69 (agree) and physician mean response was 6.18 (agree), p=0.079.

FERTILITY & STERILITY®
CONCLUSIONS: Both patients and physicians agreed that social media can be a patient education tool and that the role of a physician should extend beyond the physical practice. However, patient and physician responses on using social media accounts as a tool for emotional support did not align. This may be due to the prevalence of social support groups on social media that offer extensive emotional support. Additionally, while physicians reported higher satisfaction in patients that follow them on social media, patients who did so did not report higher satisfaction. Although both patients and physicians agreed that social media is a tool for patients to see a side to their doctors beyond medicine, there was a significant difference between their responses—physicians agreed with this statement more strongly than patients. Trust is a critical component of the physician-patient relationship, and appropriate physician social media use allows to optimize this relationship in the digital age, especially when working with a younger patient population.

P-262 Tuesday, October 15, 2019 6:30 AM

DOES FERTILE YOGA CLASS REDUCE STRESS AND SADNESS AND PROVIDE HOPE FOR INFERTILE PATIENTS IN TREATMENT IN A PRIVATE FERTILITY PRACTICE? Lisa Rosenthal, BA, MA; Hannah Shakartzi, M.D.; Shehzeen Kamal, M.D.; Robin Mangieri, M.A.; Mark Leonidres, M.D.; Spencer S. Richlin, M.D. Reproductive Medicine Associates of Connecticut, Norwalk, CT; The Stamford Hospital Dept of OB/GYN, Stamford, CT.

OBJECTIVE: Does Fertile Yoga reduce stress and sadness and provide hope for infertility patients undergoing treatment in a private fertility practice?

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Students completed an unidentified pre- and post-class questionnaire. Results were blinded from the yoga teacher. During class, two techniques were introduced: 1) one-minute mantra, “I am strong, healthy, resilient, capable, hopeful and fertile,” 2) seven movements of the spine which included forward flexion, back bend extension, lateral left bend, lateral right bend, left rotation twist, right rotation twist and axial extension. Primary outcomes were stress, sadness and levels of hopefulness before and after class using a scale of 0 to 10. 0 indicated no stress, sadness or hope and a score of 10 indicated high stress, sadness, and maximum hope. Secondary outcomes evaluated if the mantra and spine movements were helpful and likely to be used in the future. We analyzed data based on age and months conceiving. Age was subdivided into < 35, 35-37, 38-42, and > 42 years of age. Months conceiving were divided into 6-12, 12-18, 18-24, and > 24 months. Statistical analysis was performed with SPSS version 25.0.

RESULTS: 55 patients completed pre- and post-test questionnaires. Ages were < 35 (32.7%), 35 to 37 (23.6%) 38 to 42 (29.1%) and > 42 years of age (14.5%). Months conceiving was divided into 6 to 12 (7.3%), 12-18 (27.3%), 18-24 (34.5%) and > 24 months (30.9%). There was a statistically significant decrease in stress, sadness (p<0.001), and an increase in hopefulness (p<0.001) after class (Table 1) for all age groups. All age categories felt that the mantra and seven movements were helpful during class and that they would use them in the future (ANOVA). Scheffe Test revealed that the 6 to 12-month cohort was less likely to use the mantra in the future and found that the seven movements in class were less helpful compared to the older students.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pretest Mean</th>
<th>Pretest SD</th>
<th>Posttest Mean</th>
<th>Posttest SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress</td>
<td>6.96</td>
<td>2.14</td>
<td>4.00</td>
<td>2.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sadness</td>
<td>5.67</td>
<td>2.99</td>
<td>3.11</td>
<td>2.37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hopefulness</td>
<td>6.78</td>
<td>2.25</td>
<td>7.78</td>
<td>1.90</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Fertile Yoga class decreased student stress and sadness and increased hope. Students reported that they were likely to continue to use the mantra and spine movements during their infertility journey. Given that many infertility patients stop treatment prematurely due to stress and feelings of discouragement, the techniques used in Fertile Yoga class could ultimately provide our patients the emotional energy and skills necessary to continue with fertility treatment and succeed. Data is being collected to better elucidate the role of Fertile Yoga on our patients’ fertility journey.

Reference: None.

SUPPORT: None.

P-263 Tuesday, October 15, 2019 6:30 AM

EFFECT OF MUSIC IN REDUCING PATIENT ANXIETY DURING COLPOSCOPY: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS. Ahmed M. Abdelhakim, MBBC; Ahmed Samy, MD; Ahmed M. Abbas, MD; Kar Al-Ainy Faculty of Medicine, Cairo University, Cairo, Egypt; Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: Music therapy has been used greatly in various medical procedures to reduce associated anxiety and pain. This review aims to evaluate the evidence from published randomized clinical trials (RCTs) about the effect of music therapy in reducing patient’s anxiety during the colposcopy.

DESIGN: Systematic review and meta-analysis.

MATERIALS AND METHODS: We performed a comprehensive literature search using four electronic databases (PubMed, Cochrane library, Scopus and ISI Web of science) using the following search terms: (Music OR Symphony OR Rhythm OR Orchestra OR Song) AND (Colposcopy OR cervicoscope OR colposcope). All RCTs assessing the effect of music therapy versus no music in reducing anxiety during colposcopy were considered. Eighty-five studies were identified of which five studies deemed eligible for this review. The extracted outcomes were; anxiety, pain during and after the procedure, and satisfaction levels. Continuous outcomes were pooled as weighted mean difference (WMD) and standardized mean difference (SMD) using the Mantel-Hansel method with 95% confidence intervals (CI). All statistical analyses in this study were completed by the RevMan software package.

RESULTS: We included five studies with a total number of 836 patients in our final analysis. We found no effect of music therapy in reducing the anxiety levels when compared with the control group (SMD= -0.11, 95% CI [-0.36, 0.14], p=0.4). No difference between music and control groups regarding pain during and after the procedure respectively (SMD= -0.20, 95% CI [-0.58, -0.18], p=0.31) and (SMD= -0.10, 95% CI [-0.30, -0.10], p=0.33). The pooled SMD showed a similarity between the music group in comparison with no music intervention group (SMD= 0.16, 95% CI [-0.02, 0.34], p=0.08).

CONCLUSIONS: This systematic review suggests that music therapy has no great positive effect in reducing anxiety and pain levels and no effect in increasing satisfaction levels when compared with control groups during the colposcopy procedure.

SUPPORT: None.

P-264 Tuesday, October 15, 2019 6:30 AM

DIETARY PATTERNS ARE ASSOCIATED WITH OVARIAN RESERVE IN OVERWEIGHT AND OBESE WOMEN IN A REPRODUCTIVE AGE COHORT. Ashley Eskew, MD, MSCL; Bronwyn Bedrick, BA; Joan Riley, PhD, HCLD; Jorge E. Chavarro, MD, Sc.D.; Emily S. Junheim, MD, MSCL; Washington University School of Medicine, St. Louis, MO; Washington University in St. Louis, Saint Louis, MO; Washinton University School of Medicine, St. Louis, MO; Harvard School of Public Health, Boston, MA.

OBJECTIVE: The objective of this study was to examine the relationship between dietary patterns and markers of ovarian reserve as measured by serum antimullerian hormone (AMH) levels and antral follicle count (AFC) in a reproductive age cohort of women.

DESIGN: Cross-sectional cohort study.

MATERIALS AND METHODS: Women aged 18 to 44 years with regular menstrual cycles were recruited for this study. Women who were pregnant, had a history of infertility, ovarian surgery or major chronic illness were excluded. AFC was determined by transvaginal ultrasound. AMH was measured with a Roche cobas e411 analyzer. A validated food frequency questionnaire (FFQ) and the Kaiser Physical Activity Survey were used to

CONCLUSIONS: Both patients and physicians agreed that social media can be a patient education tool and that the role of a physician should extend beyond the physical practice. However, patient and physician responses on using social media accounts as a tool for emotional support did not align. This may be due to the prevalence of social support groups on social media that offer extensive emotional support. Additionally, while physicians reported higher satisfaction in patients that follow them on social media, patients who did so did not report higher satisfaction. Although both patients and physicians agreed that social media is a tool for patients to see a side to their doctors beyond medicine, there was a significant difference between their responses—physicians agreed with this statement more strongly than patients. Trust is a critical component of the physician-patient relationship, and appropriate physician social media use allows to optimize this relationship in the digital age, especially when working with a younger patient population.
assess diet and exercise patterns over the prior year. After assessment of physical activity and BMI, women with a caloric intake < 500 or > 5000 kcal/day were excluded. We assessed adherence to one of two dietary patterns: 1) the fertility diet (FD), characterized by a higher intake of vegetable protein, low fat dairy, reduced ratio of monounsaturated to trans-fats, iron supplementation and a daily multivitamin, and 2) the pro-fertility diet (PFD), characterized by higher intakes of B12,olic acid, vitamin-D, dairy, and whole grains, low pesticide residue produce and soy or seafood as preferential protein sources. Adherence to a dietary pattern was defined by a factor score with higher values indicating greater adherence. Linear regression was used to control for potential confounders.

RESULTS: Two-hundred women were recruited and 175 were included in the analysis. Subjects were a mean age of 31.0 (±6.6) years and had a mean BMI of 27.7 (±7.0) kg/m². After stratifying by BMI and adjusting for age, smoking and physical activity level, adherence to the PFD in overweight and obese women (BMI > 25 kg/m²) was linearly associated with higher AMH concentrations. Women in the third and fourth quartiles of the PFD had mean AMH levels 1.45 ng/mL (95%CI 0.33-2.56, p=0.01) and 1.67 ng/mL (95%CI 0.60-2.74, p=0.003) higher than women in the lowest quartile respectively. The highest adherence with the PFD was also associated with a higher AFC in overweight and obese women (B=7.8, 95%CI 0.003-15.34, p=0.049). The FD was not significantly associated with AMH or AFC in overweight or obese women. Dietary patterns were not associated with markers of ovarian reserve in normal weight women.

CONCLUSIONS: Consumption of low pesticide residue produce and adherence to a PFD has been associated with improved reproductive outcomes in women undergoing IVF. Our study is the first to demonstrate that increased adherence to a PFD is linearly associated with AMH in an over-weight and obese reproductive aged cohort of women. It is critical that further studies examine dietary patterns in at-risk populations to determine the potential impact on ovarian reserve in reproductive age women.


SUPPORT: Research reported in this publication was supported by the National Center For Advancing Translational Sciences of the National Institutes of Health under Award Numbers and KL2 TR000450 and TL1 TR002344. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

P-265 Tuesday, October 15, 2019 6:30 AM

OBESITY CAUSES SIGNIFICANT CHANGES TO THE HUMAN SPERM PROTEOME. Taylor Pini, PhD,a Jason C. Parks, BS,a Monika Dzieciatkowska, PhD,a Kirk C. Hansen, PhD, b William B. Schoolcraft, MD, b and Mandy G. Katz-Jaffe, PhD. aColorado Center for Reproductive Medicine, Lone Tree, CO;bAffiliation not provided. cUniversity of California, Los Angeles, Los Angeles, CA. dAffiliation not provided; eUniversity of California, Los Angeles, Los Angeles, CA.

OBJECTIVE: Increased lipid content is thought to reduce oocyte tolerance to cryopreservation (1-3) and this has been reported to be particularly troublesome in some mammalian species (3, 4). Elevated intracellular insulin, triglycerides and free fatty acids have been described among obese women and incubation of mouse oocytes in human lipid-rich follicular fluid has been reported to cause oocyte lipid accumulation (5, 6). However, no human studies have described the effects of obesity on oocyte cryosurvival. Therefore, our objective was to investigate the effects of obesity, estimated by body mass index (BMI), on oocyte post-warming cryosurvival after vitrification.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Oocyte warming cycles of women who underwent oocyte cryopreservation with vitrification from January 2000-February 2018 were identified using the etVF database (PracticeHwy, Dallas, TX). Age at retrieval, BMI, total number of oocytes warmed and oocyte cryosurvival after vitrification were extracted from the database. Outcomes for obese (BMI ≥ 30 kg/m²) patients were compared to non-obese (BMI <30 kg/m²) patients using t-test or Wilcoxon rank-sum test where appropriate. A pre-test power calculation revealed a need for 204 subjects to detect a 25% reduction in cryosurvival in obese vs. normal subjects assuming 15% of all patients undergoing oocyte cryopreservation would be classified as obese.

RESULTS: A total of 535 oocyte warming cycles from 30 US clinics were included. There were 69 obese and 466 non-obese patients with a mean BMI of 36.1 and 22.8 kg/m² respectively. There were no differences in age at retrieval (36.5±5.1 vs. 37.0±5.4 years, p=NS) between obese and non-obese

<table>
<thead>
<tr>
<th>TABLE 1.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
</tr>
<tr>
<td>&lt;20</td>
</tr>
<tr>
<td>20 to &lt;25</td>
</tr>
<tr>
<td>25 to &lt;30</td>
</tr>
<tr>
<td>30 to &lt;35</td>
</tr>
<tr>
<td>35 to &lt;40</td>
</tr>
<tr>
<td>≥40</td>
</tr>
</tbody>
</table>

FERTILITY & STERILITY® e211
subjects. There was a trend towards an increased number of oocytes warmed in obese subjects (8.1±7.5 vs. 6.3±6.9, p=0.06). There was no difference in oocyte cryosurvival after vitrification between obese and non-obese (Median IQR: 100% (70-100%) vs. 100% (80-100%), p=NS). Mean cryosurvival in the obese group was 79%±SD 32% vs. 85%±SD 27.5% in the non-obese group. Oocyte cryosurvival by BMI sub-group is depicted in Table 1.

CONCLUSIONS: Obesity does not appear to impact post-warming cryosurvival after oocyte vitrification. In humans, the intra-oocyte lipid stores that could result as a consequence of obesity may not meaningfully impact tolerance to cryopreservation unlike other mammalian species. Additional adequately powered studies are required to determine the impact of class III obesity on post-warming cryosurvival after oocyte vitrification.


SUPPORT: None.

P-267 Tuesday, October 15, 2019 6:30 AM

OBEITY IS ASSOCIATED WITH INCREASED QUANTITY BUT NO DIFFERENCE IN QUALITY OF OOCYTES AND EMBRYOS IN WOMEN WITH LOW ANTI-MULLERIAN HORMONE LEVEL. Guang Xu, M.D., Ph.D., a Catherine Racowsky, PhD, b Brigham and Women’s Hospital, BOSTON, MA; bBrigham and Women’s Hospital, Boston, MA.

OBJECTIVE: Both obesity and low AMH levels are associated with reduced oocyte, embryo and clinical outcomes. Whether obesity further diminishes outcomes in women with low AMH is unclear. In this study, we aimed to fill the knowledge gap by testing the hypothesis that obese women with low AMH have lower oocyte and embryo yields with reduced quality compared with women of normal weight.

DESIGN: Retrospective cohort of 1,542 cycles from 876 patients who underwent autologous IVF/ICSI cycles from March 2013 to October 2018.

MATERIALS AND METHODS: Patients at a single center undergoing IVF. BMI versus %BF were not different in investigating preterm delivery or body mass index (BMI), which may be an inaccurate metric for detailing body composition. This study also explores use of bioelectric impedance analysis (BIA) and its estimation of adiposity as a more precise method of defining obesity in patients undergoing IVF.

RESULTS: Pregnancy outcome data for 1,037 females who underwent IVF from June 2016 – March 2019 were offered utilization of the InBody 770 BIA scale at time of vaginal oocyte retrieval to determine their body composition. Participant demographics, BMI, percentage body fat (%BF), IVF outcome, pregnancy, and delivery data were recorded prospectively.

RESULTS: Pregnancy outcome data for 1,037 females who underwent frozen embryo transfers were collected during this study period. Delivery data was obtained for 873 cycles. The positive predictive values (PPV) of BMI versus %BF were not different in investigating preterm delivery or

Adjusted oocytes and embryos outcomes of low AMH women stratified by BMI

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Normal weight (N=827)</th>
<th>Overweight (N=388)</th>
<th>Class I obese (N=160)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>Odds Ratio (95% CI)</td>
<td>Odds Ratio (95% CI)</td>
</tr>
<tr>
<td>No. oocytes</td>
<td>6.7</td>
<td>7.3 (1.08, 1.03 — 1.13) *</td>
<td>8.2 (1.22, 1.15 — 1.29) *</td>
</tr>
<tr>
<td>No. MII</td>
<td>5.0</td>
<td>5.4 (1.07, 0.98 — 1.16)</td>
<td>6.5 (1.29, 1.14 — 1.44)</td>
</tr>
<tr>
<td>No. 2PN</td>
<td>3.4</td>
<td>3.6 (1.05, 0.93 — 1.17)</td>
<td>4.4 (1.28, 1.09 — 1.47)</td>
</tr>
<tr>
<td>Quality % MII/Total</td>
<td>77.3</td>
<td>75.6 (0.91, 0.78 — 1.04)</td>
<td>81.4 (1.29, 0.96 — 1.61)</td>
</tr>
<tr>
<td>% 2PN/MII</td>
<td>68.1</td>
<td>66.9 (0.95, 0.78 — 1.12)</td>
<td>69.7 (1.08, 0.81 — 1.35)</td>
</tr>
<tr>
<td>D5 embryo grading</td>
<td>5.1</td>
<td>5.1 (-0.02, -0.22 — 0.18) #</td>
<td>4.9 (-0.21, -0.5 — 0.08) #</td>
</tr>
<tr>
<td>% D5 usable embryo / 2PN</td>
<td>59.5</td>
<td>56.0 (0.87, 0.70 — 1.04)</td>
<td>61.0 (1.06, 0.80 — 1.33)</td>
</tr>
<tr>
<td>No. GQ D5 embryos</td>
<td>0.4</td>
<td>0.4 (0.97, 0.60 — 1.34)</td>
<td>0.6 (1.64, 0.90 — 2.38)</td>
</tr>
</tbody>
</table>

# = Mean difference (OR, 95% CI)

SUPPORT: None.
P-269 Tuesday, October 15, 2019 6:30 AM

LIFESTYLE MODIFICATIONS IN MALE PARTNERS OF SUBFERTILE COUPLES IN WHICH THE SPOUSE IS OBSESE IMPROVES THE CHANCES OF THE COUPLE TO CONCEIVE. Matea Belan, MSc, a Belina Carranza-Mamane, MD, a Youssef AinMelk, MD, a Marie-Hélène Pesant, MD, a Karine Duval, PhD, a Farrah Jean-Denis, MSc, a Marie-France Langlois, MD, a Jean-Patrice Baillargeon, MD a Research Center of the Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC, Canada; bUniversité de Sherbrooke, Sherbrooke, QC, Canada; cUniversité de Sherbrooke - Department of Obstetrics and Gynaecology, Sherbrooke, QC, Canada; dUniversité de Sherbrooke, Department of Medicine, Sherbrooke, QC, Canada.

OBJECTIVE: 1) To evaluate the impacts of an exposition of male partners of infertile couples to a lifestyle intervention, already targeted to their spouse. Therefore, engaging more actively male partners in the lifestyle intervention that is already indicated for their spouse with obesity can potentially further improve the couple’s fertility.

P-270 Tuesday, October 15, 2019 6:30 AM

IMPACT OF BMI ON PREGNANCY OUTCOMES WITH RESPECT TO DIFFERENTIAL TSH LEVELS. Maria Bustillo, M.D., a Ineabelle Collazo, BS, b Jessica Lapalme Ricard, BS, b Juergen Eisermann, M.D., a Nicholas Hendon, BS, b Himanshu Arora, Ph.D. b IVFMD, South Florida Institute for Reproductive Medicine, MIAMI, FL; cUniversity of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: Serum thyroid-stimulating hormone (TSH) levels are routinely screened in women with infertility because thyroid disease may exert negative effects on ovulation and menstrual function. Women with clinical hypothyroidism (TSH levels > 4 uIU/mL) are treated with thyroid replacement. However, it is unclear whether subclinical hypothyroidism, defined as TSH levels > 2.5 uIU/mL (and < 4 uIU/mL) can affect pregnancy outcome. In the present study, we evaluated the IVF treatment/pregnancy outcomes with respect to BMI in euthyroid women and in those with subclinical hypothyroidism.

DESIGN: A retrospective study of 1,160 IVF cases.

MATERIALS AND METHODS: Patients were categorized into three groups. Group 1, euthyroid, consisted of 919 women, had pre-IVF TSH levels < 2.5 uIU/mL. Group 2 included 74 women with subclinical hypothyroidism (TSH levels > 2.5 uIU/mL who were not treated). Group 3 included 167 women who were treated. All the patients were subgroup based on their BMI (< 30). All women underwent standard IVF protocols following usual individualized practice in our IVF clinic.

RESULTS: Table below shows the classification of patients with respect to their pregnancy outcomes, by TSH levels, BMI and treatment respectively.

<table>
<thead>
<tr>
<th>Group 1- EUTHYROID</th>
<th>Group 2- SCI Hypo T Untreated</th>
<th>Group 3- SCI Hypo T Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre, TSH&lt;2.5, BMI &lt;30</td>
<td>Pre, TSH&lt;2.5, Non Treated BMI &lt;30</td>
<td>Pre, TSH&gt;2.5, Treated BMI &lt;30</td>
</tr>
<tr>
<td>Mean Age</td>
<td>Mean Age</td>
<td>Mean Age</td>
</tr>
<tr>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Not Pregnant</td>
<td>Pregnant</td>
<td>Sab</td>
</tr>
<tr>
<td>No of Patients</td>
<td>177*</td>
<td>601</td>
</tr>
<tr>
<td>% Mean Age</td>
<td>22.7</td>
<td>77.2</td>
</tr>
<tr>
<td>35.1</td>
<td>34.6</td>
<td>34.8</td>
</tr>
<tr>
<td>32</td>
<td>109</td>
<td>15</td>
</tr>
<tr>
<td>22.7</td>
<td>77.3</td>
<td>10.6</td>
</tr>
<tr>
<td>35.7</td>
<td>36.4</td>
<td>39.3</td>
</tr>
<tr>
<td>23*</td>
<td>40</td>
<td>9</td>
</tr>
<tr>
<td>36.5</td>
<td>63.5</td>
<td>14.3</td>
</tr>
<tr>
<td>36.0</td>
<td>33.3</td>
<td>33.6</td>
</tr>
<tr>
<td>3</td>
<td>37</td>
<td>2</td>
</tr>
<tr>
<td>27.3</td>
<td>72.7</td>
<td>18.2</td>
</tr>
<tr>
<td>40.3</td>
<td>35.1</td>
<td>38.5</td>
</tr>
<tr>
<td>37</td>
<td>105</td>
<td>14</td>
</tr>
<tr>
<td>26.1</td>
<td>73.9</td>
<td>9.9</td>
</tr>
<tr>
<td>35.6</td>
<td>33.8</td>
<td>33.4</td>
</tr>
<tr>
<td>8</td>
<td>17</td>
<td>2</td>
</tr>
<tr>
<td>32.0</td>
<td>68.0</td>
<td>8.0</td>
</tr>
<tr>
<td>39.3</td>
<td>29.3</td>
<td>33.5</td>
</tr>
</tbody>
</table>

*p = 0.013

FERTILITY & STERILITY®


e213
BMI. A BMI 25 - 29.99 are more likely to have CP with IUI compared to normal treatment strategies. Considering parameters such as the presence of TPO antibodies and specific dose thyroid supplementation may be beneficial. Further studies are ongoing considering parameters such as the presence of TPO antibodies and specific treatment strategies.

Support: This work was supported in part by the IVFMD, South Florida Institute for Reproductive Medicine.

P-271 Tuesday, October 15, 2019 6:30 AM

THE EFFECT OF BODY MASS INDEX (BMI) ON INTRAUTERINE INSEMINATION (IUI) CYCLE SUCCESS. Rachel M. Whynott, M.D.; Karen M. Summers, MPH ChE; Amy E. Sparks, Ph.D.; Rachel Mejia, D.O. University of Iowa Hospitals and Clinics, Iowa City, IA; University of Iowa, Iowa City, IA; University of Iowa Center for Advanced Reproductive Care, Iowa City, IA.

Objective: To determine if BMI affects IUI success.

Design: Retrospective cohort study.

Materials and Methods: Inclusion: IUI patients from 7/2009-12/2018. Exclusions: if weight (wt) or pregnancy outcome unavailable, or if BMI <18.5 (due to low n), for a total of 1319 patients and 3244 IUI cycles. Primary outcome was clinical pregnancy (CP) by BMI, defined as intrauterine pregnancy (IUP) with heartbeat (HB) on ultrasound (US). Secondary outcomes were live birth (LB), multiple gestation (MG), and abnormal pregnancy (AP) (defined as hCG without an IUP with HB at US). Chi-square was used to compare outcome data between groups. Generalized estimating equations were used to examine relationships between individual factors and outcome of CP. Initial odds ratios (OR) were calculated for all hypothesized individual factors: maternal age, smoking, gravity, parity, diagnosis, antral follicle count (AFC), cycle order, and treatment cycle type. Age and factors meeting criteria of p < 0.25 were entered into regression model. Through an iterative process of variable selection, covariates were removed from model if they did not meet significance of a = 0.1 or were not found to change any remaining parameter estimate by >15%. After the iterative process of deleting, refitting, and verifying, each variable not selected for inclusion in the original multivariate model was added back one at a time, with any significant at a = 0.1 retained.

Results:

<table>
<thead>
<tr>
<th>BMI</th>
<th>CP (n=3329)</th>
<th>AP (n=3329)</th>
<th>LB (n=3244)</th>
<th>MG (n=355)</th>
<th>Multiple Delivery (n=312)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI 18.5-24.99</td>
<td>192/1545 (12%)</td>
<td>55/152 (4%)</td>
<td>146/1521 (10%)</td>
<td>13/157 (8%)</td>
<td>8/150 (5%)</td>
</tr>
<tr>
<td>BMI 25-29.99</td>
<td>38/153 (15%)</td>
<td>38/153 (5%)</td>
<td>72/788 (9%)</td>
<td>6/91 (7%)</td>
<td>5/77 (7%)</td>
</tr>
<tr>
<td>BMI ≥ 30</td>
<td>115/813 (14%)</td>
<td>128/886 (14%)</td>
<td>77/854 (9%)</td>
<td>10/99 (10%)</td>
<td>9/79 (11%)</td>
</tr>
</tbody>
</table>

p

CONCLUSIONS: After controlling for potential confounders, patients BMI 25 - 29.99 are more likely to have CP with IUI compared to normal BMI. A BMI ≥ 30 does not have an impact on IUI CP rate or LB at a clinic requiring BMI <50. However, women BMI ≥ 30 are more likely to have AP which is consistent with prior studies in spontaneous and in vitro fertilization pregnancies.

Support: None.

P-272 Tuesday, October 15, 2019 6:30 AM

DIET, OBESITY, AND OVARIAN RESERVE IN A HEALTHY REPRODUCTIVE AGE COHORT. Bronwyn Bedrick, BA; Ashley Eskew, MD; Jorge E. Chavarro, MD, Sc.D.; Joan Riley, PhD, HCLD; Emily S. Junghem, MD, MSCI; Washington University in St. Louis, St. Louis, MO; Washington University School of Medicine, St. Louis, MO; Harvard School of Public Health, Boston, MA; Washington University School of Medicine, St. Louis, MO.

Objectives: The objectives of this study were to (1) describe dietary patterns in a cohort of healthy, reproductive-age women, (2) examine socioeconomics and demographic factors associated with adherence to these dietary patterns, and (3) assess the association between these dietary factors obesity and ovarian reserve.

Design: Cross-sectional study of healthy women age 18-44 in St. Louis with no history of infertility, chronic disease, or ovarian surgery.

Materials and Methods: A total of 185 women completed a validated food frequency questionnaire. Women with daily caloric intakes <500 kcal or >5000 kcal were excluded. Principal component analysis with varimax rotation was used to combine 40 food groups into 2 independent factors, or dietary patterns, for greater interpretability. Adherence to dietary patterns was defined by each participant’s factor score, such that women with higher scores for a specific dietary pattern were considered to be more adherent to that dietary pattern. Markers for ovarian reserve, serum anti-mullerian hormone (AMH) and antral follicle count (AFC) was measured via a Roche cobas e411 analyzer and transvaginal ultrasound, respectively. Logistic regression was used to examine the association between dietary patterns and obesity. Linear regression was used to assess the association between dietary patterns and markers of ovarian reserve.

Results: Two dietary patterns were identified: a “Prudent” pattern characterized by consumption of fruits, vegetables, olive oil, and nuts, and a “Traditional” pattern characterized by consumption of meat, refined carbohydrates, and high calorie drinks. African American women and those without college degrees were more adherent to the Traditional pattern and less adherent to the Prudent pattern. Income and employment were not associated with dietary adherence. Thirty percent of our cohort was obese. On multivariate regression, odds of obesity were higher for African American women (OR 3.11, 95% CI 1.23 to 7.89) and lower for physical active women (OR 0.30, 95% CI 0.10 to 0.93) after controlling for diet, physical activity, education, and income. There was a dose-dependent increase in odds of obesity with increasing adherence to the Traditional dietary pattern, but there was no relationship between obesity and adherence to the Prudent pattern. No associations were seen between either dietary pattern and markers of ovarian reserve.

Conclusions: A growing body of evidence has demonstrated that diet, irrespective of maternal BMI, influences fertility, pregnancy outcomes, and newborn health. In order to identify women for wellness interventions in the preconception period, it is necessary to understand local context. In this cohort of reproductive age women in St. Louis, we describe dietary patterns that are associated with obesity, but not with markers of ovarian reserve. Future research is needed to elucidate the relationship between diet and markers of ovarian reserve.

Support: Research reported in this publication was supported by the National Center For Advancing Translational Sciences of the National Institutes of Health under Award Numbers and KL2 TR000450 and T1LITR002344. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.
OBJECTIVE: To investigate whether switching GnRH antagonist (GnRHant) to medroxyprogesterone acetate (MPA) could effectively prevent premature LH surge in GnRHant protocols when patients turned out to have a high risk of OHSS during controlled ovarian stimulation (COS) and a freeze-all strategy was chosen.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This study recruited patients (<38 years old) who received a GnRHant protocol in their first IVF/ICSI cycle. Daily rFSH and GnRHant were started on cycle day 2 or 3, and stimulation day 5, respectively. During COS, the patients turned out to be at a high risk of developing OHSS (more than 13 follicles of ≥11 mm in diameter) before reaching the ovulation trigger criteria. It is our policy to freeze-all in this circumstance. GnRH antagonist was used to trigger ovulation. All the grade A or B embryos were vitrified on day 3 and frozen embryo transfer (FET) was performed on the subsequent cycle. In the study group (from August 2016 to July 2017) GnRHant was switched to MPA of 10mg daily till the day of ovulation trigger once freeze-all was determined (switch protocol). In the control group (from August 2015 to July 2016), GnRHant was maintained till the day of ovulation trigger as traditional GnRHant protocols. The primary outcome measure was the incidence of premature LH surge. Secondary outcome measures were the duration of GnRHant/MPA administration, duration of dose of rFSH administration, number of oocytes retrieved, numbers of embryos frozen, implantation and live birth rate in the first FET cycle.

RESULTS: A total of 401 cycles met the inclusion criteria for analysis: 205 in the control group and 196 in the study group. Premature LH surge did not occur in both groups. The characteristics of ovarian stimulation were similar between the two groups except the duration of GnRHant/MPA administration. The duration of GnRHant treatment was significantly lower in the switch protocol compared with the GnRHant protocol (3.1±1.2 days vs. 6.5±1.2 days). Majority of the patients (173/196=88.3%) received 2-4 days of GnRHant treatment before switching to MPA. Majority of the patients (185/196=94.4%) received 2-5 days of MPA treatment. The mean (±SD) duration of MPA administration was 3.6±1.1 days. No significant differences were observed in the duration (10.6±1.1 days vs. 10.5±1.2 days) and dose (1929±450 IU vs. 2005±483 IU) of rFSH administration; trigger day serum LH levels (2.0±1.4 IU/L vs. 1.8±1.1 IU/L); number of oocytes retrieved (17.0±6.4 vs. 16.9±5.9); number of embryos frozen (7.8±3.1 vs. 7.9±2.8); or live birth rate (50.5% vs. 49.8%) between switch and GnRHant protocol.

CONCLUSIONS: This study showed that MPA could replace GnRHant and effectively prevent premature LH surge after several days of GnRHant. This study showed that MPA could replace GnRHant and effectively prevent premature LH surge after several days of GnRHant administration in this group of patients. Switch protocol could individualize freeze-all policy in contrast to freeze-all for all in the progesterin primed ovarian stimulation. It could also reduce patients’ injection burden.

P-275 Tuesday, October 15, 2019 6:30 AM

WITHHOLDING LUTEAL HCG IS ASSOCIATED WITH DECREASED LIVE BIRTH (LB) IN WOMEN AT HIGH RISK FOR OVARIAN HYPERSTIMULATION SYNDROME (OHSS) DESPITE "INTENSIVE" LUTEAL SUPPORT WITH INTRAMUSCULAR PROGESTERONE (IMP). Lauren A. Bishop, MD,1 Natalie Clark Stenz, MD, MSCE,2 Micah J. Hill, DO,3 Kate Devine, MD,4 Saioa Torrealday, MD,e Eric A. Widra, MD,f Alan H. DeCherney, MD,g Frank E. Chang, MD,h NIH, Bethesda, MD;2Shady Grove Fertility, Atlanta, GA;National Institute of Child Health and Human Development, NIH, Bethesda, MD;3Shady Grove Fertility, Washington D.C., DC;1 Walter Reed Military Medical Center, Bethesda, MD;5SG Fertility, Washington, DC;5Shady Grove Fertility, Rockville, MD.

OBJECTIVE: To determine if the absence of hCG for luteal support results in reduced LB rates from IVF with fresh embryo transfer (ET) when “intensive” luteal support with IMP is given after GnRH agonist (GnRHa) trigger.

DESIGN: Retrospective Cohort Study.

MATERIALS AND METHODS: Fresh autologous IVF cycles from 2014-2017 with ≥24 oocytes retrieved were analyzed. Patients who did not undergo a fresh ET and those who received both hCG and GnRHa to trigger oocyte maturation were excluded. HCG trigger patients received luteal support with 100mg vaginal progesterone three times a day starting the day after retrieval. The same luteal support was used following GnRHa trigger if 1500 IU hCG was administered post retrieval. If OHSS risk was assessed as unacceptable high, hCG was held following GnRHa trigger and “intensive” luteal...
support with 50mg daily IMP was administered starting the day after retrieval. All patients received 2mg twice daily oral estradiol starting the night of retrieval. Multivariable logistic regression was used to compare laboratory and pregnancy outcomes in patients receiving hCG trigger (control) to those with GnRHa trigger with and without post retrieval hCG. Adjusted models accounted for age, BMI, number of embryos transferred, embryo quality, and serum progesterone level on day of trigger. Greater efficacy and receiver operator curves were used to determine if serum estradiol and progesterone concentrations on the day of trigger were associated with LB in each treatment group.

RESULTS: 984 autologous IVF cycles met inclusion criteria, distributed as follows: 235 hCG trigger, 236 GnRHa trigger with hCG post retrieval and, and 454 GnRHa trigger with no hCG post retrieval. GnRHa trigger patients were older, had a higher peak estradiol level, more embryos available for vitrification, and fewer embryos transferred (P < 0.001) compared to hCG trigger. Patients without hCG exposure had lower clinical pregnancy (CP) (42% vs 52%, P = 0.01) and LB (35% vs 44%, P = 0.01) rates compared to those using hCG trigger in both analysis models. Patients with GnRHa trigger who received post retrieval hCG had similar CP (56%, P = 0.43) and LB (46%, P = 0.42) to the hCG trigger cohort. There were no statistically significant differences in biochemical pregnancy, spontaneous abortion, and ectopic pregnancy. Patients without hCG exposure had lower rates of OHSS (<1%, P < 0.001) compared to hCG trigger (11%) and GnRHa patients (6%). LB did not vary by peak serum estradiol in any treatment arm.

CONCLUSIONS: Patients receiving GnRHa trigger who did not receive hCG post retrieval had lower CP and LB rates from fresh ET despite “intensive” luteal support. This was largely due to implantation failure as pregnancy loss was similar in all treatment groups. Adjusted analysis demonstrated that higher peak serum estradiol levels in the GnRHa without hCG group did not mediate this effect. Post retrieval hCG was associated with LB outcomes equivalent to hCG trigger, but at the cost of increased OHSS relative to the no hCG group. These data suggest when hCG luteal support cannot be given due to high OHSS risk a freeze all strategy should be strongly considered.


P-276 Tuesday, October 15, 2019 6:30 AM

MATERNAL AND FETAL OUTCOMES AFTER OVARIAN HYPERSTIMULATION SYNDROME: A ROCHESTER EPIDEMIOLOGY PROJECT (REP) STUDY.
Ajieta Sangtani, MD, Zaraq Khan, MD, Maryama Ismail, BS, Mayo Clinic Rochester, MN.

OBJECTIVE: The objective of this study was to determine the effect of ovarian hyperstimulation syndrome (OHSS) on maternal and fetal outcomes.

DESIGN: This was a retrospective cohort design.

MATERIALS AND METHODS: IRB approval was obtained. Using the Rochester epidemiology project, residents of Olmsted County and the surrounding 9 counties with OHSS after in vitro fertilization were identified between 1995 and 2017. Matched controls were then screened as matches on age, parity, and cause of infertility. Two controls were identified for each patient with OHSS. Patients were included if they had a pregnancy lasting ≥ 20 weeks gestation after the diagnosis of OHSS. Background demographics, pregnancy outcomes were collected via chart review. Data was then analyzed using a t-test and ANOVA.

RESULTS: Patients with and without OHSS did not differ on BMI, number of stimulation days, amount of gonadotropin use. Patients with OHSS has significantly more follicles (p < 0.0001) and more oocytes (p < 0.0001) as well as a higher peak estradiol (p = 0.004)[table1]. Rates of intrauterine fetal death, gestational diabetes, placental abruption, deep venous thrombosis, pulmonary embolism, gestational hypertension, number of liveborn infants, infant birthweight, and use of antenatal steroids did not differ between the groups. One and 5 minute Appgars did not differ between the two groups either [table1].

CONCLUSIONS: The incidence of OHSS after assisted reproduction is approximately 3%. OHSS did not affect maternal or neonatal outcomes in a subsequent pregnancy in our report. Further analyses are underway to determine if outcome outcomes differ in women who have a fresh transfer after OHSS diagnosis compared to those that undergo freeze all of embryos with a planned frozen embryo transfer.

P-277 Tuesday, October 15, 2019 6:30 AM

PREDICTION OF SEVERE OVARIAN HYPERSTIMULATION SYNDROME IN WOMEN UNDERGOING IN VITRO FERTILIZATION USING DAY 3 ESTRADIOL LEVELS, COLLECTED OVA, AND THE NUMBER OF FOLLICLES.
Ivan Madrazo, MD,1,2 Ginna Milena Ortiz, MD,a Juan José Suárez, MD,a Josue J. Hidalgo, MD,a Monserrat Fabiola Vélez, MD,a Esther López-Bayghen, PhD “Ingenes Mexico, Mexico City, DF, Mexico,” Affiliation not provided; “Centro de Investigación y Estudios Avanzados IPN, México, EM, Mexico.

OBJECTIVE: Ovarian hyperstimulation syndrome (OHSS) is a potentially life-threatening iatrogenic condition that can occur during in vitro fertilization (IVF). The worst outcome is hydrothorax, hypovolemia, higher risk of deep venous thrombosis and oliguria. With severe OHSS patients are required to postpone embryo transfer for an undetermined amount of time. Presence of OHSS or a high risk of developing OHSS is mainly based on serum estradiol (E2) levels, but other factors, such as female age, BMI, ovarian volume, antral follicle count (AFC), and polycystic ovary syndrome, are speculated to be predictive. Here, we aimed to determine if E2 levels at Day 3 and its fold change at day ten as well as antral follicle count and ova collected are predictive factors for severe OHSS.

METHODS: Retrospective cohort study.

MATERIALS AND METHODS: Patient chart review was performed between January 2008 and December 2017 at Ingenes in Mexico City. Three hundred twenty-seven women were selected. E2 >3000 ng/L usually on the last day of stimulation (day 10 with three 18 mm-follicles) was defined as OHSS (n=151). Culdocentesis was performed on a patient when upon clinical assessment patient presented features such as nausea, vomiting, oral intolerance and ascites identified by endovaginal ultrasound and abdominal ultrasound (renal and hepatic areas with visible ascites) that do not respond to conservative management (n=55 severe OHSS). Predictability was evaluated by measuring the area under the receiver-operating characteristic (AUC). Differences between groups were determined by t-test.

RESULTS: The OHSS positive group, when compared to the non-OHSS group, was higher with respect to E2 Day 3 levels (150±230 v 250±177 ng/L), E2 fold change (24.5±23.6 v 32.9±29.1), AFC (11.6±3.5 v 18.2±9.1), and Ova collected (10.1±6.4, 21.1±9.0, p < 0.0001). E2 Day 3 levels (AUC=0.76, 95%CI: 0.71-0.82), E2 fold change (AUC=0.71, 95%CI: 0.65-0.77), AFC (AUC=0.75, 95%CI: 0.70-0.81), and Ova collected (AUC=0.85, 95%CI: 0.81-0.89) were predictive of OHSS. For Culdocentesis, E2 Day 3 levels (190±221 v 223±158 ng/L) were not different between the subjects who received culdocentesis, whereas the E2 fold change (24.5±26.6 v 32.9±28.8, p=0.038), AFC (13.7±9.0 v 19.8±8.9, p=0.003), and Ova collected (13.7±8.9, 23.3±8.1, p<0.001) were higher. Interestingly, all variables were predictive of subjects who would qualify for culdocentesis (E2 Day 3 levels: AUC=0.63, 95%CI: 0.55-0.70; E2 fold change: AUC=0.63, 95%CI: 0.55-0.71; AFC: AUC=0.74, 95%CI: 0.68-0.80; and Ova collected: AUC=0.80, 95%CI: 0.75-0.85).

CONCLUSIONS: Here, we demonstrate the E2 levels, as well as the ova production parameters, are indicators of IVF patients who could develop severe OHSS and may require culdocentesis.

SUPPORT: Conacyt/15 205068.
**OVARIAN STIMULATION**

P-278 Tuesday, October 15, 2019 6:30 AM

**EFFECTIVENESS AND OPTIMAL DOSE OF CHLORMADINONE ACETATE (CMA) AS PROGESTIN-PRIMED OVARIAN STIMULATION.** Airi Kobayashi, RN, Emiko Funahashi, RN, Chiharu Tanaka, RN, Sachiko Nonaka, RN, Atsuko Tanaka, RN, Marina Kiuichi, RN, Yumi Suzuki, Medical doctors clark, Chiyuri Kuma, BS, Mizuho Takahashi, BS, Noriyuki Okuyama, MSC, Nobuya Aono, Ph.D., Toshihiro Tai, M.D., Ph.D., Mayumi Toya, M.D., Ph.D., Hideki Igarashi, M.D., Ph.D., Suguru Kikuchi, M.D., Ph.D., Tomoko Hashimoto, M.D., Ph.D., Koichi Kyono, M.D., Ph.D., Kyono ART Clinic Takanawa, Tokyo, Japan; Kyono ART clinic, Human Ovarian-tissue Preservation Enterprise (HOPE), Tokyo, Japan.

**OBJECTIVE:** The aim of this study was to clarify the effectiveness and optimal dose of chlormadinone acetate (CMA) as progesterin-primed ovarian stimulation (PROS).

**DESIGN:** This study was a prospective study conducted at Kyono ART Clinic Takanawa in Japan from August 2018 to April 2019 and performed with the consent of the Kyono ART Clinic Ethical Committee.

**MATERIALS AND METHODS:** Study 1: The subjects were classified into two groups. In both groups, either FSH/hMG was administered on day 3. Group A comprised 32 cycles (32 patients) using 12mg CMA from day 3; group B comprised 28 cycles (28 patients) using 0.25mg GnRH antagonist when mean dominant follicle diameter reached 14 mm. All embryos were cryopreserved at the blastocyst stage for later transfer. Study 2: The optimal dose of CMA (12mg, 6mg, 4mg, and 2mg) was examined. RESULTS: Study 1: Premature LH surge was not observed (0/32) in group A, whereas it was observed in 21.4% of cases (6/28) in group B; however, ovulation was not observed in either groups. Clinical outcomes in groups A and B were as follows: mean number of oocytes retrieved, 13.4±7.0 vs. 15.4±9.9; fertilization rate, 80.2% vs. 76.7%; blastocyst rate, 55.3% vs. 51.1%; good blastocyst rate, 43.6% vs. 44.0%; clinical pregnancy rate, 58.3% (7/12) vs. 62.0% (12/20); ongoing pregnancy rate, 50.0% (6/12) vs. 50.0% (10/20); miscarriage rate, 14.3% (1/7) vs. 16.7% (2/12). Thus, there were no significant differences between the two groups. Study 2: Premature LH surge was not observed: 0% (0/12), 0% (0/21), 0% (0/32), 0% (0/32) in CMA 2mg, 4mg, 6mg, and 12mg, respectively.

**CONCLUSIONS:** To our knowledge, this is the first report of CMA worldwide. PROS using CMA completely inhibited premature LH surge and clinical outcomes equal to those of GnRH antagonist treatment. CMA is oral medicine, cheaper and effective as PROS, and 2mg CMA may be the optimal dose. Further studies are needed.

**P-279 Tuesday, October 15, 2019 6:30 AM**

**DOES EXTENDING CONTROLLED OVARIAN HYPERSTIMULATION DURING A GNRH ANTAGONIST PROTOCOL IN VITRO FERTILIZATION CYCLE AFFECT OOCYTE QUALITY?** Sydney Chang, MD, Tanaseh Gharib Nazem, MD, Carlos Hernandez-Nieto, MD, Dmitriy Gounko, MA, Beth McCavey, MD, Daniel E. Stein, MD, Alan B. Copperman, MD, Icahn School of Medicine at Mount Sinai, New York, NY; Reproductive Medicine Associates of New York, New York, NY.

**OBJECTIVE:** The number of oocytes retrieved during an in vitro fertilization (IVF) cycle is an important determinant of success. Timing of the oocyte maturation trigger during controlled ovarian hyperstimulation (COH) must be optimized to maximize oocyte yield while avoiding hyperstimulation syndrome and impaired oocyte quality. A common protocol prescribes triggering administration when ≥ 2 follicles reach ≥ 18 mm. Periodically, clinicians delay the trigger to allow medium-size follicles to “catch up.” A recent study segregated 200 IVF cycles into: delayed trigger despite ≥ 2 mature follicles and trigger administration with ≥ 2 mature follicles, and found no difference in clinical pregnancy rate (CPR) and live birth rate (LBR). The clinicians transferred 1-2 fresh, unscreened embryos, which limits success with characteristics. To eliminate confounders with multi-embryo transfer and the effect of supraphysiologic hormone levels on the endometrium, we asked whether rates of oocyte maturation, fertilization, blastulation, and euploidy were affected by prolonging COH.

**DESIGN:** Retrospective, cohort study.

**MATERIALS AND METHODS:** The study included patients at a single academic center who underwent GnRH-antagonist IVF cycles from 2012-19. Cycles were grouped: (1) delayed trigger despite the presence of ≥ 2 mature follicles, and (2) administration of trigger in the presence of ≥ 2 mature follicles. Primary outcome was oocyte metaphase II (MII) rate. Secondary outcomes were rates of fertilization, blastulation, and euploidy. Statistical analysis was performed with R. Two-tailed P < 0.05 was considered significant.

**RESULTS:** Of the 7,976 antagonist IVF cycles from 6,478 patients, trigger was administered in the presence of ≥ 2 mature follicles in 6521 (81.8%) cycles, 1 day beyond in 1334 (16.7%) cycles, and 2 days beyond in 121 (1.5%) cycles. Univariate analysis demonstrated differences in age, antral follicle count, peak estradiol, gravidity, and trigger type. After controlling for these confounders, no significant association was observed for continuing COH beyond visualization of ≥ 2 mature follicles and MII rate (OR 1.01 [95% CI 0.90-1.13]), fertilization rate (OR 0.98 [95% CI 0.88-1.10]), blastulation rate (OR 0.97 [95% CI 0.87-1.08]), or euploidy rate (OR 0.90 [95% CI 0.78-1.04]). A sub-analysis was performed for SART age group E, which also showed no differences in cycle outcomes when COH was extended.

**CONCLUSIONS:** In the largest study of GnRH antagonist protocol IVF cycles looking at oocyte developmental competence when trigger was delayed in the presence of ≥ 2 mature follicles, we demonstrated no significant difference in rates of maturation, fertilization, blastulation, and euploidy, even in patients >42 years old. Our study suggests that continuing COH up to 2 days in select patients does not negatively affect outcomes. While reassuring, the effects of COH prolongation on genomic and non-genomic factors must be investigated. Well-controlled prospective studies assessing CPR and LBR will be needed before we can definitively quantify the limits around optimal COH duration.

**REFERENCES**


**SUPPORT:** None.

**P-280 Tuesday, October 15, 2019 6:30 AM**

**CIRCULATING MiRNA LEVELS AS A PREDICTOR OF OVARIAN RESPONSE IN WOMEN UNDERGOING CONTROLLED OVARIAN STIMULATION.** Maria Gabriela Mulato, BSc, Daniela Paes de Almeida Ferreira Braga, PhD, Amanda Souza Setti, MSc, Assumpoto Iaconelli, Jr, MD, Edison Borges, Jr, PhD, Murilo Vieira Geraldo, PhD, UNICAMP, Campinas, Brazil; Fertility Medical Group / Sapienctiae Institute, Sao Paulo, Brazil.

**OBJECTIVE:** The main objective of individualization of assisted reproduction treatments is to offer every woman the best treatment tailored to her unique characteristics. However, the success of individualized controlled ovarian stimulation (COS) depends on finding a reliable method for predicting ovarian response to stimulation. Therefore, the goal for the present study was to identify circulating microRNAs (miRNAs) biomarkers of the response to COS.

**DESIGN:** Cohort study.

**MATERIALS AND METHODS:** For the present study, 90 serum samples were collected prior to COS for intracytoplasmic sperm injection (ICSI). Samples were collected in a private university-affiliated IVF center, between Jan 2017 and Jan 2018, and were split into three groups, depending on the patient’s response to COS: Poor Response Group: < 4 retrieved oocytes (PR group, n=30), Normo Response Group: ≥ 4 and ≤ 12 retrieved oocytes (NR group, n=30), and Hyper Response Group: > 25 retrieved oocytes (HR, n=30). Samples were used for two experimental sets. For the first experimental set, 5 samples from each group were pooled together and used to identify aberrantly expressed miRNAs in experimental groups, by using a large-scale microRNA expression analysis platform. For the second experimental set, 25 samples from each group were individually analyzed and the expression of specific miRNAs, determined by the first step, was investigated.

**RESULTS:** Twenty two miRNAs presented a twofold increase level in the PR or HR groups when compared with the NR group. From those miRNAs, 9 presented poor dissociation curves and were excluded from further analysis. Based on the quality of the amplification, observed in the manual analysis, the detection pattern in the experimental groups, and literature data, three miRNAs with exclusive detection in the HR group (miR-181d-5p, miR-221-3p and miR-92a-1-5p) and one miRNA with exclusive detection in the PR group (miR-29a-3p, miR-223-3p and miR-
miR-200c, let-7d-3p and miR-150-5p were selected for a subsequent validation set. The results showed that the serum levels of miR-181d-5p was also positively correlated with the number of aspirated follicles (p<0.0001), number of retrieved oocytes (p<0.0001), and number of mature oocytes (p=0.0002).

CONCLUSIONS: The quantification of miR-181d-5p prior to the COS may discriminate patients who will respond in an exacerbated manner to those who will respond insufficiently to the COS. The use of this tool associated with other previously described parameters may allow the individualization of the treatment, increasing treatment success while decreasing patients’ risks and physical, emotional and economic burden.


P-281 Tuesday, October 15, 2019 6:30 AM

PHYSICIANS SHOULD AVOID CHANGING A PATIENT’S OVARIAN STIMULATION PROTOCOL FOR THE PURPOSE OF IMPROVING LABORATORY OUTCOMES. Kaitlyn Wald, MD, Eleni A. Greenwood, MD, MSc, Marcelle I. Cedars, MD, Mitchell P. Rosen, MD, HCLD. University of California San Francisco, San Francisco, CA.

OBJECTIVE: Providers consider a number of factors when selecting a stimulation protocol and may switch protocols when a patient has a suboptimal stimulation or laboratory outcome. We sought to determine whether providers’ choice in stimulation is associated with laboratory outcomes.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: IVF cycles from 1/2010 to 3/2019 were reviewed. Cycles were categorized as: (1) E2 priming antagonist (2) Antagonists +/- OCP priming (3) Long luteal (4) Lupron stop (5) Flare. Mini-stimulations were excluded. Laboratory outcomes for first stimulations only and repeated cycles within a patient were compared. For first stimulation cycles, linear and logistic regression were used. For repeated cycles, those who completed the same stimulation were compared to those who changed, using cluster analyses for pairwise comparison. A subgroup of patients who had a low blast progression in their first cycle was also analyzed. Outcomes were adjusted for number of eggs collected and patient age.

RESULTS: 5209 patients underwent ovarian stimulation for IVF. When comparing between stimulation types, fertilization rate, blast progression and euploid rate were not statistically different. 2477 of these patients underwent a second cycle: 50% repeated the same and 50% completed a different protocol. The fertilization rate and blast progression were not statistically different between those who repeated the same protocol and those who changed. There was a statistically significant improvement in eggs collected, usable embryos and euploid rate for those who repeated the same stimulation, after adjustment (table). Of those with low blast progression in the first cycle, a significant improvement occurred in the second cycle, however, repeating the same protocol resulted in a slightly greater improvement (coefficient 0.03 (0.01-0.04)).

CONCLUSIONS: All conventional ovarian stimulation protocols result in comparable laboratory outcomes. By enlarge, the variations seen from cycle to cycle within a patient cannot be explained by stimulation type. If anything, there is a subtle benefit to staying with the same protocol, for reasons yet to be determined, but likely inherent to the patient. Until these factors are further understood, physicians should avoid changing stimulation protocols for the purpose of improving laboratory outcomes.

### Table 1: Laboratory Outcomes in First and Second Stimulations

<table>
<thead>
<tr>
<th>Outcome</th>
<th>First Stimulation</th>
<th>Second Stimulation</th>
<th>Coefficient (p)</th>
<th>Adjusted Odds Ratio (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td># Eggs</td>
<td>11.8</td>
<td>10.7</td>
<td>1.0 (0.46-1.53)</td>
<td></td>
</tr>
<tr>
<td>Fertilization Rate</td>
<td>0.78</td>
<td>0.76</td>
<td>1.0 (0.92-2.8)</td>
<td></td>
</tr>
<tr>
<td># Usable Embryos</td>
<td>3.9</td>
<td>3.11</td>
<td>1.25 (0.79-1.72)</td>
<td></td>
</tr>
<tr>
<td>Blast Progression</td>
<td>0.51</td>
<td>0.48</td>
<td>0.03 (-0.01-0.08)</td>
<td></td>
</tr>
<tr>
<td>Euploid Rate</td>
<td>0.34</td>
<td>0.34</td>
<td>1.39 (1.01-1.93)</td>
<td></td>
</tr>
</tbody>
</table>

P-282 Tuesday, October 15, 2019 6:30 AM

CAN TREATMENT CHOICE AFFECT COST OF THERAPY IN PATIENTS PREDICTED TO BE HIGH-RESPONDERS? RESULTS OF AN ECONOMIC ANALYSIS OF THE MENOOPUR IN GNRH ANTAGONIST SINGLE EMBRYO TRANSFER - HIGH RESPONDER (MEGASET-HR) TRIAL. Andrew F. Khair, PhD, MBA, Winnie Nelson, PharmD, MS, MBA, Anshul Sinha, B.Tech, Masakazu Ando, PhD, Patricia W. Heiser, PhD, Jared C. Robins, MD, Gaurang S. Daftary, MD, MBA. Ferring Pharmaceuticals, Inc, Parsippany, NJ; Northwestern University, Chicago, IL.

OBJECTIVE: To determine difference in treatment cost associated with cumulative live birth between highly purified-human menotropin (HP-hMG, Menopur®) and recombinant follicle stimulating hormone (rFSH, Gonal-F®) in predicted high responder women undergoing assisted reproductive technology.

DESIGN: Cost analysis of a multicenter, randomized, open label, assessorblind, non-inferiority trial.

MATERIALS AND METHODS: Ovulatory women aged 21-35y with BMI 18.0-30 kg/m² and serum anti-Müllerian hormone (AMH) ≥ 5 ng/mL (N=620) were randomized 1:1 to a 150 IU start dose of HP-hMG or rFSH in a GnRH antagonist cycle with dose adjustments allowed on day 6 of stimulation. All embryos were fertilized by intracytoplasmic sperm injection and underwent Day 5 trophectoderm biopsy for preimplantation genetic screening (PGS). Whereas morphology guided single, fresh blastocyst transfer, PGS results were only available to guide frozen blastocyst transfers. Live birth outcomes resulting from all fresh and any frozen transfers occurring within 6 months of randomization were collected. A decision tree of all per protocol trial outcomes and their associated probabilities was constructed. The resultant model was then used to perform a cost analysis using real-world trial site procedural costs and wholesale acquisition cost (WAC) of medication from when the trial began (September 2015) inflation-adjusted to 2019 cost.

RESULTS: Demographics for the HP-hMG and rFSH arms were similar. The primary non-inferiority end-point was met, and the cumulative live birth rate was 50.6% (157/310) for HP-hMG and 51.5% (159/309) for rFSH (difference: -0.8%; 95% CI: -8.7, 7.1). Mean total dose of HP-hMG was 616 IU greater, while patients with rFSH underwent 43 more transfers, had a higher cumulative early pregnancy loss rate (-11.0%; 95% CI: -18.8, -3.1) and higher adverse event rate of ovarian hyperstimulation syndrome (-11.7%; 95% CI: -17.3, -6.1). Results of the cost analysis showed that per patient treatment cost of HP-hMG was lower at $14,744 compared to $15,759 with rFSH.

CONCLUSIONS: Cost analysis of data from the MEGASET-HR trial shows that treatment of predicted high-responders with HP-hMG may be associated with lower treatment costs compared to rFSH, despite potentially higher initial medication cost. The savings were driven by fewer embryo transfers needed and lower rate of adverse events associated with HP-hMG therapy.

SUPPORT: This trial was sponsored by Ferring Pharmaceuticals, Inc.

P-283 Tuesday, October 15, 2019 6:30 AM

A SIMULATED USE STUDY OUTLINING DIFFERENCES IN HANDLING ERRORS AND PREFERENCE BEFORE AND AFTER USE OF CURRENTLY AVAILABLE RECOMBINANT HUMAN FOLLICLE-STIMULATING HORMONE (R-HFSH) PEN INJECTORS. Salvatore Longobardi, MD, Anke Seidler, MBA, Julian G. Martins, MA, Francois P. M. Beckers, PhD.
OBJECTIVE: This study compared handling errors and preference ratings before and after use of four currently available r-hFSH pen injectors tested by women with infertility and fertility nurses.

DESIGN: This was a simulated use study comparing the GONAL-f® (Merck KGaA, Germany), Bemfola® (Gedeon Richter PLC, Hungary), Rekovelle® (Ferring Pharmaceuticals Ltd, UK) and Ovaleap® (Teva BV, The Netherlands) pen injectors in Germany, Poland and the UK.

MATERIALS AND METHODS: Injector-naïve women with infertility and injector-experienced fertility nurses tested pen injectors with masked labels in a randomized testing order. Simulated injections were made into a foam pad following the instructions for use (IFU) and injectors were rated before and after use. Handling errors were noted by the moderator during the study. After the study, errors were grouped according to severity and used steps indicated in the IFU. Ordinal or Poisson linear mixed models were applied, adjusted for injector and testing order with an unstructured correlation matrix between measures (or with non-convergence, non-parametric or normal approximation to the Poisson methods). All analyses were exploratory by nature without any correction for multiplicity.

RESULTS: A total of 120 women with infertility and 60 fertility nurses participated. All participants tested GONAL-f and Bemfola injectors. Because of their similarity, participants tested either Rekovelle (71 women; 30 nurses) or Ovaleap (49 women; 30 nurses) injectors. Before simulated use, mean ratings from women with infertility were similar between the GONAL-f® and other pen injectors. After use, the ratings from women were higher for GONAL-f® vs other pen injectors (p < 0.001 for all comparisons). Fertility nurses rated the GONAL-f® injector higher than the other pen injectors both before and after simulated use, with the difference in ratings larger after simulated use (p < 0.001 for all comparisons vs GONAL-f®). Adjusted rates of total handling errors for both women with infertility and fertility nurses were lower with the GONAL-f® pen injector (p < 0.001 for all comparisons vs GONAL-f®). Adjusted rates of total handling errors (95% CI) for women with infertility were 1.02 (0.84, 1.20), 1.64 (1.41, 1.87), 2.07 (1.68, 2.45) and 3.16 (2.50, 3.81) with GONAL-f®, Bemfola, Rekovelle and Ovaleap pen injectors, respectively. For fertility nurses, corresponding adjusted rates were 0.31 (0.16, 0.45), 1.30 (1.00, 1.60), 1.19 (0.71, 1.66) and 1.64 (1.06, 2.21), respectively. The most difficult use-steps (i.e. during which most errors were recorded with all pen injectors) were "priming" and "giving the injection". Significantly lower error rates were recorded during these use-steps with the GONAL-f® pen injector vs the other pen injectors (p < 0.05 for all comparisons).

CONCLUSIONS: In this study, the GONAL-f® injector was rated significantly higher than other pen injectors after use. This may be a result of more handling errors, including those that may affect treatment outcomes, observed with the Bemfola, Rekovelle and Ovaleap pen injectors.

SUPPORT: Funded by Merck KGaA, Darmstadt, Germany.

**Table 1. Comparisons of Key Parameters Before and After Use of Pen Injectors Tested by Women with Infertility**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TT (n=84)</th>
<th>TC (n=72)</th>
<th>CC (n=25)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age yrs.*</td>
<td>28.5±5.6</td>
<td>29.4±5.9</td>
<td>29.5±6.1</td>
<td>0.58&lt;</td>
</tr>
<tr>
<td>Infertility Duration yrs.*</td>
<td>4 (0-19)</td>
<td>4.5 (0-18)</td>
<td>4 (1-19)</td>
<td>0.85SS</td>
</tr>
<tr>
<td>Basal FSH m IU/mL</td>
<td>4.8 (1.2-10.5)</td>
<td>5 (1-11.1)</td>
<td>4.9 (1.9-11.9)</td>
<td>0.60&lt;</td>
</tr>
<tr>
<td>Causes of infertility: n(%)</td>
<td></td>
<td></td>
<td></td>
<td>0.77&lt;</td>
</tr>
<tr>
<td>Male (n = 69)</td>
<td>33 (39.3)</td>
<td>25 (34.7)</td>
<td>11 (44)</td>
<td></td>
</tr>
<tr>
<td>PCOS (n = 20)</td>
<td>12 (14.4)</td>
<td>7 (8.3)</td>
<td>1 (4)</td>
<td></td>
</tr>
<tr>
<td>Tubal infertility (n = 29)</td>
<td>13 (15.4)</td>
<td>11 (12.5)</td>
<td>5 (20)</td>
<td></td>
</tr>
<tr>
<td>Combined (n = 32)</td>
<td>14 (16.6)</td>
<td>13 (16.6)</td>
<td>5 (20)</td>
<td></td>
</tr>
<tr>
<td>Unexplained (n = 31)</td>
<td>12 (14.3)</td>
<td>16 (22.2)</td>
<td>3 (12)</td>
<td></td>
</tr>
<tr>
<td>Gn Rh protocol n(%)</td>
<td></td>
<td></td>
<td></td>
<td>0.19&lt;</td>
</tr>
<tr>
<td>Agonist, (n = 81)</td>
<td>32 (38.4)</td>
<td>34 (47.2)</td>
<td>14 (56)</td>
<td></td>
</tr>
<tr>
<td>Antagonist (n = 100)</td>
<td>52 (61.6)</td>
<td>58 (25.8)</td>
<td>11 (44)</td>
<td></td>
</tr>
<tr>
<td>Gonadotropin dose IU*</td>
<td>1888.4±481.9</td>
<td>1958.3±526.9</td>
<td>2067.2±548.6</td>
<td>0.28&lt;</td>
</tr>
<tr>
<td>Eggs retrieved*</td>
<td>10 (1-23)</td>
<td>9 (1-31)</td>
<td>7 (1-35)</td>
<td>0.33SS</td>
</tr>
<tr>
<td>Ovarian response n(%)</td>
<td></td>
<td></td>
<td></td>
<td>0.04&lt;</td>
</tr>
<tr>
<td>POR (n=23)</td>
<td>9 (10.7)</td>
<td>7 (9.8)</td>
<td>7 (28)</td>
<td></td>
</tr>
<tr>
<td>Normal response (n=144)</td>
<td>70 (83.4)</td>
<td>60 (83.3)</td>
<td>14 (56)</td>
<td></td>
</tr>
<tr>
<td>High response (n=14)</td>
<td>5 (5.9)</td>
<td>5 (6.9)</td>
<td>4 (16)</td>
<td></td>
</tr>
</tbody>
</table>

* = (mean ± SD), *(median, range);< Anova test, SS=Kruskal-Wallis Test, < = chi square test


P-285 Tuesday, October 15, 2019 6:30 AM

EFFECT OF OVARIAN STIMULATION OF OOCYTE DONORS ON IN-VITRO FERTILIZATION OUTCOMES. Heather S. Hipp, M.D.,* Audrey J. Gaskins, Sc.D.,* Zsolt Peter Nagy, MD, PhD,† Sarah M. Capelotto, MD,‡ Daniel B. Shapiro, MD,§ Jessica B. Spencer, MD, MSc,¶ Emory University, Atlanta, GA; Reproductive Biology Associates, Atlanta, GA; †The University of Texas, Southwestern Medical Center, Dallas, TX.

OBJECTIVE: To determine the effect of ovarian stimulation in oocyte donors on in-vitro fertilization (IVF) outcomes for recipients.

DESIGN: Retrospective cohort study of data from a frozen donor oocyte bank from 2008 to 2015.

MATERIALS AND METHODS: A total of 350 oocyte donors underwent 553 ovarian stimulation cycles with an antagonist protocol. Mature oocytes were vitrified and later warmed in individual cohorts among 989 unique recipients who underwent 1745 embryo transfer cycles. The associations between ovarian stimulation characteristics and rates of oocyte warm survival, fertilization, and usable embryos (combination of number of embryos transferred and cryopreserved for future use) per oocyte warmed as well as the rate of live birth per embryo transfer cycle were modeled using cluster-weighted generalized estimating equations adjusted for donor age, body mass index (BMI), race, retrieval year, and recipient age (live birth only).

RESULTS: The donors were 21-32 years old with BMI <30 kg/m². Per stimulation cycle, the median number of oocytes retrieved was 30 (range: 9-95). The majority of recipients, 78.6%, had 6-8 donor oocytes warmed. Multivariate linear regression analysis showed that percentage of oocytes that survived warm, were successfully fertilized and were usable was 93.6% (11.5%), 79.8% (18.2%) and 53.9% (21.8%) respectively. Donors with more oocytes retrieved had a lower percentage of usable embryos per oocyte warmed (<15: 62.5% [95% Confidence interval (CI) 52.7-71.4], 15-30: 58.9% [95% CI 55.0-62.6], 31-50: 53.6% [95% CI 49.6-57.5], > 50: 52.0% [95% CI 40.5-57.9%]). Of the transfers, 856 (49.1%) resulted in a live birth. There was no difference in the probability of live birth according to number of oocytes retrieved in a donor. For example, the adjusted odds of live birth among recipients was 0.93 (95% CI 0.67, 1.31) if the donor had >50 oocytes retrieved compared to 15-30 oocytes retrieved.

CONCLUSIONS: Oocyte donors represent an excellent model to determine the impact of ovarian stimulation on IVF outcomes given a relatively uniform uterine environment. Although high donor oocyte yields result in more oocytes available, there are less usable embryos per oocyte warmed as number of retrieved oocytes increases. These differences in early outcomes, however, do not translate into differences in live birth rate.

SUPPORT: REDCap grant support at Emory was provided through UL1 TR000424.

P-286 Tuesday, October 15, 2019 6:30 AM

THE IMPACT OF FOLLISTATIN HORMONE ON OVARIAN RESPONSE. Yahia Mohamed El-Faiass, M.D., M.Sc.,* Alaa Amer, B.Sc.,* Mohamed A. Aboulghar, M.D.,* Gamal Serour, M.D.,* Ragaa Mansour, M.D., Ph.D.,†* Cairo University, Cairo, Egypt; †The Egyptian IVF-ET center, Maadi, Cairo, Egypt; *Cairo University, Egyptian IVF center, Cairo, Egypt; **The Egyptian IVF-ET center, Maadi, Al Azhar University, Cairo, Egypt.

OBJECTIVE: We aimed in this study to find the role of serum level of Follistatin in the process of folliculogenesis. Noticing the variability of Follistatin levels between women, we wanted to uncover a modifying role that Follistatin plays, resulting in a variable individual ovarian response.

DESIGN: A Prospective cross-sectional observation study, including 200 women undergoing an IVF program with the long stimulation protocol in the Egyptian IVF Center in Maadi, Cairo, Egypt.

MATERIALS AND METHODS: Patients were matched regarding age, BMI, ovarian reserve (based on AMH and AFC) and HMG initial doses (150-225mgIU/day). Serum Follistatin was measured in the blood sample withdrawn from the patient 12-14 days after starting the GnRHa, to test for correlations and regulation, prior to HMG administration. Two primary parameters were set. Parameter 1: the time needed to reach a satisfactory initial response (Point A set as: “the number of days needed by the patient to reach at least 2 follicles on each side with a minimum of 12 mm diameter”). Parameter 2 was set as: “the time needed to reach mature Graafian follicles (Point B set at: 20 mm follicular diameters or more and concomitant Estradiol levels corresponding to at least 200 pg/mL per follicle”).

RESULTS: Patients were divided into four groups based on their Follistatin levels, ranging between the minimal and the maximal readings recorded in our study, using an increment of 1000 pg/ml between each group (Group 1: 100-200, Group 2: 200-300, Group 3: 300-400, Group 4: 400-500). The number of days to reach Point A was significantly higher in Group 4 compared to the other groups (Point B was reached in Group 1 after 8 days in 82.1% and 100% after 10 days. At 12 days of stimulation the percentage of those who reached Point B was 92.2% in Group 2, 4.5% in Group 3 and 0% in Group 4. In that last group, 73.7% of patients needed 16 days to reach Point B, with a remaining 26.3% needed 18 days or more to reach it. Using Pearson’s correlation, a strong positive correlation was found between serum Follistatin levels and Parameter 1 & 2 (r=0.899 & 0.91, respectively). The correlations between Follistatin and Age, BMI and AMH were statistically insignificant.

CONCLUSIONS: In this study, serum Follistatin levels had a clear effect on ovarian response. The detected inverse correlation between Follistatin levels and the ovarian response time suggests a role of serum Follistatin levels assessment prior to starting an ovarian stimulation protocol. Follistatin could act as a reliable independent predictor of the magnitude of ovarian response in cases undergoing controlled ovarian hyperstimulation for IVF. This could be used to properly tailor the dose for those patients, reducing the need for dose modification and subsequently duration of stimulation. It could equally help to predict OHSS or slow response.

SUPPORT: None.

P-287 Tuesday, October 15, 2019 6:30 AM

ORAL OVULATION INDUCTION MEDICATIONS VERSUS GONADOTROPINS FOR UNEXPLAINED INFERTILITY: A SYSTEMIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS. Jessica R. Zolton, DO,a Peter G. Lindner, M.D.,b Nancy Terry, B.S., M.L.S.,c Alan H. DeCherney, MD,a Micah J. Hill, DO. aNational Institute of Child Health and Human Development, NIH, Bethesda, MD; bWalter Reed National Military Medical Center, Bethesda, MD; cNIH, Bethesda, MD.

OBJECTIVE: To compare live birth and multiple gestation in gonadotropins versus oral ovulation induction agents for patients with unexplained infertility.

DESIGN: Systematic review and meta-analysis

MATERIALS AND METHODS: A systematic review of PubMed and Embase was performed for RCTs comparing gonadotropins versus clomiphene citrate (CC) or letrozole in IUI cycles for patients diagnosed with unexplained infertility. Primary outcomes were live birth and multiple gestation. Random effects models were used for all comparisons, due to clinical heterogeneity or I2 > 50%. Primary meta-analysis was performed on an intent-to-treat and per patient basis, with sensitivity analyses of per protocol, per cycle, and fixed effects models performed.

RESULTS: Eight total trials were identified that met inclusion criteria and constituted 2,989 patients undergoing 6,590 cycles. One study reported a significant increase in live births and multiple gestations with gonadotropins in comparison to letrozole and CC. All other studies compared CC and gonadotropins. Three of these studies found no difference in live birth or multiple gestations. One study found a lower live birth rate with CC but no difference in multiple gestations. Moderate heterogeneity was suggested by the Q test (Q=0.08) and the I² index (I²=53%) for live birth comparisons. The overall likelihood of live birth was not significantly increased in patients randomized to gonadotropins (RR 1.10, 95% CI 1.00-1.21, P=0.05). Similarly, the risk of multiple gestations was significantly increased in patients assigned gonadotropins (RR 1.09, 95% CI 0.97-1.21, P=0.15). The number needed to treat with gonadotropins was 15 to have 1 additional live birth. For every 1 additional live birth from
gonadotropins, an additional 0.88 twin pregnancies occurred. Singleton birth per cycle was similar between the two groups. The results did not change in per protocol, per cycle, or per cycle analysis after model sensibility analyses.

CONCLUSIONS: In women with unexplained infertility, letrozole did not increase the likelihood of live birth. For every birth gained with the use of gonadotropins, an almost identical increase in the risk of twins occurred. The randomized data do not support the use of gonadotropins for superovulation in women with unexplained infertility.

P-288 Tuesday, October 15, 2019 6:30 AM

OVULATION RATE WITH LETROZOLE STAIR-STEP PROTOCOL AND IN SUBSEQUENT LETROZOLE CYCLE. Reeva B. Makhijani, MD,1 Chantal Bartels, MD,1 Jeffrey Thorne, MD,1 Grow R. Daniel, MD,1 John Nulsen, MD,1 Lawrence Ekgmann, MD,1 Claudio Benadiva, MD,1 Center for Assisted Reproductive Services, University of Connecticut School of Medicine, Farmington, CT;1Center for Advanced Reproductive Services, University of Connecticut School of Medicine, Farmington, CT.

OBJECTIVE: Stair-step (SS) protocols have been successfully used for anovulatory women who fail to ovulate with the initial dose of clomiphene citrate (CC), with the additional benefit of decreased time to ovulation and increased ovulation rates compared with more traditional protocols. Letrozole is now considered first-line therapy for ovulation induction (OI). However, ovulation rate with the letrozole SS protocol has never been reported. We sought to determine the effectiveness of the letrozole SS protocol for inducing ovulation, as well as the ovulation rate in the subsequent cycle with the letrozole dose that achieved ovulation through SS.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Anovulatory patients who underwent OI using the letrozole SS protocol at our center between 2013-2019 were included for analysis. Baseline and cycle characteristic data was collected from our electronic medical record. Ovulation was confirmed by positive result on urinary ovulation predictor kit, serum LH level >20 IU/mL, or the presence of a follicle >15 mm on ultrasound. Ovulation rate was the primary outcome. Student’s t-test and chi squared test was used for continuous and categorical variables, respectively. A p-value of 0.05 was considered statistically significant.

RESULTS: Of 108 patients who underwent letrozole SS for OI, 83.3% (90/108) of patients became ovulatory. 38.9% (35/90) patients ovulated with the 5 mg dose and 61.1% (55/90) ovulated with the 7.5 mg dose. 88.9% (80/90) and 61.1% (55/90) ovulated with the 7.5 mg dose and 61.1% (55/90) ovulated with the 7.5 mg dose, respectively. Of the ovulatory patients, 61 underwent a subsequent letrozole cycle and 91.8% (56/61) ovulated at the ovulatory dose established in the previous cycle.

CONCLUSIONS: The letrozole SS protocol is successful in inducing ovulation in a majority of patients as well as in a subsequent cycle with the previously established ovulatory dose. Higher BMI may contribute to letrozole resistance.

P-289 Tuesday, October 15, 2019 6:30 AM

SINGLE DOSE VERSUS 5 DAY DOSING OF AN AROMATASE INHIBITOR FOR OVULATION INDUCTION. Kaitlin McGrail, MD,a Susan C. Conway, MD,a7 John Stormert, MD,b Sarah Buzhardt, MD,a Neil Chappell, MD, MSC,a7 LSU OB/GYN (Baton Rouge) Residency Program, Baton Rouge, LA;7Fertility Answers, Baton Rouge, LA.

OBJECTIVE: Compare the efficacy of single dose letrozole (1D) with standard five day (5D) course for ovulation induction (OI).

DESIGN: A retrospective cohort study of all patients undergoing OI and intrauterine insemination (IUI) with letrozole from January 2015 through December 2017 at a single institution.

MATERIALS AND METHODS: All patients undergoing their first OI/IUI cycle with letrozole from January 2015 to December 2017 were included in the study. Patients either received a one time dose of 25mg letrozole (1D) on cycle day 3 or dose of 5mg daily for five days (5D) from cycle days 3-7. The primary outcome was pregnancy rate (PR). Secondary outcomes included live birth rate (LBR), multiple gestation (MG), and miscarriage (SAB). Student’s T test, chi square, and Fisher’s exact statistical analysis were utilized where appropriate.

RESULTS: Of a total of 586 patients, the 1D group had 302 patients and the 5D group had 284 included in the study. There was no difference in smoking status, primary vs secondary infertility, or total motile concentration (TMC). Comparing 1D to 5D, there was a statistically significant, though not clinically relevant difference in both age and BMI (31 yrs vs. 31.8 yrs, p=0.03; 26.2 vs. 27.4, p=0.02), respectively. There were no differences between 1D and 5D in PR (14.2% vs. 11.6%), LBR (9.6% vs 7%), MG (16.2% vs 13.8%), or SAB (16.2% vs 13.8%).

CONCLUSIONS: A single dose protocol with Letrozole in an OI/IUI cycle may be considered as an alternative to standard five day dosing protocols with potential for improved compliance and similar reproductive outcomes.
rhFSH dose in IU was lower in the PC vs HC (1848.4 [700.5] vs 2237.8 [772.6]); clinical pregnancy rate was improved in the PC vs HC (per embryo transfer cycle: 50.3% vs 40.7%; per initiated cycle: 35.3% vs 37.8%). OHSS incidence was significantly lower in the PC vs HC (1.5% [27/1873] vs 4.0% [57/1419], p<0.001); most events were mild/moderate. 5.0% [89/1783] of patients had ≥ 1 AE and 1.9% [33/1783] of patients had ≥ 1 serious AE in the PC.

CONCLUSIONS: Pts using the RPI required a significantly lower rhFSH dose per oocyte retrieved vs pts using OID in this Asian population. Clinical outcomes were improved and OHSS incidence was significantly lower in the PC vs HC.

SUPPORT: Merck KGaA, Darmstadt, Germany.

P-291 Tuesday, October 15, 2019 6:30 AM

USE OF LUTEINIZING HORMONE SUPPLEMENTATION FOR OVARIAN STIMULATION IN IVF/ICSI CYCLES OF WOMEN WITH GOOD OVARIAN RESERVE. Liang Hsuan Chen, MD, Tzu-Hsuan Chin, MD, Ya-Chiung Hsu, MD, Shang Yu Huang, MD, Hsien-Ming Wu, MD, PhD, Chia-Lin Chang, MD, Hong-Yuan Huang, MD, Hsin-Shih Wang, PhD, Yung-Kuei Soong, MD. Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital Linkou Medical Center, Taoyuan, Taiwan R.O.C., Taipei, Taiwan.

OBJECTIVE: To declare current evidence exploring the added value of LH supplementation to FSH following GnRH antagonist protocol in women with good ovarian reserve.

DESIGN: We conducted a retrospective analysis exploring the benefit for pregnancy achievement of LH supplementation to GnRH antagonist cycles in women with AMH level over 5 ng/mL.

MATERIALS AND METHODS: A total of 255 women with AMH ≥ 5 undergoing IVF/ICSI using a GnRH antagonist protocol was included. Of these, 148 were received treatment with recombinant FSH (r-FSH) + human menopausal gonadotrophin (HMG) and 107 with r-FSH alone through the ovarian stimulation.

RESULTS: We observed a significantly lower serum LH levels at the beginning of cycle, the day of GnRH antagonist administration and the day of oocyte triggering in the combination of r-FSH+HMG group. The treatment days and total gonadotropin dose was significantly higher in r-FSH+HMG group compared with r-FSH alone group. Nevertheless, there were no significant differences between the two groups with respect to the number of oocytes retrieved, maturation, fertilization, and blastocyst formation rate. The OHSS occurred 8% of the r-FSH+HMG group, whereas 8% OHSS developed in the r-FSH alone group. There were no difference in pregnancy outcome between the two groups.

CONCLUSIONS: LH supplementation to r-FSH following GnRH antagonist does not seem to significantly augment serum E2 level on the trigger day and further pregnancy outcome in patient with good ovarian reserve. However, LH supplementation seems to have a benefit in some normo-gonadotropic women, who developed LH deficiency following GnRH antagonist. An accurate definition of the LH threshold in GnRH antagonist cycles may contribute to the discussion of which subgroups of women may benefit from adjuvant LH therapy.

P-292 Tuesday, October 15, 2019 6:30 AM

CHOOSING THE OPTIMUM MEDICATION AND DOSE IN OVULATION INDUCTION-INTRAUTERINE INSEMINATION CYCLES (OI-IUI) TO AVOID MULTIPLE GESTATION PREGNANCIES. M. Blake Evans, DO,† Micah J. Hill, DO,† Kate Devine, MD,§ Alan H. DeCherney, MD,§ Natalie Clark Stentz, MD, MSCE,§ “NIH-NICH, Bethesda, MD;§ Shady Grove Fertility, Washington D.C., DC;§ Shady Grove Fertility, Atlanta, GA.

OBJECTIVE: Does dosing or choice of ovulation induction medication impact clinical pregnancy or multiple gestation rate?

DESIGN: Retrospective cohort

MATERIALS AND METHODS: 8,911 patients underwent 15,453 oral ovulation induction-IUI (OI-IUI) cycles from 2004-2018. Primary exposure: Medication (clomiphene citrate (CC) versus letrozole (LTZ)) and dose. Primary outcome: singleton/multiple clinical pregnancy rate (CPR). Statistical associations were determined using chi square analysis and multivariable logistic regression models. Age, BMI, AMH, baseline FSH and AFC were considered as clinically relevant covariates. Generalized estimating equations were used to account for multiple cycles in the same patient. To isolate medication effect, those couples with total motile sperm counts <5 million were excluded from analysis. Cycles using gonadotropins were excluded.

RESULTS: When considering the overall cohort, clinical pregnancy rates were comparable between patients who received CC and LTZ (18.1% CC vs 18.7% LTZ, p=0.580). LTZ was associated with a decreased likelihood of multiple pregnancy compared to CC among those with a clinical IUP (20.3% CC vs 12.5% LTZ p=0.001). Increasing doses of CC or LTZ were not associated with an increased chance of pregnancy or risk of multiple pregnancy.

In ovulatory women (11,449 cycles), LTZ use was associated a similar CPR (17.2% CC vs 15.5% LTZ, p=0.168) and a similar multiple pregnancy rate (22.0% CC vs 19.2% LTZ, p=0.423) when compared to CC. Increased CC dosing from 50 to 100 mg decreased the chance of clinical pregnancy (CC50 (18.2%) vs CC100 (16.3%), p=0.014) while increasing the chance of multiple pregnancy (CC50 (19.8%) vs CC100 (25.7%), p=0.004). Increased LTZ dosing above 2.5 mg did not increase the chance of IUP (p=0.354) but an increase from 2.5 to 5 mg did increase the chance of multiple pregnancy (LTZ 2.5 (7.7%) vs LTZ22 (8.8%), p=0.040). In women with ovulatory dysfunction (4,004 cycles), LTZ was associated with a similar CPR compared to CC (22.8% LTZ vs 21.0% CC, p=0.271) with a significantly decreased risk of multiple pregnancy (6.5% LTZ vs 15.6% CC, p=0.002). Increasing dose was not associated with increased multiples for either CC or LTZ.

CONCLUSIONS: To maximize clinical pregnancy rates while minimizing the chance of multiples in CC-IUI cycles, medication and dose should be chosen carefully. LTZ vs CC had similar pregnancy rates in the overall population. In ovulatory women, consideration should be given to starting CC at 50mg, as higher doses were associated with an increased risk of multiple

---

<table>
<thead>
<tr>
<th>Ovarian stimulation</th>
<th>r-FSH (n=107)</th>
<th>r-FSH+m-LH (n=148)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total gonadotropin dose(IU)</td>
<td>1498+/-386</td>
<td>2408+/-701</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total FSH dose(IU)</td>
<td>1498+/-386</td>
<td>2005+/-526</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total LH dose(IU)</td>
<td>-</td>
<td>403+/+276</td>
<td></td>
</tr>
<tr>
<td>Duration of stimulation(days)</td>
<td>8.5+/-1.1</td>
<td>9.1+/+1.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LH on day of antagonist(IUL)</td>
<td>4.1+/+4.6</td>
<td>2.7+/+2.9</td>
<td>0.005</td>
</tr>
<tr>
<td>E2 on day of antagonist(pg/mL)</td>
<td>807.8+/412.3</td>
<td>723.8+/483.7</td>
<td>0.148</td>
</tr>
<tr>
<td>LH on day of trigger(IUL)</td>
<td>3.1+/+2.5</td>
<td>2.1+/+1.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E2 on day of trigger(pg/mL)</td>
<td>2901.6+/1516.9</td>
<td>2449.1+/1406.0</td>
<td>0.017</td>
</tr>
<tr>
<td>No. of oocytes</td>
<td>18.2+/+8.0</td>
<td>17.4+/+8.5</td>
<td>0.464</td>
</tr>
<tr>
<td>No. of metaphase II</td>
<td>15.7+/+8.1</td>
<td>14.3+/+8.2</td>
<td>0.176</td>
</tr>
<tr>
<td>Blastocyst formation rate(%)</td>
<td>57.7+/+31.7</td>
<td>62.6+/+54.8</td>
<td>0.419</td>
</tr>
<tr>
<td>No. of transferred embryos</td>
<td>2.0+/+0.5</td>
<td>2.1+/+0.5</td>
<td>0.836</td>
</tr>
<tr>
<td>No. of cryopreserved embryos</td>
<td>6.2+/+3.8</td>
<td>6.4+/+3.9</td>
<td>0.761</td>
</tr>
<tr>
<td>Ovarian hyperstimulation(%)</td>
<td>10 (9)</td>
<td>12 (8)</td>
<td>0.730</td>
</tr>
<tr>
<td>Pregnancy rate per ET(%)</td>
<td>48/52(59)</td>
<td>65/96(68)</td>
<td>0.209</td>
</tr>
<tr>
<td>Live birth rate per ET(%)</td>
<td>27/82(33)</td>
<td>45/96(47)</td>
<td>0.715</td>
</tr>
<tr>
<td>Cumulative live birth rate(%)</td>
<td>63/107(59)</td>
<td>91/148(61)</td>
<td>0.585</td>
</tr>
</tbody>
</table>
gestation without improvement in CPR. Patients with ovulatory dysfunction may benefit from lower multiple pregnancies with LTZ utilization.

P-293 Tuesday, October 15, 2019 6:30 AM

DO INFERTILE PATIENTS WHO TEST POSITIVE FOR GROWTH DIFFERENTIATION FACTOR 9 (GDF9) POLYMORPHISM C447T EXHIBIT AN ALTERED RESPONSE TO CONTROLLED OVARIAN STIMULATION (COH)? Jenna Friedenthal, MD.a Dmitry Goukou, MA.a Joseph A. Lee, BA.b Teresa A. Caccinone, MS, CGC.b Alan B. Coppersman, MD.b "Icahn School of Medicine at Mount Sinai, New York, NY; "Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: GDF9 is a protein coding gene responsible for promoting granulosa cell proliferation while inhibiting FSH-induced steroidogenesis [1]. GDF9 also potentiates the final stages of follicle growth and supports metabolic cascades such as sterol biosynthesis. Single nucleotide polymorphisms (SNPs) in GDF9 are associated with an increased risk for primary ovarian insufficiency and diminished ovarian reserve [2]. Fortilome®, a multi-togene panel test, reports GDF9 SNPs as part of a multigene targeted sequencing panel and is often suggested in poor responding patients. We sought to evaluate ovarian stimulation outcomes in patients who tested positive for the GDF9 SNP C447T.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The study included patients at a single academic center who underwent COH and Fortilome® testing from 2016 to 2018. Cases included patients who screened positive for the GDF9 SNP C447T. Control cases included patients who screened negative. Patients testing positive for a Fragile X premutation or abnormal karyotype were excluded. Our primary outcome was number of oocytes retrieved. Secondary outcomes were number of metaphase II (MII) oocytes, number of fertilized oocytes, blastulation rate, and euploidy. Data were analyzed using student’s t-test, with p < 0.05 considered significant.

RESULTS: A total of 96 patients who underwent 214 COH cycles and Fortilome® testing were assessed in the study. A total of 80 patients (170 cycles) tested positive for the GDF9 SNP C447T, while 16 patients (44 cycles) tested negative for the GDF9 SNP. Although there was a difference in BMI between groups (23.59 vs 21.42, P = 0.0005), no differences in age or AMH were observed. We demonstrated no differences in the total number of oocytes retrieved or MII oocytes. Last, there was no difference in the fertilization, blastulation, or embryo euploidy between groups.

CONCLUSIONS: A majority of patients who experienced poor response to IVF stimulation tested positive for the GDF9 SNP C447T. However, the presence of the SNP did not affect oocyte retrieval count or MII maturation. Thus, although the GDF9 gene may be important in follicular development and maturation, detection of SNP C447T is not associated with worse outcomes during COH. Patients can be reassured that testing positive for the SNP C447T does not translate to impaired ovarian stimulation and oocyte retrieval outcomes.

<table>
<thead>
<tr>
<th>GDF SNP positive</th>
<th>GDF SNP negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Oocytes retrieved</td>
<td>12.70</td>
</tr>
<tr>
<td>MII oocytes</td>
<td>9.27</td>
</tr>
<tr>
<td>Fertilized oocytes</td>
<td>6.86</td>
</tr>
<tr>
<td>Blastocysts</td>
<td>4.57</td>
</tr>
<tr>
<td>Blastulation rate (%)</td>
<td>60.82</td>
</tr>
<tr>
<td>Euploidy (%)</td>
<td>45.97</td>
</tr>
</tbody>
</table>

REFERENCES

SUPPORT: None.

P-294 Tuesday, October 15, 2019 6:30 AM

OCYOTE RECRUITMENT OF PATIENTS SUBMITTED TO THE NEW OVARIAN STIMULATION REGIMEN USING PROGESTIN TO BLOCK THE LH SURGE. - Michelli Suemi Tanada, BSc, Elen Souto Vieira Porto, BSc, Ivan Henrique Yoshida, BSc, MSc, Renato de Oliveira, MD, PhD, Emerson Barchi Cordts, MD, MSc, Caio Parente Barbosa, MD, PhD. Instituto Idecia Fertil de Saúde Reprodutiva, Santo André, Brazil.

OBJECTIVE: To evaluate the recruitment and oocyte maturity of a new low cost and easy administration ovarian stimulation regimen, which uses progestin as an alternative to the GnRH analogue.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: It was analyzed 100 patients who underwent Assisted Human Reproduction between June 2018 and January 2019. Of those patients, 50 used the progestin protocol as an alternative to the GnRH analogue, to suppress the premature LH surge during the follicular phase. The other 50 patients used the standard protocol with antagonist. The total number of oocytes retrieved and the classification for maturity and viability were analyzed between the groups. Variables such as age and body mass index (BMI) were considered as well. The qualitative variables were presented by absolute and relative frequency and the quantitative variables by means of a 95% confidence interval, using a normality test of the Shapiro-Wilk data (p < 0.05). The Mann-Whitney test and Chi-square test were used to compare the variables according to the two induction protocols. The Chi-square test was used for the comparative analysis of the BMI. For all analyzes, the level of significance was p < 0.05. The statistical program used was Stata version 11.0.

RESULTS: No statistically significant results were found in relation to the number of oocytes retrieved in the conventional ovarian stimulation cycles with antagonist compared to the cycles using progestin to block the LH surge (283 versus 247, p = 0.54). Similarly, there was no difference in the degree of oocyte maturation (mature 79.72% / 77.43%, immature 13.52% / 15.68%), altered, degenerated or oocytes with ruptured zona pellucida (2.54% / 2.19%, 1.13% / 1.88%, 3.10% / 2.82%, p = 0.88). The body mass index (BMI) was also evaluated without significant differences after analysis (p = 0.87). When separated by age (up to 37 years and ≥ 38 years), the groups also did not present statistically significant differences in any of the analyzed variables.

CONCLUSIONS: The use of progestin in the induction protocols to block the LH surge seems to be an option in the substitution of GnRH analogues, since it presented similar results, more accessible cost and a route of administration more comfortable for the patients.

P-295 Tuesday, October 15, 2019 6:30 AM

COMPARISON OF TRADITIONAL AND STEP UP PROTOCOLS WITH LETROZOLE. Shelin Tsai, MD, Stephanie Smeltzer, MD, Thomas M. Price, MD. Division of Reproductive Endocrinology and Infertility, Duke University Medical Center, Durham, NC.

OBJECTIVE: To compare time to ovulation between traditional and step up protocols with letrozole.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Patients were identified through Duke Fertility Center’s Intrauterine Insemination database, which stores information about each ovulation induction cycle including patient’s age, body mass index (BMI), last menstrual period, trigger date, and outcomes. The electronic medical record was used to obtain missing data points. Patients requiring induction with letrozole for ovulation dysfunction between January 1, 2010 and March 3, 2018 were included. Patients were excluded if they received gonadotropins or if they switched to a different ovulation induction agent. In the traditional protocol, patients had an increase in letrozole dose following spontaneous menstruation or medroxyprogesterone-one-induced withdrawal bleed if there were no follicles at 16mm or greater on ultrasound by cycle day 20. Patients were excluded if they delayed starting a cycle with the increased dose. In the step up protocol, patients had an immediate increase in letrozole dose by cycle day 20 at the latest if no developing follicle was detected. A separate cohort of those who underwent a step up protocol with clomiphene was also included for comparison. The primary outcome was time to ovulation, defined as the number of days between the last menstrual period and the detection of a follicle at 16mm or greater on ultrasound. A secondary outcome was clinical pregnancy. Student’s t-test or Wilcoxon rank sum tests were used to compare variables. Statistical analyses were conducted using R version 3.5.1 (Vienna, Austria).

FERTILITY & STERILITY®
RESULTS: 49 patients were included: 21 in the traditional letrozole cohort, 15 in the step up letrozole cohort, and 13 in the step up clomiphene cohort. All cycles with traditional protocols occurred before January 2014 while step up protocols occurred after. The median age and IQR of patients in the traditional letrozole protocol cohort was 33 (31-35) vs. 28 (27-30) in the step up letrozole protocol, and the median BMI was 29 (25-36) vs. 34 (27-39). The time to ovulation was twice as long at 50.6 days for patients who underwent traditional letrozole protocol compared to the 21.9 days for those who underwent the step up letrozole protocol (p<0.0001). There was no difference in clinical pregnancy rate per cycle (10% [2/20] vs. 0% [0/14], p=0.16). In comparing letrozole step up cycles with clomiphene step up cycles, there was no difference in time to ovulation (21.9 vs. 21.1 days, p=0.47) or clinical pregnancy rate per cycle (0% [0/14] vs. 16.7% [2/12], p=0.17). No significant side effects were reported in any group.

CONCLUSIONS: The step up letrozole protocol allows for faster time to ovulation in initially nonresponsive patients with ovulatory dysfunction. Similar to findings seen with clomiphene, it is not essential to have menstruation prior to increasing letrozole doses for ovulation induction.

P-296 Tuesday, October 15, 2019 6:30 AM
CORIFOLLITROPIN ALFA IN THE ULTRASHORT GONADOTROPIN-RELEASING HORMONE ANTAGONIST (GnRHA) PROTOCOL: A NOVEL PATIENT-FRIENDLY ALTERNATIVE. Tzu-Ning Yu, MD, MS,a Yung-Liang Liu, MD,b Chi-Huang Chen, MD, PhD,c Chi-Ruey Tzeng, MD, MPHd. aTaipei Medical University Hospital, Taipei, Taiwan; bTri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan.

OBJECTIVE: To compare the outcomes of in vitro fertilization (IVF) and fresh embryo transfer (ET) using corifollitropin alfa in ultrashort GnRHa protocol and GnRH antagonist protocol.

DESIGN: A retrospective observational analysis conducted in a university-affiliated infertility center.

MATERIALS AND METHODS: A total of 245 unselected patients undergoing IVF/ET were enrolled between January 1 and December 31, 2017, including 135 treated with ultrashort GnRHa protocol and 110 treated with antagonist protocol. The primary outcomes were the duration of stimulation, dosage of additional gonadotropin for ovarian hyper stimulation, number of total injections and outpatient department (OPD) visits before ovulation triggering, ovarian response, and ovarian hyper stimulation syndrome (OHSS) rate. The secondary outcomes were rates of pregnancy, clinical pregnancy, and live birth.

RESULTS: Patients treated with ultrashort GnRHa required less additional gonadotropin, fewer total injections, but had better ovarian responses, including more oocytes retrieved, more metaphase II oocytes, and more blastocysts than those treated with antagonist did. A premature LH surge occurred only in six patients treated with antagonist protocol. The OHSS rate was similar in the two groups. The rates of pregnancy (37.0% vs. 43.6%), clinical pregnancy (25.2% vs. 34.6%), and live birth (19.3% vs. 30.0%) did not differ significantly between the two groups.

CONCLUSIONS: In unselected patients using corifollitropin alfa, the ultrashort GnRHa protocol needed low dose of additional gonadotropin and fewer injections but produced similar pregnancy outcomes than antagonist protocol did, suggesting that the ultrashort GnRHa protocol could be an alternative.

P-297 Tuesday, October 15, 2019 6:30 AM
FLEXIBLE VERSUS FIXED GONADOTROPIN RELEASING HORMONE ANTAGONIST (GnRH-ANT) STARTING DAY DURING CONTROLLED OVARIAN HYPERSTIMULATION FOR IN VITRO FERTILIZATION (IVF): A SYSTEMATIC REVIEW & META-ANALYSIS. Clara Q. Wu, M.D., Cheng Wei Xiao, M.D., Paul Claman, M.D., Doron Shumorgun, M.D., Ottawa Fertility Centre, Ottawa, ON, Canada.

OBJECTIVE: To obtain the up-to-date evidence on fertility outcomes when comparing flexible and fixed start gonadotropin releasing hormone antagonist (GnRH-ant) protocols during controlled ovarian hyperstimulation for In Vitro Fertilization (IVF).

DESIGN: This study is a systematic review and meta-analysis of published randomized controlled trials (RCT). A systematic search of the literature, using keywords GnRH antagonist, fixed, flexible, pregnancy, and live birth, was performed across the Cochrane Library, EMBASE, and MEDLINE databases from 1996 to January 2019.

MATERIALS AND METHODS: Studies were selected for inclusion in the systematic review and meta-analysis if they were 1) RCTs, 2) that compared flexible versus fixed start GnRH antagonist protocols, 3) reported IVF outcomes, 4) on patients who were normo-responders. Data involving patient characteristics, IVF protocols, and fertility outcomes were extracted independently by two reviewers. Collected variables include IVF protocol used; total gonadotropin dosage; median estradiol level on day of GnRH-ant start; number of oocytes retrieved; fertilization rate; number of good quality embryos; clinical pregnancy rates; premature LH rises and cycle cancellation. Study quality assessment was performed using the Cochrane Collaboration’s tool for assessing risk of bias in randomized trials.

RESULTS: Six hundred and thirty-eight articles were identified through database searches and five full text RCTs (701 IVF cycles) were included in our analysis. There is no statistically significant difference in clinical pregnancy rates between flexible and fixed GnRH-ant protocols (OR = 0.74, 95% CI = 0.53-1.03, p = 0.07) with a trend towards higher clinical pregnancy rate in the fixed GnRH-ant protocol. There is no significant difference in total oocytes retrieved between the flexible and fixed GnRH-ant protocols (Pooled mean difference = 1.02, 95% CI = -0.09-2.12, p = 0.07). There is a trend towards lower total gonadotropin dosage used in the flexible GnRH antagonist protocol (Pooled mean difference = -124.18, 95% CI = -325.36-76.99, p = 0.23); however, the difference is not statistically significant. There is no difference in the incidence of premature LH surge between the two protocols (OR = 1.11, 95% CI = 0.56-2.18, p = 0.76).

CONCLUSIONS: There is sufficient evidence to demonstrate whether flexible and fixed GnRH-ant protocols yield different IVF outcomes.
OBJECTIVE: Poor ovarian response (POR) is an increasingly common indication for IVF, accounting for 31% of cycles in the USA in 2016, compared to 12% in 2005. These patients are especially challenging as POR results in higher rate of cycle cancellation, lower number of embryos available for transfer, and overall lower pregnancy rates. Autologous platelet-rich plasma (PRP) is rich in growth factors and cytokines and has been used as an agent that induces tissue regeneration. PRP also promotes follicle development in vitro and two studies reported a total of 7 cases of POR, where PRP was utilized. The aim of the current study was to investigate whether intraovarian injection of autologous PRP is associated with improved ovarian reserve and IVF outcomes in patients with POR.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Reproductive age women diagnosed with POR based on Ovarian Reserve criteria and with a history of at least one failed IVF cycle were recruited for the study between December 15, 2018, and April 15, 2019. Antral follicle count (AFC), serum anti-mullerian hormone (AMH), and early follicular phase serum follicle stimulating hormone (FSH) levels were determined at baseline. Autologous blood obtained from peripheral vein was used to prepare PRP following standard protocols. PRP injection was performed under sedation anestheisa, using a 35 cm 17 G needle under transvaginal ultrasound guidance. On the 2-4th days of the first three menstrual cycles following the procedure, AFC, AMH, and FSH levels were re-assessed. Patients with at least one antral follicle were started on ovarian stimulation for IVF-ICSI, followed by embryo banking at cleavage stage for PGT-A. Markers of ovarian reserve (AFC, FSH, AMH) and IVF outcome parameters (number of MII oocytes, 2PN and cleavage stage embryos) were followed and compared to previous cycle.

RESULTS: At the time of this submission, a total of 152 patients (mean age ± SD: 39.3 ± 5.6) with the diagnosis of POR were included in the study. The PRP treatment resulted in higher AFC (6.2 ± 2.8 vs 2.6 ± 1.6; p<0.001) and AMH (0.54 ± 0.30 vs 0.41 ± 0.28; p=0.01, respectively), and lower FSH (17.5 ± 4.7 vs 20.3 ± 5.4; p<0.001) levels. Number of MII oocytes, 2PN and cleavage stage embryos were also increased following the PRP procedure (4.2 ± 2.9 vs 2.5 ± 1.9; 3.8 ± 2.6 vs 2.2 ± 1.7, 3.4 ± 1.8 vs 2.0 ± 1.6, respectively; p<0.01 for all).

In 118 patients (12.5%), no changes were observed in AFC after the PRP procedure. Another 43 patients (25.3%) failed IVF due to stimulation failure, another 43 patients (25.3%) failed IVF due to stimulation failure, and 48 patients (21.7%) did not achieve a pregnancy

CONCLUSIONS: Intraovarian injection of autologous PRP might be an alternative experimental treatment option for women with poor ovarian response to stimulation. Whether this treatment is clinically effective will need to be further investigated using a prospective randomized clinical trial design.

P-300  Tuesday, October 15, 2019 6:30 AM  
TWELVE PREGNANCIES AFTER SURGICAL ACTIVATION OF FOLLICLES IN POOR RESPONDER PATIENTS. Atsushi Tanaka, M.D., Ph.D.; Motoi Nagayoshi, M.D.; Izumi Tanaka, Ph.B.; Takashi Yamaguchi, M.D., Ph.D.; Motoharu Ohno, M.D.; Masayuki Shimada, Ph.D.; Kazuhiro Kawamura, M.D., Ph.D.; Saint Vincent Hospital, Houston, TX; Kita-Toyo University, Japan; 4Graduate School of Biosphere Sciences, Higashi-Hiroshima, Japan; 5International University Health and Welfare School of Medicine, Narita, Japan.

OBJECTIVE: The success of IVF treatment in poor responder (POR) patients is low due to decreases in the number of retrieved oocytes. Recent studies demonstrated that the disruption of Hippo signaling in ovarian follicles by surgical fragmentation of ovaries induced growth of secondary follicles in mice and human. The aim of this study is to improve the clinical outcome of IVF treatment in POR patients through induction of secondary follicle growth to increase viable embryos by surgical activation.

DESIGN: A prospective non-randomized control study using historical control.

MATERIALS AND METHODS: Under ethical approval (Clinical trial registration# UMIN000028031), 66 patients who received written informed consent and met the Bologna criteria for POR were enrolled from May 2016 to October 2018. We dissected partial ovarian cortices from one side of ovary under laparoscopic surgery. The ovarian cortices were fragmented into 1-2 mm cubes followed by auto-transplantation beneath the serosa of Fallopian tubes and between cortex and medulla in ovaries. After the surgery, patients received ovarian stimulation under short protocol while maintaining normal LH levels (<10 mU/ml) until oocyte retrieval. The primary endpoint is increase the number of growing follicles after the surgery under trans-vaginal ultrasound monitoring, whereas we evaluate the number of retrieved oocytes, fertilization rate, cleavage rate, clinical pregnancy rate, and miscarriage rate as secondary endpoints.

RESULTS: The median age of enrolled patients was 43.0 [36-45]. Clinical outcome was shown in Table 1.
**TABLE 1. Clinical outcome of laparoscopic ovarian surgical activation**

<table>
<thead>
<tr>
<th>Patients (n=60)</th>
<th>Growing follicle number within four months until operation* (mean ± SD)</th>
<th>Number of retrieved oocytes (mean ± SD)</th>
<th>Fertilization rate (% n)</th>
<th>D3 8cell stage rate (% n)</th>
<th>Clinical pregnancy rate (% n)</th>
<th>Miscarriage rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-op (203 cycles)</td>
<td>1.34±1.03*a</td>
<td>1.13±0.98*b</td>
<td>57.7 (79/137)</td>
<td>25.6* (33/129)</td>
<td>0*a (0/23)</td>
<td>-</td>
</tr>
<tr>
<td>Post-op (216 cycles)</td>
<td>2.81±2.02*a</td>
<td>1.53±1.39*b</td>
<td>68.2 (163/239)</td>
<td>40.6* (95/234)</td>
<td>17.1*b (127/0)</td>
<td>58.3% (7/12)</td>
</tr>
</tbody>
</table>

(a-a’, b-b’: p < 0.05, t-test, c-c’, d-d’: p < 0.05, Chi-squared test)

*(a) including cycles without operation due to small number

**CONCLUSIONS:** Our procedure significantly increased the number of growing follicles with increase in viable embryos, resulting in twelve successful clinical pregnancies and five babies. Also, it might improve embryo quality based on disruption of Hippo signaling pathway.

**REFERENCES**


**P-301** Tuesday, October 15, 2019 6:30 AM

**APPLICATION OF CONTROLLED OVARIAN HYPER-STIMULATION WITH AGONIST-ANTAGONIST PROTOCOL IN POSEIDON GROUP 3 AND GROUP 4 PATIENTS WITH DIMINISHED OVARIAN RESERVE.** Rui Yang, Doctor, a Xiaoguo Du, Master, a Liuxie Chen, M.D, b Xinna Chen, Professor. aPeking University Third Hospital, Beijing, China; bAffiliation not provided.

**OBJECTIVE:** By comparing standard antagonist regimen and agonist-antagonist protocol (AAP regimen), a combination of a microdose flare-up GnRH agonist with a GnRH agonist in Poseidon group 3 and group 4 patients with diminished ovarian reserve, this article aims to study if AAP regimen could improve the clinical outcomes in low prognosis patients.

**DESIGN:** This is a retrospective study.

**MATERIALS AND METHODS:** The clinical data of 646 cycles of prospective poor ovarian response POR patients (POSEIDON group 3 and 4) who received in vitro fertilization and embryo transfer (IVF-ET) in Peking University Third Hospital reproductive medical center from January 2016 to May 2018 were retrospectively analyzed. The total number of APP cycle was 323, and the control group was selected from the database with 1:1 matching of prospective low prognosis patients (POSEIDON group 3 and group 4) with similar age and approaching date of oocyte retrieval. Patients’ general information, ovarian hyperstimulation indicators and clinical outcomes were studied.

**RESULTS:** AAP group had fewer antral follicle count (3.04±2.05 vs. 3.84±2.17, p < 0.05) and similar AMH level (0.62±0.64 and 0.63±0.49, p > 0.05) compared with control group. AAP group had shorter (0.84±2.59 vs. 10.31±2.23, p = 0.015) and lower dosage (2754.18±973.37 vs. 3246.7±1044.20, p < 0.05) of Gn using, and had similar number of oocytes obtained compared with control group (4.06±2.89 vs. 4.16±2.65, p = 0.649). Under the same proportion of fertilization schemes (routine or ICSI methods), AAP group had higher fertilization rate (74.1% vs. 69.1%, p = 0.004) and good quality embryo rate (62.6% vs. 56.9%, p = 0.014), and ultimately had higher embryo implantation rate (22.3% vs. 15.8%, p = 0.020) and cumulative clinical pregnancy rate (32.5% vs. 22.9%, p = 0.018).

**CONCLUSIONS:** For POSEIDON patients with low prognosis and poor ovarian reserve, controlled ovarian hyperstimulation with agonist-antagonist protocol had better clinical outcomes compared with conventional antagonist regimen.

**SUPPORT:** None.

**P-302** Tuesday, October 15, 2019 6:30 AM

**CONVENTIONAL PROTOCOL VERSUS MINIMAL OVARIAN STIMULATION IN PATIENTS WITH POOR PROPOSED PROGNOSIS ACCORDING TO POSEIDON CRITERIA.** Mauro Cozzolino, M.D, a Gustavo N, Cecchino, M.D, b Nicolas Garrido, PhD. aFundación IVI, Valencia, Spain; bIVIRMA Madrid, Madrid, Spain; cIVI Foundation, IIS La Fe, Valencia, IIS, Spain.

**OBJECTIVE:** to analyze whether minimal ovarian stimulation (MOS) is as effective as conventional controlled ovarian stimulation (COS) for patients belonging to different groups according to the Poseidon criteria.

**DESIGN:** Observational retrospective multicenter cohort.

**MATERIALS AND METHODS:** Considering that advanced reproductive age is the main factor affecting reproductive outcomes, we evaluated women from the Poseidon’s group 2 and 4 (1,2) undergoing in vitro fertilization (IVF) with either MOS or conventional COS between January 2014 and October 2018. Exclusion criteria were as follows: irregular menstrual cycles, oocyte donation, severe male factor, and contraindication to pregnancy or COS. While patients from the conventional stimulation group received a GnRH antagonist protocol using high doses of gonadotropins, the MOS group received usual doses of clomiphene citrate along with low doses of gonadotropins, as previously described (3). The continuous variables were reported as mean ± standard deviation and compared using the t-Student test. Fisher’s Exact test and Odds Ratio were used in order to compare reproductive outcomes, as appropriate. Statistical significance was set at p < 0.05.

**RESULTS:** A total of 2,944 patients underwent 4,450 embryo transfers (MOS = 737 and COS = 3,713). Baseline characteristics of patients were similar between groups. While comparing MOS vs. conventional COS in Poseidon’s group 2, there were no significant differences in biochemical pregnancy (OR 1.27, CI 0.96-1.66; p = 0.079), clinical pregnancy (OR 1.24, CI 0.94-1.63; p = 0.123), ongoing pregnancy (OR 1.1, CI 0.83-1.46; p = 0.531), and live birth rates (OR 0.98, CI 0.73-1.33; p = 0.941). Similarly, no differences were found regarding Poseidon’s group 4, as shown by comparable biochemical pregnancy (OR 1.2, CI 0.98-1.48; p = 0.079), clinical pregnancy (OR 1.19, CI 0.96-1.48; p = 0.094), ongoing pregnancy (OR 1.2, CI 0.98-1.52; p = 0.117), and live birth rates (OR 1.14, CI 0.95-1.45; p = 0.282). Although the number of embryos obtained was statistically higher for patients receiving conventional COS in Poseidon’s group 4, also number of embryos not viable was higher.

**CONCLUSIONS:** MOS is a good alternative when conventional COS has failed or even as a first-line treatment for patients belonging to the Poseidon groups 2 and 4. Randomized controlled trials are needed before incorporating this strategy in daily clinical practice. Future studies should investigate potential benefits of minimal and mild-stimulation protocols, such as improved neonatal outcomes and lower maternal complication rates.

**P-303** Tuesday, October 15, 2019 6:30 AM

**THE EFFECTIVENESS OF TRANSDERMAL TESTOSTERONE GEL 1% (ANDROGEL) FOR POOR RESPONDERS UNDERGOING IN VITRO FERTILIZATION.** Anjali Chaudhary, MD DNB, CONSULTANT AAROGYA HOSPITAL, Delhi, India.

**OBJECTIVE:** To investigate the effectiveness of treatment with transdermal testosterone gel (TTG) 1%(androgel) before ovarian stimulation (COS) using GnRH antagonist in low responders undergoing IVF/intracytoplasmic sperm injection (ICSII).
PREIMPLANTATION GENETIC TESTING

P-305 Tuesday, October 15, 2019 6:30 AM

IMPACT OF PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) ON GESTATIONAL CARRIER (GC) CYCLES IN THE UNITED STATES. Reeva B. Makhjani, MD, a Madeline Coulter, BA, a Jeffrey Thorne, MD, a Chantal Bartels, MD, a John Nulsen, MD, a Lawrence Engmann, MD, a Claudio Benadiva, MD, a Grow R. Daniel, MD, a Center for Assisted Reproductive Services, University of Connecticut School of Medicine, Farmington, CT. bCenter for Advanced Reproductive Services, University of Connecticut School of Medicine, Farmington, CT.

OBJECTIVE: We analyzed the SART registry to determine the impact of PGT-A on GC in vitro fertilization (IVF) cycles in the United States. DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: SART data was analyzed from 4,470 autologous IVF cycles that used a GC between 2014-2016. Cycles were excluded if donor oocytes were used, multicellular embryos (5) was transferred or embryo transfer was not attempted. The cycles were separated into 4 groups defined by use of PGT-A and number of embryos transferred as follows: (A) PGT and single embryo transfer (SET); (B) PGT and multiple embryo transfer (MET); (C) no PGT and SET (D) no PGT and MET. The primary outcome was live birth rate (LBR). Secondary outcomes were clinical pregnancy rate (CPR), clinical loss rate (CLR) and multiple pregnancy rate (MPR). One-way ANOVA or Student’s t test and X2 tests were used to compare continuous and categorical variables, respectively. Multivariate logistical regression was done to control for potential confounders. A p-value of 0.05 was considered statistically significant.

RESULTS: Groups significantly differed in terms of intended parent (IP) age, GC age, IP BMI, smoking status and parity. In MET groups, significantly fewer embryos were transferred when PGT was used (Group B: 2.0 ±0.2 v. Group D: 2.1 ±0.4, p<0.01). When comparing groups by number of embryos transferred (A to C, B to D), LBR and CPR were significantly higher with PGT. MPR was significantly lower with SET. After controlling for potential confounders, a significant difference in LBR remained among groups (p<0.01). Of potential confounders, only IP age was significantly predictive of live birth (OR 0.9574, 95% CI 0.9453 - 0.9697, p<0.01).

CONCLUSIONS: This study shows that euploid SET does not compromise LBR and significantly reduces MPR. It highlights an opportunity to increase GC safety as well as widen access to this already restricted service. SUPPORT: None.
**P-306 Tuesday, October 15, 2019 6:30 AM**

**NGS EUPLOID EMBRYOS HAVE HIGHER DELIVERY RATES THAN THOSE DIAGNOSED AS EUPLOID BY ACGH/SNP.** Caroline McCaffrey, Ph.D., David H. McCulloh, Ph.D., Xinjian He, MS, Patty Ann Labella, BS, Melicia Clarke-Williams, BA, Mary Elizabeth Fino, MD, James A. Grifo, MD, PhD, NYU Langone Fertility Center, New York, NY.

**OBJECTIVE:** To review outcomes of all STEET procedures based on PGT-A platform used to determine Ploidy status.

**DESIGN:** Retrospective review of all STEET procedures over an 8 year period at a single center.

**MATERIALS AND METHODS:** More than 3200 STEET procedures performed over an 8 year period (2011 to 2018) at a single center were reviewed based on the PGT-A platform (NGS, aCGH or SNP) utilized. Our main outcome measures were: Implantation Rate (IR), Clinical Preg rate (FH) and Live Birth (LB) rate. Only embryos reported as euploid were included in the analysis- embryos reported as mosaic or those not yielding a result were omitted. Statistical significance was determined using contingency X^2 with 1 degree of freedom.

**RESULTS:** TABLE 1. Comparison of STEET outcomes depending on PGT-A Platform

<table>
<thead>
<tr>
<th>NGS1</th>
<th>aCGH + SNP2</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age at Freeze</td>
<td>36.60±4.34</td>
<td>36.54±4.60</td>
</tr>
<tr>
<td>Implantation rate (sacs/embryo)</td>
<td>70.1% (1330/1897)</td>
<td>62.4% (858/1375)</td>
</tr>
<tr>
<td>Clinical Preg rate (FH/embryo)</td>
<td>66.7% (266/1897)</td>
<td>55.9% (768/1375)</td>
</tr>
<tr>
<td>SAB/ Cln Preg</td>
<td>10.3% (87/845)</td>
<td>12.6% (97/770)</td>
</tr>
<tr>
<td>Live Births (Live born/embryo)</td>
<td>61.7% (750/1216)</td>
<td>53.2% (657/1235)</td>
</tr>
</tbody>
</table>

1 Only included FETs of embryos with NGS performed in the Fresh IVF cycle.
2 SNP cases were included with aCGH due to low number
3 Live Birth rate calculated through 2017 only (results for 2018 cycles pending)

STEET following PGT-A via NGS resulted in a significantly higher IR compared to aCGH /SNP combined (70.1% vs 62.4%). Similarly, ongoing Pregnancy rates and LB rates were significantly improved when NGS was utilized vs aCGH or SNP. SAB rates were not significantly different between platforms but all methods reduced SAB rates compared to age matched controls without PGS (18% ) (Ref 1). CONCLUSIONS: STEET results in high IR, high clinical pregnancy rates and high LB rates across all age groups. However, in advances in PGT-A platforms we can continue to improve outcomes and increase safety of ART by maximizing the potential of every ET procedure. With continuing development of PGT-A platforms and interpretation methods used to determine ploidy we can further improve outcomes and safety by transferring a single embryo with the highest implantation potential every time.

**REFERENCE**
SUPPORT: None.

**P-307 Tuesday, October 15, 2019 6:30 AM**

**PREIMPLANTATION GENETIC TESTING ALTERS THE SEX RATIO: AN ANALYSIS OF 44,939 CYCLES FROM THE SOCIETY FOR ASSISTED REPRODUCTIVE TECHNOLOGY DATABASE.** Kathryn L. Shaia, MD, MHA,a Benjamin S. Harris, MD, MPH,b Tracy Truong, MS,c Carl F. Pieper, DrPH,c Anne Z. Steiner, MD, MPHb. aDuke Center for Applied Therapeutics, Department of Surgery, Durham, NC, bDuke University Medical Center, Durham, NC; cDepartment of Biostatistics & Bioinformatics, Duke University Medical Center, Durham, NC.

**OBJECTIVE:** Preimplantation genetic testing (PGT) is commonly used to assess for aneuploidy. Consequently, chromosomal sex is revealed, allowing couples to select the offspring’s sex when multiple euploid embryos are available for transfer. The sex ratio (SER), defined as the ratio of male to female births in the population normalized to 100, is typically standard at 105. We sought to determine the extent to which the use of PGT shifts the SER in vitro fertilization (IVF) cycles and whether this trend differs by region or parity.

**DESIGN:** Society for Assisted Reproductive Technologies (SART) database analysis.

**MATERIALS AND METHODS:** National IVF data from 2014-2016 was requested from SART including fresh and frozen transfer cycles. Women who had a singleton live birth following a fresh or frozen autologous embryo transfer of a 1) PGT blastocyst, 2) non-PGT blastocyst, or 3) non-PGT cleavage stage embryo were included. The SER for each group was calculated and compared using chi-square analysis. Subsequently, modified Poisson regression was used to model the relative risk (RR) of having a male infant compared to a female infant among PGT embryo transfers versus both non-PGT cleavage and blastocyst transfers adjusting for age, BMI, smoking status, race, parity, number of oocytes retrieved, and clinic regions. Lastly, we investigated whether the risk of having a male infant differed by parity (parous or nulliparous) or clinic region by testing the significance of the interaction term. P<0.05 was considered statistically significant.

**RESULTS:** The SER was 110 among PGT offspring compared to 106 among non-PGT blastocyst offspring (p = 0.01) and to 99 among cleavage offspring (p < 0.0001). After adjusting for covariates, the risk of having a male infant was 4% higher among PGT cycles compared to non-PGT cleavage cycles (RR 1.04; 95% Confidence Interval (CI): 1.02, 1.07). The risk was 2% higher among PGT cycles compared to non-PGT blastocyst cycles (RR 1.02; 95% CI: 1.01, 1.04). The association between PGT and infant gender did not differ by parity. The RR point estimate favored boys in all regions compared to girls.

**REFERENCES**
SUPPORT: None.

**P-308 Tuesday, October 15, 2019 6:30 AM**

**BLASTOCYST CONVERSION RATE AND PLOIDY IN TRANLOCATION CARRIERS.** Iris Insogna, MD, MBE, Andrea Lanes, PhD, Ann M. Thomas, PhD, Lori J. Dobson, MS, LCOG, Elizabeth S. Ginsburg, MD, Catherine Racowsky, PhD, Elena Yanushpolsky, MD, Brigham & Women’s Hospital, Boston, MA.

**OBJECTIVE:** To determine if women intending to undergo in vitro fertilization (IVF) with preimplantation genetic testing for structural rearrangements (PGT-SR) have a poorer rate of blastocyst conversion and an increased risk of aneuploidy compared to patients undergoing IVF with PGT-A (PGT for aneuploidy).

**MATERIALS AND METHODS:** National IVF data from 2014-2016 was requested from SART including fresh and frozen transfer cycles. Women who had a singleton live birth following a fresh or frozen autologous embryo transfer of a 1) PGT blastocyst, 2) non-PGT blastocyst, or 3) non-PGT cleavage stage embryo were included. The SER for each group was calculated and compared using chi-square analysis. Subsequently, modified Poisson regression was used to model the relative risk (RR) of having a male infant compared to a female infant among PGT embryo transfers versus both non-PGT cleavage and blastocyst transfers adjusting for age, BMI, smoking status, race, parity, number of oocytes retrieved, and clinic regions. Lastly, we investigated whether the risk of having a male infant differed by parity (parous or nulliparous) or clinic region by testing the significance of the interaction term. P<0.05 was considered statistically significant.

**RESULTS:** The SER was 110 among PGT offspring compared to 106 among non-PGT blastocyst offspring (p = 0.01) and to 99 among cleavage offspring (p < 0.0001). After adjusting for covariates, the risk of having a male infant was 4% higher among PGT cycles compared to non-PGT cleavage cycles (RR 1.04; 95% CI: 1.02, 1.07). The risk was 2% higher among PGT cycles compared to non-PGT blastocyst cycles (RR 1.02; 95% CI: 1.01, 1.04). The association between PGT and infant gender did not differ by parity. The RR point estimate favored boys in all regions compared to girls.

**REFERENCES**
SUPPORT: None.
**TABLE 1. Comparison of laboratory outcomes and ploidy results following blastocyst biopsy for patients using PGT-A versus PGT-SR**

<table>
<thead>
<tr>
<th>Variable</th>
<th>PGT-A Mean ± SD</th>
<th>PGT-SR Mean ± SD</th>
<th>aRR (95% CI)</th>
<th>Referent: PGT-A</th>
</tr>
</thead>
<tbody>
<tr>
<td>% 2PN/MII</td>
<td>82% ± 18</td>
<td>80% ± 20</td>
<td>1.02 (0.98-1.06)</td>
<td></td>
</tr>
<tr>
<td>% Blastocysts/2PN</td>
<td>66% ± 24</td>
<td>72% ± 22</td>
<td>1.07 (1.01-1.13)</td>
<td></td>
</tr>
<tr>
<td>% D5 Biopsied/Total blastocysts</td>
<td>67% ± 30</td>
<td>69% ± 27</td>
<td>1.08 (1.00-1.18)</td>
<td></td>
</tr>
<tr>
<td>% D6 Biopsied/Total blastocysts</td>
<td>46% ± 33</td>
<td>38% ± 30</td>
<td>0.79 (0.65-0.96)</td>
<td></td>
</tr>
<tr>
<td>% Euploid blastocysts</td>
<td>42% ± 33</td>
<td>29% ± 23</td>
<td>0.86 (0.73-1.00)</td>
<td></td>
</tr>
<tr>
<td>% Blastocysts with no result</td>
<td>4% ± 13</td>
<td>2% ± 5</td>
<td>0.70 (0.39-1.26)</td>
<td></td>
</tr>
</tbody>
</table>

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** Autologous cycles with the intention of pursuing PGT-A or PGT-SR with biopsy on either day 5 or 6 were identified from all IVF cycles performed in our program from 1/2012 to 10/2018. Outcome variables assessed included fertilization rate (%2PN/MII), blastocyst conversion rate (% total blastocysts/2PN), proportion of biopsiable blastocysts (% blastocysts of adequate quality for biopsy on days 5 or 6/total blastocysts), % euploid embryos, and % embryos with inconclusive biopsy results. GEE modeling was used to control for patients with more than one cycle during the study period. Rate ratios (RR) were calculated using a Poisson regression with offset model with PGT-A cycles as the referent group, adjusted for patient age, total number of mature oocytes, BMI and intracytoplasmic sperm injection (ICSI).

**RESULTS:** 566 cycles from 388 patients were included (462 PGT-A and 104 PGT-SR cycles). Demographic information and cycle characteristics were similar between groups in terms of age, AMH, and day 3 FSH, with small differences in BMI and use of ICSI. The laboratory outcome data are shown in the Table 1. Blastocyst conversion rate was statistically significantly higher in the PGT-SR group, although there was no difference between groups in the percentage of blastocysts biopsied on either day 5 or day 6, or the percentage of biopsies that were noninformative. Of note, in the PGT-A group, 42% of biopsied embryos were euploid, compared to only 29% in the PGT-SR group (aRR 0.86; 95% CI 0.82-0.90). Notably, blinded sectioned analysis also confirmed the overall high clinical efficacy of preimplantation genetic testing for aneuploidy screening from a TE biopsy and low incidence of chromosomal mosaicism.

**CONCLUSIONS:** This study validated the strength and robustness of NGS for diagnosis of chromosomal deletions in TE biopsies. These small chromosomal deletions can result in clinically recognizable genetic syndromes, such as chromosome 1p36 and chromosome 3q29 deletion syndromes, cautioning their selection for transfer. Notably, blinded sectioned analysis also confirmed the overall high clinical efficacy of preimplantation genetic testing for aneuploidy screening from a TE biopsy and low incidence of chromosomal mosaicism.

**SUPPORT:** None.

**P-310** Tuesday, October 15, 2019 6:30 AM

**IMPACT OF DIFFERENT DEGREES OF GENETIC MOSAICISM IN THE KINETIC PROFILE OF THE HUMAN EMBRYO.** Angel M. Bastida, MSc; Carmen Vidal, M.D., Ph.D.; Lorena Rodrigo, Ph.D., Amparo Mercader, PhD; Carmen Rubio, PhD; Juan Giles, M.D., Ph.D.; Jose Alejandro Remohi, MD, Ph.D.; Ma José de los Santos, Ph.D.; IVIRMA Valencia, Valencia, Spain; Igenoxim Spain, Paterna (Valencia), Spain; IVIRMA Valencia, Valencia, Spain.

**OBJECTIVE:** Current publications have shown that embryos classified after PGT-A as mosaics may lead to healthy live births. Some clinics transfer them under certain clinical circumstances, while others opt not to. These embryos, whose developmental potential is generally compromised compared to their euploid counterparts, still await morphokinetic characterization. The aim of this study is to examine whether embryos showing different degrees of mosaicism exhibit characteristic kinetic profiles. This may provide additional information about their viability, hence easing clinical decisions in the IVF daily practice.

**DESIGN:** Retrospective, observational study including 688 embryos from 172 patients that underwent PGT-A ICSI cycles in IVI RMA Valencia from March 2018 to April 2019 and used time-lapse technology for embryo culture.

**MATERIALS AND METHODS:** Timings of the following preimplantation events were annotated during embryo culture: time of extrusion of the PB2 (tPB2), time of PN appearance (tPNa) and fading (tPNf), time to compaction (tSC), time to hatching blastocyst (tHb), time to expanded blastocyst (tEB) and time to hatching blastocyst (tHB). At day 5-6 of development, trophectoderm biopsies were analyzed by NGS and classified according to their relative content of aneuploid cells: euploid mosaic (<50%), low-degree mosaic (50-70%), and aneuploid mosaic (>70%). The remaining 12 (22.2%) blastocysts were concordant, displayed evidence of a diploid cell line in ≥1 analyzed section and also included two blastocysts showing the reverse chromosome duplication in both ICM and TE sections. Blinded sectioned re-analysis of the 21 euploid and 87 full aneuploid blastocysts also strongly validated the original TE diagnosis for 95.2% and 97.7% of the embryos, respectively. In both sets of data, the non-concordant blastocysts were identified as euploid mosaic (n=2; 4.8%) and aneuploid mosaic (n=2; 2.3%).

**CONCLUSIONS:** This study validated the strength and robustness of NGS for diagnosis of chromosomal deletions in TE biopsies. These small chromosomal deletions can result in clinically recognizable genetic syndromes, such as chromosome 1p36 and chromosome 3q29 deletion syndromes, cautioning their selection for transfer. Notably, blinded sectioned analysis also confirmed the overall high clinical efficacy of preimplantation genetic testing for aneuploidy screening from a TE biopsy and low incidence of chromosomal mosaicism.

**SUPPOR:** None.
vs. aneuploid. However, embryos showing low and high degree of genetic mosaicism exhibited a similar kinetic behavior with all the parameters examined. Significant differences were not found for the assessed variables between euploid and low-degree mosaics, nor between high-degree mosaics and aneuploid embryos.

CONCLUSIONS: This preliminary study shows that mosaic embryos have a similar kinetic behavior with the cut-off values considered to establish the mosaicism degree. Our results suggest that kinetic variations between euploid and low-degree mosaics, and between aneuploid and high-degree mosaics, may be subtle or even non-existent. These findings recall the importance of a critical interpretation of any mosaics data, especially when working with limited sample sizes.

SUPPORT: Research supported by CDTI n. 20190022.

P-311 Tuesday, October 15, 2019 6:30 AM

FOUR YEARS OF PROSPECTIVE MOSAIC EMBRYO TRANSFER: A SINGLE CENTER’S EXPERIENCE.

Andria G. Besser, MS,a Jennifer K. Blakemore, MD,b, Elizabeth J. Del Buono, MS,c Caroline McCaffrey, Ph.D., David H. McCulloh, Ph.D., James A. Grifo, MD, PhD, NYU Langone Fertility Center, New York, NY; NYU Langone School of Medicine, New York, NY; Sarah Lawrence College, Bronxville, NY; New York Langone Health, NYU Fertility Center, New York, NY; NYU Langone Health, New York, NY; NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: It is now well-established that embryos diagnosed as chromosomally mosaic can result in healthy live births. Our aim was to report on our clinic’s outcomes associated with mosaic embryo transfer (MET), determine which parameters predict MET success, and compare MET outcomes to single thawed euploid embryo transfer (STEET).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All STEET cycles after in vitro fertilization, trophoderm biopsy, and preimplantation genetic testing for aneuploidy (PGT-A) by next-generation sequencing were identified as controls. Cases included all MET cycles. Statistical analysis included chi-square with p < 0.05 considered significant.

RESULTS: A total of 645 PGT-A frozen embryo transfer cycles occurred during the selection period. STEET occurred in 569 cycles (mean age = 35.8), and MET occurred in 70 cycles (mean age = 39.6) with 76 embryos. 47 embryos were diagnosed as segmental mosaic (SM) and 29 embryos were diagnosed as whole chromosome mosaic (WCM, including monosomies and trisomies). 28/47 (59.6%) SM embryos and 10/29 (38.5%) WCM embryos implanted, compared to 408/569 (71.7%) euploid embryos. The ongoing pregnancy/live birth rate was significantly higher in SM embryos (22/47; 46.8%) compared to WCM embryos (5/29; 19.2%; p < 0.01). MET resulted in significantly more ongoing pregnancies (358/569; 62.9%) than both SM (p = 0.03) and WCM (p < 0.01) embryos. For SM embryos, there was no significant difference in outcomes when stratified by the percentage of mosaicism in the biopsy; however, WCM embryos with 20-40% mosaicism in the biopsy had significantly higher ongoing pregnancy rates compared to those with 41-80% mosaicism (p = 0.03). 8/8 WCM embryos with more than 1 chromosome involved failed to implant. There were no significant differences when comparing embryos with a deletion vs. a duplication or a monosomy vs. a trisomy. Maternal age at testing was not associated with differences in pregnancy outcomes in the MET or STEET groups. 15/27 fetuses conceived by MET were reported to be tested by amniocentesis (including 9 with chromosomal microarray), and none were found to have evidence of mosaicism involving the chromosome in question.

CONCLUSIONS: In the absence of euploid embryos, MET may be considered. While embryos diagnosed as SM have higher reproductive potential compared to those diagnosed as WCM, both categories have inferior outcomes when compared to STEET. While neonatal outcomes are reassuring, additional studies are needed to explore long-term outcomes from babies born following MET.

P-312 Tuesday, October 15, 2019 6:30 AM

PREIMPLANTATION GENETIC TESTING (PGT) AND FROZEN EMBRYO TRANSFER (FET) SYNERGISTICALLY DECREASE PRE-TERM DELIVERY IN PATIENTS UNDERGOING IN VITRO FERTILIZATION (IVF).

Luke Y. Ying, M.D.a, Mark D. Sanchez, M.D.a, James Baron, M.D.,a Ying Ying, Ph.D.b, HCA West Florida GME Consortium/Brandon M.D.,a Ying Ying, MS,a John A. McCulloh, M.D.,a, bHCA West Florida GME Consortium/Brandon M.D.,a Ying Ying, Ph.D.b, HCA West Florida GME Consortium/Brandon M.D.,a, Ying Ying, MS,a John A. McCulloh, M.D.,a, bHCA West Florida GME Consortium/Brandon M.D.,a, Ying Ying, Ph.D.b

X2 tests for trend analysis of term, pre-term and very pre-term delivery: FET vs ET (P = 0.04); FET/PGT vs ET (P < 0.0001) and FET/PGT vs FET (P = 0.02).

Regional Hospital, Brandon, FL; aUniversity of South Florida Department of Obstetrics and Gynecology, Tampa, FL.

OBJECTIVE: To study the effects of PGT on pregnancy outcomes in patients undergoing IVF with elective single embryo transfer (eSET).

DESIGN: Retrospective cohort Society for Assisted Reproductive Technology (SART) data study.

MATERIALS AND METHODS: A retrospective cohort study was conducted using the publicly available data in the SART National Summary Report from 2014 to 2016. Cycle inclusion criteria were eSET, fresh embryo transfer (ET), and frozen embryo transfers (FET) with or without PGT. Exclusion criteria were use of gestational carriers and donor eggs. Pregnancy outcomes included live births and gestational age at delivery (term: > 37 weeks, pre-term: 32-37 weeks, and very pre-term: < 32 weeks). X2 test was used to compare variables between groups. A P value of < 0.05 was considered statistically significant.

RESULTS: A total of 104154 eSETs were analyzed for the effect of PGT on IVF outcome and pre-term deliveries including 31670 ETs, 39228 FETs and 33256 frozen embryo transfers post PGT (FET/PGT). The main outcome was summarized in Table 1. Live birth rate in patients with FET/PGT was significantly higher than those in ET (52.2% vs 47.0%, P < 0.0001) and FET without PGT (52.2% vs 42.5%, P < 0.0001). FET was associated with a statistically lower pre-term and very pre-term deliveries than ET (P = 0.04), though live birth rate was significantly lower than that in ET (42.5% vs 47.0%, P < 0.0001). FET/PGT significantly reduced pre-term and very pre-term deliveries when compared with ET (P < 0.0001). Pre-term/very pre-term deliveries in FET/PGT was also statistically lower than those in the FET without PGT (P = 0.02), suggesting that PGT has an additive effect on FET in decreasing pre-term delivery.

CONCLUSIONS: PGT has been integrated into one of the most important roles in IVF treatment. This study using large cohort SART data demonstrates that PGT significantly improves IVF outcome. Moreover, this study shows that patients undergoing PGT accompanied with subsequent FET had significantly reduced pre-term as well as very pre-term deliveries. Lower incidence of pre-term delivery associated with PGT should be taken into account when counseling patients seeking infertility treatment.

P-313 Tuesday, October 15, 2019 6:30 AM

HOW MANY SINGLE EMBRYO TRANSFERS WOULD BE NEEDED TO PERFORM AN EUPLOID EMBRYO TRANSFER ACCORDING TO THE AGE OF THE PATIENT?

Carmen Rubio, PhD,a Monica Clemente-Ciscar, PhD,a Lorena Rodrigo, PhD,b Jorge Jimenez-Almazan, PhD,b Carlos Simon, MD, PhD,b Igenomix Spain, Paterna (Valencia), Spain; University of Valencia, Igenomix Foundation-INCLIVA, Valencia, Spain.

OBJECTIVE: To estimate the number of single embryo transfers (SETs) using morphological criteria and the number of stimulation cycles needed to find an euploid embryo for transfer.

DESIGN: This retrospective study includes 215,723 blastocysts corresponding to 59,451 cycles of preimplantation genetic testing for aneuploidy (PGT-A) performed using Next Generation Sequencing (NGS). Results of trophectoderm biopsies performed from January 2016 to December 2018 were stratified according to the origin of the oocytes (own or donated). Ovum donors were under 30 years of age. Cycles performed with own oocytes were divided according to the female age in the following categories:
TABLE 1.

<table>
<thead>
<tr>
<th>OD</th>
<th>27</th>
<th>28</th>
<th>29</th>
<th>30</th>
<th>31</th>
<th>32</th>
<th>33</th>
<th>34</th>
<th>35</th>
<th>36</th>
<th>37</th>
<th>38</th>
<th>39</th>
<th>40</th>
<th>41</th>
<th>42</th>
<th>43</th>
<th>≥44</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of euploid embryos</td>
<td>0.6</td>
<td>0.7</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.4</td>
<td>0.4</td>
<td>0.3</td>
<td>0.3</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Minimum number of blastocysts to obtain a euploid embryo</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Mean number of blastocysts</td>
<td>5.7</td>
<td>4.9</td>
<td>4.8</td>
<td>4.8</td>
<td>4.7</td>
<td>4.7</td>
<td>4.5</td>
<td>4.2</td>
<td>4.1</td>
<td>3.9</td>
<td>3.7</td>
<td>3.4</td>
<td>3.2</td>
<td>3.0</td>
<td>2.8</td>
<td>2.6</td>
<td>2.4</td>
<td>2.3</td>
</tr>
<tr>
<td>Minimum number cycles to obtain a euploid embryo</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Expected number of SET to transfer a euploid embryo</td>
<td>1.5</td>
<td>1.4</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.6</td>
<td>1.6</td>
<td>1.7</td>
<td>1.7</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2.5</td>
<td>3</td>
<td>3.3</td>
</tr>
</tbody>
</table>

≤27 years, individually from 28-43 years, and ≥44 years (range: 20-45). The percentage of euploid embryos and the mean number of biopsied blastocysts at each age group were computed for the mathematical model based on the empirical data to estimate the stimulation cycles and the expected number of SETs needed to obtain a euploid embryo.

MATERIALS AND METHODS: The incidence of chromosomal abnormalities ranged from 34.6% to 82.5% and the mean number of blastocysts per cycle varied from 5.7 to 19.1, in the youngest versus oldest patients, respectively. To estimate the minimal number of blastocysts and cycles needed to obtain a euploid embryo at each group, these empirical data were used. To compute the expected number of SETs to be performed, a hypergeometric probability distribution was applied, using the probability-weighted average of all possible values. To obtain the final value, we applied a smooth method, computing running medians of odd span (J.H. Friedman and W. Stuetzle, Technical report, 1982). This calculation was performed starting from the minimal number of expected blastocysts at each age category.

RESULTS: A summary of the results is presented in Table 1 according to maternal age in years (OD means ovum donation). Each row represents the frequency of euploid blastocysts, the mean number of blastocysts per cycle, the minimum number of blastocysts and stimulation cycles needed to obtain a euploid embryo and expected number of SETs needed to transfer a euploid embryo if PGT-A would not have been performed.

CONCLUSIONS: This mathematical model shows the potential benefits of selecting the euploid embryo in the first SET in PGT-A, compared to standard SET in which embryo selection is performed according to morphological criteria. These data as well as the number of cycles needed to obtain an euploid embryo according to the female age are valuable information for reproductive counselling.

REFERENCE

SUPPORT: None.

P-314 Tuesday, October 15, 2019 6:30 AM

ARTIFICIAL VISION AND MACHINE LEARNING DESIGNED TO PREDICT PGT-A

RESULTS. Alejandro Chavez-Badiola, MD, Adolfo Flores-Saiffe Farias, MSc, PhD, Gerardo Mendizabal-Ruiz, PhD, Andrew J. Drakeley, MD FRCOG, Rodolfo Garcia-Sanchez, MSc, John J. Zhang, MD, PhD, New Hope Fertility Center Mexico, Mexico City, Em, Mexico; New Hope Fertility Center, Guadalajara, JA, Mexico; Departamento de Ciencias Computacionales, Universidad de Guadalajara, Guadalajara, JA, Mexico; Hewitt Centre for Reproductive Medicine, Liverpool Women’s Hospital, Liverpool, United Kingdom; New Hope Fertility Center Mexico, Guadalajara, JA, Mexico; New Hope Fertility Center, New York, NY.

OBJECTIVE: To assess the ability of a computing tool based on artificial vision and machine learning to predict aneuploidy based on single blastocyst pictures.

DESIGN: Double blind, prospective, longitudinal cohort study.

MATERIALS AND METHODS: A self developed computing tool (CT) with artificial vision and machine learning capabilities was tested for its ability to segment images, extract features of each segment, and to predict aneuploidy on digital images of blastocysts collected between October 2018 and February 2019 from a single IVF center. All embryos were subject to embryo biopsy for PGT-A analysis with next generation sequencing (NGS). Pictures from all embryos were taken before trophectoderm biopsy. Results were assessed using a confusion matrix: PGT-A results matched against CT’s predictions. Mathematicians performing biopsy and PGT-A providers were blind to CT’s predictions. Mathematicians feeding information to our CT were also blind to PGT-A results until analysis was performed.

RESULTS: A total of 241 blastocysts were analyzed with the use of our artificial vision and machine learning computing tool. Positive predictive value for aneuploidy was 79.5%, sensitivity of 70.1%, specificity of 73.2% and accuracy of 71.4%. F1 Score was 74.5%. Negative Predictive Value, which is the ability of the algorithm to predict euploidy, was 62.3%.

CONCLUSIONS: Sensitivity, specificity and accuracy with our current Artificial Vision and Machine Learning tool is not yet comparable to embryo biopsy and NGS for euploidy prediction and, at this stage, are not ready to substitute what is still considered the gold standard for euploidy screening. However, a positive predictive value for euploidy estimated at 72% is for now good enough to guide embryologists during the embryo selection process in those cases where PGT-A was not performed. Further studies with a larger image database are already underway aiming to improve predictive capabilities of our software.

P-315 Tuesday, October 15, 2019 6:30 AM

REBIOPSY OF BLASTOCYSTS REVEALS THAT NEXT GENERATION SEQUENCING PROVIDES EXCELLENT CLINICAL ACCURACY DESPITE MINOR DISCORDANCES. David H. McCulloh, Ph.D., Nidhhee Sachdev, MD, Caroline McCaffrey, Ph.D., James A. Grifo, MD, PhD, NYU Langone Health, New York, NY; OC Fertility, Newport Beach, CA; NYU Langone Health, NYU Fertility Center, New York, NY; NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: PGT-A on TE biopsies (TE Bx/NGS) provides a method of selecting blastocysts with excellent prognosis for establishing clinical pregnancies, minimizing miscarriages and improving live birth rates per ART procedure. However some practitioners distrust the reliability of TE Bx/NGS because mosaicism is seen in normal placentae (derived from the TE) and small numbers of TE cells biopsied may not represent the fetus (derived from the inner cell mass). We examined rebiopsy specimens from the TE and the ICM to determine the reliability of the clinical biopsy to characterize the blastocyst. In particular, we determined concordance between the clinical biopsies and rebiopsy specimens, focusing on 1) chromosomal concordance for disomic results, aneuploid results or mosaic results in the clinical biopsy and 2) clinical concordance (whether biopsy of the ICM was concordant with the initial biopsy’s result of “Euploid” vs “NOT euploid”).

DESIGN: Rebiopsy of blastocysts with known results of clinical PGT-A MATERIALS AND METHODS: Results of initial, clinical TE biopsies were obtained from Cooper Genomics. Vitriified blastocysts from patients consenting to research were selected for groups that had no aneuploidy (N = 10), aneuploidy with 1 or 2 aneuploid embryos (N = 4) or 1 aneuploid chromosome and 1 mosaic result (N = 18). Blastocysts were rewarmed and cells from the TE and ICM were biopsied separately, obtaining as many re-biopsy specimens as possible. Biopsy specimens were subjected to WGA and NGS in our university’s core laboratory. NGS results for rebiopsies were compared with results of the clinical biopsy. Rebiopsy chromosomes were considered concordant when the same chromosomal diagnosis was observed.

RESULTS: Chromosomal concordances were 97.0%, 74.3%, and 13.7% per chromosome, respectively, for disomic (D), aneuploid (An) and mosaic (Mo) chromosomes in the clinical biopsy. Discordant chromosome results were predominantly mosaic results (2.6%) for D, mosaic or complementary results (21.6%) for An, or were not seen or non-mosaic aneuploid results (74.5%) for Mo observed for the same chromosome that was seen in the clinical biopsy. These minor discordances can be considered concordant since
they mainly confirm the initial results. Counting them as concordant leads to concordances 99.6% for Di, 95.9% for An, and 88.2% for Mo per chromosome. Rebiopsies of inner cell mass were clinically concordant for 100% of the blastocysts (biopsy result of ICM agreed with the clinical result of “euploid” or “not euploid”).

CONCLUSIONS: Despite small number of biopsied cells (required to avoid damage to the blastocyst) and mosaicism (demonstrated by rebiopsy specimens) the excellent chromosomal concordance for rebiopsy specimens (99.6% and 95.9%) and clinical concordance for ICM biopsies (100%) indicate that TE biopsy/NGS provides excellent accuracy in its assessment of ploidy. Within this non-randomly selected subset of blastocysts, mosaics detected in the clinical biopsy outnumbered mosaics detected only by rebiopsy 2.25:1 (18:8).

SUPPORT: None.

P-316 Tuesday, October 15, 2019 6:30 AM

A UNIVERSAL SINGLE TUBE PCR-BASED LIBRARY PREPARATION FOR PG-T AG ALLOWING CROSS-PLATFORM NGS SEQUENCING. Melinda Jane Jasper, PhD, Steven Anthony Myers, PhD, Kimberly Warren, B Tech, (Hons), Lann Tay, B Sc, Sandra Protapisalis, Associate Diplomas Medical Laboratory Science, PerkinElmer Health Sciences (Australia) Pty Ltd, Thebarton, SA, Australia; Affiliation not provided; PerkinElmer Health Sciences, Adelaide, SA, Australia.

OBJECTIVE: There are several methods to prepare trophectoderm biopsy samples for Preimplantation Genetic Testing for Aneuploidy (PG-T-A) by Next Generation Sequencing (NGS). Most methods use a two-step approach of Whole Genome Amplification (WGA) followed by library preparation. However, combining WGA with library preparation by utilising PCR-based library preparation approaches offers several advantages over traditional two-step methods, including protocol time efficiencies and reduced hands-on time. In addition to these advantages, a novel combined approach developed based on the PerkinElmer DOPify® WGA kit offers the capability for cross-platform sequencing validation of a single biopsy.

DESIGN: Here we describe the development of a novel PG-T-A approach which allows PCR-based library preparation of trophectoderm biopsies for cross-platform NGS using either Illumina® or Ion Torrent® sequencing technology.

MATERIALS AND METHODS: Five-cell samples representative of trophectoderm biopsies were manually sorted from aneuploid cell lines (Coriell Institute) and euploid lymphocytes. Cell lysis and WGA were performed using a modified DOPify® kit protocol (PerkinElmer) followed by incorporation of Illumina®-specific adapter sequences and unique indexes in a single tube. Amplified, indexed 5-cell samples were purified, quantified then pooled before 48 sample multiplex and 1x75bp read length sequencing on the MiSeq® Instrument (Illumina). Sequencing data was analysed for correct ploidy calling using the PG-Find™ software (PerkinElmer).

RESULTS: A total of 105 5-cell samples were processed. Three samples were excluded from final analysis due to weak amplification (2.8%) with a further five samples failing to pass quality control checks (4.8%). The 48 sample multiplex generated an average of 510,000 reads per sample with 98.9% of reads mapping to hg19. All samples that passed quality control metrics displayed the expected karyotype when analysed with the PG-Find™ software. The PCR-indexing protocol took on average 4.5 hours (2.5 hours hands on) to process 48 samples from sample receipt to NGS instrument loading.

CONCLUSIONS: This novel PCR-based indexing workflow provides rapid, scalable and economical sequencing for PG-T-A and provides the capability for cross-platform sequencing validation of a single embryo biopsy for PG-T-A. This flexible workflow allows customisable throughput and tailorable resolution to detect smaller segmental aberrations.

SUPPORT: None.

P-317 Tuesday, October 15, 2019 6:30 AM

HOW IMPORTANT IS IT TO VISUALIZE 2PN IN ZYGOTES DESTINED FOR PG-T A TESTING BY NEXT GENERATION SEQUENCING (NGS)? Caroline McCaffrey, Ph.D., David H. McCulloh, Ph.D., Frederick L. Lisciardi, M.D., James A. Grifo, MD, PhD, Hsiao-Ling Lee, M.S., Xinjian He, MS, Andrea G. Besser, MS, New York Langone Health, NYU Fertility Center, New York, NY; NYU Langone Health, New York, NY; NYU Langone Prelude Fertility Center, New York, NY; New York University Fertility Center, New York, NY; NYU Langone Fertility Center, New York, NY.

OBJECTIVE: To determine the incidence of euploidy in Blastocysts derived from 0PN and 1PN compared with 2PN embryos.

DESIGN: Single center retrospective review of PG-T-A cases over a 4 year period (2015-2018) where a biopsy and ploidy determination was performed on blastocysts (blasts) derived from zygotes where pronuclei (PNs) were either not evident (0 PN) or only 1 pronucleus (1 PN) was evident at the time of fertilization check.

MATERIALS AND METHODS: At NYULMC fertilization checks are conducted ~18 hours post insemination or ICSI. The number of PN in each egg is recorded and zygotes are cultured individually. Cases where ≤50% of the mature eggs exhibit 2PN are routinely rechecked later on Day 1. In cases for PG-T-A, all viable inseminated eggs excluding those with ≥3 PN remain in culture to Day 6/7. Good quality blastocysts with a distinct Inner cell mass and cohesive trophectoderm are considered for PG-T-A regardless of whether they were 0PN, 1PN or 2PN at fertilization check. PG-T-A results are shown in Table 1 along with PG-T-A sex of blasts derived from each group.

RESULTS:

CONCLUSIONS: Prior to utilization of PG-T-A and/or timelapse zygotes not exhibiting 2PN at fertilization check were routinely discarded. However, it is now obvious that a percentage of these, albeit small, are fertilized normally and are euploid. Though they account for only a small percentage these may be the only euploid blasts available. Implantation rates and LB rates following transfer of these blasts are similar to those for 2PN blastocysts. Of interest, ratios of XX:XY for only a small percentage these may be the only euploid blastocysts derived from 0PN and 1PN zygotes were ~2:1 while those from 2PN zygotes were ~1:1. It should be noted that NGS cannot detect pure haploidy (23, X0) or triploidy (69, XXX) thereby possibly mis-diagnosing these as euploid although our IR and LB results indicate otherwise.

SUPPORT: None.

TABLE 1.

<table>
<thead>
<tr>
<th>All Patient Ages</th>
<th>2PN</th>
<th>1PN</th>
<th>0PN</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conventional insemm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number Blasts B’x’d</td>
<td>11287</td>
<td>428</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Number Euploid (% B’x’d)</td>
<td>3864 (34%)</td>
<td>113 (26%)</td>
<td>11 (35%)</td>
<td></td>
</tr>
<tr>
<td>Ratio XX:XY (%)</td>
<td>47.52</td>
<td>61.39</td>
<td>64.36</td>
<td></td>
</tr>
<tr>
<td><strong>ICSI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number Blasts B’x’d</td>
<td>6553</td>
<td>CONCLUSIONS: This 76 147</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number Euploid (% B’x’d)</td>
<td>2189 (33%)</td>
<td>29 (38%)</td>
<td>35 (24%)</td>
<td></td>
</tr>
<tr>
<td>Ratio XX:XY</td>
<td>50:50</td>
<td>86:14</td>
<td>54:46</td>
<td></td>
</tr>
<tr>
<td><strong>Conventional insemm+ ICSI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IR (sac/ ET) (%)</td>
<td>x/1809 (68%)</td>
<td>x/40 (60%)</td>
<td>x/10 (80%)</td>
<td></td>
</tr>
<tr>
<td>LB / ET with known outcome (%)</td>
<td>52%</td>
<td>44%</td>
<td>66%</td>
<td></td>
</tr>
<tr>
<td>LB Ratio XX:XY</td>
<td>362:394</td>
<td>11:5</td>
<td>4:2</td>
<td></td>
</tr>
</tbody>
</table>

Of 11726 embys biopsied from conventional insemination, 4% developed from 1PN. Less than 1% was from 0PN. Of 6553 ICSI embys biopsied, 1% was from 1PNs, 2% were from 0PNs. Of the 11 XX 1PN LB N 10 (10/ 17) are from insem, 1 (1/6) from ICSI. Of the 4 XX 0PN LB N LB insem, 1 (1/1) is from ICSI.
INDIVIDUAL CHROMOSOME MOSAICISM RATES AFTER PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY: IMPLICATIONS FOR MECHANISMS RELATED TO THE EARLY STAGES OF EMBRYO DEVELOPMENT. Amy Jones, MS, Ping Zou, PhD, Minjae Kwon, MS, Melissa Wilmarth, BS, Cecilia Rios, CG, Ashlie M. West, BS, Jordan Clarke, MS, Ovation Fertility, Franklin, TN; Ovation Genetis, Henderson, NV.

OBJECTIVE: Next generation sequencing (NGS) provides evidence of mosaicism in the blastocyst stage embryo. Mosaic profiles are often graded as low or high to denote levels of risk. Here we assess mosaicism as it pertains to specific chromosomes and determine rates of high and low level mosaicism for individual chromosomes.

DESIGN: Retrospective study.

MATERIALS AND METHODS: A total of 6525 samples were assessed during the time period of this study. Mosaicism rates were determined as a percentage of total samples, total mosaicism event and per chromosome. Additionally, we evaluated the frequency of high and low level mosaics for each chromosome.

RESULTS: Of the 6525 samples that underwent PGT-A testing 931 (14%) displayed whole aneuploid mosaicism. High and low level mosaicism was observed in 47% and 53% of the samples respectively. Male and female samples showed autosomal mosaicism disproportionately at 44% and 56% respectively. Mosaicism and high level mosaicism in chromosome 22 occurred at a higher rate than other chromosomes, while mosaicism rates were lowest in chromosomes 12 and 17. Data are summarized in Table 1.

### Table 1. Rates of mosaicism, segmental errors, and “no call” results based on embryologist performing the biopsy

<table>
<thead>
<tr>
<th>Embryologist</th>
<th>Mosaicism</th>
<th>Segmental Error</th>
<th>“No Calls”</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>891/15803</td>
<td>5.6</td>
<td>1697/15803</td>
</tr>
<tr>
<td>B</td>
<td>428/9969</td>
<td>4.3</td>
<td>896/9969</td>
</tr>
<tr>
<td>C</td>
<td>209/3754</td>
<td>5.6</td>
<td>395/3754</td>
</tr>
<tr>
<td>D</td>
<td>83/1373</td>
<td>6.1</td>
<td>136/1373</td>
</tr>
<tr>
<td>All</td>
<td>1607/30899</td>
<td>5.2</td>
<td>3124/30899</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Bridging the gap between preimplantation genetics and prenatal cytogenetics has the potential to be a powerful tool for clinicians treating infertility couples. The literature has reported that mosaicism is clinically relevant. This report evaluates the rates of mosaicism for individual chromosomes providing a basis on which to correlate the incidence of preimplantation mosaicism in specific chromosomes with mosaicism observed in prenatal samples. Additionally, the data highlights the putative uneven distribution of mosaicism in male and female samples.

P-318 Tuesday, October 15, 2019 6:30 AM

RATES OF EMBRYONIC MOSAICISM ARE CONSISTENT AMONGST EMBRYOLOGISTS PERFORMING OR LOADING TROPHECTODERM BIOPSIES FOR PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY. Emily K. Osman, MD, Shelby A. Neal, MD, Ashley W. Tieg, MD, Brent M. Hanson, MD, Julia G. Kim, MD, MPH, Jason M. Fransasiak, MD, Richard Thomas Scott, Jr., MD, IVI-RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: The introduction of next-generation sequencing (NGS) for preimplantation genetic testing for aneuploidy (PGT-A) has led to increased detection of mosaicism and segmental errors. It has been suggested that the incidence of such abnormalities varies between reference laboratories where the biopsy is analyzed. Additionally, the technical aptitude of the embryologist performing or handling the biopsy specimen may contribute to mosaicism, segmental errors, and “no call” outcomes including nonconcurrent or unamplified results.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Patients undergoing in vitro fertilization (IVF) cycles with PGT-A at a single center were included. Embryos were cultured to the blastocyst stage and biopsies were performed on days 5, 6 or 7. PGT-A was performed using the NexCCS NGS platform. An embryo was designated as mosaic if the DNA copy number ranged from 0.3 to 0.7. Segmental errors were defined as chromosomal duplications or deletions that were ≥ 5 Mb. A chi-squared analysis was utilized to compare the primary outcome of mosaicism and secondary outcomes of segmental errors and “no call” results between embryologists. An alpha error <0.05 was considered significant. Given the large sample size, differences <2% were determined to be clinically irrelevant despite statistically significant.

RESULTS: Four embryologists performed a total of 30,899 embryo biopsies and 6 individuals loaded biopsy specimens into designated tubes. PGT-A results of embryologists performing the biopsy are listed in Table 1. Given the immense sample size, all biopsy performing embryologists had statistically separable differences in both primary and secondary outcomes. However, individuals performed within 1% of the mean; these differences were not of clinical significance. Similarly, differences in rates of mosaicism (5.0-5.9%), segmental errors (9.7-10.4%) and inconclusive results (1.1-2.8%) amongst different embryologists performing biopsy loading were clinically irrelevant.

CONCLUSIONS: Rates of mosaicism, segmental abnormalities, nonconcurrent and unamplified PGT-A results are highly consistent amongst embryologists. Variation in PGT-A results can be attributed to differences in reference laboratories. With increasing utilization of PGT worldwide, reproducible results are critical for optimizing clinical outcomes during IVF cycles.

P-320

WITHDRAWN

P-321 Tuesday, October 15, 2019 6:30 AM

IN VITRO FERTILIZATION (IVF) WITH PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) IS NOT COST EFFECTIVE TO ACHIEVE A LIVE BIRTH COMPARED TO IVF ALONE IN DONOR OOCYTE CYCLES. Maria Facadrio Antero, MD, Bhichitra Singh, M.D., MPH, MS, Megan E. Gornet, MD, William G. Kearns, MD, PhD, Valerie L. Baker, MD, Mandy S. Christianson, MD, John Hopkins University School of Medicine, Lutherville, MD; Johns Hopkins School of Medicine, Baltimore, MD; John Hopkins University School of Medicine.
OBJECTIVE: The process of using donor oocyte can be costly for patients and in some cases it is not covered by insurance. For some patients, oocyte donation comes as their last resort after they have exhausted their financial limit. Optimizing every aspect of oocyte donation is important not only to improve outcomes but also reduce cost to patients. Preimplantation genetic testing for aneuploidy (PGT-A) has been shown to be cost effective in certain subpopulations of infertile patients undergoing IVF[1][ii]. The objective of this study is to determine whether IVF with PGT-A is cost effective to achieve a live birth compared to IVF alone in donor oocyte cycles.

DESIGN: Cost-effectiveness study

MATERIALS AND METHODS: A decision analytic model was constructed using TreeAge Pro 2019 (TreeAge Software Inc, Williamstown MA) to compare the cost of IVF with PGT-A versus IVF alone to achieve a live birth. The model assumed donor oocytes were obtained from healthy females younger than 30 years old, with laboratory evidence of normal ovarian reserve, and no infertility diagnosis. The model analyzed a hypothetical single fresh oocyte donor IVF cycle with PGT-A versus IVF alone and followed the progression of a single embryo through the different decision nodes. Cost estimates of relevant clinical events and incorporated probabilities were based on data from published literature including the Society for Assisted Reproductive Technology (SART) database. Cost data was converted to 2018 US dollars. The primary outcome was the cost to achieve a live birth using IVF with PGT-A for donor egg cycles compared to IVF alone, and Monte Carlo sensitivity analyses were performed to assess for model robustness.

RESULTS: The model demonstrates IVF with PGT-A on average costs $37,940 to achieve a live birth with a donor oocyte cycle across all combined age groups. In base-case analysis, IVF with PGT-A did not increase the overall effectiveness of increasing live birth rate at an additional cost of $4,650. This yielded an incremental cost-effectiveness ratio (ICER) of - $1142.66; IVF alone with donor eggs had a net monetary benefit (NMB) of $124,044 per live birth rate. The ICER was above the willingness to pay cost of $40,000 for achieving one live birth assuming the live birth rate of 61.3% and $37,940 per cycle for this patient population. Monte Carlo simulations demonstrated that IVF+PGT-A is not cost-effective in nearly all iterations at an acceptability cut off of $40,000.

CONCLUSIONS: This model suggests that the addition of PGT-A to IVF in donor oocyte cycles is not cost effective compared to IVF alone over a wide range of probabilities and costs. To better understand the dynamics of cost effectiveness in this population, the willingness to pay per live birth should be refined or the motivation to pay for PGT-A needs to be further investigated.

REFERENCES


P-322 Tuesday, October 15, 2019 6:30 AM

THE COST-EFFECTIVENESS OF PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A): AN ANALYSIS OF 153,865 SART CYCLES. Malinda S. Lee, MD, MBA, Katherine T. Lofgren, MPH, Ann M. Thomas, PhD, Andrea Lanes, PhD, Randi H. Goldman, M.D., Elizabeth S. Ginsburg, M.D., Mark D. Hornstein, M.D. Brigham and Women’s Hospital, Boston, MA; 1Harvard University, Cambridge, MA; 2Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: To determine the cost-effectiveness of PGT-A at cycle start for the treatment of infertility in the United States

DESIGN: Retrospective analysis of linked cycles from 1/2014–12/2016 from the Society for Assisted Reproductive Technology Clinic Outcomes Reporting System (SART CORS) applied to a decision analytic model.

MATERIALS AND METHODS: All first fresh autologous cycles of women undergoing IVF between 1/2014–12/2015 plus linked FET cycles from 1/2014–12/2016 were included. Banking, frozen egg, PGT-M and PGT-SR cycles were excluded. Cycles were categorized by intent to perform PGT-A.

Clinical and cost outcomes of IVF compared to IVF with PGT-A were estimated using a decision analytic model. Transitions between treatment stages relied on probability estimates from SART CORS. Patients progressed through the model until they achieved a live birth, exhausted their embryos or at one year after stimulation. Two payer perspectives were considered: patient and societal. Expected costs accounted for age-specific projections from SART CORS, such as number of embryos biopsied and total gonadotropin use.

RESULTS: 114,182 fresh and 39,683 linked FET cycles were included. Of fresh cycles, 18,470 (16.2%) planned PGT-A and 95,712 (83.8%) did not. Across all age groups, non-PGT-A cycles used more gonadotropin, had fewer embryos, and had higher cancellation and failed fertilization rates, suggesting that patients utilizing PGT-A represent a more favorable prognosis group. Cumulative live birth (CLBR) and twin live birth rates (TLBR) per cycle start are presented. From the patient perspective, costs incurred with PGT-A were higher in every age group when compared to IVF alone (differential $4,551–5,137). From the societal perspective, costs incurred with PGT-A were lower in the <35 age range (-$4,233), equivalent at age 35, and higher at every other age ($955–6,905).

CONCLUSIONS: From the societal perspective, IVF with PGT-A can be cost-effective for certain ages. From a patient perspective, IVF with PGT-A is costlier at every age. Up to age 35, at which CLBR are equivalent between IVF with and without PGT-A, PGT-A incurs an additional cost to the patient of $4,551-4,742.
Preimplantation genetic testing for monogenic diseases (PGT-M) is the process in which embryos created via in vitro fertilization (IVF) are tested for diseases like SCD; unaffected embryos may then be selected for transfer. In the United Kingdom, this technology is available to couples with SCT; in the United States, it is not routinely offered. Whether the costs of IVF with PGT-M (IVF+PGT-M) to avoid the birth of a child with SCD outweigh the lifetime medical costs of a person with SCD is unknown.

DESIGN: Cost effectiveness analysis.

MATERIALS AND METHODS: We conducted a decision analytic model using TreeAge Pro 2019 (TreeAge Software Inc, Williamstown, MA) for couples known to both have SCT, attempting to conceive with natural conception (NC) versus IVF+PGT-M. The primary outcome variable was quality adjusted life years (QALYs) for children born with or without SCD. The model incorporated probabilities and cost estimates of relevant clinical events using data from published literature. The total cost for each potential child included the cost of conception, lifetime medical care, and future potential income. We assumed all patients undergoing IVF+PGT-M also test embryos for aneuploidy (PGT-A); data were thus derived for euploid embryo transfers for all IVF+PGT-M patients. To determine whether IVF+PGT-M is cost effective, we calculated the incremental cost effectiveness ratio (ICER). Here, the ICER is defined as the ratio of the difference between the per patient per QALY costs of IVF+PGT-M compared with NC. Costs were converted to 2018 U.S. dollars. To examine the impact of changes in model input parameters, a sensitivity analysis was performed. We assumed a willingness to pay of $30,000 which is equal to the average cost of trying to conceive a non-SCD child in one IVF+PGT-M cycle with embryo transfer.

RESULTS: Healthy adults in the US have an average life expectancy of 79 years, versus 54 for individuals with SCD. By avoiding SCD, IVF+PGT-M for SCD offers a 23.27% increase in QALYs. The mean cost of SCD-related care is $26,319 per patient per life-year, while the average cost of IVF+PGT-M is $24,750 per non-SCD embryo transferred. The ICER for IVF+PGT-M as compared with NC was $22,881 per QALY added to the lifespan. Therefore, the cost per QALY of conceiving a healthy child with IVF+PGT-M is $22,881 less than the cost of SCD-related care. The ICER was less than the expected willingness to pay, and improved substantially with a decrease in the willingness to pay of $22,881 less than the cost of SCD-related care. The ICER for IVF+PGT-M. Offering this option to SCT couples on a more widespread basis might help families avoid the financial, emotional and familial burdens of raising a child with SCD, and decrease the societal costs of SCD.

P-325 Tuesday, October 15, 2019 6:30 AM

TRANSMITTED SELECTED EMBRYOS, AFTER PGT-A DIAGNOSED AS “ABNORMAL,” WHERE PATIENTS WERE FERTILIZED WITH TRANSFERS AT THEIR ORIGINAL IVF CENTERS: David H. Barad, MD, MS, Sarah K. Darmon, PhD, David F. Albertini, PhD, Norbert Gleicher, MD, Center for Human Reproduction, New York, NY.

OBJECTIVE: To report outcomes of IVF cycles in which, by PGT-A “abnormal,” embryos were transferred after such transfers had been earlier refused at the patients’ original IVF centers.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Since 2014, our center has been offering couples with only chromosomally “abnormal” embryos after PGT-A (“aneuploid” or “mosaic”), selective transfers of such embryos under an experimental consent. We at ASRM 2015 reported the first healthy births following such transfers in the world.1 Since our center does not recommend PGT-M, we uniformly had their IVF cycles elsewhere and transferred their embryos to or center after being refused transfers at their original centers. Written informed consent pointed out risks of a chromosomal abnormality, miscarriage risks, did not differentiate between “mosaic” and “aneuploid” embryos and excluded transfers from embryo transfers with non-lethal and with >3 abnormalities. Patients also consented to early pregnancy diagnosis and termination of pregnancy, should the pregnancy be aneuploid.

RESULTS: Since our original report with collaborating colleagues from 2 other centers in 2015 where we reported 5 normal pregnancies,1 we counselled 38 patients who moved their embryos to CHR. Among those, so far 22 have elected to have a transfer, with 7 (26.9%) achieving clinical pregnancy; 3/7 miscarried (42.8%); 1 was aneuploid pregnancy, 1 was 46XX, with maternal contamination ruled out and a third is currently pending a genetic result. Three pregnancies delivered normal offspring. Most IVF centers were cooperative in transferring embryos, though one transfer only occurred after the couple engaged a lawyer.

CONCLUSIONS: Here reported pregnancy and live birth rates are slightly lower than we reported in our initial series1 and others reported,2 but patients here were much older (44.2 ± 4.4 years). Considering age, the miscarriage rate was actually relatively low, confirming earlier reports. Since some of the original clinics had asked PGT-A laboratories not to report “mosaicism,” accurate separation of “mosaic” and “aneuploid” transfers was not possible. Current definitions, based on percentages of aneuploid DNA within a single trophoctoderm biopsy, however do, anyhow, have no empiric basis.3 Here presented data, therefore, suggest that, due to still excellent, pregnancy and delivery chances, embryos with alleged lethal aneuploid DNA should not be disposed. Because of downstream self-correction of human embryos, even intrauterine transfers of non-lethal “abnormalities” may have to be considered when no other embryos are available for transfer.

REFERENCES
2 Munné et al., Fertil Steril. 2017; 108(1), 62-71
3 Kushnir et al., Reprod Biol Endocrinol.2018; 16(1):6

SUPPORT: Intramural funds from The Center for Human Reproduction and grants from The Foundation for Reproductive Medicine.
CONCLUSIONS: The findings of this study are valuable for understanding the clinical results after SET with low/high-grade level mosaic embryos. We demonstrated that the high-grade mosaic embryos have the probability of resulting in implantation and healthy newborn but with higher abortion rate than low-grade mosaic embryos.

TABLE 1. Likelihood of Euploid Embryos

<table>
<thead>
<tr>
<th>Age</th>
<th>% of PGT cycles with at least 1 euploid embryo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-3 embryos</td>
</tr>
<tr>
<td>Egg Donor</td>
<td>84%</td>
</tr>
<tr>
<td>&lt;35</td>
<td>81%</td>
</tr>
<tr>
<td>35-37</td>
<td>73%</td>
</tr>
<tr>
<td>38-40</td>
<td>57%</td>
</tr>
<tr>
<td>41-42</td>
<td>33%</td>
</tr>
<tr>
<td>43-45</td>
<td>19%</td>
</tr>
<tr>
<td>All</td>
<td>59%</td>
</tr>
</tbody>
</table>

SUPPORT: Invitae

P-327 Tuesday, October 15, 2019 6:30 AM

PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) AND TECHNOLOGY PLATFORM: DOES PLATFORM INFLUENCE EUPLIDY CALL RATES AND/OR SUBSEQUENT PREGNANCY OUTCOMES? Eleni A. Greenwood, MD, PhD; Charles E. McCulloch, PhD; Kaitlyn Wald, MD; Salustiano Ribeiro, MD; Phil Marsh, BS; Marcellie I. Cedars, MD; Mitchell P. Rosen, MD; HCLD. aUniversity of California San Francisco, San Francisco, CA; bUCSF, San Francisco, CA; cUniversity of California - San Francisco, San Francisco, CA; dUniversity of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: With the evolution in technology platforms for PGT-A over the past decade, benefits to genetic testing companies include increased speed and reduced expense. Whether benefits have concurrently accrued to patients in terms of pregnancy outcomes is unclear. We sought to 1) compare euploid call rates by technology platform, and 2) determine whether pregnancy outcomes after single embryo transfer (SET) of a euploid blastocyst varied as a function of platform.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Trophectoderm biopsies for PGT-A for the past decade had at least one euploid embryo for transfer. Consistent with previous reports, the likelihood of transfer and euploid rates, stratified by egg age, fertilization type, day of biopsy, and clinical indication were assessed.

RESULTS: The dataset consisted of 138,643 embryos from 29,624 cycles. Egg age ranged from 18-55 years (mean of 35). The average number of biopsy samples per case was 4.5. Of resulted samples, 56% were euploid; 77% of all cycles had at least one euploid embryo (Table 1). As previously reported, the only factors affecting euploid rates were egg age and day of biopsy.1-3 Excluding embryos from known tr anslocation carriers, 10% of embryos had a segmental abnormality, 32% were observed in conjunction with at least one whole chromosome abnormality. Segmental changes were seen in all chromosomes and the rate of independent of egg age.

Out of 75,726 samples analyzed with our SNP enhancement, 1.6% were polyploid. These polyploid samples consisted of 924 triploid, 164 haploid/WG-UPiD and 154 tetraploid, many of which would have been misclassified as euploid or mosaic with other NGS-based assays.3 Of 1,574 transfers for which outcome data was provided, the observed clinical pregnancy rate was highly variable across clinics, with a range of 38%-80% (mean of 61%). The mean ongoing/live birth rate per transfer was 57%, with a clinic-specific rate range of 38%-80% (mean of 61%). The mean ongoing/live birth rate per transfer was 57%, with a clinic-specific rate range of 38%-80% (mean of 61%). The mean ongoing/live birth rate per transfer was 57%, with a clinic-specific rate range of 38%-80% (mean of 61%). The mean ongoing/live birth rate per transfer was 57%, with a clinic-specific rate range of 38%-80% (mean of 61%).

CONCLUSIONS: The majority of patients in this dataset had at least one euploid embryo for transfer. Consistent with previous reports, an age-related decline in euploidy was observed, and segmental aneuploidy was independent of age.5 Our data, stratified by egg age and number of embryos tested, is a valuable counseling tool for patients considering PGT-A.

REFERENCES

SNP array

<table>
<thead>
<tr>
<th>Age</th>
<th>SNP array</th>
<th>Array CGH</th>
<th>NGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>37.9 (4.0)</td>
<td>17.9 (0.3)</td>
<td>42.1%</td>
<td>56.0%</td>
</tr>
<tr>
<td>37.9 (3.6)</td>
<td>17.7 (10.3)</td>
<td>48.0%</td>
<td>50.8%</td>
</tr>
<tr>
<td>37.5 (4.0)</td>
<td>16.0 (8.8)</td>
<td>46.1%</td>
<td>52.7%</td>
</tr>
<tr>
<td>Total</td>
<td>37.9 (3.9)</td>
<td>17.4 (9.4)</td>
<td>44.2%</td>
</tr>
</tbody>
</table>

Mean (SD) or %

*p=NS
**p=0.01
***p<0.001
(coefficient 0.29, 95% CI 0.08, 0.51, p < 0.01). Rates of live birth or ongoing pregnancy after euploid SET (n = 987 transfers) did not differ by platform (Table; p = 0.83).

CONCLUSIONS: Euploid call rates differ as a function of PGT-A technology platform after adjusting for age and eggs collected. However, these differences do not seem to translate into different pregnancy outcomes after SET of a “euploid” blastocyst. Further investigation should attempt to reconcile these differences and clarify if and how advances in PGT-A technology platforms translate to patients.

P-328 Tuesday, October 15, 2019 6:30 AM
PREVIOUSLY VITRIFIED EMBRYOS CAN BE SUCCESSFULLY WARMED, BIOPSIED OR REBIOPSIED, AND PROVIDE RESULTS. Nicole George, BS, Carolyn MacDonough, BS, Christopher Hibray, BS, Lynn B. Davis, MD, MS, G David Ball, Ph.D., Seattle Reproductive Medicine, Seattle, WA.

OBJECTIVE: This study aimed to evaluate whether vitrified embryos could be warmed, biopsied or rebiopsied, and provide meaningful preimplantation genetic testing for aneuploidy (PGT-A) results. The vitrified and warmed embryos include both those biopsied for the first time, as well as those biopsied for a second time (rebiopsied) due to inconclusive results.

DESIGN: This was a retrospective study performed at a large, private IVF center which included 242 embryos being warmed and biopsied for the first time and 28 embryos being warmed and rebiopsied.

MATERIALS AND METHODS: Day 5 and 6 embryos of good and fair quality were vitrified for potential future use. Embryos were warmed, given time to re-expand, and biopsied. Some embryos that initially survived the warming process were unable to be biopsied due to degeneration or developmental arrest prior to re-expansion. Samples were sent to a third-party testing laboratory for PGT-A testing via aCGH, SNP array or NGS.

RESULTS: Two hundred forty-two embryos were warmed and biopsied for the first time. One hundred seventy-eight (74%) reached a stage and quality suitable for biopsy. One hundred ten of these embryos (62%) were euploid. When classified by age group, patients 37 years and under yielded a euploid rate of 66%, while patients 38 years and older yielded a euploid rate of 44%. Twenty-eight embryos were warmed for rebiopsy. Twenty-two (79%) reached a stage and quality suitable for biopsy. Twelve of these (55%) were euploid. When classified by age group, patients 37 years and under yielded a euploid rate of 62%, while patients 38 years and older yielded a euploid rate of 50%. Overall, 96% of thawed embryos (258/270) survived the warming process, and 78% of surviving embryos (200/258) were able to be biopsied or rebiopsied.

CONCLUSIONS: Embryo thaw survival rates are high, but approximately one in five embryos (22%) degenerate or arrest prior to re-expansion and cannot be biopsied. The majority of vitrified embryos can be successfully biopsied or rebiopsied and provide meaningful PGT-A results. With informed consent, embryo thaw and biopsy or rebiopsy is a reasonable clinical option.

P-329 Tuesday, October 15, 2019 6:30 AM
ARTIFICIAL INTELLIGENCE: NON-INVASIVE DETECTION OF MORPHOLOGICAL FEATURES ASSOCIATED WITH ABNORMALITIES IN CHROMOSOMES 21 AND 16. Matthew David VerMilyea, PhD.a Jonathan M. Hall, PhD.b Don Perugini, PhD.b Andrew P. Murphy, BS.b Tuc Nguyen, PhD.c Cecilia Rios, CG, c Alicia Picou, M.S., a Andrew Miller, MS, a Andrew W. Dinsmore, BS.a Kaylen Silverberg, MD.a Michelle Perugini, PhD.a ‘‘Life Whisperer, Adelaide, SA, Australia; ’’Ovation Genetis, Henderson, NV; ’’Californi Fertility Partners, Los Angeles, CA; ’’Texas Fertility Center, Austin, TX.

OBJECTIVE: To examine whether Artificial Intelligence (AI) algorithms and computer vision technology can non-invasively identify embryos with key morphological features associated with abnormalities of chromosome 21 and 16.

DESIGN: AI Analysis of embryo images in private reproductive technology programs.

MATERIALS AND METHODS: Approximately 2,000 static 2D images of Day 5 blastocysts with related pregnancy and pre-implantation genetic testing for aneuploidy (PGT-A) outcomes were assessed. Images were divided into three groups: training, validation, and blind test sets. Two AI models were trained, validated, and tested on embryo images by a further blind set test of 461 images with known PGT-A outcomes.

RESULTS: Our results show a high level of accuracy with the use of AI in detecting embryological morphological changes associated with additions to chromosome 21 or an additional full copy of the chromosome. A blind data set of 54 images achieved an accuracy of 81.5%. To expand the model to include all abnormalities of chromosome 21, we achieved an accuracy of 71% from 214 images. This reduction in accuracy is most likely the result of increased morphological variability between embryos with different (broader) abnormalities in chromosome 21. Using the same methodology, an accuracy of 73.1% was obtained when we were able to determine abnormalities of chromosome 16 in 214 images.

CONCLUSIONS: Embryonic chromosomal abnormalities are known to lead to implantation failure, pregnancy loss, severe chromosomal diseases (e.g. Down and ATR-16 syndromes) and have recently been associated with developmental disorders including Autism1. One of the major limitations of PGT-A analysis by traditional genetic analysis is the presence of chromosomal mosaicism within the developing embryo2. Recent advances in non-invasive embryo ploidy determination by either morphokinetic analysis by time-lapse imagery3 or cell free DNA isolation from either spent conditioned culture medium4 or blastocoel fluid5 have shown promise, but concordance studies have shown otherwise6. This study presents, for the first time, that AI can non-invasively determine whether certain morphological features of a Day 5 blastocyst are associated with specific chromosomal abnormalities of human embryos. Additional studies and analyses are under way.

<table>
<thead>
<tr>
<th>1st Biopsy</th>
<th>Total # of patients</th>
<th>Average Age</th>
<th>Warmed</th>
<th>Survival</th>
<th>Biopsied</th>
<th>Euploid</th>
<th>Aneuploid</th>
<th>Other*</th>
</tr>
</thead>
<tbody>
<tr>
<td>48</td>
<td>35.3</td>
<td>242</td>
<td>232</td>
<td>96%</td>
<td>178</td>
<td>110</td>
<td>56</td>
<td>12</td>
</tr>
</tbody>
</table>

*Other = 9 mosaic, 2 no DNA amplification, 1 no call

<table>
<thead>
<tr>
<th>Rebiopsy</th>
<th>Total # of patients</th>
<th>Average Age</th>
<th>Warmed</th>
<th>Survival</th>
<th>Biopsied</th>
<th>Euploid</th>
<th>Aneuploid</th>
<th>Other*</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>36.2</td>
<td>28</td>
<td>26</td>
<td>93%</td>
<td>12</td>
<td>8</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

*Other = 1 mosaic, 1 no DNA amplification
way to increase specificity and explore other chromosomal abnormalities by including larger data sets.

**REFERENCES**


**P-330**

**Tuesday, October 15, 2019 6:30 AM**

**IF ANY MOSAICISM IS IDENTIFIED IN THE TROPHECTODERM, THERE IS A 26% CHANCE OF MOSAICISM BEING PRESENT IN THE INNER CELL MASS; A CLINICAL PARADOX, DO YOU TRANSFER MOSAIC EMBRYOS?**

**P-331**

**Tuesday, October 15, 2019 6:30 AM**

**PRE-IMPLANTATION GENETIC TESTING (PGT-A) USING FAST-SEQS NGS OF IN VIVO CONCEIVED BLASTOCYSTS RECOVERED BY UTERINE LAVAGE.**

**P.330**

**Tuesday, October 15, 2019 6:30 AM**

**IF ANY MOSAICISM IS IDENTIFIED IN THE TROPHECTODERM, THERE IS A 26% CHANCE OF MOSAICISM BEING PRESENT IN THE INNER CELL MASS; A CLINICAL PARADOX, DO YOU TRANSFER MOSAIC EMBRYOS?**

Paul Robert Brezina, M.D.,a Kyle J. Tobler, M.S.,a Cameron F. Bagby, M.D.,a Elizabeth M. Strott, M.D.,a Kyle L. Robinson, M.D.,a David R. Schulte, M.D.,a Marisa D. Seraj, M.D.,a Rebecca L. Guzman, M.D.,a E. Hunter Lee, M.D.,a Jesse S. Meng, M.D.,a

**OBJECTIVE:** To determine the correlation of mosaicism identified in the trophectoderm (TE) to the rate of mosaicism within the inner cell mass (ICM).

**DESIGN:** Prospective

**MATERIALS AND METHODS:** 78 patients (631 embryos) underwent IVF and PGT-A was performed. All patients underwent IVF due to repeat pregnancy loss, previous unsuccessful IVF cycles, decreased ovarian reserve or unexplained infertility between 2012 and 2016. Embryos were first biopsied at the cleavage stage and if aneuploid, remained in culture to the blastocyst stage. At the blastocyst stage of development, the ICM and TE were separated and blindly analyzed. Molecular karyotypes were performed by enhanced next generation sequencing (NGS) using a Personal Genome Machine (PGM) or S5. By deep sequencing and proprietary algorithm’s, we can detect mosaicism at approximately the 10% level. This sequencing provided a minimum of over 3.5 million reads with a median sequencing fragment of 186bp.

**RESULTS:** 55% (350/631) of cleavage stage embryos were aneuploid. Of these, 37% (131/350) differentiated to the blastocyst stage. 26% (34/131) of these embryos were found to have mosaicism within both the TE and ICM.

**CONCLUSIONS:** Our results indicate that using an enhanced NGS technology, a significant percentage (26%) of embryos with detectable levels of mosaicism as determined by PGT-A in the TE population will be associated with mosaicism within the ICM as well. Clinically, an aneuploid mosaic fetus may result in a live birth with significant mental and physical deficits. Given this risk, we strongly recommend that the transfer of mosaic embryos only be considered as a last resort for very poor prognosis patients following comprehensive informed consent by a geneticist.

**P-331**

**Tuesday, October 15, 2019 6:30 AM**

**PRE-IMPLANTATION GENETIC TESTING (PGT-A) USING FAST-SEQS NGS OF IN VIVO CONCEIVED BLASTOCYSTS RECOVERED BY UTERINE LAVAGE.**

Charlene A. Alouf, PhD,a Sam Najmabadi, MD,b Steven T. Nakajima, MD,c John E. Buster, MD,d Nicole Faulkner, PhD,d Invitae, San Francisco, CA; Center for Reproductive Health & Gynecology, Beverly Hills, CA; Stanford University School of Medicine, Stanford, CA; Professor Emeritus of Obstetrics and Gynecology, Brown University, Providence, RI.

**OBJECTIVE:** To report the chromosomal characterization of in vivo conceived embryos utilizing a FAST-SeqS NGS-based PGT-A assay.

**DESIGN:** Reported rates of euploidy per oocyte age differ amongst fertility programs. The most striking range reported, with a relatively homogenous group of oocyte donors, suggests that stimulation, culture conditions and manipulation may impact ploidy. IVF/PGT-A reduces the transfer of abnormal embryos but may be cost prohibitive even with minimal stimulation. A preliminary report demonstrated success with retrieving in vivo created embryos for PGT-A using a patented uterine lavage system. In vivo culture would reduce the financial burden and the potential untoward effects of the in vitro environment.

**MATERIALS AND METHODS:** Twenty women underwent ovulation induction and donor insemination, with uterine lavage 5 days later, as previously described. The study had IRB approval and oversight by the Ministry of Health. TE biopsy was performed after lavage or following in vivo culture and donor insemination.

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Total # embryos at lavage (day 5)</th>
<th>Day 5 Grade</th>
<th>Day 6 Grade</th>
<th>Bx Day</th>
<th>Interpretation</th>
<th>Misc Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>186</td>
<td>4</td>
<td>6 cell frag</td>
<td>3CC</td>
<td>6</td>
<td>Aneuploid</td>
<td>delt(1)(q41)</td>
</tr>
<tr>
<td>187</td>
<td>11</td>
<td>4AA</td>
<td>6AA</td>
<td>6</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>187</td>
<td>9cell</td>
<td>3CC</td>
<td>6 Normal</td>
<td>6</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>192</td>
<td>6 cell vac</td>
<td>3cc</td>
<td>6 Aneuploid</td>
<td>6</td>
<td>Monosomy 8</td>
<td></td>
</tr>
<tr>
<td>197</td>
<td>8 cell, vac</td>
<td>2 (early)</td>
<td>6 Aneuploid</td>
<td>6</td>
<td>53.X,+1,+2,+3,+8,+9,+17,+20,+21</td>
<td></td>
</tr>
<tr>
<td>193</td>
<td>12 cell, vac</td>
<td>4AB</td>
<td>6 Mosaic</td>
<td>6</td>
<td>trisomy 22 (mos)</td>
<td></td>
</tr>
<tr>
<td>185</td>
<td>10 cell, vac</td>
<td>3CC</td>
<td>6 Mosaic</td>
<td>6</td>
<td>delt(4)(q32) (mos)</td>
<td></td>
</tr>
<tr>
<td>196</td>
<td>2</td>
<td>6BB</td>
<td>6 Anueploid</td>
<td>6</td>
<td>Monosomy 13</td>
<td></td>
</tr>
<tr>
<td>200</td>
<td>2</td>
<td>6CC</td>
<td>5 Normal</td>
<td>5</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>202</td>
<td>1</td>
<td>5BB</td>
<td>5 Normal</td>
<td>5</td>
<td>Normal</td>
<td></td>
</tr>
</tbody>
</table>
vitro culture. Biopsies were analyzed using Invitae’s FAST-SeqS NGS bioinformatics pipeline which detects whole chromosome and segmental aneuploidies (≥ 10 MB). Whole genome uniparental Isodisomy (WG-UPID or haploidy), all forms of triploidy, and most single chromosome UPiD are also identified from this analysis.3

RESULTS: Thirty-five viable embryos were recovered from 15 patients. Five blasts were biopsied on day 5 and 13 biopsied on day 6 from 10 patients total. Mean egg age for the resulting biopsied embryos was 26 (range 21-30). In all (n=18), 12 embryos (67%) were euploid, 4 were aneuploid (22%) and 2 mosaic (5.7%). Of interest, all 5 embryos biopsied on day 5 were euploid regardless of grade; the day 6 aneuploidy rate was 46%.

CONCLUSIONS: In this small sample, the higher aneuploidy rate in day 6 biopsies was consistent with Invitae’s previous report. Additionally, the euploid rate for egg age (<= 30) and the mosaic rate are consistent with Invitae’s internal data (68% and 5%-7%, respectively). Uterine lavage is an effective alternative to IVF for the recovery of viable embryos for PGT-A.

Additional studies are planned to confirm these findings.

REFERENCES

SOMY USING OWN OOCYTES: IS A SUITABLE PGT-A (PREIMPLANTATIONAL GENETIC TESTING) FOR ANEUPLOIDY, ALL FORMS OF TRIPLOIDY, AND MOST SINGLE CHROMOSOME UPiD, REGARDLESS OF GRADE; THE DAY 6 ANEUPLOIDY RATE WAS 46%.

RESULTS: Mean egg age for the resulting biopsied embryos was 26 (range 21-30). Five blasts were biopsied on day 5 and 13 biopsied on day 6 from 10 patients total. Mean age and body mass index was 38.1 y (37.3-39). RESULTS: Mean age and body mass index was 38.1 y (37.3-39) vs. 36.1 y (35.3-37.8). 24.6 kg/m² (23.4-25.8) vs. 23.6 kg/m² (22.9-24.2) for PGT-A (MTS) vs. OD (MTS/PTS) respectively, without significant differences found.

OBJECTIVE: Evaluate the reproductive outcome of preimplantational genetic diagnosis (PGT-A) in patients with mosaic Turner’s syndrome (MTS) using own oocytes, compared to mosaic and pure Turner syndrome (PTS) using ova.

DESIGN: Prospective cohorts study from January 2011 until December 2017, scrutinizing >120,000 IVF cycles from 14 infertility clinics in Spain, searching for pure or mosaic TS, confirmed by the karyotype.

MATERIALS AND METHODS: University-affiliated private-infertility centre. 67 PGT-A in MTS patients (FISH/arrays-NGS), on which 65 searches for pure or mosaic TS, confirmed by the karyotype.

CONCLUSIONS: Despite being the largest sample size ever reported with PGT-A in MTS the number of patients included is still low. Subsequently, the conclusions reached should be taken carefully until a larger body of evidence will be available.

Oocyte donation (OD) seems to be the best reproductive option in female who are missing one of the X chromosomes, with or without mosaicism presents.

Nevertheless, based on the previous data, PGT-A is a valid therapeutic option in patients with mosaic Turner’s syndrome (MTS) using own oocytes and OD should not necessarily be recommended directly as the treatment of choice.

REFERENCES

P-333 Tuesday, October 15, 2019 6:30 AM

PGT-A (PREIMPLANTATIONAL GENETIC SCREENING) IN PATIENTS WITH PARTIAL X MONOSOMY USING OWN OOCYTES: IS A SUITABLE INDICATION? Juan Giles, M.D., Ph.D.,a

Amparo Mercader, Ph.D.,b Carmen Rubio, Ph.D.,c Carmen Vidal, M.D., Ph.D. b Lucia Alegre, Ph.D.,d Martina Trabalon, MD Ph.D,c Marcos Meseguer, Ph.D.,d IVI-IVMA Valencia, Valencia, Spain;e IVIRMA Valencia, Valencia, Spain;e Igenomix Spain, Paterna (Valencia), Spain;f IVIRMA Global, Valencia, Spain;f IVIRMA Murcia, Murcia, Spain;f IVIRMA Global, Valencia, Spain, Tel Aviv, Israel.

OBJECTIVE: Evaluate the reproductive outcome of preimplantational genetic diagnosis (PGT-A) in patients with mosaic Turner’s syndrome (MTS) using own oocytes, compared to mosaic and pure Turner syndrome (PTS) using ova.

PGT-A (PREIMPLANTATIONAL GENETIC TESTING FOR ANEUPLOIDY DETECTION) IN PATIENTS WITH TURNER’S SYNDROME: OBJECTIVE: Evaluate the reproductive outcome of preimplantational genetic diagnosis (PGT-A) in patients with mosaic Turner’s syndrome (MTS) using own oocytes, compared to mosaic and pure Turner syndrome (PTS) using ova.


OBJECTIVE: The absence of standardised culturing conditions or molecular testing methodologies, including whole genome amplification (WGA) used for non-invasive preimplantation genetic testing of spent embryo culture media for aneuploidy (NI-PGT-A) may explain the variable rates of
concordance reported between the spent embryo culture media and embryo biopsy results to-date. Culture conditions impact the accumulation of embryonic and contaminating DNA in spent embryo culture media and optimisation of either the cultivating conditions, molecular testing methodologies, or both, should yield the highest level of concordant results for NI-PGT-A.

DESIGN: This study examined rates of ploidy concordance between spent embryo culture media and embryo biopsies to evaluate the impact of cultivating conditions on NI-PGT-A results.

MATERIALS AND METHODS: Spent embryo culture media was collected from single embryo culture droplets following biopsy of the embryo for PGT-A then stored at -20°C, with ethics approval. Equivalent volumes of spent embryo culture media samples from 10μl-60μl culture droplets, from either continuous (n=4 labs) or two-step cultures (n=4 labs) were whole genome amplified using DOP-It® kit reagents (PerkinElmer). WGA DNA yield was assessed by gel electrophoresis and high sensitivity quantification using a Qubit® instrument (Thermo Fisher® Scientific). Next generation sequencing libraries were generated according to the PG-Seq™ kit 48 sample protocol and sequencing was performed on a MiSeq® instrument (Illumina/8). Data was bioinformatically aligned to hg19, and WGA DNA yield, NGS metrics, and whole chromosome aneuploidy concordance with the PGT-A result for the embryo biopsy were determined.

RESULTS: Whole genome amplification using the DOP-It® kit reagents resulted in the amplification of 78-100% of spent embryo culture media samples (WGA failure rate 0-22%). Ploidy concordance with the embryo biopsy ranged from 29-75% for autosomal chromosomes and 47-94% for sex chromosomes using a single-step culturing system (n=4), compared with concordance rates of 67-90% and 50-97% respectively when media was changed during the 5-6 day culture (n=4). DNA yield was not affected by embryo culture media droplet volume, or continuous or two-step culture. Sex chromosome concordance varied between individual labs, suggesting that embryological processes are important in NI-PGT-A testing. Further statistical analysis during the ongoing larger scale collaborative study will determine quality control parameters for acceptance of NI-PGT-A results.

CONCLUSIONS: Successful NI-PGT-A using spent embryo culture media will possibly require specific culturing conditions and/or specialised molecular analysis during the ongoing larger scale collaborative study will determine quality control parameters for acceptance of NI-PGT-A results.

P-335 Tuesday, October 15, 2019 6:30 AM
APPLIED OF WHOLE GENOME NEXT GENERATION SEQUENCING (NGS) ANALYSIS OF PRODUCTS OF CONCEPTION AFTER FRESH EMBRYO TRANSFER. Siwei Chen, MD,a Rina Abramov, MSc,b Ran Antes, PhD,a Valeriy Kuznetsov, PhD,a Svetlana Madjunkova, MD,a Clifford Lawrence Librach, MD. aCreate Fertility Centre, Toronto, ON, Canada; bCREAte fertility centre, Toronto, ON, Canada; cCREAte Fertility Centre, Toronto, ON, Canada.

OBJECTIVE: Genetic assessment of tissue from products of conception (POC) can elucidate the reason for miscarriage in approximately 50-70% of first trimester miscarriages. Assessment of the fetal chromosomal composition may be very helpful in counselling and management of parents experiencing miscarriages, especially after IVF, or in patients with recurrent pregnancy losses. However, obtaining fetal tissue from early miscarriages is often compromised by maternal cell contamination (MCC). Here we present the results from assessing early POC samples (<10 GW) after IVF single embryo transfer, controlling for MCC, using whole genome NGS at the CREAte Fertility Centre.

DESIGN: A retrospective study.

MATERIALS AND METHODS: POC samples (n=294) (Jan, 2016-Apr, 2019) from early pregnancy losses after IVF treatment were obtained by suction D&C collection. Four representative samples of fetal tissue and/or chorionic villi were separated from decidual tissue and blood using a dissecting microscope. A maternal/paternal blood sample was obtained for DNA extraction to test for MCC. MCC was determined using analysis of short tandem repeats-STRs (AmpFlSTR Identifier Plus kit) of maternal and fetal DNA (fDNA). After confirmation of fetal DNA origin, whole genome NGS was carried out using VeriSeq kit. GeneMapper (Applied Biosystems) and BlueFuse Softwarev4.4 (Illumina) were used to analyze the STR and NGS data.

RESULTS: In total, we analyzed 294 POC samples (8.45±1.8 weeks) from patients undergoing IFV. Overall, mean maternal age was 36.8±8.5 years. DNA confirmation by STR MCC analysis was obtained from 45.6% (n=134) of the samples. NGS analysis for chromosomal aberrations showed increased MCC (n=134) of the POC samples were euploid (46,XX n=37, 46, XY n=29), 14.2% of fDNA samples (19/134) were from euploid embryos tested by NGS for aneuploidy at blastocyst stage. All these 19 POC samples were confirmed to be euploid and 100% sex concordant with preimplantation result. Aneuploidy was detected in 46.3% (62/134) [trisomy- T16,12.9%; T21, 12.9% ; T22, 11.3%; T15,9.7%; T20, 6.5%; T14, 4.8%; T3 and T18, 3.2%; 1.6% of each T9,T12,T14,T13, T15+16,T5+15, T15+22, T17; monosomy – X, 17.7%, and 4.8% were trisloid (69,XXX)]. Mosaicism was detected in 4.5% (6/134): (x-X,30%;+XX,60%; 1/6); (-X;1p11.2-1q21.33, 36Mb, 60%, -Xq21.33-qter, 40%, 1/6); (+Y,60%;1/6); (+8,50%;+9,50%, 1/6);(+12q,30%, 1/6)).

CONCLUSIONS: MCC is high in POC samples from early pregnancies and controlling for it is warranted. NGS results from euploid embryo transfers were fully concordant with PGT-A results. Establishing STR MCC and NGS analysis of POC on a larger scale would improve diagnostic accuracy, and could aid in patient counselling and management.

CREATE Support Centre.
OBJECTIVE: Clinical studies have shown a difference in perinatal outcomes following fresh versus frozen embryo transfer. With the advent of pre-implantation genetic testing (PGT), many clinics have moved towards "freeze-all" cycles in conjunction with PGT, though there do remain many clinics who perform PGT before fresh embryo transfer. This study aims to assess the differences in perinatal outcomes of autologous fresh embryo transfer using embryos that underwent biopsy for PGT versus those that did not.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: The Society for Assisted Reproductive Technology (SART) database was used to identify fresh embryo transfer cycles that did and did not undergo PGT from 2014 and 2015. Cycles in which embryos were transferred on days 5, 6, or 7 were included. Log binomial regression models were used to assess for associations between embryo biopsy and pregnancy and perinatal outcomes. Models were adjusted for covariates including maternal age, race, BMI, smoking, prior IVF cycles, prior preterm/full-term births and cause of infertility.

RESULTS: The mean age of the no biopsy patients (N=52,754) and biopsy patients (N=1,003) was 33.9 and 35.2 years, respectively (P<0.01). Compared to patients whose embryos were not biopsied, patients whose embryos were biopsied were significantly more likely to have a clinical pregnancy (61.2 vs. 57.3%, adjusted relative risk (aRR) 1.16, 95% confidence interval (CI) 1.07, 1.26) and live birth (54.4 vs. 48.4%, aRR 1.17, 95% CI 1.10, 1.29). Of the live births (N=25,462) no biopsy, N=543 biopsy, the incidence of large for gestational age (LGA) neonates was significantly higher in the biopsy group compared to the non-biopsy group (12 vs. 10.3%, aRR 1.45, 95% CI 1.04, 2.02). There were no differences in the incidence of LBW (24.9 vs. 28.8%, biopsy vs. no biopsy, aRR 0.83, 95% CI 0.61, 1.12) or preterm delivery (PTD) (20 vs. 22.6%, aRR 0.84, 95% CI 0.70, 1.00).

CONCLUSIONS: Evaluating the subset of patients whose had fresh embryos transferred following PGT allows for the assessment of the effects of PGT itself without the confounding effects of embryo cryopreservation. While there was a difference seen in the incidence of LGA babies, there were otherwise no differences seen in perinatal outcomes between fresh transfer with and without embryo biopsy. Future studies should assess potential etiology for the observation of an increase in LGA babies following fresh transfer after embryo biopsy.

SUPPORT: None.

P-337 Tuesday, October 15, 2019 6:30 AM

ACCURACY OF CELL-FREE EMBRYONIC DNA TESTING FOR EUPLOIDY AND ANEUPLOIDY IN COMBINED SPENT EMBRYO CULTURE MEDIUM AND BLASTOCOELE FLUID SAMPLES WITH OR WITHOUT USING A CELL LYSIS STEP BEFORE AMPLIFICATION. Valeriy Kuznyetsov, PhD,a Svetlana Madjunkova, MD,a Rina Abramov, MSc,a Ran Antes, PhD,a Iryna Kuznyetsova, PhD,a Clifford Lawrence Librach, MD,a 1CREAte Fertility Centre, Toronto, ON, Canada; 2CREAte fertility centre, Toronto, ON, Canada.

OBJECTIVE: Blastocoele fluid (BF) and spent embryo culture medium (SEM) both contain cell-free embryonic DNA (cfedNA). Attempts to use cfedNA for non-invasive preimplantation genetic testing (NIPGT), brings to light several factors that could affect the accuracy of this approach. These include maternal contamination by cumulus/corona cells and DNA degradation. The objective of this study was to determine the accuracy, efficacy and reliability of whole genome amplification (WGA) to determine ploidy status (euploid/aneuploid) of the blastocyst using combined SEM+BF samples with or without using a cell lysis step before amplification.

DESIGN: Controlled prospective study. Two NIPGT samples (SEM+BF) from each culture medium droplet were used for amplification and subsequent testing of chromosomal abnormalities. Results were compared with the corresponding trophectoderm (TE) biopsy sample used as control.

MATERIALS AND METHODS: Laser zona opening was performed on Day 5, and embryos were transferred to fresh 20ul droplets of Global Cycles medium with HSA. Thirty nine human blastocysts were collapsed by a laser pulse, and then both SEM and BF samples were collected together as one.

RESULTS: Multiplex ligation-dependent probe amplification (MLPA) and methylation testing was performed to evaluate for Prader-Willi syndrome (caused by 15q11.2-13 paternal deletions) on the affected boy. This testing incidentally diagnosed an extra paternal copy of 15q11.2-q13. Chromosomal microarray [Dian Diagnostics] confirmed a 5.76MB duplication at 15q11.2-13. The boy was diagnosed with 15q duplication syndrome, a highly variable condition associated with developmental delays, autism spectrum disorders, and a phenotype influenced by parental origin of the duplication (maternal vs paternal). Retrospective analysis of his PGT-A results was requested per clinic protocol. Review of archived profile images of the original NGS data [BlueFuse Multi, Illumina Inc] 5/7 embryos were diagnosed as euploid and FET of two euploid male embryos resulted in the birth of healthy twin boys. By 8 months of age one twin had failed to meet his developmental milestones, developed marked obesity, and had abnormally low growth hormone and insulin levels.

RESULTS: Clinical studies have shown a difference in perinatal outcomes following fresh versus frozen embryo transfer. With the advent of pre-implantation genetic testing (PGT), many clinics have moved towards “freeze-all” cycles in conjunction with PGT, though there do remain many clinics who perform PGT before fresh embryo transfer. This study aims to assess the differences in perinatal outcomes of autologous fresh embryo transfer using embryos that underwent biopsy for PGT versus those that did not.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: The Society for Assisted Reproductive Technology (SART) database was used to identify fresh embryo transfer cycles that did and did not undergo PGT from 2014 and 2015. Cycles in which embryos were transferred on days 5, 6, or 7 were included. Log binomial regression models were used to assess for associations between embryo biopsy and pregnancy and perinatal outcomes. Models were adjusted for covariates including maternal age, race, BMI, smoking, prior IVF cycles, prior preterm/full-term births and cause of infertility.

RESULTS: The mean age of the no biopsy patients (N=52,754) and biopsy patients (N=1,003) was 33.9 and 35.2 years, respectively (P<0.01). Compared to patients whose embryos were not biopsied, patients whose embryos were biopsied were significantly more likely to have a clinical pregnancy (61.2 vs. 57.3%, adjusted relative risk (aRR) 1.16, 95% confidence interval (CI) 1.07, 1.26) and live birth (54.4 vs. 48.4%, aRR 1.17, 95% CI 1.10, 1.29). Of the live births (N=25,462) no biopsy, N=543 biopsy, the incidence of large for gestational age (LGA) neonates was significantly higher in the biopsy group compared to the non-biopsy group (12 vs. 10.3%, aRR 1.45, 95% CI 1.04, 2.02). There were no differences in the incidence of LBW (24.9 vs. 28.8%, biopsy vs. no biopsy, aRR 0.83, 95% CI 0.61, 1.12) or preterm delivery (PTD) (20 vs. 22.6%, aRR 0.84, 95% CI 0.70, 1.00).

CONCLUSIONS: Evaluating the subset of patients whose had fresh embryos transferred following PGT allows for the assessment of the effects of PGT itself without the confounding effects of embryo cryopreservation. While there was a difference seen in the incidence of LGA babies, there were otherwise no differences seen in perinatal outcomes between fresh transfer with and without embryo biopsy. Future studies should assess potential etiology for the observation of an increase in LGA babies following fresh transfer after embryo biopsy.

SUPPORT: None.
patient’s three remaining euploid embryos were also then reanalyzed via PGTa and 2/3 embryos were reaffirmed to be euploid. The third embryo was found to have the same 15pter-q13.1 duplication as the affected boy, also in the mosaic range (78%), suggesting that the variant may be inherited.

**CONCLUSIONS:** This may be the first case in which correlation between a mosaic PGT-A result and the same finding postnatally, in non-mosaic form and likely resulting in an abnormal phenotype, has been made. This case is highlights the significant challenges of predicting mosaic embryo transfer outcomes. Transfers of mosaic result embryos may not always result in binary outcomes, an essential consideration for genetic counseling of families considering this option.

**P-339 Tuesday, October 15, 2019 6:30 AM**

**OUTCOMES OF A SIMPLIFIED MOSAIC RANKING SYSTEM.** Andrijana Jovasevic, Bachelor of Science (Molecular Genetics and Biotechnology),1 Mark Livingstone, Genea Deputy Medical Director, MB, ChB, FRANZCOG, CREI, MM,2 Maria Victoria Traversa, MScMed,3 Jolene Stockton, Bachelor of Science,4 Steve Grkovic, PhD,4 Steven J. McArthur, BSc, PLD (Harvard Business School),5 Genea, Sydney, NSW, Australia; 6Genea Sydney, Sydney, NSW, Australia.

**OBJECTIVE:** Investigating outcomes of transferring mosaic embryos according to a simplified classification system that replaced our more complex 1-9 ranking system.

**DESIGN:** Following previous implementation of a comprehensive mosaicism classification system, a review of our mosaic embryo outcome data, together with that of recent literature (Spinella et al 2018, and Munne et al 2017) was conducted. The goal was to introduce a more simplified classification system – using an A-D grading – which ranks mosaic embryos for clinical use (as per table below). The study included 158 single transfers of embryos (between April 2016 to February 2019) which exhibited a mosaic shift (ranging from 20-79%) using NGS technology.

**RESULTS:**

| TF-A | NAD (no abnormality detected) – first choice for transfer |
| TF-B | Noisy result/low level mosaicism <=40% – second choice |
| TF-C | MOSAIC (significant mosaicism detected >40% <=80%) - third choice, further stratified by: |
| TF-D | ABN (abnormal) – not available for transfer |

- C1: -segmental low-risk chromosomes
- C2: high risk chromosomes
- C3: mosaic detected (>40% <80%)
- C4: second choice
- C5: third choice

**CONCLUSIONS:** Overall, the positive bHCG and fetal heart outcomes support the simplified classification system and the concept of preferentially transferring low level before high level whole chromosome mosaics in the absence of NAD embryos. Single segmental mosaic embryos have improved clinical outcomes compared to whole chromosome mosaic embryos and should be considered for preferential transfer ahead of other types of mosaic findings. Whole chromosome mosaics should be considered last choice.

**P-340 Tuesday, October 15, 2019 6:30 AM**

**EVALUATION OF THE IMPACT OF THE PULLING AND FLICKING TROPHECTODERM BIOPSY PROCEDURES ON THE INTEGRITY OF THE BIOPSIED CELLS AND THEIR CORRELATION TO PGT-A RESULTS.** Marina Benavent, MSc,5 Maria Escriba, MSc,2 Clara Miret, MSc,6 Ivette Vanrell, MSc,6 Nuno Costa-Borges, PhD,7 Gloria Calderón, PhD,8 Juana Crespo, MD,9 Jose Teruel, MSc,10 Equipo Juana Crespo, Valencia, Spain; 1Embryotools, Barcelona, Spain.

**OBJECTIVE:** Blastocyst biopsy is currently the gold standard in PGT-A. However, because trophectoderm (TE) cell excision is technically challenging, results can vary depending on how the procedure is performed. To ensure successful results, it is important not only to avoid harming the blastocyst during the biopsy procedure, but also to ensure a minimal damage on the biopsied cells. In this study, we aimed to evaluate the impact of two different TE biopsy techniques (pulling and flicking) on the integrity of the biopsied cells and to correlate their status with the chromosome screening results of the two methods.

**DESIGN:** This is a retrospective observational study that includes the data analysis of 268 TE biopsies performed on blastocysts from 83 patients (mean age – 39.1 y/o) that underwent a PGT-A cycle between October 2018 and April 2019. Chromosome screening analysis were carried out by an accredited genetics laboratory. Indications for PGT-A cycles included advanced maternal age, recurrent implantation failure, recurrent miscarriage and/or severe male factor.

**MATERIALS AND METHODS:** Trophectoderm biopsies were performed with the assistance of a dynamic laser. Assisted hatching was performed on Day 3 and biopsied day 5 blastocysts with hatching cells not completely hatched were biopsied with the “pulling” or “flicking” techniques. In the pulling method, blastocysts were held firmly with the holding pipette and the biopsy needle used to pull TE cells away from the blastocyst, while laser pulses were applied. In the flicking method, laser pulses were used to allow TE cells to be drawn inside the biopsy pipette and subsequently the TE cells were excised with a quick movement of the biopsy pipette against the holding pipette. Biopsied cells were then photographed and classified according to their integrity status as follows: intact (A); partially lysed (B); completely lysed (C). After biopsy, the cells were washed and transferred into PCR tubes to be processed for chromosome screening by NGS. Statistical significance was assessed by Students t-test or Fisher’s exact test.

**RESULTS:** A total of 118 blastocysts were biopsied with the pulling method and 150 with the flicking technique and no differences were found in terms of mean age of the patients (39.5±1.1 and 38.5±3.2, respectively) or average number of laser pulses used (4.2±1.1 vs 3.9±0.9, respectively). Overall, the pulling technique resulted in higher (p=0.0009) percentage of pieces graded as A (74.6%, n=88) than the flicking method (54.7%, n=82), but no differences were found among the two groups in terms of euploidy rates (28% and 36%, respectively). Regardless of the technique used, all cells graded as A were majorly (80-100%) diagnosed as chromosomally abnormal compared to those that were classified as morphologically intact (43.9-62.5%) or partially lysed (52.4-62.5%).

**CONCLUSIONS:** These results indicate that the pulling and flicking methods do not differ in terms of rates of chromosomally normal blastocysts as long as both procedures are applied correctly. The integrity of the cells seems to affect the results of aneuploidy rates, which might depend on blastocyst morphology.

**SUPPORT:** Institutional funding.

**P-341 Tuesday, October 15, 2019 6:30 AM**

**DEVELOPMENT OF A NEXT GENERATION SEQUENCING METHOD (PGT-SR PLUS) TO DETERMINE CARRIER STATUS OF BALANCED TRANSLOCATION PATIENT EMBRYOS.** Hua Jin, PhD, Hui Zheng, MA, Alysha Nicole Sábatos, BS, Robert Snyder, BS, ManLi, MD, PhD, Lian Liu, MD, PacGenomics, Agoura Hills, CA.

**OBJECTIVE:** Currently, PGT-SR is the only PGT option in the United States for patients with a balanced translocation. While PGT-SR does...
reliably screen for chromosomal copy number normal embryos and avoid the transfer of unbalanced translocation embryos, PGT-SR cannot determine the carrier status of embryos. Our objective is to develop a generic genome-wide next generation sequencing method (PGT-SR Plus) that can determine the carrier status of balanced translocation patient embryos, regardless of the type or location of translocation. This will allow patients the option to transfer embryos without the structural chromosomal abnormality.

**DESIGN:** Feasibility and validation study.

**MATERIALS AND METHODS:** The feasibility of the PGT-SR Plus method has been tested on 10 cases involving various chromosomes, including Robertsonian and reciprocal translocations. Parental blood was collected to determine the balanced translocation allele. Then, PGT-SR was performed on all embryos to identify those with a normal chromosomal copy number. These identified embryos, along with one unbalanced embryo, were then tested with PGT-SR Plus. The unbalanced embryo is used as a reference for phasing the parental carrier’s balanced translocation allele. The carrier status of each embryo was then determined based on whether or not the embryo carries the parental balanced translocation allele.

**RESULTS:** All 10 translocation cases that have been tested with PGT-SR Plus have had definitive results for the carrier status of the balanced translocation embryos. 7 of these 10 cases were also tested on the illumina karyomapping microarray platform and the same carrier statuses were identified, indicating that our generic next generation sequencing method and bioinformatic analysis pipeline are encouraging for screening structural chromosomal abnormalities.

**CONCLUSIONS:** The next generation sequencing-based PGT-SR Plus is a promising method for determining the carrier status of balanced translocation patient embryos. As a genetic method, it does not rely on the design of patient specific primers. It is applicable to all currently identified structural chromosomal abnormalities and is therefore very affordable.

---

**IMPACT OF TROPHOECTODERM BIOPSY FOR PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) ON EARLY BETA-HCG TRENDS IN SINGLE FROZEN EMBRYO TRANSFERS (FET) RESULTING IN LIVE BIRTH.** Laura Perez Soriano, BA,a Joshua Stewart, M.D.,b Steven Spandorfer, M.D.,b Zev Rosenwaks, M.D.b. aWeill Cornell Medical College, New York, NY; bThe Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

**OBJECTIVE:** Newer techniques in PGT-A allow blastocyst biopsy removing 6-10 trophectoderm cells for genetic analysis. As syncytiotrophoblasts produce beta-hCG, our objective was to determine the effect of trophectoderm biopsy for PGT-A on early serum beta-HCG trends in pregnancies resulting in a singleton live birth.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** All patients undergoing an FET cycle of a single blastocyst between January 2015 to December 2017 were analyzed. Cycles were divided into those with PGT-A and without. For PGT-A cycles, only euploid embryos were included. Inclusion criteria: 2 serum BhCG results obtained 2 days apart, delivery of a live singleton. Exclusion criteria: cycles utilizing donor oocytes, multiple gestation pregnancies. Primary outcomes were initial serum BhCG and 2-day increase in BhCG. Secondary outcomes were serum estradiol (E2) and progesterone (P4). Groups were further stratified by FET protocol, natural cycle or medicated.

**RESULTS:** 487 cycles met inclusion criteria, 279 with PGT-A and 208 without. There was no difference in mean initial BhCG or second serum BhCG levels between the cycles with PGT-A and those without PGT-A despite controlling for age and protocol. The median 2-day increase in BhCG was significantly higher in the PGT-A group versus the cycles without PGT-A (247.9% vs 238.9%, respectively, p<0.02). There was no difference in the 2-day rise of serum E2 or P4 levels between the groups.

**CONCLUSIONS:** BhCG is commonly used as a marker of trophoblast differentiation and to assess pregnancy viability, but little is known about the impact of trophectoderm biopsy on BhCG trends. Our results reveal no difference in initial BhCG between cycles with PGT-A and without. While there was a significantly greater 2-day increase in BhCG in the PGT-A group, the clinical relevance of this minimal difference is unclear. However, it is clinically reassuring that trophectoderm biopsy does not impair BhCG rise. This contributes to previous studies that suggest trophectoderm biopsy does not affect implantation or early pregnancy steroidogenesis, adding to the overall safety of PGT-A to achieve healthy pregnancies.

**REFERENCES**


CONCLUSIONS: Hematological differences exist between women who successfully conceive following a fresh IVF cycle, as demonstrated by increases in neutrophil and lymphocyte counts in women who had a positive hCG versus those who did not conceive. There are also differences in estradiol and progesterone early when pregnancy is diagnosed. Waist hip ratio was increased in neutrophil and lymphocyte counts in women who had a positive two- to three-day test and-tilt and cooxon tests; data presented as mean ± standard deviation with the significance threshold set at p < 0.05.

RESULTS: The mean age of subjects at retrieval was 32 ± 3.7 years, mean BMI 25.5 ± 3.9 kg/m², with no significant differences between women based on conception status. Half of the women conceived with the initial fresh IVF cycle. Women who conceived had a lower waist:hip circumference ratio (0.77 ± 0.05) compared to those who did not (0.9 ± 0.04), p = 0.003. There were differences in android tissue fat and android:gynoid fat ratio based on conception status (not statistically significant). There were no other differences in body composition or bone mineral density age matched z-scores between groups.

CONCLUSIONS: Hormonal and hematological characteristics of women undergoing in vitro fertilization (IVF).

OBJECTIVE: To determine if averaged nocturnal vaginal temperature measurements recorded during non-menstruation by use of the OvuSense system (OS), could describe atypical patterns potentially associated with reduced fertility.

RESULTS: Three novel atypical temp patterns were identified: (a) 'Crash To Baseline' first nightly averaged temp falls by >0.2 degrees Celsius (C) to lowest cycle temp point (baseline) – final temp >0.9 degrees C, (b) 'False Ovulation' rise of >0.1 degrees C followed by a return to baseline temp followed by ovulation two or more days later in the cycle - 981 cycles (9.4%); 939 users (14.1%), (c) 'Crash After Ovulation' final temp >0.2 C lower than the post ovulatory peak temperature - 1,259 cycles (12.0%); 1,062 users (16.0%). Additionally, Short Luteal Phase (SLP) (d) was noted with menstruation 9 or fewer days post-ovulation - 871 cycles (8.3%); 793 users (12.0%).

Support: This work was supported by NIH grant number R01HD057110 (COS); SCB was supported by NIH training grant number T32HL07692.
133 cycles; 128 users, with (b) 155 cycles; 153 users, with (c) 7 cycles; 7 users. SLP co-existed with pattern (a) + (b) 33 cycles; 32 users, and as in low frequency with (a) + (c) 1 cycle; 1 user; and (b) + (c) 2 cycles; 2 users. Therefore 3,721 cycles exhibited one or more ‘atypical’ patterns (a), (b), or (c) = 35.6%.

CONCLUSIONS: It is likely OS continuous vaginal temp patterns closely reflect luteal progesterone changes, hence describe subtle progesterone secretion or metabolism anomalies, which not yet have been recognised. (a) suggests high progesterone early in the cycle, (b) suggests a small progesterone rise which does not result in a sustained ovulatory rise, but is followed by an ovulatory rise later in the cycle, (a) and (b) would be expected to occur in women with PCOS, and further studies are planned to examine this within the OS population. (c) suggests that progesterone may fall sharply in some women before onset of menses, and it is possible that fertility may be impaired in these cycles. Relatively strong correlation between SLP and patterns (a), (b), and/or (c) indicates vaginal, core-body temp monitoring may represent a promising method of identifying previously undetectable causes of infertility in women with “normal” ovulation.

References:

SUPPORT: This study was financially supported by Fertility Focus Ltd.

P.346 Tuesday, October 15, 2019 6:30 AM

IGF-1 AND IGFBP-3 SERUM CONCENTRATIONS IN PATIENTS UNDERGOING PROGRAMMED FROZEN-THAVED EMBRYO TRANSFER OF EUPLOID PGT-A EMBRYOS. Robert Setton, MD, Antonia Athanasiou, MD, Dayton James, PhD, Steven Spandorfer, M.D., The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: IGF-1 has been shown to induce embryonic development in vitro, but at high concentrations it exerts toxic effects by decreasing embryonic glucose uptake. IGFBP-3 binds IGF-1, modulating its bioavailability and is essential to its function. Prior reports have associated elevated follicular phase IGF-1 with pregnancy loss in frozen-thawed embryo transfer in natural cycles (n-FET), but an association in programmed (p-FET) cycles or in the luteal phase has not been analyzed. We sought to determine whether serum levels of IGF-1 and IGFBP-3 correlate with the outcome of p-FET cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients who underwent p-FET of single, good quality (Grade ≥2BB), PGT-normal embryos were included in the study. GnRH-agonist suppression was started in the preceding luteal phase, overlapped with estradiol patches, and stopped with the start of progesterone. Serum samples were collected on cycle day 2 (CD2), the day of progesterone start (CDP4), and cycle days 28 (CD28) and 30 (CD30). Embryo transfer occurred on the 7th day of P4 administration. Serum levels of IGF-1 and IGFBP-3 were compared between those who did not achieve pregnancy, those who had a live birth, and those who had a pregnancy loss. Serum IGF-1 and IGFBP-3 levels were measured by chemiluminescent immunoassays using the Immulite 2000 XPi. Statistical analysis was performed using Chi-square and Fisher’s exact test. P <0.05 was deemed statistically significant.

RESULTS: A total of 102 patients who underwent p-FET of single euploid embryos over 2 years were analyzed. The mean age at retrieval was 35.7 ± 4.1 years, BMI 24.2 ± 4.8 kg/m2, gravity 1.8 ± 1.6, parity 0.4 ± 0.6 and peak endometrial thickness 9.7 ± 2.0 mm. 76.5% of patients were pregnant and 78.2% of those had a live birth. Among women who conceived, those who had a subsequent pregnancy loss had significantly higher serum IGF-1 levels on CDP4 and CD28 compared to those who achieved live birth when analyzing patients whose serum IGF-1 levels were above the mean value of IGF-1 level on CDP4 (136 ng/ml, p = 0.044) and CD28 (138 ng/ml, p = 0.007), and between patients with CD28 IGF-1 levels one standard deviation above the mean (≥ 160 ng/ml, p = 0.007). There was no significant difference in the serum levels of IGFBP-3 in any of the treatment cycle days.

CONCLUSIONS: In p-FET cycles with transfer of a single, euploid, high quality embryo, IGF-1 serum levels on day of progesterone start and CD28 are significantly higher in patients who subsequently had a pregnancy loss compared to those who had a live birth. This is in contrast to the findings of prior studies in n-FET.

Reference: None.

SUPPORT: None.

REPRODUCTIVE BIOLOGY - BASIC

P.347 Tuesday, October 15, 2019 6:30 AM

UPREGULATION OF THE LONG NON-CODING RNA TUG1 INHIBITS GRANULOSA CELL APOPTOSIS AND AUTOPHAGY IN POLYCYSTIC OVARY SYNDROME BY REGULATING ERK/MAPK PATHWAY. Ying Li, M.D., Shi-ling Chen, PhD. Nanfang Hospital, Southern Medical University, Guangzhou, China; Center for Reproductive Medicine, Department of Gynecology and Obstetrics, Nanfang Hospital, Southern Medical University, Guangzhou, China.

OBJECTIVE: Polycystic ovary syndrome (PCOS) is the most common cause of anovulatory infertility in women of reproductive age, and its etiology remains poorly understood. Evidence has indicated that the increase in granulosa cell (GC) proliferation is associated with PCOS. Altered activities of long non-coding RNAs (lncRNAs) have been associated with human diseases and development. Tumor suppressor gene 1 (TUG1), an evolutionarily conserved lncRNA, has been shown to play an oncogenic role in various cancers. However, little is known about the role of TUG1 in PCOS. Therefore, the aim of this study is to explore the potential role of TUG1 in the pathogenesis of PCOS.

DESIGN: We measured TUG1 lncRNA expression levels in GCs from 58 PCOS patients and 58 controls. Also, TUG1 was knocked down in a human GC tumour-derived cell line, KGN, to investigate the role of TUG1 and its molecular mechanism in cell apoptosis and autophagy.

MATERIALS AND METHODS: GCs were collected from women with or without PCOS undergoing IVF or ICSI treatment. The PCOS diagnosis was based on the Rotterdam revised criteria, and control patients were limited to male factor or tubal disease and had a normal ovarian reserve. Quantitative real-time PCR was used to measure the differential expression levels of TUG1 between PCOS patients and controls. The receiver operating characteristic (ROC) curve was drawn to evaluate the diagnostic values of TUG1 in PCOS. In the KGN cell line, TUG1 was knocked down with locked nucleic acid GapmeRs. Cell counting kit-8 assays, ethynyl-2-deoxyuridine assays and flow cytometry were used to study the role of TUG1 in cell proliferation and apoptosis, and western blotting was performed to detect the potential underlying mechanism.

RESULTS: We first found that TUG1 IncRNA was significantly upregulated in PCOS GCs and was associated with the antral follicle count (R = 0.264, P < 0.01 versus control). The ROC curves illustrated strong separation between all the PCOS patients and the control group (AUC: 0.627; 95% CI: 0.526–0.728; P = 0.017). TUG1 was primarily localized in the nuclei of GCs. TUG1 knockdown in KGN cells inhibited cell proliferation and promoted cell apoptosis. In addition, TUG1 knockdown induced an increase in the protein levels of bax, bak, cleaved caspase-3, caspase-9, cleaved caspase-9, LC3B and phosphorylated ERK (p-ERK), and a decrease in the protein levels of bax, bak, cleaved caspase-3, caspase-9, cleaved caspase-9, LC3B and phosphorylated ERK (p-ERK). Therefore, the aim of this study is to explore the potential role of TUG1 and its molecular mechanism in cell apoptosis and autophagy.

REFERENCE: None.
P-348 Tuesday, October 15, 2019 9:30 AM

EFFECT OF ADRIAMYCIN, BLEOMYCIN, VINBLASTINE AND DACarbazine (ABVD)-TREATMENT ON FEMALE MICE REPRODUCTIVE FUNCTION. Yubing LIU, Sr., Ph.D., a Xinmei LU, Sr., Master, b Xiaocan LEI, Sr., Ph.D., a Richeng Chian, Sr., Ph.D., b Shanghai 10th People’s Hospital of Tongji University, Shanghai, China; c Zhongshan Hospital, Fudan University, Shanghai, China; Zunyi Medical University, Zunyi, China.

OBJECTIVE: Adriamycin, bleomycin,vinblastine and dacarbazine (ABVD) combined treatment is the standard first-line treatment for early stage Hodgkin lymphoma (HL). With this treatment, over 90% of early-stage patients achieve long-term remission and can be considered cured. It is clinically believed that ABVD combined treatment has little effect on fertility and no risk of POL but there is serious gonadal toxicity when adriamycin treatment alone. Researchers even found an increase in the number of primitive follicles in the ovaries of patients after ABVD treatment. Only limited data is available on long-term female gonadal toxicity following ABVD combined treatment, and most of them are descriptive clinical studies. The purpose of this study is to investigate the effects of ABVD treatment on reproductive function of female mice.

DESIGN: Experimental study on mouse model of ABVD treatment.

MATERIALS AND METHODS: Eight weeks female mice were injected i.p. with vehicle or ABVD once weekly for 4 weeks. Estrous cycles were monitored daily after first injection(n=5 each). Body weight, ovary weight, number of follicles at each stage and serum AMH were analyzed after finishing treatment and estrous cycles recovered to normal(n=5 each). Natural mating trials were undertaken when the estrous cycles recovered(n=5 each). Offspring data (number of pups per litter and pup weight at postnatal Day 2) were recorded.

RESULTS: Most mice were completely lost estrous cycle after 1 week of first ABVD injection. After 4 weeks treatment, the body weight change(3.05±1.52 vs. 0.42±2.05g, P<0.01), the gross ovarian weight(11.68±1.89 vs. 3.48±2.41mg, P<0.01), the ovary organ index(36.87±5.50 vs. 12.51±8.56, P<0.01) were significantly lower than the control group. Follicle counts revealed a significantly decrease in the number of primordial follicles (363±45.997 vs. 138.3±17.88, P<0.01), secondary follicles (61.74±5.08 vs. 46.36±12.81, P<0.05), antral follicles (51.46±20.46 vs. 16.32±3.81, P<0.05), mature follicles(26.36±16.03 vs. 4.06±1.63, P=0.05)and total follicles (753.1±109.5 vs. 401.1±42.63, P<0.01) after 4 weeks treatment. Estrus cycles returned to normal after 4 weeks ABVD removed. Then there were no differences on the 401.1

ESTRUS L crude after 4 weeks ABVD removed. Then there were no differences on the number of primordial follicles (121.5±15.12 vs. 364.1±133.1, P<0.05), primary follicle(130.7±18.14 vs. 312.4±101.5, P=0.05)and total follicles 527.6±3.81 vs. 191.3±269.2, P<0.05)were significantly increased. The number of offspring in ABVD group was less than that in control group (12.2±1.79 vs. 9.4±0.55, P<0.05), but there was no significant difference in offspring weight between ABVD group and control group(1.64±0.13 vs. 1.64±0.19, P=0.95).

CONCLUSIONS: ABVD treatment can affect the estrus cycle of mice, but the reproductive function can be restored and the fertility reserve ability can be recovered following drug withdrawal.


P-349 Tuesday, October 15, 2019 6:30 AM

THE IMPACT OF BOTULINUM TOXIN A (BOTA) TREATMENT ON ENDOMETRIAL BLOOD FLOW. Yoon-Jung Kang, Ph.D., a Sooyeon Kim, MD, b Siwon Lee, MD, c Hwang Kwon, MD, Ph.D., d Jung-Jae Ko, Ph.D., e Kyung-A. Lee, Ph.D., f Hwa Seon Koo, MD, f CHA University, Seongnam-si, Korea, Republic of (South); g CHA Bundang Medical center, Seongnam-si, Korea, Republic of (South); h Department of obstetrics and gynecology, Mound Sinai Medical Center, Miami Beach, FL; i Fertility Center, Seongnam-si, Gyeonggido, Korea, Republic of (South).

OBJECTIVE: Most embryos produced in vitro fail to produce live offspring after transfer. There is a dearth of research activity addressing this problem despite the significant population of women suffering repeated failure of implantation after transfer of high-quality embryos. We hypothesize that a proportion of these failures arises due to failure of construction of functional endometrium with the proficient blood flow. We have investigated the impact of treatment with Botulinum toxin A (BOTA), which is widely used in the field of plastic and reconstructive surgery with the specific purpose of enhancement in wound healing, to induce endometrial angiogenesis to improve the endometrial blood flow and increase the vessel formation at the site of uterine cavity.


MATERIALS AND METHODS: I in vitro: BOTA (0.5, 2, 10 IU/ml) was exposed to human endometrial epithelial carcinoma (Ishikawa) cells and stromal (CRL4003) cells in culture condition for 24h and 72h. Proliferation and migration of the 2 cell types were observed in response to BOTA treatment. Quantitative RT-PCR was used to quantify the expression levels of HIF1a and VEGFca, well-known surrogates of angiogenic effects. Data were normalized to β-actin mRNA and analyzed using the ordinary one-way ANOVA with Tukey’s multiple comparisons. II in vivo: BOTA was injected to the intrauterine cavity of female mice and uterine tissues were harvested at day 3 and 8. Changes in endometrial histology and CD31 immunoreactivity in response to BOTA treatment were examined to assess the levels of endometrial angiogenesis.

RESULTS: BOTA treatment enhances the capacity of proliferation of wound healing of both endometrial epithelial and stromal cells. QRT-PCR results revealed that soluble BoTA treatment induced increment (β~3 fold) and IL-8 (~2 fold) mRNA in both endometrial epithelial (Ishikawa cells) and stromal cells (CRL4003). The expression levels of HIF1a (~1.5 fold, p<0.001) and VEGF2 (~4 fold, p<0.001) were significantly increased in BoTA-treated Ishikawa cell compared to untreated group. In CRL4003 cells, Vimentin (~1.5 fold, p<0.001) and IL-6 (~2.5 fold, p<0.001) were significantly higher in groups with BOTA treatment compared to control group. Of note, little impact was observed in 10 IU BoTA-treated cells and no toxic effect was induced by BoTA treatment. Significantly, intrauterine injection of BoTA induced higher expression of CD31 in uterine tissues compared to saline-treated group displaying higher numbers of blood vessel formation near uterine cavity.

CONCLUSIONS: Our findings indicate that BoTA treatment has a beneficial effect on reconstruction of functional endometrium prior to embryo implantation by increasing endometrial blood flow near the uterine cavity suggesting BoTA treatment as a potential therapeutic strategy for in vitro fertilization-embryo transfer (IVF-ET) cycles.

P-350 WITHDRAWN

P-351 Tuesday, October 15, 2019 6:30 AM

HORMONE SECRETION IN A MICROFLUIDIC OVARY-ON-A-CHIP PLATFORM USING ENGINEERED FOLLICLES. Young Bin Won, M.D., a Inha Lee, M.D., a Jae Hoon Lee, M.D., b Sihyun Cho, M.D., b, c Hee Dong Chae, M.D., Ph.D., d Siwon Lee, M.D., Ph.D., d Young Suk Choi, M.D., Ph.D., a Yong University College of Medicine, Severance hospital, Seoul, Korea, Republic of (South); b Yong University

Support: This work was supported by the National Natural Science Foundation of China (grant No. 31601197).
OBJECTIVE: Although organ-on-a-chip platforms to reproduce physiological functions have been developed in a variety of tissues, there have been only a few reports on ovary-on-a-chip platforms. The human ovarian follicle is the functional unit of an ovary which consists of granulosa and theca cells interacting in an intimate relationship to produce reproductive hormones such as estradiol and progesterone. The aim of this study was to develop a dynamic microfluidic, ovary-on-a-chip platform comprising of multilayered engineered follicles that could demonstrate ovarian endocrine function in vitro.

DESIGN: In vitro animal study.

MATERIALS AND METHODS: Granulosa and theca cells were isolated from the ovaries of 3-5 week old rats. After aggregation of cells into a spheroid shape, the engineered follicles were placed in a PDMS platform for structural support and dynamic microfluidics was constructed in a three-dimensional network of gelatin hydrogels fabricated with thermoresponsive sacrificial poly(N-isopropylacrylamide) microfibers. Two types of engineered follicles were crafted through forced aggregation of theca and granulosa cells; Bi-layered follicle with inner granulosa cells surrounded by outer theca cells (BF), and tri-layered follicle with a 5% matrigel basal membrane between the two cell layers (TF). Three dimensional static and dynamic cultures were observed for 30 days. The dynamic culture medium was continuously perfused at a flow rate of 7 μL/min. Hormone secretion was measured by ELISA. Spheroid circularity was assessed to determine the effect of morphological factors on hormone secretion. F-actin staining to assess the overall shape and structure of the cells and live/dead assay to assess the cell viability were performed.

RESULTS: The structure and viability of engineered follicles were maintained for both the static and dynamic cultures up to the observed 30 days. The circularity of TF was maintained better than that of BF in both static and dynamic culture. The dynamic TF produced 17β-estradiol for longer without decrease as opposed to the dynamic BF which tapered off starting from day 15. The same was true for progesterone production. Progesterone secretion peaked at day 21 and remained elevated longer for dynamic TF compared to the dynamic BF. Hormone production, both 17β-estradiol and progesterone, were maintained uniformly stagnant without increasing during static culture and significantly lower compared to that of the dynamic culture. Statistically significant differences in testosterone levels were not observed among all static and dynamic cultures.

CONCLUSIONS: This microfluidic ovary-on-a-chip platform using engineered follicles with a matrigel basal membrane yielded better hormone secretion. F-actin staining to assess the overall shape and structure of the cells and live/dead assay to assess the cell viability were performed.

DESIGN: The structure and viability of engineered follicles were maintained for both the static and dynamic cultures up to the observed 30 days. The circularity of TF was maintained better than that of BF in both static and dynamic culture. The dynamic TF produced 17β-estradiol for longer without decrease as opposed to the dynamic BF which tapered off starting from day 15. The same was true for progesterone production. Progesterone secretion peaked at day 21 and remained elevated longer for dynamic TF compared to the dynamic BF. Hormone production, both 17β-estradiol and progesterone, were maintained uniformly stagnant without increasing during static culture and significantly lower compared to that of the dynamic culture. Statistically significant differences in testosterone levels were not observed among all static and dynamic cultures.

CONCLUSIONS: This microfluidic ovary-on-a-chip platform using engineered follicles with a matrigel basal membrane yielded better hormone secretion results. This platform may provide an opportunity to research ovarian physiology and to establish a novel in vitro disease model.

P-352 Tuesday, October 15, 2019 6:30 AM

LOW MOLECULAR WEIGHT HYALURONAN INDUCES INFLAMMATORY GENE EXPRESSION IN OVARIAN STROMAL CELLS AND IMPAIRS GAMETE DEVELOPMENT IN VITRO.

Jennifer E. Rowley, MS,a
Farners Amargant Riera, PhD,a
Michele T. Pritchard, PhD,b
Francesca E. Duncan, PhD,b
Center for Reproductive Science, Northwestern University, Chicago, IL.a, Department of Pharmacology, Toxicology, & Therapeutics, Kansas University Medical Center, Kansas City, KS.

OBJECTIVE: Female reproductive aging is characterized by a decline in gamete quantity and quality. We recently identified that the ovarian stroma becomes inflamed with age. The ovarian stroma is the microenvironment in which gametes develop, and we predict that this pro-inflammatory milieu impairs gamete quality. In other tissues, age-associated inflammation is partially driven by extracellular matrix (ECM) degradation products, such as low molecular weight hyaluronan (LMW-HA). HA is a major component of the ovarian ECM, and enzyme expression data suggests that ovarian HA is increasingly fragmented into LMW-HA with age. Thus, we hypothesized that LMW-HA fragments stimulate an inflammatory response in the ovarian stroma, which negatively impacts ovarian function.

DESIGN: Two tightly controlled in vitro mouse model systems to examine the effect of LMW-HA on the stroma and follicle compartments of the mammalian ovary.

MATERIALS AND METHODS: Isolated ovarian stromal cells or secondary ovarian follicles were treated with physiologically relevant (10 μg/mL or 100 μg/mL) concentrations of 200 kDa LMW-HA. Ovarian stromal cells were treated for 6 hours and expression of 84 inflammatory genes was analyzed using a qPCR array. Isolated follicles were cultured with LMW-HA for 12 days. Follicle survival, growth, morphology, estradiol production and markers of gamete quality were assessed using brightfield microscopy.

RESULTS: Primary ovarian stromal cells treated with both concentrations of LMW-HA exhibited increased expression of inflammatory genes. Most notably, eotaxin receptor Ccr3-4.07 and 3.57-fold change following 10 μg/mL or 100 μg/mL treatment, respectively and a suite of Ccr3-related, eosinophil activation genes (p = 0.044) were significantly regulated by LMW-HA. Interestingly, these findings were consistent with an age-dependent increase in ovarian stromal expression of Ccr3, a major CCR3 ligand (1.86-fold change, p = 0.0002). In follicle cultures, LMW-HA treatment did not affect follicle survival, growth, or morphology but the 100 μg/mL condition did significantly reduce estradiol production (p = 0.0098). With respect to gamete quality, follicles grown in 10 μg/mL LMW-HA produced a higher proportion of morphologically abnormal gametes relative to controls (50.7% vs. 17.1%, p = 0.0035). Strikingly, only 48.1% of morphologically normal gametes reached a mature metaphase-II (MII) stage (versus 90.0% of control normal gametes, p = 0.0213) and MII eggs had significantly smaller diameters (p = 0.0013). Moreover, the ovarian stimulation was also performed to determine the duration of the gonadotoxicity caused by multiple-dose paclitaxel and to investigate the protective effect of GnRHa to ovaries from paclitaxel remains unclear.

OBJECTIVE: Chemotherapeutic agents have numerous side effects. However, we observed that paclitaxel (1 dose per 3 days) or an equal volume of vehicle was given intraperitoneally to 7-week-old female ICR mice. These mice were given 1 mg/kg GnRHa(every day) or normal saline for one estrous cycle before, during and another estrous cycle after chemotherapy. On the 1st, 6th, 11th or 16th day after the multiple-dose paclitaxel, the mice were managed in several ways: follicle counting (n=5/group/time point), acquisition of oocytes (n=5/group/time point) and immunofluorescence.


RESULTS: The follicle counting showed that paclitaxel only destroyed antral follicles for 2 estrous cycles after chemotherapy and induced increasing atretic follicles without affecting follicles in other stages. Add GnRHa to paclitaxel significantly reduced the amount of atretic follicles (0.67 times versus 6.30, P<0.05). Moreover, the ovarian stimulation was also performed to determine the duration of the gonadotoxicity after multiple-dose paclitaxel. The acquisition of MII oocytes in paclitaxel-only group was extremely less on the 1st and 6th day after the last dose of the treatment(D1: 1.00±0.00 versus 30.40±5.27, P<0.01; D6: 17.20±4.25 versus 31.33±4.67, P<0.05). Compare to the control, mice, with the protection of GnRHa, ovulated even more MII oocytes on the 6th day after chemotherapy(46.80±3.44 versus 31.33±4.67, P<0.05). And...
up to 2 estrous cycles after the last dose, the quantity of MI oocytes in all groups showed no statistical difference. Meanwhile, the morphology of oocytes was observed by immunofluorescence.

CONCLUSIONS: These results indicated that paclitaxel mainly impacted antral follicles and the gonadotropin toxicity lasted no more than 2 estrous cycles of mice. The protective effect of GnRHa on ovaries was significant. This study provides a laboratory evidence for the impact of paclitaxel and the effectiveness of GnRHa in clinical practice.

E248 ASRM Abstracts

P-354 Tuesday, October 15, 2019 6:30 AM

ESTABLISHMENT OF DECREASED OVARIAN RESERVE MOUSE MODEL BY CONSECUTIVE SUPEROVULATION. XiaoweiNie, M.D. Daorong Hou, Ph.D. Embryologist, NANJING, China.

OBJECTIVE: This study investigated the effect of consecutive superovulation on the ovaries and established a decreased ovarian reserve (DOR) model in mice.

DESIGN: One hundred fifty C57BL/6 female mice aged 7–8 weeks and thirty C57BL/6 female mice aged 44 weeks were used. The mouse POF model was induced by 5-15 consecutive superovulation treatments with pregnant mare serum gonadotropin (PMSG), human chorionic gonadotropin (HCG) and prostaglandin F2α (PGF2α). Normal adult mice were compared with mice displaying natural ovarian aging.

MATERIALS AND METHODS: The following serum biochemical parameters were measured: including follicle-stimulating hormone (FSH), luteinizing hormone (LH), progesterone (P), estradiol (E2), inhibin (INH B), malondialdehyde (MDA), total superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) levels. Follicles were counted using H&E staining. Levels of 8-hydroxyguanosine (8-OHdG), 4-hydroxynonenal (4-HNE), Nitrotyrosine (NTY), anti-Mullerian hormone (AMH) and Cdx2NAp16 (p16) were detected using immunohistochemical staining. Reactive oxygen species (ROS) levels were measured using dihydroethidium (DHE) staining. Cell apoptosis was detected using an in situ TUNEL fluorescence staining assay. Levels of proteins involved in ROS-related pathways and the p16 protein were detected using Western blotting. Sod1, Sod2 and Sod3 mRNA levels were detected using quantitative polymerase chain reaction (Q-PCR). Oocyte quality was evaluated using in vitro fertilization (IVF) and zygote culture.

RESULTS: Consecutive superovulation groups presented lower F2, E2, SOD, GSH-Px and INH B levels, significantly higher FSH, LH, MDA and ROS levels, and significantly fewer primordial follicles compared with the control group. Consecutive superovulation groups presented significantly increased levels of Sod2, 8-OHdG, 4-HNE, NTY, significantly increased levels of the SIRT1 and FOXO1 proteins, significantly increased levels of the senescence-associated protein p16, as well as decreased AMH, Sod1 and Sod3 levels and increased granulosa cell apoptosis compared with the control group.

CONCLUSIONS: Consecutive superovulation significantly decreased ovarian function and oocyte quality and increased oxidative stress and apoptosis. The mechanism involves a mechanism involving the p16 and SIRT1 FOXO1 signaling pathways. These findings suggest that consecutive superovulation may be used to establish a mouse model of ovarian aging.


P-355 Tuesday, October 15, 2019 6:30 AM

CHARACTERIZING MEIOTIC AND MITOTIC ERRORS IN THE INNER CELL MASS AND TROPHOCDERM OF POOR QUALITY PREEMBRYONIC EMBRYOS. Christine Briton-Jones, PhD, HCLD.a

Lucky Sekhon, MD.a

Ethan Ellis, BS.b

Joseph A. Lee, BA,a

Eric E. Schadt, PhD,b

Robert P. Sebra, PhD,a

Alan B. Copperman, MD.b

aReproductive Medicine Associates of New York, New York, NY;
bIcahn School of Medicine at Mount Sinai, New York, NY; cSema4, a Mount Sinai Venture, Stamford, CT.

OBJECTIVE: Human blastocysts that undergo trophoderm (TE) cell biopsy for pre-implantation genetic testing for aneuploidy (PGT-A) are capable of achieving normal morphological development despite having gains or losses in chromosome copy number. Occasionally in clinical embryo culture we see nonviable blastocysts with morphology of few or no inner cell mass (ICM) cells and good quality TE cells. Also the reverse is seen, a blastocyst with good quality ICM but few elongated TE cells. These embryos are not suitable for biopsy or clinical use. However, these morphologically abnormal blastocysts provide a novel glimpse at the earliest stages of human cell differentiation. The aim of the study was to compare rates of meiotic and mitotic errors resulting in loss, gain or mosaicism of chromosomes in cells from poor quality blastocysts.

DESIGN: Experimental study on human embryos donated for research.

MATERIALS AND METHODS: The study included embryos donated by patients from fresh cycles between January and June of 2016. Embryos reaching the blastocyst stage of development but ineligible for TE biopsy (<4CC, Modified Gardner), were biopsied and 5-6 cells were evaluated for aneuploidy by NGS. Ploidy status including mosaicism was identified based on bioinformatical interpretation of chromosome copy number falling within disomic (between 1.8 - 2.2), aneuploid thresholds (less than 1.2 and more than 2.2) and mosaic (between 1.2-1.8 and 2.2-2.8). The mean number of monosomy, trisomy and mosaic calls was determined and compared for each study group. Kruskal Wallis was used to determine statistically significant differences, where p<0.05.

RESULTS: Of the 15 blastocysts, with isolated poorly graded ICM (n=9) or trophoderm (n=6), that underwent NGS. Of the embryos with poor ICM and good TE: 7 were euploid; 2 were mosaic and 1 was aneuploid. Of the embryos with good ICM and poor TE grade: 2 were euploid and 4 had complex aneuploidy. Blastocysts with good ICM grade but poor TE grade had significantly higher incidence of mosaicism and aneuploidy (p<0.0001).

CONCLUSIONS: As embryo development reaches the blastocyst stage, the incidence of aneuploidy is significantly reduced. The reason for this reduction in incidence of aneuploid cells between cleavage stage and blastocyst stage embryos is believed to be that the burden of aneuploidy leads to embryonic arrest. This study showed that embryos with many copy number variants are still capable of growing a morphologically normal ICM. In contrast the blastocysts with morphologically normal trophoderm had fewer aneuploid calls, despite having none or few ICM cells present. Our study’s findings suggest that the consequence of aneuploidy is less severe in ICM cells compared to TE cells, as at this specific time point in embryonic development, ICM cells are more closely related to the cleavage stage blastomeres than the differentiated trophoderm. Our current work is focused on identifying differential gene expression in these embryos, which allow a unique opportunity to study the roles of ICM and TE cells largely independent of each other.

Reference: None.

SUPPORT: None.
configuration, which has been hypothesized to be critical for the ordered exodus of the paternal genome following fertilization. This model describes centromeres clustering in the center (chromocenter), with p- and q-chromosome arms stretching toward the nuclear periphery. However, we recently presented a novel model to target the chromocenters and to further investigate these findings and their relationship to the hairpin-loop model we examined the 3D configurations of chromosomes in human sperm nuclei.

**DESIGN:** Transversal laboratory study.

**MATERIALS AND METHODS:** This study was approved by the local IRB, five normozoospermic males were recruited. Three-color fluorescence in-situ hybridization (FISH) was utilized to target the centromeres, and chromosome p- and q-arms of eight chromosomes (2, 3, 6, 8, 10, 12, 16, and 18). Wide-field fluorescence microscopy and 3D modeling was employed to image and visualize sperm cells and FISH probes in 3D. The radial organization of each targeted loci was established by measuring the distance of the geometric center of each loci to the nearest nuclear periphery. Nonrandom organization of was established using the Chi-squared goodness-of-fit test (p<0.05). Furthermore, hairpin-loop configurations were determined by the angle created between the p- and q-arms. A minimum of 30 cells per subject, per chromosome were studied.

**RESULTS:** Distinct reproducible chromosome-specific patterns of organization emerge. All chromosomes were found to possess nonrandom radial organization (p<0.05), with the exception of the chromosome 12 centromere. Chromosome arms were found to form discrete hairpin-loop configurations. However, different chromosomes were observed to preferentially form narrower or wider hairpin loops that were largely reproducible between the five subjects enrolled. We did not find evidence to support the existence of a centralized chromocenter(s) with 68.3% of investigated centromeres being more distally localized within the sperm nucleus than one (30.5%) or both (37.8%) of their respective chromosome arms.

**CONCLUSIONS:** We report reproducible nonrandom hairpin-loop organization of chromosomes that partially supports the proposed hairpin-loop model of organization. However, our findings do not support the existence of a centralized chromocenter. This provides further evidence to support a more segmented chromosome organization in the human sperm nucleus, which could result in specific genomic regions being exposed, remodeled and activated first, following fertilization. The sequential exodus and remodeling could impact patterns of gene activation observed within the early embryo, perturbations in which, could negatively impact fertilization and early embryogenesis. Further research is warranted to evaluate the functional relevance of the nonrandom hairpin-loop organization of chromosomes in sperm observed in this study, and how this may impact spermatogenesis, fertilization and embryogenesis.

**P-357**

Tuesday, October 15, 2019 6:30 AM

**THE UBQINONE MITOCHONDRIA-TARGETED ANTIOXIDANT AMENDS THE EFFECT OF MATERNAL AGE ON OOCYTE SPINDLE FORMATION AND DEVELOPMENTAL COMPETENCE.** Usama I. Al-Zubaidi, PhD; Ozgur Cinar, Prof; Deepak Adhikari, PhD; Rebecca Robker, Prof; John Carroll, Prof.* Development and Stem Cell Program, Department of Anatomy and Developmental Biology, Melbourne, VIC, Australia; Department of Histology and Embryology, School of Medicine, Ankara, Turkey; The Robinson Research Institute, School of Medicine, Adelaide, SA, Australia.

**OBJECTIVE:** To examine the effect of maternal age on mitochondrial function and spindle formation in maturing oocytes, and to investigate whether in vitro treatment with mitochondria-targeted antioxidants (AOs) can reverse the impact of aging on oocyte quality.

**DESIGN:** Preclinical models of oocyte quality were used for this study. In experiment 1, oocytes were obtained from young (1-month-old) mice and treated with hydrogen peroxide (H2O2) to induce oxidative stress or with H2O2 and mitochondria-targeted AOs. In experiment 2, oocytes were collected from young and old (>12 months) mice and treated with mitochondria-targeted AOs during in vitro maturation (IVM). End point assays in both experiments were stage of maturation reached, mitochondrial function and spindle quality.

**MATERIALS AND METHODS:** Cumulus-free oocytes were cultured in vitro for 14 h in M2 or M16 medium, or in the same medium containing H2O2 (25μM), with or without AOs (experiment 1). In a separate experiment, oocytes from young and old mice were cultured in vitro in the presence and absence of mitochondria-targeted AOs. At the end of the culture period mitochondria membrane potential (MMP) was measured by ratioing the fluorescence intensities of Tetramethylrhodamine methyl ester (TMRM), and Mitotracker green (MTG). Oocytes were fixed to label the microtubules and DNA. ImageJ software was used to analyze spindle dimensions and chromosome alignment. Student’s t-test and ANOVA were applied to compare between groups and a P value below 0.05 were considered statistically significant.

**RESULTS:** We find oxidative stress causes a decrease in MMP (P<0.001) and an increase in the frequency of disrupted spindles and misaligned chromosomes (P<0.001). Co-treatment with H2O2 and AOs reversed the MMP and spindle disruption to control levels. Oocytes from old mice matured to the MII stage in vitro also showed decreased MMP and disrupted spindles. These age-related perturbations were completely reversed by incorporating antioxidants in the culture media. Furthermore, for the first time we have performed live-cell ratiometric imaging of TMRM and MTG for the full time-course of maturation in young and old eggs. This study reveals that MMP increases significantly during IVM in young oocytes (P<0.001) but not in old oocytes.

**CONCLUSIONS:** Oxidative stress and maternal age are both associated with decreased MMP and spindle disruption and chromosome misalignment. Time-lapse imaging suggests that mitochondria in young oocytes undergo an adaptive increase in MMP during IVM and that this capacity is lost in mitochondria of old oocytes. The compromised mitochondrial function in maternal aging and the ability of the mitochondria-targeted AOs treatment to mitigate against aging and oxidative stress-induced mitochondrial and spindle disfunction, suggests that mitochondria may be a useful therapeutic target for improving oocyte quality.

**P-358**

Tuesday, October 15, 2019 6:30 AM

**LOSS OF MITOCHONDRIAL FUSION PROTEIN MFN2 RESULTS IN A REPRODUCTIVE AGING PHENOTYPE WITH TELOMERE SHORTENING, REDUCED FERTILITY, AND ACCELERATED DEPLETION OF FOLLICULAR POOL.** Man Zhang, M.D, Ph.D;* Muhammed Burak Bener, B.S; Zongliang Jiang, Ph.D; Tianran Wang, M.D., Ph.D.; Ecem Esencan, M.D.; Richard Scott III, B.S;* Emre Seli, M.D.;* Yale School of Medicine, New Haven, CT;* Louisiana State University, Baton Rouge, LA;* Foundation for Embryonic Competence, Basking Ridge, NJ;* Foundation of Embryo Competence, Basking Ridge, NJ.

**OBJECTIVE:** Mitochondria change their shape through fusion and fission in order to adapt to their metabolic milieu and respond to environmental stress. Mitofusin-2 (MFN2) is a key regulatory protein in this process, mediating mitochondrial fusion and interaction with endoplasmic reticulum. The aim of the present study was to determine the role of MFN2 in female reproductive competence using a mouse model with oocyte-specific deletion of MFN2.

**DESIGN:** Experimental study.

**MATERIALS AND METHODS:** Mfn2<sup>fl/wt</sup> mice were crossbred with Zp3-Cre mice to produce mice with oocyte-specific Mfn2 deletion (Mfn2<sup>fl/wt</sup> mice). To evaluate fertility, 25-30 days old wild type (WT) female mice were mated with adult WT males of proven fertility for 12 weeks. Follicle development was assessed in serial ovarian sections stained with hematoxylin and eosin. Ability to generate oocytes (germinal vesicle [GV] and metaphase II [MII]), 2-cell embryos, and blastocysts was assessed after injection with PMSG (3IU) or PMSG and hCG (5IU) and mating with WT males as indicated. RNA sequencing analysis was performed using pooled Mfn<sup>−−</sup> and WT GV oocytes and secondary follicle enclosed oocytes (SFOs) (n=3 mice per group). Protein and mRNA expression were assessed using immunofluorescence and qRT-PCR, respectively. Telomere length was assessed using quantitative real-time PCR.

**RESULTS:** Mature female Mfn<sup>−−</sup> mice exhibited reduced fertility compared to WT females (5.21 ± 0.39 vs 7.63 ± 0.31 paps per litter, p<0.001). They had decreased number of antral follicles (93.3 ± 3.33 vs 30.67 ± 1.67, P<0.001), and generated a significantly lower number of GV oocytes (16.33 ± 2.0 vs 29.33 ± 0.67, P<0.001), MII oocytes (10.58 ± 21.33 ± 1.20, P<0.01), 2-cell embryos (8 ± 0.58 vs 20.33 ± 0.88, P<0.001) and blastocysts (6.33 ± 0.88 vs 13 ± 0.58, P<0.001). RNA-seq analysis revealed 363 and 1041 genes that were differentially regulated in Mfn2<sup>−−</sup> and WT GV oocytes, respectively. Affected pathways included telomere biology and GV oocyte follicle degeneration (apoptosis) signaling in SFOs (P<0.01). Pro-apoptotic protein caspase 6 and apoptotic markers were significantly increased in Mfn<sup>−−</sup> SFOs. Telomere length in Mfn<sup>−−</sup> GV oocytes was shorter compared to WT with decreased expression of telomere protective protein TRF1. When we assessed changes in follicular pool across mouse reproductive lifespan, we found Mfn<sup>−−</sup> ovaries to have significantly lower number of
primordial, secondary, and antral follicles at 6 months (p<0.05), and dramatically decreased number of follicles at all stages at 12 months (p<0.0001), compared to WT.

CONCLUSIONS: Targeted deletion of Mfn2 in oocytes results in female subfertility associated with impaired oocyte maturation and follicle development. Oocytes lacking MFN2 show shortened telomeres and increased apoptosis, resulting in compromised oocyte quality and accelerated follicle depletion, consistent with a reproductive aging phenotype.

P-359 Tuesday, October 15, 2019 6:30 AM

THE ROLE OF AKAP13 INHIBITORS AND ACTIVATORS AND MATRIX STIFFNESS IN HIPPO PATHWAY SIGNALING FOR PRIMORDIAL FOLLICLE ACTIVATION. Jacqueline Yano Maher, MD, MA, Md, Soriful Islam, PhD, Szu-Chi Su, MS, James Segars, MD. Johns Hopkins University, School of Medicine, Baltimore, MD.

OBJECTIVE: Signaling pathways of primordial follicle activation are incompletely understood. Disruption of Hippo pathway signaling promotes gonadotropin independent follicle activation in granulosa cells. F-actin formation increases primordial follicle activation through Hippo signaling inhibition, and A-Kinase Anchoring Protein-13 (AKAP13) possesses a Rho- guanine exchange region (GER) that promotes actin nucleation. Our objective was to test whether pharmacologic manipulation with AKAP13 inhibitor (A13) or AKAP13 activator (A02) affected Hippo signaling in a human granulosa cell line. Second, we tested whether activation of RhoA by manipulation of substrate stiffness affected Hippo signaling.

DESIGN: Translational research using COV434 cells, derived from a human granulosa cell tumor.

MATERIALS AND METHODS: Downstream Hippo signaling targets, Yes-associated protein (YAP) and transcriptional co-activator with PDZ-binding motif (TAZ), bind to the Tea Domain Family of transcription factors (TEAD). Since TEADs mediate nuclear YAP/TAZ function, we used a TEAD luciferase reporter (TEAD-luc) to assess gene activation by YAP/TAZ. TEAD-luc was previously reported endogenous AKAP13 levels in COV434 cells as determined by immunoblot. A13 and A02 are small molecules previously identified by virtual screening for molecules that altered Rho-GEF activity of AKAP13 (Dianvia et al., 2016). COV434 cells were plated at 200K/well x 1 day and serum starved the second day. The third day, cells were transfected with 500ng TEAD-luc and either a control vector, an AKAP13 expression construct, 10uM A13, or 10uM of A02. In some experiments, four hours later, FSH was added as a treatment. After 24 hours, cells were lysed, assayed for luciferase activity and normalized with an MTS assay. Next, we assessed changes in TEAD-luc activity among stiff polystyrene (2-4 GigaPascals) vs. 3 different soft silicone Flexcell® plates: untreated, laminin-coated, or pronectin-coated. Student’s t-tests were used to determine statistical significance.

RESULTS: Addition of AKAP13 did not augment TEAD-luc reporter activity, possibly due to high levels of endogenous AKAP13 in COV434 cells, as determined by immunoblot. Of note, treatment with A13 reduced TEAD-luc activity by 69% (p<0.0001) and A02 increased TEAD-luc activity by 73% (p<0.0001). FSH treatment or vehicle control did not affect TEAD-luc reporter activity. In the second series of experiments, there was a significant decrease in TEAD-luc activity between the polystyrene plate and all 3 silicone Flexcell type plates (p<0.0001).

CONCLUSIONS: These data indicate that TEAD-luc reporter activity in COV434 cells could be decreased or increased by inhibition or activation of AKAP13 activity, respectively. If supported by in vivo data, these data suggest that pharmacologic manipulation of Hippo signaling might represent a new strategy for follicle activation.


P-360 Tuesday, October 15, 2019 6:30 AM

CULTURE MEDIA WITH AND WITHOUT EXPOSURE TO HUMAN PREIMPLANTATION EMBRYOS CONTAIN EXTRACELLULAR VESICLES OF COMPARABLE SIZE. Diego Marin, M.S.; Emre Sevi, M.D.; Richard Thomas Scott, Jr., MD IVI-RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: Extracellular Vesicles (EV) are cell-derived particles with a lipid bilayer membrane ranging in size from 30 to more than 1000 nm in diameter. EVs carry a variety of biomolecules and play pivotal roles in intercellular communication. It has been evidenced that EVs secreted by human preimplantation embryos play a major role in the embryo-endometrium crosstalk during implantation and could therefore become potential biomarkers for embryonic reproductive potential. This study aimed to develop and optimize an EV isolation protocol for spent culture media (SCM) of human IVF preimplantation embryos so as to characterize the embryonic EV population and their potential as reproductive biomarkers.

DESIGN: Experimental study.

MATERIALS AND METHODS: SCM microdrops (50-100 uL) were collected following 48 hours of embryo culture from day 3 to day 5 of development. Microdrops incubated under the same conditions in the IVF lab without embryo exposure were used as negative controls. Two methods were tested for EV isolation. 1) Size exclusion chromatography (SEC): 70 SCM microdrops were pooled for each sample (2 samples exposed to ~188 embryos each) and concentrated to ~180 uL using centrifugal filters prior to SEC (Izum). After SEC, 21 fractions of 200 uL were obtained from each sample. Fractions 3, 4, and 5, the most enriched in EVs, were further pooled and re-concentrated to ~180 uL. 2) Differential centrifugation: 30 SCM microdrops were pooled for each sample (3 samples exposed to ~100 embryos each). The 3 pooled SCM samples and other 3 non-pooled single embryo culture microdrops were subjected to three rounds of centrifugation at different g forces before a final 90 minutes uncentrifuged supernatant collection. Finally, transmission electron microscopy imaging was performed in all processed samples obtained using the 2 methods in order to visualize and analyze EVs. Negative controls were processed similarly.

RESULTS: Using both SEC and differential centrifugation, spherical and highly electron-dense particles ranging from 22 to 159 nm were observed in both embryo SCM and embryo unexposed media samples. Size of nanoparticles isolated from pooled SEC fractions (3, 4 and 5) were comparable between SCM and negative control (Size: SCM= 57.05±20.06 nm, NC=44.47±14.23 nm). In addition, differential centrifugation allowed for isolation and visualization of EVs from single embryo culture microdrops, as well as from media unexposed to embryos.

CONCLUSIONS: SEC and differential centrifugation successfully isolated EVs from single and pooled embryo culture samples of human embryo SCM. Interestingly, presence of EVs was also evidenced in culture medium microdrops unexposed to embryos, which presented a size distribution comparable to the ones found in embryo SCM. These findings urge to conduct further research in order to shed light on the origin and possible effects of non-embryonic EVs in culture media, as well as the role of embryo- derived EVs during implantation and their potential as biomarkers.

P-361 Tuesday, October 15, 2019 6:30 AM

EFFECTIVENESS OF PLATELET RICH PLASMA ON PREVENTION OF CHLAMYDIA INDUCED HYDROSALPINX IN A MURINE MODEL. Sheena M. Rippentrop, MD,a Zhi Huo, PhD,b Chet Schwab, MD,c Randal D. Robinson, MD,d Guangming Zhong, MD, PhD,e* University of Texas Health Science Center San Antonio, San Antonio, TX, aChinese Society for Immunology, San Antonio, TX, bUT Health San Antonio, San Antonio, TX, c*Univ of Texas Health Science Center San Antonio, San Antonio, TX.

OBJECTIVE: To test whether oviduct delivery of platelet rich plasma (PRP) can attenuate chlamydia induction of hydrosalpinx in a mouse model

DESIGN: Intravaginal inoculation of CBA/J mice with C. muridarum can induce almost 100% bilateral hydrosalpinx, which was used as a hydrosalpinx development model for comparing the effect of FFP on hydrosalpinx development.

MATERIALS AND METHODS: A total of 16 CBA/J mice were infected intravaginally with a standard dose of C. muridarum, then PRP was instilled into one oviduct and a sham instillation with phosphate buffer solution was performed on the contralateral oviduct at the same time. Oviduct instillation was performed in four groups of mice occurring on day 7 (D7), day 7 plus day 21 (D7/21), day 21 (D21), or day 14 plus day 21 plus day 28 (D14/21/28) after infection. Vaginal and rectal shedding were monitored in all mice. Mice were then sacrificed, and pathologic evaluation performed. Statistical analysis was performed using the Mann-Whitney test.

RESULTS: Oviduct instillation of PRP on day 21 with or without additional instillations was associated with a 41.5% reduction in degree of hydrosalpinx compared to sham instillation with an average hydrosalpinx score of
1.62 and 2.77 respectively (p=0.15). Instillation of PRP on D14/21/28 was associated with a 43% reduction of hydrosalpinx, average score 1.14 and 2 for sham (p=0.56). Oviduct instillation of PRP on D21 alone was associated with a 50% reduction in degree of hydrosalpinx compared to sham instillation with an average score of 2 and 4 respectively. The average grade of inflammation on histopathology was 1.57 with any day 21 instillation vs 1.77 sham instillation (p=0.54). PRP instillation on D7 was not associated with reduction in degree of hydrosalpinx or grade of inflammatory infiltrate. No differences were observed in vaginal or rectal shedding of C. muridurium amongst the four groups.

CONCLUSIONS: Our results suggest that oviduct instillation of PRP was associated with a reduction in the degree of C. muridurium induced hydrosalpinx in CBA/J mice; however, this reduction was not statistically significant.


SUPPORT: US NIAID R01AI047997.

P-364 Tuesday, October 15, 2019 6:30 AM

ABNORMAL PHOTOPERIOD EXPOSURE BEFORE PREGNANCY AFFECTS OFFSPRING LIPID METABOLISM IN SD RATS. Yanjun Ying. B.S.Med, Dan Zhang, MD, Ph.D., Juan Liu, Doctor, Miuxue Tu, Doctor, Women’s Hospital, Zhejiang University School of Medicine, Hangzhou, China.

OBJECTIVE: Exposure to constant light or shift work impairs endogenous circadian rhythm, which can lead to metabolic diseases. Previous animal and human studies demonstrated that circadian rhythm disruption during pregnancy affects the long-term health of their progeny. But circadian rhythm disruption before pregnancy would have any effect on their offspring is not thoroughly studied. This study is designed to investigate the effects from maternal circadian disruption.

DESIGN: Randomized animal study.

MATERIALS AND METHODS: Five hundred 6-8 week-old female SD rats exposed to abnormal photoperiod (18 h:16 h light/dark cycle) and control photoperiod (12 h:12 h light/dark cycle) for 4 months. Thereafter, rats were housed in control photoperiod, mated, gestated and reared their offspring. At the age of 20 weeks, offspring were sacrificed every 8 hours. Tissue and plasma were harvested. Data were analyzed with t-tests.

RESULTS: Exposure to abnormal photoperiod results in prolonged and irregular estrous cycles with pregnancy rate decreased (p<0.05). Their ovary weight decreased (p<0.01), less corpus luteum and more expanded follicles in ovary H&E stain slides. The offspring from abnormal photoperiod group not only had significantly body weight gain (male +43.1%, female +10.1%, p<0.01), but also higher body fat rate (female +7.8%, male +7.8%, p<0.05). Their ovary weight were decreased (p<0.01), less corpus luteum and more expanded follicles in ovary H&E stain slides. The offspring from abnormal photoperiod group not only had significantly body weight gain (male +43.1%, female +10.1%, p<0.01), but also higher body fat rate (female +7.8%, male +7.8%, p<0.05). Serum cholesterol and HDL-c of male offspring decreased (p<0.05). Serum cholesterol and HDL-c of male offspring decreased (p<0.05).

CONCLUSIONS: Abnormal light-dark cycle induced maternal circadian rhythm disruption have an effect on offspring lipid metabolism disorder in rats. As shift work, artificial night lighting, jet lag are becoming increasingly prevalent. Our finding may have the implications for people to conceive and pay attention to offspring health.

SUPPORT: Grant support was provided by the National Key Research and Development Program of China (2019YFC10005003).

P-365 Tuesday, October 15, 2019 6:30 AM

CYTOKINE PROFILING REVEALS A UNIQUE INFLAMMATING SIGNATURE IN HUMAN FOLLICULAR FLUID AND THE OVARY. Jordan H. Machlin, MS,6 Seth J. Barishansky, MS,6 Sharron LaChelle Manuel, MD, PhD, MS,5 Jian-Jun Wei, MD,5 John Zhang, PhD,6 Mary Ellen Pavone, MD, MSCL,6 Francesca E. Duncan, PhD.5 Northwestern University, Chicago, IL;5 Northwestern University Professor of Pathology and Obstetrics and Gynecology, Chicago, IL.

OBJECTIVE: Reproductive aging in the ovary is characterized by a decrease in ovocyte quality and quantity that leads to adverse reproductive outcomes such as infertility, miscarriages, and birth defects. Aging is associated with a general increase in damaging chronic inflammation termed “inflammaging.” The goal of our study was to determine how inflammingaging impacts the ovary.

DESIGN: Translational.

MATERIALS AND METHODS: To examine whether inflammatory cytokines increase in the human ovary with age, we obtained human follicular fluid aspirated from the first follicle from the right or left ovary from 30 participants ranging in age from 27-74 years old undergoing oocyte retrieval. We performed cytokine antibody arrays on the follicular fluid which measured 98 unique cytokines. Cumulus cells that would have otherwise been discarded were obtained from women undergoing oocyte retrieval for...
a non-cancerous diagnosis at Fertility and Reproductive Medicine (FRM) who were ≥18 years old and ≤30kg/m². We performed immunoblot analysis on cumulus cells with a TGFβ3-specific antibody and normalized expression to the GAPDH signal. To investigate TGFβ3 expression in ovarian tissue, we generated a human ovarian Tissue Microarray (TMA) using samples from two reproductive research archives: the National Physic-ian’s Cooperative (NPC) and the Northwestern University Reproductive Tissue Library (NU-RTL). The array contained cortical tissue samples from 60 participants in two cohorts of females: 22 months-20 years old and 39-58 years old. We performed immunohistochemistry on this array with the TGFβ3 antibody and quantified expression based on age and tissue sub-structures.

RESULTS: Of the 80 cytokines measured in the follicular fluid on the cytokine antibody array, 61 were above threshold. We plotted the cytokines by both chronicologic age (years) as well as reproductive age (AMH) and found that six cytokines; IL-3 IL-7, IL-15, TGFβ1, TGFβ3, and MIP-1 showed a positive correlation with chronicologic age but were negatively correlated with AMH. Thus these cytokines represent a unique inflammatory aging signature in the ovary. To validate these follicular fluid findings, we focused on TGFβ3 which is part of the transforming growth factor beta (TGFβ) family of proteins that has unique immunoregulatory properties. To validate that TGFβ3 expression increases with age, we examined two cellular compartments – the cumulus cells immediately surrounding the oocyte and the ovarian tissue microenvironment. We did not observe an age-associated increase in TGFβ3 expression in the cumulus cell samples, suggesting that the age-associated increase in this cytokine in follicular fluid was attributable to a different cellular source. Within the human ovary, TGFβ3 localized throughout the stroma, vasculature, and within follicles. Interestingly, we observed a significant age-associated increase in TGFβ3 expression in the ovary, specifically in samples enriched in stroma and vasculature.

CONCLUSIONS: Inflammaging is a hallmark of reproductive aging in hu-man follicular fluid and ovarian-derived TGFβ3 is a central component of this signature.

P-366 WITHDRAWN

P-367 WITHDRAWN

P-368 Tuesday, October 15, 2019 6:30 AM

PREINCUBATION TIME CAN BE EFFECTIVE ON THE QUALITY AND FERTILIZATION POTENTIAL OF MOUSE MII OOCYTES. Fatemeh Mohammadi, PhD, student. Zahra Zandieh, PhD, Faculty of Medicine, Iran Univer-sity of Medical Sciences, Tehran, Iran (Islamic Republic of).

OBJECTIVE: It is demonstrated that non-optim preincubation time in IVF/ICS (in vitro fertilization/intracytoplasmic sperm injection) cycles can lead to reduction in the oocyte quality, regarding to oxidative stress condition and mitochondrial alteration, and consequently can decrease the oocyte fertilization potential. Nevertheless, there is not any explanation of standard preincubation time in ART (assisted reproductive technology) guidelines. Myo-inositol, as an antioxidant, exists naturally in the follicular fluid and is a marker of good quality in the oocytes. This study evaluated the oxidative stress condition, mitochondrial alterations and fertilization potential in mouse MII oocytes following 0, 4 and 8 hours preincubation time in the simple and myo-inositol supplemented media.

DESIGN: This was a basic experimental study that included 50 adult (6-8 weeks-old) female NMRI mice which underwent hormonal superovulation from 2018 to 2019.

MATERIALS AND METHODS: Cumulus Oocyte Complexes (COCs) which were retrieved from 6-8 weeks-old superovulated female NMRI mice were pooled and divided randomly in five experimental groups: (1) control (2) 4 hours preincubation in simple medium (3) 4 hours preincubation in 20 mmol/L of myo-inositol supplemented medium (4) 8 hours preincubation in simple medium (5) 8 hours preincubation in 20 mmol/L of myo-inositol supplemented medium. COCs in each group were denuded and intracellular Reactive Oxygen Species (ROS), glutathione (GSH), Mitochondrial Membrane Potential (MMP) and mitochondrial distribution were measured by a fluorometric assay. ATP content of oocytes also was measured using the ELISA method. Pronucleus formation was assessed for evaluation of oocytes fertilization potential.

RESULTS: Results showed that intracellular H2O2 and glutathione levels, mitochondrial distribution, mitochondrial membrane potential, ATP content, as well as fertilization rate were different between groups. Nonetheless, myo-inositol supplementation could improve levels of H2O2, glutathione, mitochondrial distribution, ATP content and fertilization rate. Unlike other variables, mitochondrial membrane potential of oocytes was not reduced after 4 hours of preincubation in either simple or supplemented medium, but 8 hours of preincubation time could decrease it significantly. Addition of myo-inositol to the medium could not ameliorate mitochondrial mem-brane potential in oocytes preincubated for 4 and 8 hours. While, ATP content did not decline in oocytes preincubated for 4 and 8 hours, supplementation of myo-inositol in medium could increase it in both groups.

CONCLUSIONS: Finally, the analysis addressed that 4 hours or more pre-incubation time can influence the oocyte quality related to alternation in H2O2, glutathione, mitochondrial integrity and mitochondrial membrane potential which ultimately leads to reduced oocyte fertilization potential. Supplementation of myo-inositol in medium improves the oocyte quality in comparison to the simple medium and saves 4 hours for preincubated oo-cytes.

P-369 Tuesday, October 15, 2019 6:30 AM

COLLAGEN AND HYALURONAN MATRICES UNDERGO AGE-RELATED CHANGES IN THE HUMAN OVARY. Sharron L. Manuel, MD, PhD, MS, Elena Antonova, PhD, Jessica E. Hornick, PhD, Farners Amargant Riera, PhD, MD, Jun-Wei Wei, MD, Mary Ellen Pavone, MD, MSCI, Michele T. Pritchard, PhD, Francesca E. Duncan, PhD, Northwestern University, Chicago, IL; Biological Imaging Facility Northwestern University, Evanston, IL; Research Associate Professor, Dept Molecular Biosciences Northwestern University, Evanston, IL; Center for Reproductive Science, Northwestern University, Chicago, IL; Northwestern University Department of Pathology, Chicago, IL; Department of Pharmacology, Toxicology, & Therapeutics, Kansas University Medical Center, Kansas City, KS.

OBJECTIVE: Female reproductive aging is characterized by a decrease in gamete number and quality, which contributes to infertility. The ovarian microenvironment in which gametes grow likely influences their development and quality, and we recently demonstrated a significant increase in age-associated fibrosis in the mouse ovarian stroma. Whether such stromal changes are conserved and occur in the human ovary is unknown. The objec-tive of this study was to examine how collagen and hyaluronan (HA), two major extracellular matrix (ECM) components, change in the human ovary with normal and pathological female age.

DESIGN: Translational.

MATERIALS AND METHODS: To examine age-associated collagen and HA content changes in the human ovary, we generated a tissue microarray (TMA) consisting of 1 mm human ovarian cortex cores from 60 individuals in four age cohorts, ranging in age from 1.8 – 58 years old. Sequential sections of the TMA were processed for hematoxylin & eosin (H&E) staining to assess tissue architecture, picrosirius red (PSR) staining to assess collagen I and III, and fluorescent-tagged HA binding protein (HABP) -mediated staining to assess HA levels. The PSR stained tissue was imaged by both light and polarized light microscopy, while HA was imaged using fluorescence microscopy. The percent area that was PSR or HA positive as well as the mean intensity (MI) were determined.

RESULTS: The amount of cortical collagen decreased between the 1.8 – 10-year-old cohort and the 11 – 20-year-old cohort (p = 0.0045) perhaps related to puberty onset. Collagen then increased between the 11 – 20-year-old cohort and the ≥51-year-old cohort, likely reflecting increased fibrosis (p = 0.0009). In contrast to collagen, there was an overall decrease in ovarian HA content between the young participants (1.8 – 20-year-olds) and the older participants (39 – 58-year-olds) (p < 0.0001). The ovarian cortex cores revealed considerable heterogeneity with some samples containing follicles, vasculature, and/or stroma. Therefore, we stratified our analyses by structural category. In the ≥51-year old cohort, we observed significant age-associated increased fibrosis in blood vessel-containing cores (p = 0.011 by percent area and p = 0.027 by MI) and stroma (p = 0.019 by MI) when compared to the 11 – 20-year-old cohort. Although fibrosis
increased and overall HA levels decreased with age, there was no correlation between HA and collagen content on an individual core basis.

CONCLUSIONS: These studies demonstrate that the human ovarian cortical ECM undergoes significant changes with age, and that ovarian stromal fibrosis is a conserved mammalian aging hallmark. Cortical ovarian collagen content is high at age extremes, and likely reflects normal stromal composition during early development but age-related pathology with advanced age. HA shows an opposite pattern and decreases with advanced reproductive age. The precise interplay between the collagen and HA matrices is currently under investigation.

SUPPORT: Supported by: National Institute of Child Health and Human Development (R01HD093726).

P-370 Tuesday, October 15, 2019 6:30 AM

THE EFFECT OF AUTOPHAGY AFTER MOUSE OOCYTE ACTIVATION TEST. Atsushi Yamamoto, MD, PhD, Naoki Yoshikawa, Bachelor of Medicine, Sae Onozuka, Bachelor of Agriculture, Akiyoshi Osaka, Bachelor of Medicine, Shin Oonota, Bachelor of Medicine, Toshiyuki Iwashita, MD, PhD, Yosihito Kobori, MD, PhD, Kouhei Sugimoto, MD, PhD, Hiroshi Okada, MD, PhD, Dokkyo Medical University Saitama Medical Center, Koshigaya, Japan.

OBJECTIVE: Autophagy is a lysosome-mediated intracellular process for protein degradation and is induced in the situation of amino acid starvation and several biological stimulations to maintain the cytoplasmic homeostasis. And previous studies in the reproductive field have shown that autophagy after fertilization and the cytoplasmic sperm injection (CSI) is a genetic test named mouse-oocyte-activation test (MOAT) to check the human sperm function after fertilization, there are no reports about the relation between MOAT and autophagy induction and we check the relations. DESIGN: Experimental Research.

MATERIALS AND METHODS: To collect MII oocytes, 8-10 weeks old female mice (C57BL/6) were superovulated. Oocytes were fertilized by intraperitoneal sperm injection (ICSI) using 1 (or 2) human sperm; MOAT mouse oocyte, or mouse sperm. After 5-hour incubation, embryos in parafomaldehyde and immunostained by microtubule-associated protein 1 light chain 3 alpha (LC3) which is the marker of autophagy. Then they were analyzed by fluorescence microscopy and LC3 puncta in each embryo were counted.

RESULTS: LC3 puncta were significantly detected in a human sperm injection more than in a mouse sperm injection. The number of puncta was almost the same in 1 sperm injection as in 2 sperm injections. The size of puncta was bigger in 1 sperm injection than in 2 sperm injections.

CONCLUSIONS: Autophagy was induced by xenogeneic sperm fertilization. The reason why autophagy was induced strongly in human sperm injection may be that the removal reaction of xenogeneic proteins occur strongly, or that the volume of autophagy inducing factor is more in the human than in mice. LC3 puncta was bigger in two-sperm injection because the proteins to remove may be much more than in one-sperm injection. Though we have to check the phenomenon quantitatively and analyze the difference autophagic induction between normal and infertile man, to detect autophagic function individually by MOAT may lead to a new evaluation of male infertility therapy.

P-371 Tuesday, October 15, 2019 6:30 AM

FUNCTIONAL ACTIVITY OF MITOCHONDRIA IN AGED OOCYTES IS ASSOCIATED WITH CYTOSKELETON STABILITY IN MICE. Jae Ho Lee, Ph.D., Hye Ran Lee, Ph.D.,* Hyun Youn Kim, Ph.D.,* Kyoungh Hee Choi, Ph.D. candidate,* Ji Hyang Kim, MD,* Hannah Kim, MD,* Chanhong Park, MD,* Soo Yeon Kim, MD,* Mi Kyong Koong, MD, PhD,* Tae Ki Yoon, M.D, Ph.D.* Sang Jin Lee, Ph.D.* CHA Fertility Center, Seoul, Korea, Republic of (South);* CHA University, Seoul, Korea, Republic of (South);* CHA Fertility Center Seoul, Seoul, Korea, Republic of (South);* CHA Fertility Center Kangnam Medical Center, Seoul, Korea, Republic of (South);* CHA Bundang Medical Center, CHA University, Seongnam-si, Gyeonggi-do, Korea, Republic of (South);* CHA Fertility Center Gangnam Medical Center, Seoul, Korea, Republic of (South);* Department of OB/GY CHA Fertility Center Seoul Station, CHA University, Seoul, Korea, Republic of (South);* CHA Fertility Center Seoul Station, Obstetrics and Gynecology, Seoul, Korea, Republic of (South);* Department of Animal Biotechnology & Resources, Sahnmyouk University, Seoul, Korea, Republic of (South).

OBJECTIVE: Dysfunctional mitochondria are strongly associated with oocyte quality and aging. However, cannot fully explain the decrease of mitochondrial activity in oocytes. Here, we studied dysfunctional mitochondria and assessed whether their functionality in aged oocytes was associated with cytoskeleton stability.

DESIGN: Experimental animal study.

MATERIALS AND METHODS: We performed time-lapse confocal live microscopy of mitochondrial motility in both young and aged oocytes. We then examined the association between cytoskeleton stability and mitochondrial motility with young oocyte, aged oocytes and 150μM cytochalasin B (CB)-treated young oocytes and analyzed the relationships between mitochondrial motility and functional activity including ATP production ratios.

RESULTS: Young oocytes showed dynamic mitochondrial motility and high ATP production levels during maturation, whereas aged oocytes did not. Cytoskeleton destabilization in CB-treated young oocytes led to a significant decrease in motility of mitochondria and to maturation ratios comparable to those of aged oocytes. Young oocytes present well development with microtubule formation in the ooplasm. But old oocytes have less development and thin microtubule formation in the ooplasm. Besides, 150μM cytochalasin B (CB)-treated young oocytes showed a lot of disconnected microtubule formation in the ooplasm like disassemble microtubule formation look like microtubule formation in the aged oocytes. It was shown that CB disturbed cytoskeleton formation in the oocytes. Therefore, low mitochondrial motility was associated with low ATP production ratios in CB-treated young oocytes and in aged oocytes.

CONCLUSIONS: In young oocytes, there was an aberrant motility and poor ATP production ratios compared to young oocytes. These findings may be related to cytoskeleton stability with a loss of motility and poor ATP production ratios of mitochondria as observed in aged oocytes. Mitochondrial motility along the cytoskeleton may play an important role for the determination of oocytes quality, depending on age.

P-372 Tuesday, October 15, 2019 6:30 AM

ROLE OF VOLTAGE DEPENDENT N AND P/Q TYPE CALCIUM CHANNEL IN MOUSE EGG FERTILIZATION. Sook Young Yoon, Ph.D.* Jin Hee Eum, Ph.D.* Miseon Park, Master,* Woo Sik Lee, M.D. Ph.D.* Fertility Center of CHA Gangnam Medical Center, Seoul, Korea, Republic of (South);* Affiliation not provided.

OBJECTIVE: During mammalian fertilization, phospholipase C zeta (PLCZ), induces repetitive changes termed Ca2+oscillations. Ca2+oscillation triggers egg activation, including cortical granule (CG) exocytosis, resumption of second meiosis, block to polyspermy, and initiating embryonic development to the blastocyst stage. The sources of Ca2+ion elevation during Ca2+oscillations are Ca2+influx from extracellular medium through the Ca2+influx receptors at the plasma membrane, Ca2+channel in the membrane. Ca2+oscillations are generated by voltage-dependent Ca2+channel (VDCs), ligand-gated Ca2+channel, and leak channel. VDCs expressed on muscle cell or neuron is specified into L, T, N, P, Q, and R type VDCs by their activation threshold and their sensitivity to peptide toxins isolated from cone snares and spiders. It has been shown that plasma membrane potentials of mammalian oocyte are changed according to their maturation stage from germinal vesicle stage to meiosis II stage that could be fertilized by sperm. Also, addition of VDCs blockers inhibits mammalian oocyte maturation or embryo development.

DESIGN: The present study was aimed to investigate that localization pattern of N and P/Q type voltage dependent calcium channel in mouse oocytes and the role in fertilization.

MATERIALS AND METHODS: Five to six week old C57BL/DBA F1 female mice were superovulated. Cumulus-enclosed eggs were retrieved from oviduct. Ca2+imaging: Oocytes were loaded with Fura 2 AM, transferred into TL-HEPES microdrops placed on a monitoring. Porcine sperm factor or adenophostin were injected by a picoinjector. 10mM SrCl2 were applied to the blastocyst stage. The sources of Ca2+ion elevation during Ca2+oscillations are Ca2+influx from extracellular medium through the Ca2+influx receptors at the plasma membrane, Ca2+channels have been characterized into voltage-dependent Ca2+channel (VDCs), ligand-gated Ca2+channel, and leak-channel. VDCs expressed on muscle cell or neuron is specified into L, T, N, P, Q, and R type VDCs by their activation threshold and their sensitivity to peptide toxins. Oocytes were incubated with acid-Tyrode’s solution and fixed in 4% PFA. Eggs were incubated with 2 μg/mL calcein-AM at 37°C for 30 min, the eggs were washed with Tyrode’s containing 0.2% BSA and mounted on a glass coverslip. Images were acquired with a Zeiss 880 LSM confocal microscope. For each experiment, at least 50 eggs were analyzed and the results were expressed as mean ± SD.

RESULTS: Ca2+oscillation were observed in Ca2+-contained medium without sperm factor or adenophostin injection. The oscillations were disappeared Ca2+-oscillation by SrCl2 or Ada microinjection. Ca2+-influx was induced in Ca2+-free medium. Other blockers including VDCs blockers inhibits mammalian oocyte maturation or embryo development. Oocytes were incubated with acid-Tyrode’s solution and fixed in 4% PFA. Eggs were incubated with 2 μg/mL calcein-AM at 37°C for 30 min, the eggs were washed with Tyrode’s containing 0.2% BSA and mounted on a glass coverslip. Images were acquired with a Zeiss 880 LSM confocal microscope. For each experiment, at least 50 eggs were analyzed and the results were expressed as mean ± SD.

RESULTS: Ca2+oscillation were observed in Ca2+-contained medium with sperm factor or adenophostin A injection. The oscillations were disappeared Ca2+free medium. Actin filament disruptor, latrunculin A abolished Ca2+oscillation by SrCl2 or Ada microinjection. Ca2+-influx was induced in Ca2+-free medium. Other blockers including VDCs blockers inhibits mammalian oocyte maturation or embryo development. Oocytes were incubated with acid-Tyrode’s solution and fixed in 4% PFA. Eggs were incubated with 2 μg/mL calcein-AM at 37°C for 30 min, the eggs were washed with Tyrode’s containing 0.2% BSA and mounted on a glass coverslip. Images were acquired with a Zeiss 880 LSM confocal microscope. For each experiment, at least 50 eggs were analyzed and the results were expressed as mean ± SD.

RESULTS: Ca2+oscillation were observed in Ca2+-contained medium with sperm factor or adenophostin A injection. The oscillations were disappeared Ca2+free medium. Actin filament disruptor, latrunculin A abolished Ca2+oscillation by SrCl2 or Ada microinjection. Ca2+-influx was induced in Ca2+-free medium. Other blockers including VDCs blockers inhibits mammalian oocyte maturation or embryo development. Oocytes were incubated with acid-Tyrode’s solution and fixed in 4% PFA. Eggs were incubated with 2 μg/mL calcein-AM at 37°C for 30 min, the eggs were washed with Tyrode’s containing 0.2% BSA and mounted on a glass coverslip. Images were acquired with a Zeiss 880 LSM confocal microscope. For each experiment, at least 50 eggs were analyzed and the results were expressed as mean ± SD.
The production of EGFR protein was higher than those on day 0. The productions of IL-8 and MMP-1 increased in the DSCs with the addition of ER. The wound repair of the DSCs was significantly enhanced compared to that of the ESCs. When ER was added, the wound repair was more enhanced. According to the RT-PCR analysis, HOXA 10 mRNA expression levels on day 12 decidual stimulation appeared to be higher than those on day 0. However, the downregulation of HOXA 10 in the DSCs were expressed on day 16.

CONCLUSIONS: Our results suggest that cell function is changed by decidualization in association with increasing EGFR expression. The up-regulation of EGFR accompanied with decidualization may contribute to have some influence on maintenance of pregnancy.

Reference: None.

SUPPORT: None.

REPRODUCTIVE GENETICS

P-374 Tuesday, October 15, 2019 6:30 AM

THE TP73 GENE (rs3765730) G>A POLYMORPHISM IS ASSOCIATED WITH OVARIAN RESPONSE DURING IVF/ICSI TREATMENT. Laura D. Vagnini, B.Sc.,a Claudia G. Petersen, Ph.D.,a Ana Lucia Mauri, B.Sc.,b Adriana Renzi, Ph.D.b Bruna Petersen, B.Sc.,b Mariana Mattila, B.Sc.,b Andrea Nicoletti, R.N.,b Felippe Dieamant, M.D.,b Joao Batista A Oliveira, M.D.,b Ricardo L. R. Baruffi, M.D.b Jose G. Franco, Jr., M.D., Ph.D.b Ricardo A. L. Brust, M.D.b

OBJECTIVE: To investigate a possible association between a TP73 gene polymorphism and ovarian response after IVF/ICSI.

MATERIALS AND METHODS: This study included 137 women submitted to IVF/ICSI cycles.

The enrolled individuals met the following inclusion criteria: age ≤37years; normal karyotype; having two ovaries as evinced in ultrasound examination; no history of ovarian surgery, endometriosis, hydrosalpinx, infection, or endocrine disorders.

DNA extracted from peripheral blood was sequenced on MiSeq(Illumina) to find single nucleotide polymorphisms (SNPs) in the TP73 gene. SNPs were identified using the TruSeq Custom Amplicon (TSCA) Panel (DesignStudio Illumina).

The findings from sequencing were associated with age, anti-Müllerian hormone (AMH) levels, antral follicle counts (AFC), total dose of recombinant FSH (r-FSH), follicle size, number of retrieved oocytes, and clinical outcome of IVF/ICSI cycles.

RESULTS: The TP73 (rs3765730) G>A SNP were identified. Although no difference was observed in ovarian reserve indicators (AMH and AFC), women with the AA genotype had significantly better ovarian response to rFSH. No difference was observed in clinical outcomes. Table 1 presents a summary of the results.

CONCLUSIONS: The TP73 rs3765730 polymorphism apparently affected ovarian response to rFSH and the clinical outcomes of IVF/ICSI.

### TABLE 1. Results

<table>
<thead>
<tr>
<th>TP73 (rs3765730) Genotypes</th>
<th>GG</th>
<th>GA</th>
<th>AA</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>51.1% (70/137)</td>
<td>37.2% (51/137)</td>
<td>11.7% (16/137)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cycles</td>
<td>47.7% (94/197)</td>
<td>42.6% (84/197)</td>
<td>9.7% (19/197)</td>
<td>0.001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>33.8±2.5</td>
<td>33.4±3.0</td>
<td>0.92</td>
<td></td>
</tr>
<tr>
<td>AMH (ng/ml)</td>
<td>2.6±3.4</td>
<td>2.9±2.8</td>
<td>0.26</td>
<td></td>
</tr>
<tr>
<td>AFC (n)</td>
<td>16.0±11.4</td>
<td>18.6±12.6</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Total dose rFSH (UI)</td>
<td>2309±1036a</td>
<td>2228±1299b</td>
<td>1674±808ab</td>
<td>0.001, 0.004</td>
</tr>
<tr>
<td>Follicles (n):Total</td>
<td>10.8±7.7a</td>
<td>10.5±7.9b</td>
<td>16.8±9.9ab</td>
<td>0.01, 0.003</td>
</tr>
<tr>
<td>Follicles (n):≥18 mm</td>
<td>3.4±2.2a</td>
<td>3.5±2.7ab</td>
<td>4.8±2.3ab</td>
<td>0.01</td>
</tr>
<tr>
<td>Retrieved oocytes (n):Total</td>
<td>7.7±5.7a</td>
<td>7.3±6.6a</td>
<td>12.5±7.2ab</td>
<td>0.001, 0.001</td>
</tr>
<tr>
<td>Retrieved oocytes (n):Metaphase II</td>
<td>5.5±4.4a</td>
<td>5.9±5.4b</td>
<td>9.6±6.1ab</td>
<td>0.006, 0.005</td>
</tr>
<tr>
<td>Fertilization rate</td>
<td>65.8%</td>
<td>68.8%</td>
<td>68.5%</td>
<td>0.55</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>29.4%</td>
<td>24.1%</td>
<td>28.0%</td>
<td>0.53</td>
</tr>
<tr>
<td>Pregnancy rate/patient</td>
<td>62.9%</td>
<td>58.8%</td>
<td>68.8%</td>
<td>0.74</td>
</tr>
<tr>
<td>Pregnancy rate/transfer</td>
<td>40.7%</td>
<td>35.7%</td>
<td>42.3%</td>
<td>0.75</td>
</tr>
</tbody>
</table>

Values within rows with the same superscript letter were significantly different.
sequences. Homozygosity of the A allele was associated with significantly better results. The identified SNP may provide an additional tool to test patients for ovarian response and thus help in the individualization of ovarian stimulation protocols. To the best of our knowledge, this is the first study associating this SNP and ovarian response.

SUPPORT: Merck Grant for Fertility Innovation (GFI-2014).

Tuesday, October 15, 2019 6:30 AM

P-375

SEQUENTIAL CLINICAL MANIPULATIONS OF EMBRYOS RESULTS IN ALTERATIONS IN EXPRESSION OF GENES INVOLVED IN INNATE IMMUNITY, APOPTOSIS, AND MITOCHONDRIAL FUNCTION. Kristin Van Heurtem, MD,1 Lisa Lam, BS,2 Michael J. Cartwright, MS,3 Brian Richardson, BS,4 Mark Cameron, PhD,5 Sam Mesiano, PhD,6 Rachael S. Weinerman, MD7 University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH;8 Affiliation not provided.

OBJECTIVE: Although data do not suggest a decreased clinical pregnancy rate with single blastocyst (blast) vitrification (vit) or blast biopsy, vit before and after biopsy has been shown to compromise embryo survival, suggesting a greater impact of cryoprotectants following trophoderm biopsy. There are also little data on the long-term safety of embryo vit. Clinical studies suggest differences in perinatal outcomes between babies born following fresh and frozen embryo transfer (FET), with higher rates of preterm birth (PTB) and pre-eclampsia (PEC) after FET, and higher rates of low birthweight (LBW) after fresh transfer. In this study, we aim to identify specific genes affected by blast vit and biopsy that may account for these phenotypic differences.

DESIGN: Laboratory research.

MATERIALS AND METHODS: Female mice were superovulated with 5 IU PMSG and 5 IU hCG and mated with male mice. Blasts were flushed on E3.5 and divided into 4 groups: no manipulation (g2), single vit/thaw (g3), IU PMSG and 5 IU hCG and mated with male mice. Blasts were flushed on E3.5 and divided into 4 groups: no manipulation (g2), single vit/thaw (g3), double vit/thaw (g4), and single vit/thaw plus biopsy and revitrified and thawed (g5). 3 sets of 15 blast per group were pooled for RNA extraction. Low input libraries were made using Takara SMART-Seq v4 and Illumina Nextera XT kits. RNA-Seq was performed on an Illumina NextSeq 550 (75 base pair, paired-end, 30 x 10^6 reads/sample). Differentially expressed genes (DEGs) were determined by two group t-tests (P < 0.05) and organized into top enrichment pathways by P value (P < 0.05) via gene set variation analysis in R Bioconductor. Our sample size achieves a power of 80% with an alpha of 0.05 to detect a >2.5 fold change in transcript expression.

RESULTS: Analysis of DEGs revealed significant alterations in multiple pathways. These differences were seen in multiple comparisons between all groups, with greater effect seen with increasing manipulations. For example, 3,340 DEGs were found between g2 and g5. STRING network analysis showed clustering in innate immunity, apoptosis, and mitochondrial function pathways. Several DEGs with plausible mechanisms for the outcomes of interest were identified, including C1qa (log fold change 2.9), Tlr2 (logFC 5.44), and Tnf (logFC -2.98).

CONCLUSIONS: In this pilot study, multiple genes involved in innate immunity exhibited altered expression with increasing levels of manipulation. C1qa, a complement system component, is significant to trophoblast invasion, and KO mice also exhibit a PEC phenotype. Decreasing levels of C1qa expression were seen with increasing manipulation in our study, suggesting a possible mechanism for the increased risk of PEC with FET. Tlr2 is a common mediator of apoptosis, and its activation has been found to trigger PTB. Our data shows decreasing Tlr2 expression with increasing manipulation, which may represent a plausible mechanism for the increased rates of PTB following fresh transfer. Tnf has been shown to be increased in placenta from PEC pregnancies; increased Tnf early in pregnancy also suppresses trophoblast invasion. We found increasing levels of Tnf expression with increasing manipulation, which may represent another mechanism for the increased risk of PEC following FET.

SUPPORT: Prelude Scientific Advisor Board Grant.

Tuesday, October 15, 2019 6:30 AM

P-376

THE MATRIX METALLOPROTEINASE-9 (MMP9) P. Gln279Arg POLYMORPHISM IS ASSOCIATED WITH OVARIAN RESERVE AND OVARIAN RESPONSE DURING IVF/ICSI TREATMENT. Laura D. Vagnini, B.Sc.,a Claudia G. Petersen, Ph.D.,b Ana Lucia Mauri, B.Sc.,c Adriana Renzi, Ph.D.,c Bruna Petersen, B.Sc.,c Mariana Mattila, B.Sc.,c Juliana Ricci, R.N.,c Felipe Dieamant, M.D.,c Joao Batista A Oliveira, M.D., Ph.D.,c Ricardo L. R. Baruffi, M.D.,c Jose G. Franco Jr., M.D., Ph.D.c Paulista Center for Diagnosis, Research and Training, Ribeirao Preto, Brazil; cCenter for Human Reproduction Prof. Franco Jr; Paulista Center for Diagnosis, Research and Training, Ribeirao Preto, Brazil; cCenter for Human Reproduction Prof. Franco Jr; Ribeirao Preto, Brazil.

OBJECTIVE: To investigate a possible association between an MMP9 gene polymorphism and ovarian response after IVF/ICSI.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: This study enrolled 135 women submitted to IVF/ICSI cycles.

The enrolled individuals met the following inclusion criteria: age ≤37years; normal karyotype; having two ovaries as evidenced in ultrasound examination; no history of ovarian surgery, endometriosis, hydrosalpinx, infection, or endocrine disorders. DNA extracted from peripheral blood was sequenced on MiSeq(Illumina) to find single nucleotide polymorphisms (SNPs) in the MMP9 gene. SNPs were identified using the TruSeq Custom Amplicon (TSCA) Panel (DesignStudio Illumina).

The findings from sequencing were associated with age, anti-Müllerian hormone (AMH) levels, antral follicle counts (AFC), total dose of recombinant FSH (r-FSH), follicle size, number of retrieved oocytes, and clinical outcome of IVF/ICSI cycles.

RESULTS: The MMP9p.Gln279Arg/Gln279Arg polymorphism was identified. Women with the Gln/Gln genotype had significantly poorer ovarian reserve indicators (lower levels of AMH and AFC), poorer ovarian response to rFSH, follicle size, number of retrieved oocytes, and clinical outcome of IVF/ICSI cycles.

TABLE 1. Results

<table>
<thead>
<tr>
<th>Gln/Gln</th>
<th>Gln/Arg</th>
<th>Arg/Arg</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>59.3% (80/135)</td>
<td>31.8% (43/135)</td>
<td>8.9% (12/135)</td>
</tr>
<tr>
<td>Age(years)</td>
<td>33.6±1.28</td>
<td>33.3±3.0</td>
<td>33.5±3.6</td>
</tr>
<tr>
<td>AMH(ng/ml)</td>
<td>2.1±3.4</td>
<td>2.6±2.2</td>
<td>3.7±5.6</td>
</tr>
<tr>
<td>AFC(n)</td>
<td>12.4±4.9</td>
<td>16.7±8.4</td>
<td>22.3±17.5</td>
</tr>
<tr>
<td>Total dose FSH(U)</td>
<td>2385±1173</td>
<td>1787±950</td>
<td>1854±1006</td>
</tr>
<tr>
<td>Follicles(n)/Total</td>
<td>10.8±7.7</td>
<td>16±10.6</td>
<td>18±10.5</td>
</tr>
<tr>
<td>Follicles(n)/≥18mm</td>
<td>3.3±2.3</td>
<td>4.6±2.8</td>
<td>4.8±2.5</td>
</tr>
<tr>
<td>Retrieved oocytes/Total</td>
<td>7.8±5.3</td>
<td>11.2±8.2</td>
<td>10.6±7.0</td>
</tr>
<tr>
<td>Retrieved oocytes/MII</td>
<td>5.9±4.0</td>
<td>8.1±6.8</td>
<td>8.2±6.0</td>
</tr>
<tr>
<td>Fertilization</td>
<td>66.6%</td>
<td>65.1%</td>
<td>81.9%</td>
</tr>
<tr>
<td>Implantation</td>
<td>26.4%</td>
<td>40.2%</td>
<td>30.8%</td>
</tr>
<tr>
<td>Pregnancy/patient</td>
<td>46.3%</td>
<td>62.8%</td>
<td>58.3%</td>
</tr>
<tr>
<td>Pregnancy/</td>
<td>39.8%</td>
<td>51.9%</td>
<td>50%</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The MMP9p.Gln279Arg polymorphism was associated with ovarian reserve and seemed to have affected ovarian response to rFSH and the clinical outcomes of IVF/ICSI cycles. Homozygosity of the Gln allele was associated with significantly poorer results. The identified SNP might provide an additional tool to test patients for ovarian response and thus help in the individualization of ovarian stimulation protocols.

SUPPORT: Merck Grant for Fertility Innovation (GFI-2014).
TOWARDS PERSONALISED REPRODUCTIVE MEDICINE: SCREENING FOR GENETIC VARIANTS AND ITS INFLUENCE IN CONTROLLED OVARIAN STIMULATION. Belen Lledo, PhD, Laura Blanco, MSc, Jose A. Ortiz, PhD, Ruth Morales, PhD, Jaime Guerrero, MSc, Ana Fabregat, PhD, Joaquín Llacer, PhD, Rafael Bernabeu, Ph D M D In- stituto Bernabeu, Alicante, Spain.

OBJECTIVE: The most studied polymorphism to assess the ovarian stimulation was N680S-FSHR, however, others genes related to follicular growth could also play an important role in determining the ovarian response. The aim of this work was to evaluate the association between ovarian stimulation and the genetic variants present in genes involved in ovarian function.

DESIGN: Oocyte donors are the most adequate model to evaluate ovarian stimulation because are young women with normal ovarian function. This prospective randomized study includes 124 healthy, normoovulatory, caucasi- an egg donors genotyped for six SNPs present in ESR1, AMH, AMHR2, GDF-9 and LHCGR and four STRs present in ESR1, SHBG, CYP19A1 and AR. All donors followed a standard ovarian stimulation protocol using a daily dose of 225UI of either uFSH or rFSH.

MATERIALS AND METHODS: SNPs were analysed by TaqMan allelic-discrimination assays (rs2234693-ESR1, rs10407022-AMH, rs2005555- AMHR2, rs10491279/rs254286-GDF-9, rs2293275-LHCGR) and the STR-polymorphism in the ESR1, SHBG, CYP19A1 and AR genes by fluores- cent-PCR. The genotypes obtained were compared to the ovarian stimulation.

RESULTS: The mean age of the oocyte donors included in the study was 23.9±3.5y. The mean AMH level was 45.4±23.5pmol/ml and the mean number of antral follicles count was 14.2±2.8. We performed a linear regression, taking into consideration confounding factors such as age, smoking, BMI and AMH. Regarding the number of retrieved oocytes, we found statistically significant differences for the ESR1 SNP (19.3±8.9 for TT vs 15.3±6.2 for CC/CT, p=0.027) and ESR1 (TA)n STR (19.1±8.3 for <17 repeats vs 14.7±6.2 for >17 repeats, p=0.020). When we combined both genotypes, the haplotype analysis showed that women that carries CC or CT in the ESR1 gene at position -397T/C (rs2234693) with a number of repeats in the ESR1 (TA)n polymorphisms higher than 17 retrieved lower oocytes (14.0±5.6) than the other genotypes (p=0.001). Regarding AMHR2 we observed an association with the length of stimulation (9.1±1.4 for AA vs 9.7±1.3 for AG/GG, p=0.021) and gonadotropin received (2050±319 for AA vs 2188±599 for AG/GG, p=0.017). No significant association among genotype, retrieved oocytes and ovarian stimulation was observed for LHCGR, CYP19A1, AMH, SHBG, AR and both of GDF-9 SNPs (p=0.08).

CONCLUSIONS: We reported that polymorphisms in the ESR1 and AMHR2 genes showed a clear association with the number of retrieved oocytes and the stimulation data, respectively. Therefore, our results suggest that polymorphisms in the genes for key reproductive hormones receptors could be used to predict the ovarian response and to personalize and adjust the stimulation drugs prior the overtaken treatment. Such pharmacogenetics approach will facilitate the selection of the optimum protocol for each patient.

TABLE 1. The result of X-chromosome STR analysis (a case of maternal origin extra-X)

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Marker</th>
<th>DXS10148</th>
<th>DXS10135</th>
<th>DXS8378</th>
<th>DXS10079</th>
<th>DXS10074</th>
<th>DXS7132</th>
</tr>
</thead>
<tbody>
<tr>
<td>Father</td>
<td>20</td>
<td>20</td>
<td>22</td>
<td>22</td>
<td>10</td>
<td>18</td>
<td>21</td>
</tr>
<tr>
<td>Mother</td>
<td>20, 22.1</td>
<td>20, 22</td>
<td>21, 22</td>
<td>21, 22</td>
<td>10</td>
<td>17, 18</td>
<td>20</td>
</tr>
<tr>
<td>Patient</td>
<td>22.1</td>
<td>22.1</td>
<td>21, 22</td>
<td>21, 22</td>
<td>10</td>
<td>18, 20</td>
<td>18</td>
</tr>
<tr>
<td>Marker</td>
<td>HPRT</td>
<td>DXS10101</td>
<td></td>
<td></td>
<td>10</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>Father</td>
<td>12</td>
<td>12</td>
<td>31, 2</td>
<td>31, 2</td>
<td>18</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>Mother</td>
<td>13, 14</td>
<td>13, 14</td>
<td>29, 31.2</td>
<td>29, 31.2</td>
<td>17, 19</td>
<td>36, 37.3</td>
<td>36, 37.3</td>
</tr>
<tr>
<td>Patient</td>
<td>14</td>
<td>14</td>
<td>29, 31</td>
<td>29, 31.2</td>
<td>17, 19</td>
<td>36, 37.3</td>
<td>36, 37.3</td>
</tr>
</tbody>
</table>

P-377 Tuesday, October 15, 2019: 6:30 AM

Brevity MAPPING UNCOVERING ABOUT 1.32% OF APPARENT BALANCED RECIPROCAL TRANSLOCATION (ABRT) CARRIERS EXISTING CRYPTIC COMPLEX CHROMOSOMAL STRUCTURAL VARIATIONS IN PREIMPLANTATION GENETIC TESTING (PGT). Shimin Yuan, Master, Yue-qi Tan, Doctor, Reproductive and Gen- netic Hospital of Citic-Xiangya, Changsha, China.

OBJECTIVE: To identify precise breakpoints, evaluate the reproduction-related risks and guide the following PGT treatment, high resolution breakpoint mapping was performed in ABRT carriers indicated by G-banding.

DESIGN: A single-center, descriptive research.

MATERIALS AND METHODS: A large sample of 833 cases with ABRT who planned to accept PGT treatment were recruited in this study. For these patients, the approach of the next-generation sequencing following microdissection (MiroSeq) of the junction region in the derivative chromosomes, and linkage analysis of the adjacent single nucleotide polymorphisms (SNPs) were performed to distinguish the carriers from noncarriers in balanced embryos. For some cases with unbalanced chromosome rearrangement in the breakpoint region, SNP-array and fluorescence in situ hybridization (FISH) techniques were further used to determine the accurate karyotype.

RESULTS: In the 833 cases with ABRT, we found 11 cases (1.32%) carried cryptic complex chromosomes structural variation, including 3 unbalanced chromosome rearrangements and 8 balanced ones in which 2 cases carried both inversion and translocation. In these 11 cases, 5 cases related to 3 chromosomes with 4 to 21 breakpoints and 6 cases involved 2 chromo- somes with 3 to 6 breakpoints. It is noteworthy that there were two cases exhibited rare chromoanagenesis, including chromothripsis and chromoplexy. Fortunately, two couples have been both successfully transplanted a normal sperms are the cause of KS. However some papers report the maternal origin. So we performed this study to investigate the origin of extra X in Kleneffel Syndrome (KS).

DESIGN: Cytogenetic analysis in KS patients and their parents.

MATERIALS AND METHODS: Blood samples from 29 KS patients were used for X-chromosome short tandem repeats (STR) analysis. The STR analysis also included data of the parents of the KS patients (24; both parents; 5; mother only; 0; father only) from January 2015 to March 2019. This study was conducted with the informed consent of all participating pa- tients and approved by The Institutional Review Boards of the St. John Obstetrics and Gynecology Clinic and adhered to JCMER criteria UMIN Clinical Trial Registry was UMIN00002452.

Blood samples of 29 KS patients and one or both of their parents were used to determine the origin of the extra X chromosome using X-chromosome haplotype markers (short tandem repeats of 12 loci), according to the method by Shrivastava et al. With DNA extracted from the samples, multiplexed PCR amplifications of the 12 X-STR loci and AMELOGENIN were conducted using an Investigator Argus X-12 QS Kit (Quiagen, Germany). The data obtained was analyzed with GeneMapper ID software.

RESULTS: X-chromosomal STR DNA profiles were compared among KS patient and their parents. In 13 of the 29 KS patients, both two X chromo- somes were maternal origin, showing that an extra X chromosome was left in an oocyte as a result of chromosomal non-disjunction at the 1st (4/13) or 2nd (9/13) meiotic division. In 15 patients, X-chromosomes were inherited from parents, suggesting that fertilization of XY-sperm is the cause of KS.

CONCLUSIONS: Although the sample number applied for X-chromo- somal STR DNA profiling is not enough, the present data may indicate that contribution of XX oocyte to the production of XXY embryos is greater than XY sperm. Namely, a XX oocyte penetration by a Y sperm is the main cause of KS. Cytogenetic analysis with smear of testicular cell mixture that was used in the studies may overestimate chromosomal abnormality.
embryo and given birth to a healthy child, and the remaining nine cases are undergoing PGT treatment.

CONCLUSIONS: In this large-scale analysis of ABRT, high resolution breakpoint mapping precisely characterized these breakpoints and uncovered 1.32% of the ABRT carriers existed cryptic complex chromosomal rearrangements. These data suggest that high resolution breakpoint mapping used in PGT can improve the accuracy of evaluating the reproduction-related risks and avoid genetic risks for the ABRT carriers.

SUPPORT: This study was supported by the National Key R&D Program of China 2018YFC1003100 (L.H.) and 2016YFC1002020 (G.L.), National Natural Science Foundation of China 81873478 (L.H.) and Merck Serono China Research Fund for Fertility Experts.

P-380 Tuesday, October 15, 2019 6:30 AM

SINGLE CELL GENE EXPRESSION OF HUMAN PUBLERTAL TESTIS DEVELOPMENT. Jingtao Guo, PhD.a Xichen Nie, BS, b Douglas T. Carrell, PhD.c James Hotaling, MD. a Bradley R. Cairns, PhD. d 1University of Utah School of Medicine, Andrology and IVF Laboratories, Salt Lake City, UT; 2Huntsman Cancer Institute, Salt Lake City, UT; 3University of Utah School of Medicine Andrology and IVF Laboratories, Salt Lake City, UT; 4Howard Hughes Medical Institute, Department of Oncological Sciences and Huntsman Cancer Institute, University of Utah School of Medicine, Salt Lake City, UT.

OBJECTIVE: We investigated the molecular mechanism underlying human testis development during puberty by single cell RNA-seq profiling.

DESIGN: We derived single cell suspensions using the testicular biopsies from 4 juvenile donors (7-14), and performed single cell RNA-seq profiling and analysis.

MATERIALS AND METHODS: We performed scRNA-seq profiling of whole testis tissues from juvenile donors (two technical replicates for each donor): one 7-year old (~3000 cells), one 11-year old (~3000 cells), one 13-year old (~3000 cells), one 14-year old (~3000 cells). This yielded a dataset composed of ~12000 single cell transcriptomes. We compared the current data-set with the single cell transcriptome from the young adult (~25 years old) and infant (~1 year old) male donors described in our previous work. We performed dimension reduction and clustering analysis using SEURAT and SDA programs, and utilized known markers to help decode cell identities. We further performed differential gene expression and gene ontology analysis to study the gene expression programs that display differential gene expression dynamics.

RESULTS: We found that spermatogonial stem cells (SSCs) commit to spermatogenesis in two sequential phases: mitotic differentiation (involving proliferation and metabolic changes) followed by subsequent commitment to meiosis, which may be induced by testosterone and activin signals. Remarkably, the early SSCs (marked by PIWI4, TSPAN33 and many other genes) were pre-determined during infancy (~1 year old), and persisted in adults. Regarding the somatic niche, we identified a common pre-pubertal cell precursor for Leydig and Myoid cells, and revealed pathways for pubertal differentiation, including the insulin signaling pathway. We have confirmed critical roles of testosterone in promoting germ cell identification and proliferation in both somatic and germline compartments. Importantly, we have developed a culture system that maintains human seminiferous tubule in vitro for three weeks.

CONCLUSIONS: The current study provided the first single cell transcriptional atlas for pre- and peri-pubertal testis development, and uncovered many important signaling pathways that may regulate both germ cell and somatic cell maturation during human puberty, which could be critical for initiation and maintenance of spermatogenesis. This can be applied to an in vitro culture system to help drive and maintain in vitro spermatogenesis using testicular tissues from prepubertal boys undergoing cytotoxic chemotherapy.

P-381 Tuesday, October 15, 2019 6:30 AM

PRE-SURROGACY OBSTETRICAL RISK ASSESSMENT FOR POTENTIAL GESTATIONAL CARRIERS. Georges Sylvestre-Margolis, MD CM, a Susanna Park, MD, b Said Daneshmand, MD, c Elmhurst Hospital Medical Center / Mount Sinai School of Medicine, New York, NY; San Diego Fertility Center, San Diego, CA.

OBJECTIVE: Develop an obstetrical risk screening system for the evaluation of women wishing to become gestational carriers.

DESIGN: Prospective Cohort Study

MATERIALS AND METHODS: Every pregnancy is associated with some maternal risk. In gestational surrogacy, the involvement of a third-party calls for caution as well-defined criteria in the evaluation of gestational carrier candidates (GCC’s) are lacking. We created a novel scoring system, the Gestational Carrier evaluation of Obstetrical Risk (GOCR) scale to rate the risk of severe maternal morbidity (SMM). Severe maternal morbidity (ACOG, Obstetrical care consensus #5, 2016) includes complications such as hysterectomy, transfusion of ≥ 4 units of PRBC, ICU admission, and stroke. The first step was the identification risk factors for SMM, from obstetrical and medical history. Examples include history of pre-eclampsia, prior cesareans, diabetes, hypertension and obesity. Based on the review of more than 75 published studies looking at individual risk factors for SMM, a score of 1 to 10 was assigned for each risk factor. Concurrently, ninety three patients were sent to a single Maternal-Fetal Medicine (MFM) provider for a pre-surrogacy evaluation. For each GCC, obstetrical and medical records were reviewed and a face-to-face, Skype or phone interview was conducted to complement the information from the records. Risk factors were abstracted and a GOCR score was assigned by adding all the risk factors scores. For each GCC, an MFM consultation report with a GOCR score was sent to referring providers and their satisfaction was recorded. A GOCR score > 10-20 suggests a high risk for SMM. The evaluation of risks of less severe maternal outcomes was also provided in the MFM report.

RESULTS: Pre-surrogacy evaluations were requested by IVF clinics (n=73) or by surrogacy agencies (n=20). Most referrals were for maternal risk concern(s) and some were for concurrent fetal/neonatal perinatal risk concern(s). Common indications for the requests were: underlying medical condition (n=54), history of pre-eclampsia (n=16), history of preterm delivery (n=16), prior cesareans (n=34), grand multiparity (n=12) and prior postpartum hemorrhage (n=6). The underlying medical conditions were varied, ranging from obesity (n=41), diabetes (n=12), hypertension (n=14), corrected cardiac defect, grade 3 uterine prolapse and multiple sclerosis. The mean GOCR score was 7.2 +/- 5.2 (range 2-22). Thirty three patients had a GOCR score ≥ 15. High GOCR scores were most often due to prior pre-eclampsia, prior postpartum hemorrhage and morbid obesity. All (100%) referring provider viewed the GOCR scoring system as simple and were satisfied with the reports.

CONCLUSIONS: This pilot study suggests that GOCR scoring combines objective, easily obtained and simplified risk factors for SMM. This approach may allow identification and screening of maternal candidates. We will continue to evaluate GCC’s to refine our scoring system and analyze data prospectively with inclusion of postpartum and perinatal outcomes. We plan to create a similar scale for fetal/neonatal risks and to adapt the GOCR scoring for planned multifetal pregnancies.

SUPPORT: N/A.

P-382 Tuesday, October 15, 2019 6:30 AM

LUTEAL PHASE-DERIVED OOCYTE-CUMULUS COMPLEXES: GENE EXPRESSION AND MITOCHONDRIAL DNA COPY NUMBER. Bella Martazanova, PhD.a Nona Mishieva, PhD., b Anna Korolkova, MD, a Khava Bogatyreva, PhD.c Maria Veykova, PhD.d Anastasia Kirillova, PhD., e Olga Burmenskaya, PhD., f Aydar Abubakirov, PhD.a aReproductive Endocrinology, Moscow, Russian Federation; bEmbryologist, Moscow, Russian Federation; cGenetic, biology, Moscow, Russian Federation.

OBJECTIVE: The double stimulation (DuoStim) became a new approach in poor responder management. However, luteal phase stimulation-derived (LPS) oocytes require further investigation. One of the methods to determine oocyte quality is investigation of the cumulus cells (CCs), which surround the oocyte and are pivotal in determining oocyte developmental competence. Several studies have revealed certain CCs genes that are correlated with oocyte competence and embryo development; also there are data, which shows that mitochondrial DNA (mtDNA) copy number is positively linked with embryo quality. However, gene expression and mtDNA quantification in CCs of LPS derived oocytes after the DuoStim approach still has not been investigated. Design: A total of 39 patients with a reduced ovarian reserve were included in the study. Inclusion criteria: age <43 years; AMH <1.2 ng/ml; AFC <6; basal FSH ≥ 11 IU/ml. Exclusion criteria: uterine fibroids ≥ 4 cm, deep endometriosis, cancer, BMI ≥ 29 kg/m², smoking, severe male infertility. Gene expression was assessed in a total of 169 CCs. 20 CCs were excluded: 4 due to mRNA impairment in the study. Inclusion criteria: age <43 years; AMH <1.2 ng/ml; AFC <6; basal FSH ≥ 11 IU/ml. Exclusion criteria: uterine fibroids ≥ 4 cm, deep endometriosis, cancer, BMI ≥ 29 kg/m², smoking, severe male infertility. Gene expression was assessed in a total of 169 CCs. 20 CCs were excluded: 4 due to mRNA impairment and 16 due to immature oocytes. A total of 149 CCMs were divided into two groups: group 1 included 55 follicular phase-derived oocytes from 15 patients and group 2 included 94 LPS - derived oocytes from 24 patients.

MATERIALS AND METHODS: The expression levels of HAS2, VCAN, ALCAM, PTGS2, GREM1, ITPKA, TRPM7, SDC4, CALM2, SP5B2, TPS313, PGR, PFKP and mtDNA were assessed using quantitative polymerase chain reaction. Statistical analysis – the Mann-Whitney test, t-test, the chi-squared test; p<0.05 was considered to be statistically significant.

RESULTS: CCs gene expression was similar between the groups. However, a significant increase in the mRNA levels of VCAN (15.542 +/- 6.8 vs.

Objectives: Poor ovarian response (POR) affects up to 20% of ART cycles and is associated with low pregnancy rates. In this review, we will describe recent advances in POR management.

Methods: A systematic review of recent publications was performed.

Results: Recent advances in POR management include: a) improvements in ovarian reserve testing, including the addition of anti-Müllerian hormone (AMH) to basal FSH for POR prediction; b) use of novel ovarian stimulation strategies, such as gonadotropin-releasing hormone (GnRH) agonist flare protocols and long agonist regimen with extremely low FSH; c) combination of GnRH agonist flare with slow release FSH for follicular recruitment; d) co-treatment with exogenous GnRH agonist and recombinant FSH or hCG for ovarian stimulation; e) use of GnRH agonist with GnRH receptor antagonist or gonadotropin-releasing hormone antagonist for antagonist cycles; and f) use of GnRH antagonist during luteal phase to improve endometrial receptivity.

Conclusion: These advances have led to improved ovarian stimulation and pregnancy rates, and the potential for improved patient outcomes.


P-384 Tuesday, October 15, 2019 6:30 AM

A "TANDEM-REFLEX" STRATEGY MINIMIZES RESULTS DELIVERY TIME FOR COUPLES UNDERGOING CARRIER SCREENING. Ashwarya Arjunan, MS, MPH, Kristjan Eerik Kaseniit, MEng, Brandon Lee, BA, Jeff Wootton, PhD, Kenny Wong, MS, Katie Johansen Taber, PhD. Myriad Women’s Health, South San Francisco, CA.

OBJECTIVE: To determine the impact of the "tandem reflex" strategy on turnaround-time and test utilization.

Expanded carrier screening aims to detect couples at risk for having children with severe and profound Mendelian disorders. As many couples are pregnant or actively trying to conceive while undergoing carrier screening, obtaining screening results in a timely manner is important. Reproductive partners are typically tested in a sequential manner: the female partner is tested first and if she is a carrier, her partner is tested for the condition(s) for which she was found to be a carrier. In current practice, this commonly necessitates a subsequent visit to a physician for submission of the partner’s sample, such that the time to receive a combined couple report is roughly double the time it takes to receive an individual carrier screening report. This need for a secondary sample submission imposes workflow challenges to the clinic and patients, reduces the likelihood of the partner getting screened, and thus may hamper detection of at-risk couples. To minimize turnaround-time and maximize the detection of at-risk couples, we implemented a "tandem reflex" strategy wherein both partners submit samples simultaneously to the carrier screening laboratory, and the likelihood of the partner getting screened, and thus may hamper detection of at-risk couples. To minimize turnaround-time and maximize the detection of at-risk couples, we implemented a "tandem reflex" strategy wherein both partners submit samples simultaneously to the carrier screening laboratory, and in that scenario, the tandem reflex strategy would not have triggered testing of the male partner.

RESULTS: 330,329 carrier testing results were reviewed. 14,258 patient samples were submitted and tested simultaneously. 41% of females were negative for all tested conditions; in this scenario, the tandem reflex strategy would not have triggered testing of the male partner.

CONCLUSIONS: Our results indicate that while differences in positivity rates within this unique patient population.

P-385 Tuesday, October 15, 2019 6:30 AM

CARRIER SCREENING IN 2019: IS SCREENING FOR MORE GENES THE NEW STANDARD OF CARE? Dana Neitzel, MS, CGC, Jocelyn Leahey, MS, CGC, Susan Glass, MS, Nicole Faulkner, PhD. Invitae, San Francisco, CA.

OBJECTIVE: To report ordering patterns within and outside of ACOG carrier screening guidelines between medical specialties.

TABLE 1. Summary of Ordering Patterns & Positive Rates

<table>
<thead>
<tr>
<th>Panel</th>
<th>REI</th>
<th>ObGyn</th>
<th>MFM</th>
<th>GC</th>
<th>Other</th>
<th>% of all orders</th>
<th>Positive Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>288 gene panel with 13 add-on genes</td>
<td>16%</td>
<td>21%</td>
<td>0%</td>
<td>18%</td>
<td>9%</td>
<td>15%</td>
<td>77%</td>
</tr>
<tr>
<td>288 gene panel</td>
<td>36%</td>
<td>27%</td>
<td>66%</td>
<td>53%</td>
<td>53%</td>
<td>41%</td>
<td>65%</td>
</tr>
<tr>
<td>46 gene panel</td>
<td>13%</td>
<td>10%</td>
<td>9%</td>
<td>3%</td>
<td>16%</td>
<td>12%</td>
<td>44%</td>
</tr>
<tr>
<td>3 gene panel</td>
<td>12%</td>
<td>24%</td>
<td>14%</td>
<td>3%</td>
<td>13%</td>
<td>14%</td>
<td>15%</td>
</tr>
<tr>
<td>Other: ACOG/ACMG ethnicity-specific genes</td>
<td>14%</td>
<td>7%</td>
<td>4%</td>
<td>2%</td>
<td>4%</td>
<td>9%</td>
<td>22%</td>
</tr>
<tr>
<td>Other: All other combinations</td>
<td>9%</td>
<td>11%</td>
<td>7%</td>
<td>21%</td>
<td>6%</td>
<td>9%</td>
<td>Varies</td>
</tr>
<tr>
<td>Total</td>
<td>7729</td>
<td>3106</td>
<td>446</td>
<td>903</td>
<td>4275</td>
<td>16459</td>
<td>51%</td>
</tr>
</tbody>
</table>

DESIGN: ACOG recommends universal carrier screening for cystic fibrosis (CF) and spinal muscular atrophy (SMA) and ethnicity-based screening when appropriate. ACOG acknowledges that expanded carrier screening (ECS) has many benefits but states ECS panels should only include high impact disorders (well-understood, severe, and common).1,2

Our laboratory offers carrier screening for up to 301 genes. These genes are available in pre-curated panels (3, 46, or 288 genes), or they can be ordered as customized panels. Thirteen additional genes (common, variable, and/or adult onset) are available as an add-on to any panel. All combinations are offered at the same out-of-pocket cost.

MATERIALS AND METHODS: Testing for up to 301 genes was performed by NGS. Ordering patterns by clinician type and positive rates were assessed.

RESULTS: In a ten-month period, 16,459 patient samples from 1,390 clinicians were tested. Almost half of all orders came from REIs and 9% of orders identified the patient/partner as pregnant. The largest pre-curated panel was ordered most frequently (n=6,699). Concurrent testing was performed for 62% of opposite-sex couple orders. Guideline-testing accounted for 23% of all orders with ObGyns having the highest adherence to guideline-based ordering (31%) and genetic counselors (GCs) having the lowest (5%). MFM was the only group that did not order all available genes (Table 1).

Of all tests, 31% were positive for 1 disorder, 21% were positive for 2 or more, and 48% were negative. The most common autosomal recessive disorders at-risk couples screened positive for (add-on genes excluded) include CFTR-related disorders, GJB2-related non-syndromic hearing loss, HBB-related hemoglobinopathies, Smith-Lemli-Optiz syndrome, SMA and phenylalanine hydroxylase deficiency (PKU).

CONCLUSIONS: Despite current guidelines, our data shows that 56% of clinicians preferred a large panel (≥288 genes), even including frequent/variable disorders and only 12% ordered the 46 gene panel with only high impact disorders. Additional investigation is needed to understand the decision tree within and between practices including the role insurance coverage and cost plays on carrier screening ordering.

References:

SUPPORT: Invitae.

P-386 Tuesday, October 15, 2019 6:30 AM

THE PROLONGED DISEASE STATE OF INFERTILITY IS ASSOCIATED WITH BLASTOCYST IMPRINTED EPIGENETIC DYSREGULATION. Michelle M. Denomme Tigna-nelli, PhD, William B. Schooler, MD, Mandy G. Katz-Jaffe, Ph.D., Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Epidemiological studies suggest that the disease state of infertility may play a role in the observed increased incidence of rare imprinting disorders in children born following infertility treatment. imprinting disorders frequently arise from epigenetic dysregulation at imprinting control regions (ICRs). Examples include loss of imprinted DNA methylation at the KvDMR ICR in ~50% of children with Beckwith-Wiedemann Syndrome, and loss of methylation at the H19 ICR in ~45% of children with Russell-Silver Syndrome. The purpose of this study was to examine the association between duration of infertility and DNA methylation at four ICRs in euploid blastocysts.

DESIGN: Research study.

MATERIALS AND METHODS: Surplus cryopreserved euploid blastocysts of transferable quality (grade ≥3BB; n=58) were donated with IRB approval and patient consent. Blastocysts were subdivided into four groups based on duration of infertility, classified as number of months of reported primary infertility prior to the oocyte retrieval that resulted in a live birth [Fertile Control: 0 months, donor oocyte/donor sperm (n=14); Infertile Short: 12-24 months (n=14); Infertile Intermediate: 36-48 months (n=14); Infertile Long: ≥60 months (n=16)]. Female age was restricted to ≤39 years. Infertility diagnoses were equally varied among the test groups. Euploid blastocyst DNA was isolated (QiAamp DNA Micro Kit; Qiagen) and bisulfite converted (EZ DNA Methylation-Direct Kit; Zymo Research) prior to PCR amplification and pyrosequencing (PyroMark Q24 Advanced system; Qiagen). Statistical analysis included Student’s t-test and one-way ANOVA where appropriate, with significance at p<0.05.

RESULTS: Extended durations of infertility ≥36 months (Infertile Intermediate + Infertile Long; mean=65 months) showed significant alterations in blastocyst imprint DNA methylation, with a decrease in methylation marks when compared to short durations ≤24 months (Fertile Control + Infertile Short; mean=10 months). The ICRs for KvDMR (39% Extended Infertility vs. 48% Short Infertility; p<0.05), H19 (29% Extended Infertility vs. 41% Short Infertility; p<0.05), and MEST (40% Extended Infertility vs. 49% Short Infertility; p<0.05) showed significant hypomethylation, while SNRPN/trended downward without significance. Infertility diagnoses, blastocyst grades, and total doses of recombinant folic acid stimulating hormone during ovulation stimulation where comparable across the groups.

CONCLUSIONS: This novel study is the first to report evidence that altered blastocyst imprint DNA methylation correlates with prolonged infertility. The prevalence of ICR hypomethylation was significant in euploid blastocysts derived from patients with an extended duration of infertility ≥36 months. Ongoing studies will investigate whether the underlying infertility leads to epigenetic errors, or if the methylation alterations themselves are perpetuating the duration of infertility? Our results contribute towards the identification of a mechanistic link between imprinted epigenetic dysregulation and infertility as a prolonged disease.

SUPPORT: None.

P-387 Tuesday, October 15, 2019 6:30 AM

ARE THERE ANY SIMILARITIES IN GENE EXPRESSION BETWEEN EUPLOID EMBRYOS AND ANEUPOID EMBRYOS COMPATIBLE WITH LIFE? Allison C. Kranayak, B.S., Alyssa Bare, B.S., Deepthi M. Athavale, B.S., Arnav Lal, na,a Jonathan L. Blalock, BS,a Shawn Zimmerman, PhD, HCLD,b T. Arthur Chang, PhD, HCLD, ELD,c Randal D. Robinson, MD, a, d J. David Winerig, PhD, HCLD, e William E. Roudebush, PhD, f Renee J. Chosed, Ph.D. g University of South Carolina School of Medicine Greenville, Greenville, SC; h Vios Fertility Institute, Swansea, IL; i University of Texas Health Science Center, San Antonio, TX; j UT Health San Antonio, San Antonio, TX; k Atlantic Reproductive Medicine Specialists, Raleigh, PA.

OBJECTIVE: Examples of human aneuploidies compatible with life include (but are not limited to) Down, Edwards, Klinefelter and Turner syndromes. Why or how are these unique aneuploid embryos able to implant and develop to term while other aneuploid embryos fail to implant or result in miscarriage? ART with PGT-A provides an opportunity not only to identify these aneuploidies but also to analyze blastocoel fluid contents. Blastocoel fluid is known to contain cell-free DNA, mRNA, extracellular vesicles and proteins, therefore comparison of the fluid components from various embryos of known ploidy status may provide insight into why some aneuploidies are compatible with life. Apoptotic remnants (i.e. mRNAs) that reside within the embryo’s blastocoel fluid may vary in relation to the embryo’s ploidy status. This study compared apoptotic gene expression in blastocoel fluid-conditioned media using Real-Time PCR from a euploid embryo resulting in a term birth, embryos harboring aneuploidies compatible with life, and aneuploid embryos incompatible with life.
**P-385** Tuesday, October 15, 2019 6:30 AM

**DEFINING A CLINICAL VALIDITY FRAMEWORK FOR PHARMACOGENOMIC BIOMARKERS OF IVF TREATMENT RESPONSE AND OUTCOMES.**

David-Emlyn Paritt, PhD, Caterina Clementi, PhD, Karen Hunter Cohn, PhD, Lili Mohelsbi, MS, Frank S. Augello, MS, Piraye Yurttas Beim, PhD Celmatix, NEW YORK, NY.

**OBJECTIVE:** To define the landscape of clinically valid genetic associations with IVF treatment response and outcomes.

**DESIGN:** The Clinical Genome (ClinGen) Resource has defined a scoring framework to evaluate the strength of the evidence linking variations in a particular gene to a phenotype. Here, we applied this framework to analyze the genetic and experimental evidence linking genes to reproductive outcomes with IVF treatment response.

**MATERIALS AND METHODS:** We optimized natural language processing algorithms to identify relevant studies published before September 18th, 2018 that examined a statistical and/or functional gene-phenotype relationship. A series of questions was developed to identify reports systematically selecting IVF treatment response and outcomes. The ClinGen framework, including the 24-domain ontologies, was used to systematically score and combine datasets. We further utilized our multi-omics ReprodGeneX software platform to characterize reported genes for their role in reproductive outcomes.

**RESULTS:** Within 9,454 studies identified, we found 55 IVF-related phenotype studies. At least one report of an association with one of 115 genes. 97 of these genes had sufficient published evidence to quantify a CVS. Of the resulting 128 gene-phenotype combinations, 8 had ‘strong’ evidence (CVS: 12-18), 26 ‘moderate’ (CVS: 7-12), 39 ‘limited’ (CVS: 0-7), and 55 ‘none’ (CVS: 0). Our study demonstrated that FSHR and LHCGR were the most extensively studied genes (examined in 34% (n=99/291) of assessed genetic studies), with strong or moderate evidence of association with ‘ovarian response to stimulation’, ‘implantation’, and ‘oocyte to embryo transition’ phenotypes. However, our analysis also highlighted genes with functions other than gonadotropin regulation: TUBB8, PAD6, and TLE5, which regulate oocyte cytoskeletal structure, had strong and moderate relationships with oocyte maturation (CVS=13.5 for TUBB8) and embryo development phenotypes (CVS=11 and 8.5 for PAD6 and TLE5, respectively). Six genes in our analysis (BDNF, HTR2A, HTR2C, ITGB3, SLCA4A, and TPH1) are well characterized for their role in serotonin signaling and had evidence of a clinically valid association with ‘implantation and early development’, ‘implantation failure’, and ‘pregnancy loss after IVF’.

**CONCLUSIONS:** We have established a machine-driven framework for rapidly analyzing and establishing the degree of clinical validity at a given time in a gene association with an IVF-related reproductive phenotype. Hundreds of new reports enter the evidence base annually. A framework and semi-automated workflow like the one designed in this study can help evaluate genetic biomarkers that show the best promise for leveraging pharmacogenomic and genetic insight to optimize IVF treatment protocols and outcomes.

**SUPPORT:** Financial support for this project was provided by Celmatix Inc. and Ferring Pharmaceuticals, Inc.

**P-389** Tuesday, October 15, 2019 6:30 AM

**ZP1 PATHOGENIC VARIANTS CAUSE ‘GENUINE’ EMPTY FOLLICLE SYNDROME: EVIDENCE FOR THE EXISTENCE OF AN INTACT OOCYTE AND A ZON A PELLUCIDA IN FOLLICLES UP TO EARLY ANTRAL STAGE.**

Can Dai, Ph.D.,a Yongzhe Chen, Ph.D.,b Ge Lin, M.D., Ph.D.c Reproductive and Genetic Hospital of CITIC-Xiangya, Changsha, China; cCentral South University, Changsha, China; cReproductive and Genetic hospital of CITIC-Xiangya, Changsha, China.

**OBJECTIVE:** Empty follicle syndrome (EFS) is the complete failure to retrieve oocytes from mature follicles after ovarian stimulation for in vitro fertilization. “Genuine” (GEFS) occurs without any human or pharmaceutical error during the ovarian stimulation process and its existence has been a question in the filed until LHCGR and ZP1 were identified as causative genes. Even so, it is still unclear what happens to these patients’ oocytes, and the pathogenesis of GEFS remains obscure. For most GEFS cases, additional β-hCG or repeated controlled ovarian hyperstimulation (COH) by different protocols does not succeed in oocyte recovery, and use of donor oocytes have been proposed as the only viable alternative choice. We sought to identify novel pathogenic variants (PVs) causing EFS and dissect follicular development in EFS patients.

**DESIGN:** COH, genetic analysis, and ovarian immunohistochemistry (IHC).

**MATERIALS AND METHODS:** Five unrelated infertility women with clinical manifestations of GEFS were included in this study, as approved by the Ethics Committee of our hospital with patient consent. We performed exome sequencing in two unrelated consanguineous families with EFS and female infertility. PV screening of ZP1 was also performed in three unrelated patients. Follicular development and zona pellucida (ZP) assembly were assessed by IHC using ovarian serial sections.

**RESULTS:** Six novel PVs and one known PV in ZP1 were identified. Studies in CHO cells showed that these PVs, except for two splice site variants, resulted in either the degradation or truncation of ZP1 protein. IHC staining demonstrated that all prefollicular follicles had normal architecture, with a thin ZP lacking ZP1 present surrounding growing oocytes. However, this thin ZP was defective in normal cumulus-oocyte complex organization during antral folliculogenesis, leading us to speculate that this might lead to oocyte degeneration or increased fragility of the oocyte during follicular puncture, eventually resulting in what presents as EFS. Our findings are complementarity to previous studies, in which oocytes lacking ZP were retrieved from patients carrying biallelic ZPI truncating mutations that were speculated to prevent the ZP formation. For these cases, we suspect that a thin ZP might actually exist within ovarian follicles, but is degraded before ovulation, or is lost during granulosa cell removal. In addition, we report a new phenotype of human ZP in the absence of ZP1 protein, which is similar to our earlier study showing that human oocytes carrying homozygous ZP1 truncating PVs form a thin ZP without ZP2.

**CONCLUSIONS:** We identified several novel ZP1 PVs causing EFS and female infertility in a recessive genetic mode, and for the first time present morphological evidence showing the normal preantral folliculogenesis with abnormal ZP assembly in EFS patients carrying biallelic ZPI PVs. Our data provides a better understanding of the biological functions of ZP1 in human ZP assembly and folliculogenesis, and gives new insights into the pathogenesis of EFS, potentially being of great inspiration for therapeutic developments.
remodeling pattern in human preimplantation embryos and revealing the epige- netic regulation of inner cell mass (ICM) and trophectoderm (TE) differentiation. DESIGN: Experimental study. MATERIALS AND METHODS: The whole ICM and partial TE were biop- sied from eight preimplantation embryos. DNA obtained from lysed samples was mix- tured using Nextera Tn5 transposase and purified by phenol-chloroform extraction. PCR was conducted using Phusion high-fidelity PCR master mix (NEB) with customized index adapter oligos. AMPure XP magnetic beads (Beck- ham Coulter) were used for Library purification. Sequencing was performed on Illumina NextSeq 550 with paired-end 150 bp reads. Sequencing reads were aligned to human genome reference Hg19 using Bowtie2. All PCR duplicates, mitochondrial, unmapped and non-uniquely mapped reads were removed. Peaking calling was conducted using MACS2 and visualizations of the peaks in a genomic context were generated. ChiPseeker was used for peak annotation and differential ATAC-seq analysis was conducted by DiffBind. The ATAC peak distribution differences were analyzed using both Fisher’s exact test and Chi-squared test. RESULTS: The assay for ATAC-seq was optimized and validated to obtain high-quality data using small sample input (10-30 cells). The ATAC-seq result of each sample for both ICM and TE groups showed a highly reprodu- cible pattern. A large fraction of the ATAC-seq peaks were located in the pro- moter and distal intergenic regions in both ICM and TE, which is consistent with the previously published data from animal models. Transcription factor binding sites (TFBS) are often accessible in the active genes and not uniformly distributed over the promoter region. Our data showed that ATAC peak distributions of the promoter regions (<1kb) and distal regions versus other regions were significantly different between ICM vs TE samples (P<0.01). We detected that higher percentage of accessible binding loci were located within 1kb of the transcription start site in ICM compared to TE (P<0.01). However, higher percentage of accessible regions were de- tected in the distal region of TE compared to ICM. In addition, 8 differential peaks with the FDR <0.05 between ICM and TE were detected and these 8 accessible locations were identified in ICM samples. CONCLUSIONS: This is the first study to characterize the landscape of the accessible chromatin between ICM and TE of human preimplantation em- bryos, which unveiled chromatin-level epigenetic regulation of cell lineage specification in early embryo development.

P-391 Tuesday, October 15, 2019 6:30 AM

AN OVARIAN COMPONENT INVOLVED IN SUBFER- TILITY OF THE NSMF KO MOUSE. Erica Louden, M.D. Ph.D. Lynn Chorich, B.S., M.S., Lawrence Layman, M.D. Augusta University, Augusta, GA.

OBJECTIVE: Genetic approaches in humans with gonadotropin releasing hormone (GnRH) deficiency causing normosmic hypogonadotropic hypogo- nadism (NHH)/Kallmann syndrome (KS) have been important to understand normal reproduction. NSMF (NDMA receptor synaptotagmin signaling & neuronal migration factor), formerly known as NELL (nasal em- bryonic LHRR factor), gene mutations have been identified in humans with either NHH/KS. However, the phenotype of the Nsfl knockout (KO) mouse is less severe than the human. The Nsfl KO females have reduced numbers of GnRH neurons and delay in vaginal opening, but normal puberty and sub- fertility. We previously showed Kiss1 mRNA expression was increased in the hypothalami of KO animals and that pituitary gonadotropin responses were not different in wild type (WT) vs Nsfl KO mouse. Our objective in this study was to identify cell types that express Nsfl in the ovary and determine if the subfertility in the female Nsfl KO mouse has a gonadal component. DESIGN: Nsfl protein cellular localization was determined in the WT mouse ovary. Kissl and Kisslr mRNA expression was characterized in the KO mouse. 8-week-old ovaries and ovarian responses to gonadotropins were studied in 3 week old Nsfl KO mice in the diestrus phase.

MATERIALS AND METHODS: Heterozygous Nsfl mice were bred to homozygosity. Ovaries from KO vs WT mice were sectioned and prepared for immunohistochemistry (IHC) using a monoclonal anti-Nsfl antibody. RNA extracted from ovaries of KO and WT animals were subjected to RT-qPCR for Kiss1 and Kisslr expression. The ΔΔCt cycle of threshold, method was used to calculate relative gene expression of Nsfl KO vs control using Gapdh expression for normalization. To determine the ovarian response to go- nadotropins, WT and KO mice 3 weeks of age were superovulated using PMSG and hCG. Mice were sacrificed and oocytes were removed from the ovi- ducts and counted. Differences were analyzed using the Mann-Whitney U test. 8-week old mice also had serum gonadotropins before and after ovariec- tomy.

RESULTS: Our preliminary findings demonstrate Nsfl mRNA expression in the ovary, and IHC studies and serum gonadotropins after ovariec- tomy are ongoing. Kisslr expression is unchanged in Nsfl hypothalami and ovary, but Kissl was upregulated in the hypothalami and the ovary. Preliminary data suggests that oocyte numbers were modestly decreased in the KO (~16/ovary) vs WT (30/ovary), but maturity has not been assessed yet.

CONCLUSIONS: A hypothalamic component appears to be involved in the subfertility of the Nsfl KO mouse, as demonstrated by a decreased num- ber of GnRH neurons as well as our finding of increased Kissl expression in the hypothalami of Nsfl KO mice, which we hypothesize is a compensatory increase secondary to deficient NSMF. Therefore we sought to characterize Kissl and Kisslr expression in the ovary. Kisslr expression was unchanged, but there was a significant increase in Kissl, which is known to be expressed in granulosa cells in mice. We also demonstrated Nsfl expression in the WT ovary. The reduced number of oocytes in the Nsfl KO mouse supports an ovarian role for NSMF in the subfertility of the Nsfl KO mouse.

P-392 Tuesday, October 15, 2019 6:30 AM

PRO-APOPTOTIC GENE EXPRESSION IN BLASTO-COEFL FLUID FROM EUPLOID DAY-5 EMBRYOS IS ASSOCIATED WITH NEGATIVE PREGNANCY OUTCOMES. Deepthi M. Athavale, B.S., Alyssa Barré, B.S., Allison C. Kranicky, B.S., Arnav Lal, na, Jonathan L. Blalock, B.S., Shawn Zimmerman, PhD, HCLD, Eld., Randall D. Robinson, MD., D. J. David Winingier, PhD, HCLD, William E. Roudebush, PhD, Renée J. Chosed, PhD. University of South Carolina School of Medicine Greenville, Greenville, SC; Vios Fertility Institute, Swansea, IL; University of Texas Health Science Center, San An- tonio, TX; UF Health San Antonio, San Antonio, TX; Atlantic Reproductive Medicine Specialists, Raleigh, PA.

OBJECTIVE: The identification of molecular markers for use during selection of embryos for intratubal implantation can enhance in vitro fertilization-embryo transfer success rates. Assessing apoptotic gene expression in blastocoeol fluid-conditioned media from human embryos with known ploidy and implantation status provides the opportunity to study patterns and processes occurring during early embryo development. Apoptosis occurs during preimplantation development and may serve to selectively eliminate aneuploid cells from the developing embryo thereby enhancing implantation potential. Therefore, apoptotic remnants (i.e. mRNAs) may reside within the embryo’s blastocoeol fluid and vary in relation to the embryo’s implantation potential. This study compared apoptotic gene expression in blastocoeol fluid-conditioned media using Real-Time PCR from euploid embryos with known implantation outcomes.

DESIGN: Retrospective analysis of day-5 euploid blastocoeol fluid apoptotic gene expression and implantation outcome.

MATERIALS AND METHODS: Blastocoeol fluid-conditioned media (25µL) was collected following trophectoderm (TE) biopsy of ICSI-generated day-5 blastocysts. Biopsied TE cells were sent for preimplantation gen- etic testing for aneuploidies using NGS. The blastocoeol fluid-conditioned media from 10 euploid embryos (6 that implanted; 4 that did not implant) were each subjected to TE biopsy prior to CDNA synthesis before as- sessing gene expression via RT-PCR using TaqMan Fast Array-Human Apoptosis plates (assessing 92 apoptosis associated genes).

RESULTS: Of the 92 genes analyzed, CASP7 and MCL1 gene expression were only detected in euploid embryos that successfully implanted. Conversely, expression of TNFRSF25 and BCL2L11 genes were only detected in euploid embryos that failed to implant. Several other apoptotic genes (BAD, BCL2L13, BCAF3, NOD1 and CARD18) were expressed more often in em- bryos that failed to implant versus those that successfully implanted.

CONCLUSIONS: This study poses that specific apoptotic remnants (mRNAs encoding apoptotic genes) may represent a molecular indicator of euploid em- bryo future implantation potential. Specifically, we detected the expression of pro-apoptotic gene expression in euploid blastocoeol fluid apoptotic gene expression and implantation outcome.

P-393 Tuesday, October 15, 2019 6:30 AM

FRAGILE X CARRIER SCREENING ACCOMPANIED BY GENETIC CONSULTATION HAS CLINICAL UTIL- ITY IN POPULATIONS BEYOND THOSE RECOMMEN- DED BY GUIDELINES. Katie Johansen Taber, PhD, Jeraldine Lim-Harashima, MS, CCg, Harris Naemi, BS, Jim Goldberg.
MD; *Myriad Women’s Health, South San Francisco, CA; †Myriad Genetics, Salt Lake City, CA; ‡Myriad Genetics, Salt Lake City, UT.

OBJECTIVE: To determine the clinical utility of FXS carrier screening by analyzing actions among FMR1 premutation carriers who do and do not meet American College of Medical Genetics and Genomics (ACMG) or American College of Obstetricians and Gynecologists (ACOG) criteria for testing.

RESULTS: A total of 122 FMR1 premutation carriers responded to the survey. Providers recommended screening for 77% of patients, while 23% of patients had requested screening themselves. 79% of screening occurred in females that did not meet the ACMG/ACOG family history criteria, and 52% occurred in those who did not meet the ACMG/ACOG fertility evaluation criteria. 99% of those screened had received post-test genetic consultation.

CONCLUSIONS: Providers recommended, and patients desired, FXS carrier screening regardless of whether the patient met current ACMG/ACOG screening criteria. Patients who did not meet screening criteria took action to reduce the risk of having an affected pregnancy to nearly the same extent as those who did meet criteria. Nearly all patients made reproductive and pregnancy management decisions informed by genetic consultation. These results support offering FXS carrier screening to all women who are pregnant or considering pregnancy.

SUPPORT: This analysis was fully funded by Myriad Women’s Health.

THE EXPRESSION OF HUMAN ENDOGENOUS RETROVIRUS SYNCYTIN IN HUMAN ANEUPLOIDY IS INSUFFICIENT COMPARED TO EUPLOIDY.

Danxia Luo, MD,* Fang Wang, PhD,† Isaac J. Chamani, B.A.,‡ David H. McCulloh, Ph.D.,# Caroline McCaffrey, Ph.D.,§ David L. Keefe, M.D.¶ *New York University School of Medicine, Department of Obstetrics and Gynecology, New York, NY; †New York University School of Medicine, New York, NY; ‡NYU Langone Health, New York, NY; §New York Langone Health, NYU Fertility Center, New York, NY.

OBJECTIVE: Retrotransposons are a group of abundant, repetitive sequences, which originated from ancient retroviral infections of our ancestral genomes. They are silenced by epigenetic marks throughout most of life, but become activated during early embryo development, with reprogramming of the epigenome. Some retrotransposons play regulatory roles during early development. Non-Long Terminal Repeat (LTR) retrotransposons (e.g. L1-1) regulate gene expression during early mammalian development. LTR retrotransposons, such as the human endogenous retrovirus HERV-W and HERV-FRD (Syncytin-1 and Syncytin-2), mediate placentation. We hypothesized that aneuploidy, which disrupts implantation, would affect expression of retrotransposons during early human development.

DESIGN: Prospective laboratory study.

MATERIALS AND METHODS: Blastocysts donated by patients who underwent IVF/PGT-A at a NYU Langone FC were thawed, stripped of zona pel lucidae by laser (to remove sperm or cumulus) and their genomic DNA and mRNA separated by the GtKseq protocol with modifications. mRNA expression and gene copy number were measured by RT-qPCR and qPCR using Bio-Rad CFX36 thermocycler and qSYBR Green mix, and the J4c and MEG-3 genes were used to express levels relative to GAPDH and SS RNA, respectively. Data were analyzed by Mann Whitney U test and Student’s T-test with GraphPad Prism 8 software.

RESULTS: Syncytin-1 was expressed in all human embryos, but its expression in euploid embryos (n=2) was significantly higher than in aneuploid embryos (n=6) (median 1.943 vs. 0.316, P=0.0019). Expression of Syncytin-2 was also extremely higher in euploid compared to aneuploid embryos (median 2.155 vs. 0.1124, P=0.0003). The copy number of ALU sequences in aneuploid embryos was greater than in euploid embryos (mean 0.943±0.067 vs 0.807±0.0716, T-test P=0.0486), but LINE1 copy number or expression did not differ between euploid and aneuploid embryos (mean 0.787±0.069 vs. 0.940±0.094, T-test P=0.1778).

CONCLUSIONS: We compared expression of a number of retrotransposons between euploid and aneuploid human blastocysts, and discovered that the human endogenous retrovirus, Syncytin-1 and Syncytin-2, are markedly decreased in aneuploid compared to euploid embryos. Given the crucial role of Syncytins in formation of human placenta, our data provide a possible mechanism of implantation failure in euploid embryos, and suggest a possible biomarker for implantation.

SPERM PHYSIOLOGY

P-396 Tuesday, October 15, 2019 9:30 AM

THE EXTRACELLULAR CUMULUS MATRIX DOES THE SPERM ZONA-ADHESION IN NORMOZOOSPERMIC PATIENTS. Rumiana Ganeva, MSc, Dimitar Parvanov, PhD, Kristina Nikolova, MSc; Magdalena Vlasileva, MSc, Ferihan Shaban, MSc, Georgi Stamoven Stamenov, MD/PhD. Nadezhdha Women’s Health Hospital, Sofia, Bulgaria.

OBJECTIVE: The aim of this study was to observe the effect of the cumulus extracellular matrix on the sperm zona-adhesion rate in healthy fertile men.

DESIGN: Comparison of the zona-adhesion rate between spermatozoa treated with cumulus extracellular matrix and non-treated spermatozoa.

MATERIALS AND METHODS: The cumulus matrix proteins used in this study were isolated from 150 cumulus complexes that were obtained from 16 donors during oocyte retrieval procedures. The cumulus cells and their extracellular matrix were separated by pipetting followed by centrifugation. The protein content in the pool of isolated cumulus matrixes (CM) was measured by Bradford method. Semen samples were obtained from 30 normozoospermic donors. After sperm washing, the motile spermatozoa were isolated by swim-up and diluted to 0.5x10^6 cells/ml. Each sample was divided into four aliquots and incubated with (1) 0.5 mg/ml CM, (2) 1.25 mg/ml CM, (3) 2.5 mg/ml CM and (4) wash medium for 30 min at 37°C. The zona-adhesion rate was evaluated by counting the adhering spermatozoa to immobilized acid-solubilized zone pellucidae from healthy donors. Results are presented as number of adhered spermatozoa per 1 mm² of the immobilized surface (sp/mm²). Statistical analysis was performed with paired t-test using IBM SPSS Software ver. 21.

RESULTS: The zona-adhesion rate of the untreated spermatozoa was 81 ± 17 sp/mm² (Mean ± SD) and ranged between 54 sp/mm² and 116 sp/mm². CM treatment of the spermatozoa dose-dependently and significantly increased the zona-adhesion rate in every patient (p < 0.05). When spermatozoa were treated with 2.5 mg/ml CM, 1.25 mg/ml CM and 0.625 mg/ml the mean sperm zona-adhesion was 128 ± 28 sp/mm², 107 ± 37 sp/mm² and 99 ± 27 sp/mm², respectively.

CONCLUSIONS: The results from this study show the important role of the cumulus matrix in the preparation of the spermatozoa before meeting the oocyte and confirm that the cumulus effect should be considered during sperm processing for ICSI.

P-397 Tuesday, October 15, 2019 9:30 AM

VARICOCELE DIMINISHES SPERM CAPACITATION FUNCTION AND THE CHANCES OF GENERATING A PREGNANCY. Philip Xie, B.S.,* Alessandra Parrella, M.Sc.,* Alexander J. Travis, VMD, PhD, Zev Rosenwaks, M.D.,* James A. Kashanian, MD, Gianpietro D. Palermo, M.D., Ph.D. aThe Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; bCornell University, Ithaca, NY; cWeill Cornell Medicine, Department of Urology, New York, NY.

OBJECTIVE: To determine whether varicocele can adversely affect sperm capacitation and therefore the probability of generating a pregnancy (PGP).

DESIGN: In 8 consenting men with grade 2 varicoceles or larger, we assessed functional semen characteristics by using Cap-Score™ to measure the percentage of sperm that can capacitate, and calculated the related PGP. Test-samples were compared to controls using paired t-tests.

RESULTS: In all experiments, Cap-Score was greater for control-CAP compared to test-CAP (p < 0.05). In the case of capacitation (CAP) and capacitation (CAP) conditions for 3 hrs, and then fixed overnight before Cap-Score determination. Test-samples were compared to controls using paired t-tests.

CONCLUSIONS: A good capacitation response was observed in the controls for all experiments, suggesting proper stimulus by the CAP condition. The ratios of semen:TCB were counted to mimic typical ejaculate volumes, such that a constant volume of extender could potentially be utilized in an at home semen collection kit that maintains sperm capacitation ability. Addition of a fixed volume of TCB to varying ejaculate volumes would limit user input. Similar Cap-Score values between the control-CAP and test-CAP, no matter the ratio, indicates that ejaculates can be maintained overnight in varying concentrations of TCB with minimal impact on next-day function. At home sample collection could lessen the burden of processing samples at clinics with limited resources. It could also encourage pursuit of workup by men whose main barrier is privacy in producing samples at clinics or bringing them to clinics. It could also broaden the geographical availability of sperm function tests to those living far from clinics, and reduce financial burdens associated with travel and time away from work.

SUPPORT: Androvia LifeSciences.

IMPACTS OF TEST (TES AND TRIS) YOLK BUFFER AND COOLING ON THE ABILITY OF HUMAN SPERM TO CAPACITATE. G. Charles Ostermeier, PhD, Cristina Cardona, PhD, Melissa A. Moody, MS, Alana J. Simpson, BS, Romeo Mendoza, MT, Alexander J. Travis, VMD, PhD aAndrovia LifeSciences, Mountainside, NJ; bCornell University, Ithaca, NY.

OBJECTIVE: Studies across several mammalian species show that Gα11 localization patterns are indicative of capacitation at the single cell level. The Cap-Score™ Male Fertility Assay reports the proportion of sperm displaying GM1 localization consistent with capacitation. Using clinical pregnancy outcomes, Cap-Score was previously shown to prospectively predict a man’s fertility and the relationship between Cap-Score and a man’s probability of generating a pregnancy was established. TES (TES and Tris) yolk buffer (TYB) can prolong the fertilization capacity of sperm. Here, we evaluated whether incubation in TYB overnight at a cool temperature affected human sperm capacitation.

DESIGN: To evaluate the impact of semen extension with TYB and cooling on sperm capacitation, ejaculates were split into control and test samples for a repeated measure design.

MATERIALS AND METHODS: Studies approved by IRB (20152233). Semen was collected, liquefied and split into control and test samples. Control samples were processed normally for Cap-Score. Test samples were extended in TYB at 1:1 (n = 5); 1:6 (n = 5) or 8:5; 1:6 ratio: 32.0 ± 0.04 vs 34.0 ± 0.03; p = 0.33; 8:5 ratio: 36.0 ± 0.02 vs 34.2 ± 0.01; p = 0.5). No differences were observed between the control-CAP and the test-CAP for any dilution (1:1 ratio: 39.7 ± 0.04 vs 40.1 ± 0.03; p = 0.16; 1:6 ratio: 32.0 ± 0.04 vs 34.0 ± 0.03; p = 0.03; 8:5 ratio: 36.0 ± 0.02 vs 34.2 ± 0.01; p = 0.5). CONCLUSIONS: A high capacitation response was observed in the controls for all experiments, suggesting proper stimulus by the CAP condition. The ratios of semen:TCB were counted to mimic typical ejaculate volumes, such that a constant volume of extender could potentially be utilized in an at home semen collection kit that maintains sperm capacitation ability. Addition of a fixed volume of TCB to varying ejaculate volumes would limit user input. Similar Cap-Score values between the control-CAP and test-CAP, no matter the ratio, indicates that ejaculates can be maintained overnight in varying concentrations of TCB with minimal impact on next-day function. At home sample collection could lessen the burden of processing samples at clinics with limited resources. It could also encourage pursuit of workup by men whose main barrier is privacy in producing samples at clinics or bringing them to clinics. It could also broaden the geographical availability of sperm function tests to those living far from clinics, and reduce financial burdens associated with travel and time away from work.

SUPPORT: Androvia LifeSciences.

RELATIONSHIP AMONG INTRACELLULAR SUPEROXIDE DISMUTASE ACTIVITY, GLUTATHIONE PEROXIDASE ACTIVITY, MOTILITY AND MORPHOLOGY IN HUMAN SEMEN. Luchezar Vasilev Itelezarska, PhD; Dimitar Parvanov, PhD, Vilyana Georgieva, MSc, Rumiana Ganeva, MSc, Philip Xie, B.S.,* Alessandra Parrella, M.Sc.,* Alexander J. Travis, VMD, PhD.
Georgi Stamenov Stamenov, MD/PhD. Nadezhda Women’s Health Hospital, Sofia, Bulgaria.

OBJECTIVE: Oxidative damage by reactive oxygen species (ROS) is one of the main causes for sperm dysfunction. Important components of the antioxidative defense systems are the superoxide dismutase (SOD) and glutathione dismutase (GPx). Therefore, our objective was to examine the relationship among sperm SOD activity, sperm GPx activity, sperm motility and morphology in human spermatozoa.

DESIGN: Prospective study.

MATERIALS AND METHODS: Sixty four patients aged between 26 and 39 years were selected. Samples were collected by masturbation after sexual abstinence for 3-5 days. After seminal liquefaction, semen analysis was performed (concentration, progressive motility and non-strict morphology) according to WHO 2010 guidelines. Sperm SOD and GPx activities were determined using Ransod and Ransel diagnostic kits (Randox Laboratories Ltd., Antrim, UK). An aliquot of the corresponding sperm suspension (20x10^6 sperm/mL) was centrifuged at 600 x g for 5 minutes and the supernatant was discarded. The remaining pellet was treated with 0.5 mL of 0.1% Triton X-100 in PBS and vortex-mixed three times for 20 seconds followed by centrifugation at 1,000xg for 5 minutes. Aliquots of the supernatant were added to the wells of the microplate and the assay was performed according to the manufacturer’s instructions. The supernatant was discarded and the pellet was treated with 0.5 mL of 0.1% Triton X-100 in PBS, vortex-mixed three times for 20 seconds, and centrifuged at 1,000xg for 5 minutes. Aliquots of the supernatant were added to the wells of the microplate and the assay was performed according to the manufacturer’s instructions. Statistical analysis was performed by Spearman’s correlation test using SPSS v.21 (IBM Corp., Armonk, NY, USA). Descriptive parameters and patient characteristics were reported as mean ± SD and median. P<0.05 was considered statistically significant.

RESULTS: The determined SOD activity ranged between 0 and 1415 U/10^9 spermatozoa with a mean of 131.82 ± 242.11 U/10^9 spermatozoa and a median of 56.64 U/10^9 spermatozoa. The observed GPx activity ranged from 0.2 to 111.57 U/10^9 spermatozoa with a mean of 5.12 ± 14.57 U/10^9 spermatozoa and a median of 1.67 U/10^9 spermatozoa. There was a significant but low positive correlation between sperm SOD and GPx activities (R=0.27; p=0.04). Sperm SOD activity did not correlate significantly with sperm motility and morphology. In contrast, sperm GPx activity showed a significant negative correlation with the progressive motility (R=-0.48; p<0.01) and negative correlation with the sperm morphology (R=-0.49; p<0.01).

CONCLUSIONS: Intracellular sperm GPx activity seem to be linked more strongly to the sperm motility and morphology parameters rather than the sperm SOD activity. Among the studied group the lower sperm motility and poor sperm morphology were associated with relatively high GPx activity.

P-401 Tuesday, October 15, 2019 6:30 AM

VARIATION IN THE PERCENTAGES OF Y-CHROMOSOME BEARING SPERM IN EJACULATES. Seth Levrant, MD, a, b; Jared Graham, BS, c; Morry B. Fiddler, Ph.D, c; Saranya Tharmakulasingam, MD, d; Rajasign Jeyendran, Ph.D, HCLD. Partners in Reproductive Health, Tinley Park, IL; Insight Medical Genetics, Chicago, IL; Androlab Inc, Chicago, IL.

OBJECTIVE: To assess the variation in the percentages of Y-chromosome bearing sperm in ejaculates for the purpose of determining an underlying etiology for sperm-based sex selection (inconsistent) outcomes.

DESIGN: Ejaculates from 50 randomly selected men testing for routine semen analysis (RSA) were analyzed for percentage of Y-chromosome bearing sperm using the Cell Lysis Buffer provided in the kit to a final concentration of 56.64 U/10^9 spermatozoa. The observed GPx activity ranged from 0.2 to 111.57 U/10^9 spermatozoa with a mean of 5.12 ± 14.57 U/10^9 spermatozoa and a median of 1.67 U/10^9 spermatozoa. There was a significant but low positive correlation between sperm SOD and GPx activities (R=0.27; p=0.04). Sperm SOD activity did not correlate significantly with sperm motility and morphology. In contrast, sperm GPx activity showed a significant negative correlation with the progressive motility (R=-0.48; p<0.01) and negative correlation with the sperm morphology (R=-0.49; p<0.01).

CONCLUSIONS: Intracellular sperm GPx activity seems to be linked more strongly to the sperm motility and morphology parameters rather than the sperm SOD activity. Among the studied group the lower sperm motility and poor sperm morphology were associated with relatively high GPx activity.

P-401 Tuesday, October 15, 2019 6:30 AM

DURAMYCIN DISRUPTS SPERM MOTILITY AND IN VITRO FERTILIZATION (IVF). Devang Sharma, MD, Claudia M. Rival, PhD, Sarah C. Krzastek, MD, Jeffrey J. Lysiak, PhD, Ryan P. Smith, MD, NICHD’s Reproductive Medicine Network, University of Virginia, Charlottesville, VA.

OBJECTIVE: The aim of our study was to investigate effects of phosphatidyethanolamine (PtdE) on mouse epididymal sperm and to evaluate the effect of Duramycin, a broad-spectrum antibiotic commonly used in animal husbandry and a compound used to detect PtdE in cell membranes, on sperm progressive motility and fertilization capacity in IVF.

DESIGN: Capacitated caudal epididymal sperm were isolated from mice and either left untreated or incubated with Duramycin. Sperm progressive motility and sperm cell death were assessed. Additionally, sperm were used for IVF and the percentage of resultant two-cell embryos was analyzed.

MATERIALS AND METHODS: Caudal epididymal sperm were isolated from >10 week-old C57BL/6 mice. To detect PtdE, capacitated sperm were incubated with biotinylated Duramycin for 30 minutes, followed by streptavidin conjugated with Texas Red, mounted, and analyzed via fluorescent microscopy. Sperm progressive motility was assessed after a 30 minute incubation with 0.1 – 2 μM Duramycin or control DMSO. The effect of Duramycin on sperm death was evaluated with 7AAD (necrosis) and staining of cleaved caspase-3 (CC3; apoptosis) by immunofluorescent microscopy. During IVF, sperm (untreated or incubated with 2 μM Duramycin) were used to inseminate oocytes isolated from super-ovulated C57BL/6 female mice. After 24 hours, the percentage of resultant 2-cell embryos was analyzed.

RESULTS: PtdE exposure was detected exclusively on the midpiece of mouse sperm. The fertilization rate of oocytes inseminated with untreated sperm was ~75%, while it was completely abolished (0%) when sperm were pre-incubated with 2 μM Duramycin. Sperm progressive motility was completely disrupted by 0.25 – 2 μM Duramycin and dramatically reduced with 0.1 μM Duramycin (% of motile sperm – Control: ~56%; Duramycin 4.2%). Sperm death increased after incubation with Duramycin (% of CC3+ cells – Control: 2.3 ± 2.3, Duramycin: 13.8 ± 4.4), while CC3+ cells were not detected.

CONCLUSIONS: Duramycin significantly impaired sperm motility even at very low concentrations. This may explain the incapacity of the Duramycin treated sperm to fertilize oocytes. Duramycin did induce cell necrosis on a fraction of sperm; however, this cannot explain the complete disruption of sperm motility. Since Duramycin binds the sperm midpiece where PtdE is present, this is possible that Duramycin disturbs mitochondrial activity depleting sperm energy and leaving the sperm immotile but alive. Environmental toxins have been implicated as a powerful contributor to the published widespread decline in semen parameters. The frequent use of Duramycin in agriculture portends frequent human exposure with unknown health and fertility consequences. Future studies are needed to examine the presence of Duramycin in our food chain.
P-402 Tuesday, October 15, 2019 6:30 AM

THE Efficacy OF OXIDATION REDUCTION POTENTIAL (ORp) IN MALE INFERTILITY AND ITS RELATIONSHIP WITH SEMINAL LEUKOCYTE CONCENTRATION. Shinnosuke Kuroda, M.D., Tepppei Takeshima, M.D., Yasushi Yamura, Ph.D, Yokohama City University, Medical Center, Yokohama, Japan.

OBJECTIVE: Reactive oxygen species (ROS) in semen has been reported to have negative effect to male fertile capacity, and recent studies reported the efficacy of oxidation-reduction potential (ORP) which reflects the balance of oxidants and antioxidant in semen. The source of ROS in semen is considered as immature spermatozoa and seminal leukocytes, but the detail is still unknown. The aim of this study is to evaluate the relationship between the concentration of seminal leukocytes and oxidative stress level using ROS, ORP.

DESIGN: Retrospective study.

MATERIALS AND METHODS: Between April 2018 and March 2019, 29 infertile males who visited Reproduction Centre of Yokohama City Medical Center were enrolled. All patients underwent semen analysis and measurement of ROS and ORP levels. The ROS level in semen was measured using Monolight 3010TM Luminometer and the ORP level was measured using MicroXSYS SystemTM. The concentration of peroxidase-positive leukocytes were evaluated using myeloperoxidase staining (Endtz test). The relationship between ROS levels, ORP levels, the concentration of leukocytes and semen parameters were evaluated using correlation analysis. The relationship between ROS levels, ORP levels, the concentration of leukocytes and semen parameters were evaluated using correlation analysis.

RESULTS: The sperm concentration and motility were 39.6±36.6 x 10^6/ml, 30.0±18.9 %, respectively. The total ROS level was 9328.9±18851 (Relative Light Units, and the ORP level was 46.1±38.7 mV. The ROS level was significantly correlated with ORP level (r=0.79, p<0.01). The concentration of leukocytes measured by Endtz test was positively correlated with both ORP level (r=0.46, p=0.023) and ROS level (r=0.82, p<0.01). ORP level was negatively correlated with sperm concentration (r= -0.41, p=0.026), while ROS level didn’t show significant correlation with every semen parameters.

CONCLUSIONS: To our knowledge, this is the first study that showed the significant correlation between ORP levels and seminal leukocytes concentration. Our study suggested that peroxidase-positive leukocyte is one of the main source of ROS in semen. Although ROS was strongly correlated with ORP level (r=0.79), p<0.01), the detail is still unknown.

P-801 WITHDRAWN

BASIC REPRODUCTIVE RESEARCH

P-802 Tuesday, October 15, 2019 9:30 AM

ANDROGENS NEGATIVELY AFFECT CILIARY FUNCTION AND ALTER GENE EXPRESSION IN THE HUMAN FALLOPIAN TUBE. Tia Jackson-Bey, MD MPH,a Angela Russo, Ph.D.,a Alexandra N. Young, B.S.,B,a Joanna E. Burdette, Ph.D. University of Illinois at Chicago, College of Medicine, Chicago, IL; University of Illinois at Chicago, College of Pharmacy, Chicago, IL.

OBJECTIVE: To evaluate the impact of androgen exposure on human fallopian tube epithelium in relation to ciliary function and gene expression.

DESIGN: Translational research

MATERIALS AND METHODS: We exposed human fallopian tube epithelium to either a hormonally physiologic (low testosterone) or hyperandrogenic (high testosterone) culture media for 7-14 days. The hyperandrogenic media was characterized by twice the concentration of testosterone (2nM) than in the physiologic media (0.8 nM). After 7 days, cilia were imaged with spinning confocal microscopy to capture ciliary beating. The cilia beating frequency was then quantified using Fiji Image J software. After 14 days, gene and protein expression was assessed via immunohistochemistry staining, qualitative PCR, RNA sequencing and ELIZA. Parallel experiments were conducted in static conditions, with the tissue on porous wools partially submerged in culture media that was exchanged every 2-3 days, as well as in microfluidic “organ on a chip” devices, in which fresh media is dynamically circulated through, and waste removed from, wells containing the human fallopian tube epithelium in culture media.

RESULTS: After 7 days, a difference was seen in the rate of ciliary beating frequency as detected by spinning disk confocal microscopy. Human fallopian tube epithelium exposed to high testosterone had a decreased rate of cilia beating compared to human fallopian tube epithelium exposed to the low testosterone media. Further, at differing testosterone concentrations, the ciliary beating frequency exhibited a dose-response decrease as concentration of testosterone increased. Changes in genes that regulate cilia structure and function were found after 14 days. RNA sequencing showed that amongst other genes, FOXJ1, SAA2, and DNAH5 were down-regulated while MAP2 and NTN4 were up-regulated respectively in the high testosterone group. These genes play major roles in ciliary motility and structure. Genes involved in hormonal signaling, including ZBTB16, were also found to be elevated in the human fallopian tube epithelium exposed to high testosterone on RNA sequencing. Immunohistochemistry staining showed that the androgen receptor was up-regulated and became localized to the nucleus in the high testosterone group, while estrogen receptor expression was reduced. qPCR also showed androgen and estrogen receptors to be up and down regulated in the high testosterone environment, respectively. In addition, qPCR showed down-regulation of OVGP1, an estrogen regulated epithelial glycoprotein important for reproductive function, and up-regulation of ZBTB16, an androgen target gene involved in cell cycle regulation. ELIZA showed decreased VEGF in the high testosterone conditions.

CONCLUSIONS: These novel findings demonstrate that elevated androgen exposure alters cilia expression and function in the human fallopian tube. These ex-vivo experiments may add to our understanding of the mechanisms of subfertility and reproductive health risks in women with living with hyperandrogenic disorders, such as PCOS, obesity and androgen producing tumors.

SUPPORT: The study PI is part of a NIAMS UG3 ES029073

P-803 Tuesday, October 15, 2019 6:30 AM

MIR-297 REPRESSES THE EXPRESSION OF PROGESTERONE RECEPTOR AND DECIDUALIZATION IN EU-TOPIC ENDOMETRIUM IN INFERTILE WOMEN WITH ENDOMETRIOSIS. Wei Huang, Ph.D. M.D., Tingting Liu, M.D. West China Second University Hospital of Sichuan University, Chengdu, China.

OBJECTIVE: Progestosterone resistance is one of the epigenetics affecting the decreased endometrial receptivity and implantation failure in endometriosis-associated infertility. Altered miRNAs expression plays an important role in the pathophysiology of endometriosis. Our previous study demonstrated that miR-297 was overexpressed in the mid-secretory eutopic endometrium in the endometriosis group compared with control. We performed our study to explore the regulation of miR-297 on the aberrant progesterone receptor expression and impaired decidualization in the endometrial stromal cells from eutopic endometrium of women with minimal or mild endometriosis.

DESIGN: Human tissue study.

MATERIALS AND METHODS: We performed our study to explore the regulation of miR-297 on the aberrant progesterone receptor expression and impaired decidualization in the endometrial stromal cells from eutopic endometrium of women with minimal or mild endometriosis. Eutopic endometrial tissues from infertile endometriosis patients (n = 20) and normal patients (n = 19) were collected in vitro analysis. Endometrial stromal cells were isolated and transfected with miR-297 mimic or miR-297 inhibitor or the respective controls. Gene expression regulation was examined by real-time-quantitative PCR, Western blot and luciferase reporter assay. Artificial decidualization assay was performed to investigate the role of miR-297 during decidualization in vitro.

RESULTS: Eutopic endometrial tissues from infertile endometriosis patients (n = 20) and normal patients (n = 19) were collected in vitro analysis. Endometrial stromal cells were isolated and transfected with miR-297 mimic or miR-297 inhibitor or the respective controls. Gene expression regulation was examined by real-time-quantitative PCR, Western blot and luciferase reporter assay. Artificial decidualization assay was performed to investigate the role of miR-297 during decidualization in vitro. The expression of progesterone receptor especially progesterone receptor B were decreased after transfected with miR-297 mimic and increased miR-297 inhibited or the respective controls. MiR-297 inhibited the decidualization of endometrial stromal cells in vitro.

CONCLUSIONS: Our study demonstrated the regulation of miR-297 on the blunted PR expression is direct.

SUPPORT: National Natural Science Foundation of China (No.81370693)
P-804 Tuesday, October 15, 2019 6:30 AM

INHIBITION OF BOTH DNA METHYLTRANSFERASES AND HEDGEHOG SIGNALING SUPPRESSES THE PHENOTYPE OF HUMAN UTERINE LEIOMYOSARCOMA CELLS. Natalia Garcia, MSc,1 Ayman Al-Hendy, MD PhD,2 Leonardo Tomiatti da Costa, MSc,3 Kátia Candido Carvalho, PhD,3 Qiwei Yang, PhD4 "University of Illinois at Chicago, Chicago, IL; 4University of Sao Paulo, Sao Paulo, Brazil.

OBJECTIVE: Uterine leiomyosarcoma (LMS) is the most common of uterine sarcoma, it is a rare and aggressive tumor with poor prognosis. Our group described previously that the hedgehog (HH) signaling was activated in LMS, which contributed to its aggressive phenotype. However, the mechanism by which HH activation in LMS is largely unknown. The objective of this work was to characterize the genetic and epigenetic mechanism in HH signaling and evaluate the anti-HH effect of DNA methyltransferase inhibitor (DNMTi) alone or in combination with GLI inhibitor (GLIi) on LMS.

METHODS AND MATERIALS: LMS cells were used to evaluate the mRNA and protein expression of DNMTi. 3a, 3b, PTCCH1, SMO and SDFU mutations were evaluated in 7 LMS patients from 3 different Brazilian institutions (CEP 477/15) using next generation sequencing Ion AmpliSeq (Thermo Fisher Scientific). The percentage of PTCCH1 methylation was determined by EpiTect Methyl II PCR array (Qiagen) in LMS cells. Proliferation, migration, invasion and apoptosis assays were performed to evaluate the inhibitory effect of DNMTi (2 μM of 5-aza-2’-deoxycytidinide) alone or in combination with GLIi (15 μM of Gant61) during 72 hours. The statistical analysis was performed using GraphPad P 5. Significance was accepted for p < 0.05.

RESULTS: No hot spot mutations on PTCCH1, SMO and SDFU sequences were detected in LMS patient samples. Uregulation of DNMTi, 3a and 3b mRNA and protein was observed in LMS compared to UTSM cells. The percentage of PTCCH1 DNA methylation in LMS was 2.3%. Treatment with DNMTi decreased the expression of DNMTi, 3a and 3b and DNA methylation of PTCCH1 to 1%. Although inhibition of DNMT did not change PTCCH1 gene expression, significant downregulation of GLIi was observed in LMS cells (p < 0.05). The DNMTi in combination with GLIi (Gant61) exhibited decreased SMO and GLIi protein expression (p < 0.05), and suppressed GLIii nuclear translocation. Moreover, the combination treatment showed more inhibitory effects on proliferation, migration, invasion and induced apoptosis in LMS cells (p < 0.05).

CONCLUSIONS: Our study demonstrates for the first time that although genetic mutations of key HH members are not observed, DNA methylation is tightly linked with LMS phenotype via HH signaling. Notably, a combined treatment of DNMTi and GLIii exhibits a more robust inhibitory effect on LMS phenotype. Further understanding the mechanism of HH pathway in LMS may lead to development of a novel treatment strategy for this aggressive cancer.

SUPPORT: Support: FAPESP 2017/24448-1, 2015/23482-6, 2015/21068-8; ROI ES028615; U54 MD007602

P-805 Tuesday, October 15, 2019 6:30 AM

INTRAUTERINE INSEMINATION CYCLES: CHARACTERISTICS ASSOCIATED WITH LIVE BIRTH AND THRESHOLDS FOR INEFFECTIVE AND FUTILE CARE. Alessandra J. Ainsworth, MD,1 Emily P. Barnard, DO,2 Sarah Baumgarten, MD, PhD,3 Camden Lopez, MS,4 Amy Weaver, MS,1 Zaraq Khan, MD5 Mayo Clinic, Rochester, MN; 1University of Pittsburgh School of Medicine, Pittsburgh, PA.

OBJECTIVE: To identify intrauterine insemination (IUI) cycle characteristics associated with live birth and to define ineffective and futile care guidelines.

METHODS AND MATERIALS: Retrospective cohort study evaluated couples pursuing IUI at Mayo Clinic from 1/2005 to 9/2017. Couples using fresh partner ejaculate were included. Female age, ejaculate and inseminate parameters, and ovarian stimulation type were evaluated for association with live birth, defined as birth after 24 weeks gestation. Outcomes were evaluated per cycle, rather than per patient.

RESULTS: A total of 2912 IUI cycles were included for 1117 women. Male infertility was the primary factor in 76% of cycles. Male factor was independently associated with live birth (p < 0.001). Models were fit using generalized estimating equation methodology with an exchangeable correlation structure to account for the correlation between cycles involving the same patient. Ineffective and futile care were defined as live birth <5% and 0%, respectively, consistent with ASRM guidelines.

CONCLUSIONS: This retrospective cohort study evaluated couples pursuing IUI at Mayo Clinic from 1/2005 to 9/2017. Couples using fresh partner ejaculate were included. Female age, ejaculate and inseminate parameters, and ovarian stimulation type were evaluated for association with live birth, defined as birth after 24 weeks gestation. Outcomes were evaluated per cycle, rather than per patient.

P-806 Tuesday, October 15, 2019 6:30 AM

WHAT IS FERTILITY FRAUD, WHAT ARE COURTS AND LEGISLATURES DOING ABOUT IT, AND HOW MIGHT IT IMPACT REPRODUCTIVE MEDICINE?. Jody L. Madeira, Ph.D., J.D.1 Susan Crockin, J.D.2 aProfessor of Law, Bloomington, IN; bSenior Scholar, Adjunct Professor of Law, Washington, DC.

OBJECTIVE: To describe the recent fact pattern associated with “fertility fraud” cases, describe new judicial rulings and legislative developments related to fertility fraud, and describe how these cases may impact ART practice.

METHODS: 1) Qualitative, semi-structured interviews with former patients who had been inseminated without consent with the sperm of their fertility physicians, and the donor-conceived children who were conceived through these procedures. Cases include 6 U.S. cases, 1 Canadian case, and 1 European case. 2) Review of existing “fertility fraud” case law and new 2019 state legislation.

RESULTS: Former patients feel physically violated and assaulted, and often feel as if seeking accountability implies a rejection of a beloved child. Donor children experience profound disruptions to personal identity, particularly if they did not know they were conceived through donor sperm IUI. Many become estranged from families after they decide to pursue relationships with new half-siblings or seek accountability from physicians. In 2019 legislative sessions, state legislatures in Indiana and Texas have taken significant steps to pass “fertility fraud” legislation. Spurred by the Donald Cline case, Indiana legislation creating a civil and criminal cause of action for fertility fraud was unanimously passed in both the House and Senate and awaits the Governor’s signature. Texas legislation that creates a criminal cause of action for fertility fraud under the state’s sexual assault law has passed the Senate and a House committee unanimously, and awaits a final vote in the House; the Governor has commented on social media approvingly about the bill.

CONCLUSIONS: Although most fertility fraud cases are decades in the past, their contemporary fallout can have important implications for today’s practitioners.

SUPPORT: None

References: Against seminal principles: ethics, hubris, and lessons to learn from illicit inseminations Madeira, Jody et al. Fertility and Sterility, Volume 110, Issue 6, 1003 - 1005
P-807 Tuesday, October 15, 2019 6:30 AM

OOCYTE DISPOSITION PREFERENCES: PLANNING FOR THE FUTURE. Anne Hutchinson, M.D., Rafael Contino, B.S., John Zhang, Ph.D., Angela K. Lawson, Ph.D., Mary Ellen Pavone, M.D, MSCM Northwestern University, Chicago, IL.

OBJECTIVE: To characterize the frozen oocyte disposition preferences of patients undergoing medical and social fertility preservation

DESIGN: Descriptive Study

MATERIALS AND METHODS: This descriptive study was performed using data collected between 2011 and 2018 in the Division of Reproductive Endocrinology and Infertility at Northwestern University. Demographic and cycle information was collected for each patient. Medical diagnosis was collected for each fertility preservation patient. Medical and social fertility preservation (FP) patients were distinguished based on documentation in their initial consult note in the electronic medical record. Disposition options included: disposal, donation to research, or donation to a specified third party which was decided at the time of initial consent and scanned into the patient chart. The demographic parameters were compared between the two groups using chi-squared analysis.

RESULTS: 578 oocyte vitrification cycles were identified between 2011 and 2018. 15 cycles were noted to have no documented disposition preference and were excluded from the analysis. 143 cycles corresponded to medical FP patients and 435 to social FP. Medical FP patients were more likely to be under the age of 35, have a higher BMI, and have had a prior live birth. In both groups, the most commonly selected option was donation to research (48.3% social, 48.3% medical), followed by donation to a specified third party (27.4% social, 27.4% medical) and finally disposal of oocytes (22.8% social, 17.5% medical).

CONCLUSIONS: Our data shows that oocyte disposition choices are similar in patients undergoing oocyte vitrification for medical and social indications. Both groups most commonly elect donation to research, followed by donation to a specified third party. Disposal of oocytes was the least common disposition choice for both groups. While oocyte vitrification is a relatively new technology, utilization of these frozen gametes is low. Disposition preferences will become increasingly important as this patient population ages and meets their reproductive goals. Formalized research protocols need to be established to accommodate this anticipated increase in oocytes available for research.

P-808 Tuesday, October 15, 2019 6:30 AM

ASSOCIATION OF BMI WITH POST-OPERATIVE MORBIDITY IN PATIENTS UNDERGOING MYOMECTOMY: AN ANALYSIS OF THE AMERICAN COLLEGE OF SURGEONS’ NATIONAL SURGICAL QUALITY IMPROVEMENT PROGRAM (ACS NSQIP). Lauren M. Kendall Rauchfuss, MD, a Tania Kim, MD, b MacKenzie P. Purdy, MD, b Elizabeth H. Habermann, PhD, c Katherine A. Bews, BA, d Amy E. Glasgow, MHA, e Zarqa Khan, MD f Mayo Clinic, Rochester, MN; g Division of Reproductive Endocrinology and Infertility, Rochester, MN; h Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery Surgical Outcomes Program, Mayo Clinic, Rochester, MD, Rochester, MN.

OBJECTIVE: To study the post-operative outcomes among different BMI classes after undergoing myomectomy.

DESIGN: A retrospective cohort study, comparing 30 day surgical outcomes after myomectomy among patients with low and normal, overweight, obese (class I and II), and morbidly obese (class III) BMI ranges.

MATERIALS AND METHODS: Following IRB approval, the ACS NSQIP was utilized from years 2010-2016. Current Procedural Technology codes were used to identify patients undergoing myomectomy. Pre-operative demographics and 30 day surgical outcomes were obtained. Primary outcomes were any wound complications and serious surgical complications which included wound disruption, sepsis, deep venous thrombosis, pulmonary emboli, acute kidney injury, and hospital readmission. Univariate analyses were performed using Chi-Square, t-test, Mann-Whitney U-test and ANOVA as appropriate. Multivariable logistic regression models were used to identify demographic factors independently associated with primary outcomes.

RESULTS: A total of 3,407 women underwent a myomectomy procedure. Univariate analyses comparing low-normal BMI patients to morbidly obese patients are shown. (table1)

Morbidity obese patients were more likely to develop wound complications after adjusting for confounders (adjusted OR 4.1; 95%CI; 1.5-11.3). Similarly, morbidly obese patients had a trend towards higher risk of serious systemic surgical complications, (adjusted OR 1.5; 95%CI; 0.6-3.8).

CONCLUSIONS: In conclusion, morbid obesity was a significant risk factor for 30 day post-operative complications in patients undergoing myomectomy. Further research is needed to identify interventions to improve post-operative morbidity after myomectomy.

Table 1. Comparison of patients across low-normal BMI to Morbid obesity (BMI Class II)

<table>
<thead>
<tr>
<th>BMI n=1042</th>
<th>Morbidly obese (BMI&gt;40) n=280</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-Normal</td>
<td>Morbidly obese</td>
<td></td>
</tr>
<tr>
<td>Pre-operative Demographics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black race</td>
<td>266 (25.5)</td>
<td>168 (60.0)</td>
</tr>
<tr>
<td>Diabetes with pharmacotherapy</td>
<td>12 (1.151)</td>
<td>30 (10.7)</td>
</tr>
<tr>
<td>Hypertension with pharmacotherapy</td>
<td>37 (3.6)</td>
<td>81 (28.9)</td>
</tr>
<tr>
<td>ASA Class III/IV</td>
<td>32 (3.1)</td>
<td>119 (42.5)</td>
</tr>
<tr>
<td>Surgical and post-operative characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal Myomectomy</td>
<td>472 (45.3)</td>
<td>160 (57.1)</td>
</tr>
<tr>
<td>Inpatient Recovery</td>
<td>498 (47.8)</td>
<td>169 (60.4)</td>
</tr>
<tr>
<td>Total Surgery Time (min)</td>
<td>131.9 ± 76.7</td>
<td>157.3 ± 84.9</td>
</tr>
<tr>
<td>Length of Hospital stay</td>
<td>1.0 (0.0-14.0)</td>
<td>2.0 (0.0-31.0)</td>
</tr>
<tr>
<td>Unplanned Hysterectomy at time of Myomectomy</td>
<td>30 (2.9)</td>
<td>20 (7.1)</td>
</tr>
</tbody>
</table>

1 Chi-Square n(%) 2 t-test mean(Standard deviation), Mann-Whitney U-test Median(Range)
DETECTION OF THE FERTILE WINDOW USING A WEARABLE MEDICAL DEVICE AND THE CALENDAR METHOD: A COMPARATIVE STUDY. Evangelia Mouriki, MSc, Alijsa Bilic, MSc, Brianana M. Goodale, PhD, Gyorgyi Hamvas, MSc, Catrin Argyle, BSc, MSc, Mohamed Shilaia, PhD, Brigitte Leeners, Dr. Prof. Ava AG, Zurich, Switzerland; University Hospital Zurich, Zurich, Switzerland.

OBJECTIVE: While many women rely on the calendar method to detect their fertile window and prevent or aid conception, recent advances in wearable sensor technology and artificial intelligence suggest a wrist-worn medical device could provide women with an accurate, individualized prediction. In this study, we compare the accuracy and precision of these two methods in identifying the six-day fertile window.

DESIGN: Retrospective analysis of data from a clinical sample MATERIALS AND METHODS: Thirty-four conception-seeking women enrolled in a trial to test the performance of a wrist-worn medical device in detecting physiological changes across the menstrual cycle. Participants wore the Ava Fertility Tracker nightly while sleeping for up to a year. Via three sensors, the Ava Fertility Tracker measures seven different biophysical parameters every 10 seconds including skin temperature and heart rate. Participants synced their bracelet each morning with the complementary smartphone app, which relies on a machine learning algorithm to predict and detect the real-time fertile window. Participants also completed a daily diary entry about their activity in the last 24 hours and recorded whether they had received a positive urinary luteinizing hormone (LH) test each morning. Women had to be older than 18 years old, not currently taking hormonal birth control, and have regular cycles (defined as 24-35 days in length) in order to be included in our analyses. For each subject, and each cycle, we retrospectively calculated the fertile window as would have been predicted by three different calendar methods: the Standard Days method, the Rhythm Method, and the Alternative Rhythm Method. Using the LH test result as an objective measure of ovulation, we compared the accuracy and precision of each calendar method to the algorithm-identified fertile window. We defined precision as the fraction of days which the method reported as fertile that aligned with the LH-detected fertile window and accuracy as the percentage of correctly classified fertile or infertile days overall.

RESULTS: The accuracy in identifying the fertile days for the wearable device was 88.1% (Standard deviation [SD] = 9.1%) compared to 76.8% (SD = 5.1%) for the Standard Days method, 69.2% (SD = 15.6%) for the Rhythm Method, and 67.6% (SD = 16.1%) for the Alternative Rhythm Method. Furthermore, the wearable fertility tracker had the highest precision of any of the methods analyzed (70.3%, SD = 21.9% vs. 42.7%-47.7% for the calendar methods [SDs = 7.6%-13.0%]).

CONCLUSIONS: Despite the ease of use and straightforward calculations driving the calendar method, using a wrist-worn medical device that records multiple physiological parameters simultaneously provides a more accurate and more precise estimation of the fertile window. Our findings have implications for women across the reproductive lifespan; whether women are trying to best time conception to maximize the number of days requiring back-up contraception, wearable technology represents a significant step forward in individualized, AI-driven healthcare.

SUPPORT: Funding for this study was provided by a grant from the Swiss Commission for Technology and Innovation (CTI) and Ava AG.

CRYO TANK ISSUES

P-810 Tuesday, October 15, 2019 6:30 AM

CRYO TANK QUALITY CONTROL: HOW TO DETECT A TANK THAT IS ‘FAILING’. James R. Graham, MS ELD, Cristina L. Applegate, MS, Seamus R. Graham, HSDG, Michael J. Tucker, PhD, 5G Fertility, Rockville, MD; 4Shady Grove Fertility, Rockville, MD; 2Student, North Potomac, MD.

OBJECTIVE: Cryo tank failure at several US and Canadian IVF clinics has been reported in the news media recently. Hundreds of patient specimens were lost. Current Quality Control (QC) measures are typically to assess liquid nitrogen (LN2) consumption and re-fill on a strict schedule. We wished to see what happens when a properly QC’d tank fails (defined as vacuum loss) to judge whether the ‘measure & fill’ approach was adequate.

DESIGN: Observational MATERIALS AND METHODS: 12 retired various model cryogenic dewars (35L+Taylor-Wharton and 47L MVE) were filled with LN2 to the neck of the tank per QC protocol. Each tank was filled with temperature sensors at mid-level and the bottom of the canister. Furthermore a temperature a probe was placed in the lid of the tank as well as the shoulder of the tank (near handle). 1mm holes were drilled either into the shoulder of the tank (external breach), or into the neck of the tank (internal breach). Temperatures were then taken from the time of the breach, and every 15 minutes thereafter until the tank was considered ‘failed’ (internal mid tank temperature rose above -150°C).

RESULTS: Boiling of the LN2 was evident within 60 seconds of the breach regardless of tank model. LN2 vapor was visible within 60 seconds of breach of each tank regardless of tank model.

Upon vacuum breach of each tank the sound of vacuum loss was audible for up to 4 hours with external breaches.

Temperature of lid due to escaping cold LN2 gas went below 5°C in the first 15 minutes of the breach regardless of model, and stayed below this level until the tank was considered failed (above -150°C). Ice “crowning” of the lid was only obvious with external breaches, but not so with internal breaches.

Time for tank to fail was dependent on tank model and type of breach.

Temperature of the external probe on the tank showed a drop in surface temperature, but this was dependent on type of breach and varied in time from when breach had occurred.

Time to tank failure depended on tank model and breach type, but for a minimum of 12hrs internal temperature were maintained above -150°C for all tanks tested.

Lid temperatures below 5°C were consistently observed until a tank’s internal temperature went above -150°C regardless of model or breach type.

CONCLUSIONS: Tanks that experience vacuum loss will almost immediately experience LN2 boiling and emit a steady stream of cold LN2 gas. Monitoring lid temperature twice daily could identify tanks that have lost vacuum. Using an infrared gun to take the lid temperature of a cryo tank twice daily (a.m. & p.m.) would be a quick and convenient way to identify tanks that have lost vacuum, and that are compromised. Tank temperatures that deviate more than 20% from the mean of other tanks in the storage area should be evaluated for failure. Additionally tanks can be fitted with remote alarmed lid temperature sensors to detect temperature drops due to LN2 boiling that would occur when a tank loses vacuum.

Weekly and even daily ‘measure & fill’ QC protocols appear inadequate without cryo-tank lid temperature monitoring.

THE ANATOMY OF LIQUID NITROGEN (LN2) CRYO DEWAR TANK FAILURES. Mitchel C. Schiewe, MS, PhD; Shane Zozula, B.S., T.S. (ABB); Erica J. Behnke, PhD; Jason Cowles, BA; Rob Manchise, BS; John B. Whitney, BS; Ovation Fertility, Newport Beach, CA; Ovation Fertility, Cincinnati, OH; Trust Gnosis, Brea, CA.

OBJECTIVE: The key factor in averting the catastrophic loss of precious gametes and embryos rests in the comprehensive implementation of quality management practices and the early detection of an unexpected failure event. The goal of our investigation was to simultaneously evaluate, interrupt and understand weight and temperature changes of induced dewar tank failures under continuous video surveillance over a 24h interval.

DESIGN: A prospective, observational study assessed a variety of induced tank failure events monitored by real-time video, weight determination and temperature changes of induced dewar tank failures under continuous video surveillance over a 24h interval.

MATERIALS AND METHODS: Using a novel Wi-Fi based, pressure sensitive weight cart devices (TrustGnosis; Brea, CA) and a hard wired temperature-based continuous monitoring alarm system (Xiltrix, Netherlands), we prospectively correlated ‘failure’ characteristics of several aged (>18 years old; n = 6) 35-36L Taylor-Wharton dewar LN2 storage tanks and one ‘recalled’ new Biocane 73L TS/Chart tank. We investigated drilled (1/16”) vacuum port of the 73L dewar and two smaller tanks (35HC, 36VHC). In phase 2, we increased the external drill (ED) opening to 1/8” and 3/16” on two 35HC tanks, while two others (35HC) where drilled (1/4”) through their inner base seam (ID) into the vacuum space. An ANOVA regression model was used to correlate the relationship between weight and LN2 levels.
RESULTS: The intentional destruction of all external dewar tanks created an aspiration noise as room air initially warmed the interstitial space outside the inner tank. Conversely, internal dewar tanks displayed overt bubbling of its inner liquid chamber and immediate LN vaporization (within 10 sec). LN vapor streaming outside the cap and neck of the external drilled tanks was also evident within 30 sec. An external thermocouple registered 5°C within 3 min. Ice was seen on the cap surface by 3 min, while gradual frost build-up occurred over several hours. Icing and condensation on the tank walls was apparent early on and throughout failure. A 20% evaporation detected by weight took about 4h, while the first internal temperature alarm at -194°C did not occur until 5.5-6.5 h. The ID tanks reached -170°C sooner (+14-15h) with 65-75% evaporation compared if >95% evaporation for the ED group (+18-19h), prior to the rapid rise of temperature for both treatments (subzero by +24-25h). The ED-treated 73L tank responded similar to the 35H tanks, but at twice the evaporation rate. The external drill size did not affect evaporation rates.

CONCLUSIONS: Tank quality and type of vacuum breakthrough can influence the rate of failure. In all cases overt physical signs of pending failure were continuously visible for >14h before critical temperatures were reached. Overall, external quality measurements and device systems represent a promising future offering greater precision, labor efficiency, and improved specimen security/safety.

SUPPORT: None

P-812 Tuesday, October 15, 2019 6:30 AM
USEFULNESS OF REMOTE, CONTINUOUS WEIGHT DETERMINATION FOR THE ROUTINE QUALITY MANAGEMENT OF CRYO DEWAR TANKS. Mitchell C. Schiewe, MS, PhD; Shane Zorula. B.S., T.S. (ABB). Tania Ochoa, BA. Jason Cowles, BA, Rob Manchse, BS, John B. Whitney, BS “Ovation Fertility, Newport Beach, CA; “Trust Gnosis, Brea, CA.

OBJECTIVE: The quality management of small volume (30-73L) LN2 dewar cryostorage tanks have historically been maintained by routine (i.e., at least weekly) internal dipstick measurements and re-filling. Meanwhile, alarm systems, if used, have been based on a designated internal temperature threshold (<-180°C) or LN2 level set point (e.g., upper canister level). The goals of our investigation were to evaluate the prospective value of real-time pressure sensitive, weight measurements of mobile dewar tanks for operational qualification (OQ) and performance qualification (PQ).

DESIGN: Real-time weight measurements were correlated to changes in LN2 volume and temperature under new tank validation (i.e., OQ) and standard tank use (i.e., PQ). Evaporation usage rates were calculated at time of fill up (t0) minus measurement prior to next fill (t1wk; usage rate = (Ew) or volume level (EL). An evaporation rate index (E vap) was defined on computer-generated tables in three groups and evaluated by weight and used to formulate a useful threshold measure assessing dewar tank retirement.

SUPPORT: None

P-403 Wednesday, October 16, 2019 6:30 AM
INFLUENCE OF COMMERCIAL EMBryo CULTURE MEDIA ON IN VITRO DEVELOPMENT, PREGNANCY, AND PERINATAL OUTCOMES AFTER IVF: A SING-LE-CENTER RCT. Masao Murakami, PhD, Keiko Tanaka, MS, Hitomi Otsubo, BS, Shigetoshi Mizumoto, Ph.D., Yozo Nagao, MS, Takeshi Kuramoto, M.D., Ph.D., Kuramoto Women’s Clinic, Fukuoka, Japan.

OBJECTIVE: Numerous embryo culture media can now be used for IVF, raising the question whether any medium is superior to others. Their ability to yield embryos in vitro does not necessarily mean that the embryos are viable. Previously, in animals, serum was commonly added to culture media to yield blastocyst stage (BS) embryos, but this impaired embryonic, fetal, and offspring health. In humans, the medium composition and culture duration as well as cryopreserved ET reportedly affect treatment efficacy and the offspring phenotype. Given the importance of media in clinical outcomes, well-designed RCTs are needed, but existing relevant data are insufficient. Here, we provide updated data on an RCT conducted to compare clinical outcome between three embryo culture media widely used in IVF.

DESIGN: A single-center RCT.

MATERIALS AND METHODS: This study included 795 healthy patients undergoing their first IVF cycle at our clinic from February 2016 to August 2017. They were randomized by computer-generated tables into three groups and underwent our standard oocyte retrieval and IVF/ICSI procedures. Embryos were cultured in G1/G2 Plus (Vitrolife) (A), Global Total (LifeGlobal) (B), or Sequential Cleav/Blasf (Origio) (C) media. Thirty-seven patients with no 2PN oocytes 18 h after insemination were excluded from the study. During embryo culture, for cycles where the patients had only one good-quality (GQ) embryo by D3, the embryos were vitrified on D2/3 (cleavage stage, CS). When the patients had ≥2 GQ embryos, vitrification was delayed on D2/3, the culture of the remaining embryos was extended, and all GQ embryos were vitrified on D5/6. Data for vitrified ET performed until the end of March 2019 were analyzed.

RESULTS: Total numbers of vitrified CS (A: 1.35 ± 0.05, B: 1.38 ± 0.04, C: 1.35 ± 0.04) and BS (A: 1.71 ± 0.14, B: 2.08 ± 0.17, C: 2.05 ± 0.15) embryos/cycle did not differ, but the number of vitrified D5 BS embryos was fewer (P < 0.005) in Group A (0.84 ± 0.09) than in Groups B (1.55 ± 0.15) and C (1.50 ± 0.12). After vitrified CS/BS ET, the clinical pregnancy rate (CPR) was lower, albeit non-significantly (P = 0.062), in Group C than in Group B (implantation rates (A: 41.2%, B: 43.2%, C: 37.2%), CPRs (A: 49.8%, B: 53.5%, C: 45.0%), ongoing/delivered PRs (ODPRs) (A: 41.0%, B: 43.0%, C: 36.7%). There were 314 live-born children (286 singletons and 28 twin children). Perinatal data for singletons were similar, except for birthweight adjusted for gestational age and gender (z-score) (A (CS: 0.17 ± 0.20, n = 25; BS: 0.21 ± 0.13, n = 71), B (CS: 0.20 ± 0.22, n = 18; BS: 0.26 ± 0.10, n = 88), C (CS: 0.40 ± 0.22, n = 13; BS: 0.47 ± 0.12, n = 71) (A (CS) vs. BS: P = 0.01, A (CS) vs. B (BS): P = 0.061).

CONCLUSIONS: A culture system yielding fewer BS embryos tended to have lower birthweight z-score, while the ODPR was comparable to or slightly better than those of other systems. Differentiation of the ability of media to support in vitro development with its ability to yield viable embryos may partly be important for better outcome. Further studies with more participants, including follow-up on the health of children born from embryo culture, are required to clarify the effects.

P-404 Wednesday, October 16, 2019 6:30 AM
EXPLORING NEW COMPLEX PROTEIN SUPPLEMENT SOLUTIONS FOR CLINICAL EMBRYO CULTURE MEDIA. John Becker, BS, Benjamin B. Goheen, BS, Dinesh, M. Lagouda, MS, Sneep K. Rajput, PhD, Courtney K. Grimm, MS, William B. Schoolcraft, MD, Leora B. Krisher, PhD, Colorado Center for Reproductive Medicine, Lone Tree, CO, CCRM, Lone Tree, CO.

OBJECTIVE: The objective of this research was to investigate the effectiveness of a novel protein supplement (GroPro; consisting of antioxidants, lactoferrin, and corn-derived antioxidants) as an alternative source of growth factor components added to in vitro embryo culture media.
growth factors, and fatty acids), to support preimplantation embryo development in vitro. ProGro was designed to act as a reliable complex protein supplement alternative for clinical ART, in order to better support embryo development and quality compared to human serum albumin (HSA) alone.

**DESIGN:** Basic Research Study. Media supplementation with ProGro, our standard recombinant HSA (AlbIX, Novozymes), or Vitrolife HSA were compared for the ability to support mouse blastocyst development, cell differentiation (inner cell mass (ICM) and trophectoderm (TE)), mitochondrial DNA (mtDNA) copy number, as well as blastocyst implantation potential and subsequent fetal development.

**MATERIALS AND METHODS:** In vivo matured oocytes were obtained from outbred C57BL/6J mice and subsequently fertilized in vitro. Zygotes were randomly assigned to sequential embryo culture media containing AlbIX (2.5mg/ml), Vitrolife HSA (5.0 mg/ml), or GroPro (5.0 mg/ml) (4 replicates, n=525). After 112h of culture, development was assessed and blastocysts were either fixed and immunostained to visualize ICM and TE cells (n=153), or flash frozen individually to determine mtDNA copy number using qPCR relative to genomic DNA (n=30). D3.5 blastocysts cultured in Vitrolife HSA and GroPro were surgically transferred into recipients (n=270 ASRM Abstracts).

**RESULTS:** There were no differences in blastocyst development (AlbIX 52.0% ± 6.5%, Vitrolife HSA 57.3% ± 5.3%, GroPro 69.0% ± 1.6%) or hatching (AlbIX 47.4% ± 5.4%, Vitrolife HSA 50.0% ± 3.9%, GroPro 58.1% ± 1.6%) between treatments. Embryos cultured in Vitrolife HSA contained significantly (p<0.05) more TE cells and total cells, while embryos cultured in AlbIX contained significantly (p<0.05) less ICM cells compared to every other treatment; the ratio of ICM to TE was not different between treatments. There was significantly lower relative mtDNA copy number in embryos cultured in AlbIX compared to embryos cultured in GroPro (p<0.05). No difference in implantation potential (Vitrolife HSA 51%, GroPro 57%) for embryos cultured in AlbIX compared to embryos cultured in GroPro (p>0.05). No difference in implantation potential (Vitrolife HSA 51%, GroPro 57%) or fetal development (Vitrolife HSA 28%, GroPro 22%) was observed.

**CONCLUSION:** These findings demonstrate that in the mouse, additional antioxidants, growth factors and fatty acids do not provide any additional benefit over HSA alone, although they are not detrimental to embryo development or quality. This novel protein supplement may be a viable alternative for the culture of human embryos, in which complex protein supplements such as SPS and SSS support better blastocyst development than HSA alone.

**SUPPORT:** None.

---

**P-405** Wednesday, October 16, 2019 6:30 AM

**COMPARISON OF HUMIDIFIED VERSUS NON-HUMIDIFIED INCUBATION WITH SEQUENTIAL CULTURE MEDIA IN A TIME-LAPSE INCUBATOR USING SIBLING OOCYTE SPLITS.** Rebecca Holmes, PhD, a Jaime Weinberg, BS, b Laurie Kalaghan, BS, b Brett Goode, BS, b William B. Schoolcraft, MD, c Jason E. Swain, PhD, c CCRM Boston, Chestnut Hill, MA; cCCRM Boston, Boston, MA; cColorado Center for Reproductive Medicine, Lone Tree, CO; cCCRM Fertility Network, Lone Tree, CO.

**OBJECTIVE:** Many modern embryo culture incubators are non-humidified. Initial studies indicate that evaporation of culture media may occur in non-humidified culture environments, even under mineral oil. This evaporation may negatively impact embryo development and quality. Controlling for other variables in the culture system while trying to study the impact of humidity may be difficult. The objective of this study was to compare outcomes following sibling zygote splits in identical culture conditions, within the same incubator, utilizing a time-lapse system that permits both dry and humidity conditions may negatively impact embryo development and quality. Controlling for other variables in the culture system while trying to study the impact of humidity can be difficult. The objective of this study was to compare outcomes following sibling zygote splits in identical culture conditions, within the same incubator, utilizing a time-lapse system that permits both dry and humidity conditions, or if using differing amounts or types of mineral oil overlay.

**MATERIALS AND METHODS:** A time-lapse incubator with individual chambers (Geri, Sirona) was utilized to culture all embryos. Three chambers were humidified by placing the supplied water chambers inside (~60% humidity) and the 3 other chambers were non-humidified. Room humidity was ~50%. All chambers were gassed using the same gas supply using 6.5% CO2 and 5% O2. pH was verified to be similar in all chambers. All embryos were grown in the supplied Geri dishes with the wells filled with 80μl Sage sequential media with 10% v/v SPS under 4 mL Paraffin oil (Life Global). Sixteen patients with > 6 MIIs at ICSI had half of their ICSI’d oocytes placed into a humidified and non-humidified chamber. All embryos were treated identically except for the absence or presence of humidity in the respective chambers. Embryos were observed and media exchanged/refreshed following 24h, 72h and 120h. Data were analyzed using Fisher’s Exact Test.

**RESULTS:** Use of a humidified chamber yielded significantly more good quality blastocysts on day 5, 6 and overall by day 7 than non-humidified chambers.

**CONCLUSIONS:** Humidified culture in the Geri time-lapse system yielded more good quality blastocysts on day 5, day 6 and overall on day 7 and than non-humidified culture. No differences in fertilization, good quality cleavage or total blastocyst development was apparent. Under the culture conditions used, evaporation may have occurred to compromise blastocyst quality, though this seems unlikely with media exchanges at 48h intervals based on prior studies within our laboratory. Results may vary with fewer media changes, in laboratories using single step media in an uninterrupted fashion, or if using differing amounts or types of mineral oil overlay.

---

**P-406** Wednesday, October 16, 2019 6:30 AM

**EFFECT OF ULTRA-LOW OXYGEN (2%) ENVIRONMENT ON MOUSE EMBRYO MORPHOKINETICS AND BLASTOCYST DEVELOPMENT.** Khaliedy Kaskar, MS, a Richard Cochran, PhD, a Daneka P. Hamilton, MPH, a Amanda David, BS, b Ralf Henkel, PhD, c William Gibbons, MD, a Chellakkann Selvanesan Blesson, PhD, a Kaskar group. aBaylor College of Medicine, Houston, TX; bTexas Childrens’ Hospital, Houston, TX; cUniver-

**OBJECTIVE:** To determine if culture of mouse embryos in an ultra-low oxygen environment could enhance blastocyst development in terms of time-lapse morphokinetics.

**MATERIALS AND METHODS:** A total of 214 commercially obtained frozen mouse embryos (B6D2F1 & B6C3F1 hybrid) were thawed and cultured in One-Step medium with 10% Serum Protein Substitute using an EmbryoScope time-lapse incubator at 37°C, 5.5% CO2, and either (1) 6.0% O2 (n=106) or (2) 2.0% O2 (n=108). Embryo images were recorded every 10 minutes for 6 days of culture. Time-lapse videos were annotated for the following time points: 2cell (t2), 3cell (t3), 4cell (t4), 5cell (t5), 6cell (t6), 7cell (t7), 8cell (t8), start of compaction (tSC), morula (tM), start of blastulation (tSB), blastocyst (tB), expanded blastocyst (tEB) and hatching.
Time points are expressed as Mean ± SD.

blastoscyt (Hb). The 2-cell stage was considered as time zero since the exact time of insemination was unknown. Time points were statistically compared between the two groups. Blastocyst development stages for both culture environments were also compared.

RESULTS: There were no statistically significant differences between the two groups in any of the time points measured up to the 8-cell stage. However, after the 8-cell stage, the 2% O₃ group showed significantly slower embryonic development in each time point up to the hatching blastocyst stage. There was no difference in the blastocyst development rate between the 6% O₂ and 2% O₂ environments (99.1% vs 95.4%, p = 0.099).

CONCLUSIONS: Culture of mouse embryos in a 2% oxygen environment did not show any improvement in blastocyst development. However, embryos cultured in 2% oxygen took significantly longer to reach the blastocyst stage than those cultured at 6% oxygen, and this delay became prominent after the 8-cell stage.

P-407 Wednesday, October 16, 2019 6:30 AM

DOES SUPPLEMENTATION OF MEDIA WITH INSULIN OR INSULIN-LIKE GROWTH FACTOR 1 (IGF-1) ENHANCE MORPHOKINETICS OF MOUSE EMBRYO DEVELOPMENT? Khaliied Kaskar, MS, Richard Cochran, PhD, Danae P. Hamilton, MPH, Amanda David, BS, Ralf Henkel, PhD, William Gibbons, MD, Chellakkan Selvanesan Blesson, PhD. \(^{a}\)Baylor College of Medicine, Houston, TX; \(^{b}\)Texas Children’s Hospital, Houston, TX; \(^{c}\)University of the Western Cape, Bellville, South Africa.

OBJECTIVE: To evaluate if adding either insulin or insulin-like growth factor 1 (IGF-1) to culture medium improves mouse embryo development and time-lapse morphokinetics.

DESIGN: Prospective study.

MATERIALS AND METHODS: A total of 305 commercially obtained frozen mouse embryos (B6D2F1 & B6C3F1 hybrid) were thawed and cultured in (1) One-Step medium only, (2) One-Step medium with 100ng/mL insulin, and (3) One-Step medium with 100ng/mL IGF-1, using an EmbryoScope time-lapse incubator at 37°C, 5.5% CO₂, and 6.0% O₂. The EmbryoScope was set to record images of each embryo every 10 minutes for 6 days of culture. The following time points were annotated: 2-cell (t2), 3-cell (t3), 4-cell (t4), 5-cell (t5), 6-cell (t6), 7-cell (t7), 8-cell (t8), start of compaction (tSC), morula (tm), start of blastulation (tSB), blastocyst (tB), expanded blastocyst (tEB) and hatching blastocyst (tHB). The 2-cell stage was considered as time zero since the exact time of insemination was unknown. All time points were statistically compared between each of the three groups with a P-value of <0.05 considered to be significant. Blastocyst development rates for each group were also compared.

RESULTS: A total of 304 blastocysts developed from the 316 embryos cultured, yielding an overall blastocyst development rate of 96.2%. When comparing the blastocyst development rate between the 3 groups, there were no significant differences between the One-Step and IGF-1 media groups (99.1% vs 96.2%). However, the insulin group showed significantly lower blastocyst rates when compared to the controls (93.3% vs 99.1%; p = 0.02). There were no statistically significant differences in any of the time points measured between the One-Step, insulin and IGF-1 groups.

CONCLUSIONS: No beneficial effects were noted by adding insulin or IGF-1 to culture media for mouse embryo development. Mouse embryos cultured with insulin showed a lower blastocyst development rate compared to un-supplemented One-Step media. No differences were seen in any of the time-lapse morphokinetics parameters by supplementing media with either insulin or IGF-1. Ongoing studies using a different more sensitive strain of mouse embryos are underway to see if any subtle changes in morphokinetics may be detected.

TABLE 1. Blastocyst development rates between two strains on mouse embryos cultured in One-step media, IGF-1 and insulin

<table>
<thead>
<tr>
<th>Culture media</th>
<th>Strain 1 (B6D2F1 &amp; B6C3F1 Hybrid)</th>
<th>Strain 2 (C57BL-6N)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-Step (n=238)</td>
<td>99.1% (n=106) (^{a})</td>
<td>80.3% (n=132) (^{b})</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>IGF-1 (n=249)</td>
<td>96.2% (n=105)</td>
<td>74.3% (n=144)</td>
<td>P &lt; 0.0001</td>
</tr>
<tr>
<td>Insulin (n=249)</td>
<td>93.3% (n=105) (^{a})</td>
<td>68.8% (n=144) (^{b})</td>
<td>P &lt; 0.0001</td>
</tr>
<tr>
<td>P-value</td>
<td>(^{a})p = 0.02</td>
<td>(^{b})p = 0.02</td>
<td></td>
</tr>
</tbody>
</table>
DEEP CONVOLUTIONAL NEURAL NETWORKS (CNN) FOR ASSESSMENT AND SELECTION OF NORMALLY FERTILIZED HUMAN EMBRYOS. Irene Dimitriadis, MD,a Charles L. Bormann, PhD,a Manoj Kumar Kanakasabapathy, MS,b Pradhvi Thirumalaraju, BS,c Raghav Gupta, B'Tech,d Rohan Pooniwal, B'Tech,d Irene Souter, MD,d Sarah T Rice, MD,e Pragati Bhownick, MD,e Hadi Shafiee, PhD,e "Massachusetts General Hospital, Harvard Medical School, Boston, MA; bBrigham and Women’s Hospital, Harvard Medical School, Boston, MA; cDivision of Engineering in Medicine, Cambridge, MA; dMassachusetts General Hospital, Harvard Medical School, Boston, MA; eMGH Fertility Center and Harvard Medical School, Boston, MA.

OBJECTIVE: To evaluate whether an artificial intelligence (AI) framework can be used to classify between normally (2PN) and abnormally (non-2PN) fertilized embryos at the pronuclear (PN) stage.

DESIGN: Historical Prospective Cohort Study.

MATERIALS AND METHODS: Embryo images from a retrospective dataset recorded by multiple optical systems at 18 hours post-insemination (hpi) were utilized. The deep convolutional neural network (CNN) model was trained and tested, with a total of 3,469 embryos, to classify between 2PN (n=2,893) and non-2PN (n=576) embryos.

The training set contained 2,366 images (6.33 2PN:1 non-2PN) while the validation set contained 154 images (0.97 2PN:1 non-2PN) with a distribution aimed at minimizing training bias. During training, the dataset was augmented through randomized rotations of the images ranging from 0 to 359 degrees, which was done using OpenCV libraries (ver. 3.1.0). In each training batch, we used 16 unique images per class supplemented by augmented data for the training class. When selecting the 947 embryos for cryopreservation, the CNN developed an algorithm with a sensitivity of 91.86% (CI: 89.94% to 93.53%) and 78.07% (CI: 73.04% to 82.39%), respectively. The area under the curve (AUC) value, established through a receiver operating characteristic (ROC) analysis, was 0.90 (CI: 0.88 to 0.92).

CONCLUSIONS: Here, we report the development and evaluation of an AI-based approach for automated human embryo assessment and selection of normally fertilized embryos at the pronuclear stage with high accuracy.

SUPPORT: This work was partially supported by the Brigham Precision Medicine Developmental Award (Brigham Precision Medicine Program, Brigham and Women’s Hospital and 1R01AI118502, R01AI138800, and R21HD092828 (National Institute of Health).
accuracy of 94.0% (95% CI: 92.4-95.7%). A one sample t-test revealed that the system performed significantly (P<0.05) better than the embryologists in selecting two embryos for transfer among which at least one will eventually form a blastocyst. The accuracy of the CNN in selecting an embryo at 70 hpi, which developed into a high-quality blastocyst (HQB) for a single embryo transfer (SET), was 63.9% that is significantly higher (P<0.05) than the average accuracy of the embryologists (52.8%; 95% CI: 48.6-57.0%). The accuracy of the CNN in selecting an embryo at 70 hpi, which developed into HQB for a double embryo transfer (DET), was significantly higher (79.4%, P<0.05) compared to the embryologists with an average accuracy of 72.4% (95% CI: 70.7-74.0%).

CONCLUSIONS: Here, we reported an artificial intelligence-based approach for predicting the developmental fate of cleavage stage embryos. Our study shows that the developed CNN outperforms an embryologist’s morphologic assessment at 70 hpi in predicting blastocyst formation. Additionally, we demonstrated that this technology might be used to select embryos with the highest in vitro developmental potential. Utilization of artificial intelligence (AI) technologies in human IVF practices may allow for more objective/standardized methods for improving embryo selection.

Reference: None.

SUPPORT: Financial Support: A This work was partially supported by the Brigham Precision Medicine Developmental Award (Brigham Precision Medicine Program, Brigham and Women’s Hospital) and 1R01AI118502, R01AI138800, and 2R1HD092828 (National Institute of Health).

---

TABLE 1. Top predictors, with regression coefficients, for positive pregnancy and LBR

<table>
<thead>
<tr>
<th>Variable</th>
<th>Regression Coefficient</th>
<th>Variable</th>
<th>Regression Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td># Stimulation cycles</td>
<td>-1.8</td>
<td># Stimulation cycles</td>
<td>-3.1</td>
</tr>
<tr>
<td>Embryo age at transfer (blastocyst transfer)</td>
<td>1.6</td>
<td>Embryo age at transfer (blastocyst transfer)</td>
<td>1.1</td>
</tr>
<tr>
<td># of blastocysts in correlating fresh cycle</td>
<td>0.8</td>
<td># of blastocysts in correlating fresh cycle</td>
<td>1.1</td>
</tr>
<tr>
<td>Endometrial thickness at transfer</td>
<td>0.6</td>
<td>Endometrial thickness at transfer</td>
<td>0.8</td>
</tr>
<tr>
<td># Miscarriages &lt; 20 weeks</td>
<td>-0.8</td>
<td># Miscarriages &lt; 20 weeks</td>
<td>-0.8</td>
</tr>
</tbody>
</table>

FERTILITY & STERILITY®
MATERIALS AND METHODS: Embryos were subject to time-lapse assessment to monitor development and perform trophectoderm biopsy for preimplantation genetic testing of aneuploidy. Fertilisation was achieved by ICSI. Time-lapse monitoring started immediately after ICSI, with a 15 min interval between consecutive observations. Of 113 embryos analysed, 55 reached the blastocyst stage (BL-group) and 58 arrested sometime after the 2-cell stage (NoBL-group). ANN analysis was performed, at this stage, only during the first two cell divisions (175 frames; 2.625 min).

RESULTS: We developed a classification platform consisting of three main steps: 1) collection of time-lapse images of preimplantation embryos; 2) evaluation of time-lapse sequence images of each embryo by a particle image velocimetry (PIV) software that detects cytoplasmic movements; 3) finally, analysis of cytoplasmatic movement patterns through an ANN that predicts developmental competence. Specifically, cytoplasmatic movements of single embryos development were measured as multivariate time series and used to train and test a Long-Short Term Memory (LSTM) neural network. LSTM displayed the capacity to learn “long-term” temporal dependences of both BL- and NoBL-group and provide a classification when challenged blind. Following a ten-fold cross validation of the training set, the specific LSTM selected was trained with 90% of data and tested on the remaining. Thus, based on the analysis of the cytoplasmatic movement occurring during the first two cell divisions of single blind embryos (test set), the trained LSTM reached an 82% classification accuracy in the prediction of development to the blastocyst stage.

CONCLUSIONS: This study represents an initial attempt to build up a robust system of classification of the quality of human preimplantation embryos totally automated from input to output. A three-steps workflow, combining time-lapse imaging, particle image velocimetry and artificial neural network (ANN) classification, predicts with high accuracy embryo ability to develop to blastocyst stage. Further refinement of the approach is expected to impact embryo assessment ability and improve efficiency in assisted reproduction treatments.

Reference: None.

SUPPORT: None.

P-415 Wednesday, October 16, 2019 6:30 AM

A MASSIVE EMBRYO MORPHOGENETICS COMPARISON SYSTEM IS ABLE TO SELECT EMBRYOS WITH HIGH IMPLANTATION POTENTIAL ENHANCING SINGLE EMBRYO TRANSFER POLICY. Lucia Alegre, PhD,a Raquel Del Gallego, PhD,a Lorena Bori Arnal, PhD,b Manuel Muñoz, MD,c Antonio Pellicer, M.D., Ph.D.,d Marcos Meseguer, PhD,e IVI-Global, Valencia, Spain; IVI-ALICANTE, Alicante, Spain; IVI-PI/RAVA-Valencia, Valencia, Spain; IVI-Global, Valencia, Spain, Tel Aviv, Israel.

OBJECTIVE: To analyze the abilities of DANA automatic embryo selection software to interpret embryo morphokinetic parameters by massive comparison with a database of embryos with known implantation potential and generate a transfer order ranking in a single embryo transfer policy.

DESIGN: DANA compares each cohort of embryos with a data cloud of KID (Known Implantation Data). This data cloud was performed from a comparison with a database of embryos with known implantation potential and cleavage and cell cycle lengths were included in the DANA software. Morphokinetic parameters were arranged on a 2D graph and the software analysis generated a transfer order ranking in a single embryo transfer policy.

MATERIALS AND METHODS: The percentage of twin gestation was calculated in our double embryo transfer cases comparing whether 1 or 2 transferred were TOP, compared to those cases in which only 1 being TOP. The twin gestation rate was significantly higher in those cases in which the two embryos transferred were TOP, compared to those cases in which only 1 being TOP. In consequence, the selection method presented is a relevant strategy to encourage single embryo transfer at least when two TOP blastocyst are available.

SUPPORT: The development of this publication was financially supported by CDTI research project IDI-20170310 from Spanish Government of Economy and competitiveness, a research grant from the Spanish Society of Embryology (SEF) and Merck S.L.U. (Spain), an affiliate of Merck KGaA, Darmstadt, Germany, through an independent medical writing grant.

P-416 Wednesday, October 16, 2019 6:30 AM

EFFECTS OF MEIOTIC SPINDLE IMAGING IN HUMAN OOCYTES FOLLOWING PIEZO-ICSI ON OOCYTE FERTILIZATION AND EMBRYO DEVELOPMENT. Kenichiro Hiraoka, Ph.D,a Takayuki Tatsumi, M.D., Ph.D.,b Makiko Tajima, M.D.,c Tomonori Ishikawa, M.D.,c Kiyotaka Kawai, M.D.Ph.D.b Kameda IVF Clinic Makuhari, Chiba, Japan; Comprehensive Reproductive Medicine, Tokyo Medical and Dental University, Tokyo, Japan; Kameda IVF Clinic Makuhari, Department of Reproductive Medicine, Tokyo, Japan; Tokyo Medical and Dental University, Tokyo, Japan; Kameda Medical Center, Kamogawa, Japan.

OBJECTIVE: Recent studies using polarized light microscopy have revealed a correlation between meiotic spindle imaging in human oocytes following intracytoplasmic sperm injection (ICSI) and fertilization rate. However, these studies have only assessed conventional-ICSI, in which a beveled and spiked micropipette is used to aspirate the cytoplasm and break the membrane before sperm are injected. To our knowledge, no studies have yet elucidated the relationship between meiotic spindle imaging in human oocytes following Piezo-ICSI, and fertilization or embryo development. In Piezo-ICSI the membrane is broken by applying a Piezo pulse, which produces ultra-fast submicron forward momentum using uniquely-shaped flat-tipped micropipettes with no bevel or spike. The objective of this study was to investigate the effect of meiotic spindle imaging in human oocytes following Piezo-ICSI on fertilization and embryo development.

DESIGN: Retrospective, case control.

MATERIALS AND METHODS: We retrospectively investigated 529 oocytes with the first polar body retrieved from 124 infertile couples (147 cycles; women’s average age, 37.8 ± 4.8; partner’s average age, 39.7 ± 4.8; expressed as the mean ± SD) who attended the Piezo-ICSI program at the Kameda IVF Clinic Makuhari between May 2016 and December 2018. Of these, 489 oocytes (92.4 %) with visible meiotic spindle comprised the Spindle (+) group, while 40 oocytes (7.6 %) not observed meiotic spindle comprised the Spindle (-) group. Meiotic spindle imaging was performed using polarized light microscopy, and the rates of oocyte survival, fertilization, good-quality day-3 embryos, blastocysts, and good-quality blastocysts were evaluated for both groups. Categorical values were compared using Fisher’s exact test. A P-value of < 0.05 was considered significant.

RESULTS: The fertilization rate of the Spindle (+) and Spindle (-) oocytes was 92.0 % (450/489) and 70.0 % (28/40), respectively. The rate of good-quality day-3 embryo formation by the Spindle (+) and Spindle (-) oocytes was 62.9 % (283/450) and 35.7 % (10/28), respectively. The rate of blastocyst formation by the Spindle (+) and Spindle (-) oocytes was 53.7 % (205/382) and 32.1 % (9/28), respectively. The rate of good-quality blastocyst formation by the Spindle (+) and Spindle (-) oocytes was 29.8 % (114/382) and 3.6 % (1/28), respectively. Significantly higher rates of fertilization, good-quality day-3 embryos, blastocysts, and good-quality blastocysts were obtained in the Spindle (+) group than in the Spindle (-) group.

CONCLUSIONS: To the best of our knowledge, this is the first study to evaluate the effect of meiotic spindle imaging in human oocytes following Piezo-ICSI on fertilization or embryo development. Spindle imaging (i.e. identifying oocytes with visible or not observed meiotic spindle) does influence the outcome of Piezo-ICSI in human oocytes, including fertilization and embryo development. Our results demonstrate that the combination of meiotic spindle imaging and Piezo-ICSI can increase the fertilization of viable oocytes without oocyte loss in human assisted reproductive technology.

P-417 Wednesday, October 16, 2019 6:30 AM

EFFECT OF DIFFERENT 6-DIMETHYLAMINOPURINE (6-DMP) TREATMENTS ON REVERSIBLE ARRESTING OF MONO- AND TRIPRONUCLEAR EMBRYOS AT THE PRONUCLEAR STAGE. Nogumori, Gila, M.D.a, Ana González-Picazo, MSc,b Nuria Soler, MSc,c María José Escrivá, Ph.D,e Xavier Vendrell, Ph.D.,f Thamara Villa, Ph.D.f IVI-VALENCIA, Valencia, Spain; IVI-Foundation, Instituto de ART LAB - EMBRYOS
OBJECTIVE: To determine the optimal duration of 6-DMAP to synchronize human zygotes at the pronuclear stage (presumably at the G2-phase of the cell-cycle) without compromising subsequent development to blastocyst, as possible pre-treatment to enhance the natural DSB repair pathways in CRISPR-Cas9 technology.

DESIGN: This study used mono- (MPN; n = 580) and tripronuclear (TPN; n = 261) human embryos. They were incubated for 6hrs in different 6-DMAP concentrations, in order to assess the arresting rate. After 6-DMAP treatment, zygotes were cultured to the blastocyst stage, in order to assess the effect of 6-DMAP on subsequent developmental competence.

MATERIALS AND METHODS: MPN and TPN zygotes were incubated in 0mM (control), 0.24mM, 0.48mM or 0.60mM 6-DMAP, in GEMS medium (Genea Biomed) for 6h at 37°C, 5%CO2 and 5%O2. Arresting rate was calculated as percentage of zygotes, blocked at PN stage when 6-DMAP treatment had finished. Then, MPN/TPN were cultured in a time-lapse incubator in 20uL GEMS for 5 days. Blastocyst rate was calculated as a percentage of blastocysts per number of pronuclear-arrested zygotes. Morphokinetic variables included the precise occurrence time of pronuclear fragmentation, any abnormality, and developmental cleavage rates at 18 h pi.

RESULTS: Concerning MPN zygotes, higher arresting rates were observed in 0.24mM and 0.48mM 6-DMAP groups (averaged: 36.1%) than in 0.24mM (44.4%; p = 0.004). In 0.24mM and 0.48mM 6-DMAP groups, some zygotes exhibited an anomalous pronuclear fragmentation at the end of 6-DMAP treatment (27.8% and 7.1%, respectively). This event was never observed in 0.60mM or control groups. Morphokinetic analysis showed that regardless of 6-DMAP concentration, PNf and cleavage occurred at comparable times (averaged: 3.9h and 8.3h, respectively). Regardless of 6-DMAP concentration, arrested MPN cleaved (78.9%) and progressed to the blastocyst stages (18.2%) at comparable rates to controls (77.8%; p = 0.3 and 18.6%; p = 0.06, respectively).

As regards TPN zygotes, they were arrested at the pronuclear stage efficiently (averaged, 92.3%), regardless 6-DMAP concentration. No PN fragmentation was observed at any 6-DMAP concentration or controls. However, at 0.24mM and 0.48mM concentrations pronuclear fade significantly (less than 0.60mM group did; 2.8-8.0h vs. 1.6-4.0h; p = 0.03). Concerning developmental stage (PN, TPN, 3PN), 6-DMAP arrested 3PN (83.1%) and progressed to the blastocyst stage (33.6%) at comparable rates to controls (81.7%; p = 0.34 and 33.6%; p = 0.6, respectively), regardless 6-DMAP concentration.

CONCLUSIONS: MPN and TPN zygotes, incubated in 0.60mM 6-DMAP for 6h did efficiently arrest the first cell-cycle at the G2-stage without compromising subsequent development. This finding could have a potential applicability in CRISPR-Cas9 technology due to DSB repair pathways are critical for 6h did efficiently arrest the first cell-cycle at the G2-phase without compromising subsequent development to blastocyst, as possible pre-treatment to enhance the natural DSB repair pathways in CRISPR-Cas9 technology.

USE OF A SPECIFIC GRAVITY DEVICE TO PREDICT BLASTOCYST SEX. Alex L. Schaubhut, B.S., Charles L. Bormann, Ph.D., Manoj Kumar Kanakasabapathy, M.S., Hemanth Kandula, B.S., Hadi Shafiee, Ph.D. Brigham and Women’s Hospital, Harvard Medical School, Boston, MA. Massachusetts General Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: Failure to fertilize oocytes can be associated with both the male and female factors. However, for certain women especially with premature ovarian failure, diminished ovarian reserves or genetically transmittable diseases, donor egg may be the only available option in giving birth to a healthy child. Addition of donor eggs to a cycle significantly increases the patient’s out-of-pocket costs. Obtaining premium quality eggs that have a high chance of success may help reduce the uncertainty in patients, while potentially improve rates of pregnancy. Currently, there is no objective system that can evaluate oocyte quality and predict its developmental potential. The high predictive power of the trained network can help identify oocytes with the highest fertilization potential. Our evaluation in the network achieved a maximum predictive power of 86.0% (95% CI: 77.3% to 92.4%). In 0.6133 obtained through a ROC analysis confirmed that the network was able to differentiate between the outcomes with a reasonable degree of accuracy. After establishing that the neural network was able to differentiate oocytes based on their fertilization potential, we tuned the network to conservatively identify oocytes with the highest fertilization potential. Our results suggest that a neural network can be used to help identify the highest quality oocytes objectively based on their fertilization potential. The high predictive power of the trained network can carefully select the oocytes with the promise of improving the patient prognosis.

Support: This work was partially supported by the Brigham Precision Medicine Developmental Award (Brigham Precision Medicine Program, Brigham and Women’s Hospital) and R01AI118502, R01AI138800, and R21HD092828 (National Institute of Health).
A CLINICAL MODEL PREDICTING SUPERNUMERARY EMBRYOS IN WOMEN UNDERGOING FREEZE-ALL CYCLES UTILIZING SART CORS DATA. Yetunde O. Ibrahim, MD,⇑ Greg Stoddard, MS,⇑
Erica Johnstone, MD⇑ Utah Center for Reproductive Medicine, Salt Lake City, UT; 2Affiliation not provided; 3University of Utah, Salt Lake City, UT.

OBJECTIVE: The field of IVF has focused on embryo selection technology and multiple methods have been utilized including metabolomics, time lapse imaging and PGT-A. PGT-A was touted as the optimal method but it has recently come under scrutiny due to some evidence of euploid births from embryos found to be aneuploid on testing [1-3]. A selection method can only enhance the chances of success if we have a cohort of embryos to select from and yet, we have inadequate counseling tools for patients on their chances of having supernumerary embryos for a selection method to be applicable. We have identified factors predictive of having supernumerary embryos in freeze-all cycles. Therefore, we sought to create a clinical prediction model using those identified factors for clinical counseling.

DESIGN: Retrospective cohort study of women who underwent freeze-all cycles in 2014.

MATERIALS AND METHODS: Data were obtained from the Society for Assisted Reproductive Technology. We defined supernumerary as having two or more embryos cryopreserved. We utilized previously identified predictors and entered them into a logistic regression model presenting a receiver operating characteristic curve (ROC) for all predictors. Any predictor that did not alter the area under the curve for the ROC was removed from the prediction model. We then utilized methods described by Sullivan and colleagues [4] to modify the final model into a risk index. The number of points assigned to each significant covariate equaled its regression coefficient divided by the parameter estimated in the model with the smallest value rounded to the nearest whole number. The accuracy equaled its regression coefficient divided by the parameter estimated in the model into a risk index. The number of points assigned to each significant covariate equaled its regression coefficient divided by the parameter estimated in the model with the smallest value rounded to the nearest whole number. The accuracy equaled its regression coefficient divided by the parameter estimated in the model into a risk index. The number of points assigned to each significant covariate equaled its regression coefficient divided by the parameter estimated in the model with the smallest value rounded to the nearest whole number. The accuracy equaled its regression coefficient divided by the parameter estimated in the model into a risk index. The number of points assigned to each significant covariate equaled its regression coefficient divided by the parameter estimated in the model with the smallest value rounded to the nearest whole number.

RESULTS: Of 31,537 freeze-all cycles in 2014, 18,250 produced supernumerary embryos. We included 16,395 cycles into the logistic regression model after excluding cycles with missing AMH as this was a very strong predictor of the outcome. Table 1 demonstrates the points assigned to each necessary predictor. The area under the curve (AUC) for the ROC was 0.84.

CONCLUSIONS: Age, AMH and number of eggs retrieved are necessary predictors for the model. The AUC for the ROC is considered excellent discrimination and therefore, this model can be used to counsel patients undergoing freeze-all cycles on their probability of having supernumerary embryos for a selection method to be applicable.

TABLE 1. Points assigned to each significant covariate

<table>
<thead>
<tr>
<th>Variable (Referent)*</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&lt;35)</td>
<td>35 - 37</td>
</tr>
<tr>
<td></td>
<td>38 - 40</td>
</tr>
<tr>
<td></td>
<td>41 - 42</td>
</tr>
<tr>
<td>AMH (1.0 – 3.0)</td>
<td>&gt;42</td>
</tr>
<tr>
<td></td>
<td>&lt;1.0</td>
</tr>
<tr>
<td></td>
<td>&gt;3.0</td>
</tr>
<tr>
<td># eggs retrieved (0 – 3)</td>
<td>4 - 8</td>
</tr>
<tr>
<td></td>
<td>9 - 13</td>
</tr>
<tr>
<td></td>
<td>14 - 20</td>
</tr>
<tr>
<td></td>
<td>21 - 45+</td>
</tr>
</tbody>
</table>

*Referent category is assigned zero (0) Points Score = sum of all Points in a given individual.

*Scores = Score + 5 (automatically sets the minimum summative score to zero).


SUPPORT: None.

BLASTOCYST AND EMBRYO SCREENING SELECTION TEST (BESST): AN ULTRAFAST NON-INVASIVE EMBRYO SELECTION TEST FOR USE IMMEDIATELY PRIOR TO EMBRYO TRANSFER. Raminta Zmuidinaite, MSc,a Ricardo J. Pais, PhD,a Ray K. Ilies, PhDb, Fady I. Sharara, M.D.,c Christian Jardine, BEng,c Stephen A. Butler, PhDb. aMAP Sciences Ltd, Bedford, United Kingdom; bMAPSciences Ltd, Bedford, United Kingdom; cVirginia Center for Reproductive Medicine, Reston, VA; dTrainee software engineer, Bedford, United Kingdom; eMAP Sciences, Bedford, United Kingdom.

OBJECTIVE: Development and implementation of a novel embryo selection workflow immediately prior to transfer during routine fertility cycles.

DESIGN: A scoring algorithm for the selection of embryos based on a mass spectral profile of culture media has been developed previously. Here the algorithm was adapted and optimized to be integrated into the current routine practices of a fertility centre in the USA. The applicability and advantages of using this workflow were analyzed retrospectively using post implantation data outcomes from the cohort.

MATERIALS AND METHODS: A total of 1190 embryo cell culture media were collected and frozen prior to implantation from a single IVF clinic in the USA between March 2014 and March 2018. Samples were stored in 50μl aliquots and subsequently 1 μl was applied directly onto prepared stainless-steel plates with α-Cyano-4-hydroxycinnamic acid matrix. After drying on a hot plate, the sample plate was loaded to a Shimadzu benchtop MALDI-ToF mass spectrometer. To score embryos, we used the Blastocyst and Embryo Screening and Selection Tool (BESST) software, previously installed on the instrument. This tool provides an embryo score from mass spectral features of between 0 and 5, with 5 being the best chance of implantation and ongoing pregnancy and 0 being the least.

RESULTS: The time responses of our workflow were monitored starting from sample preparation to embryo scores reporting for candidate embryos. The total time obtained ranged between 6 to 8 minutes, which is a reasonable time to give an informative response before embryo implantation. In each cohort, comparison of blastocysts, showed substantial differences between embryos from the same cycle; indicating that some embryos had a greater chance of success when compared to others. Statistically, embryos selected with higher scores (>4) correlated with more cases of successful implantation and ongoing pregnancy with a positive predictive value of 76.9%. In comparison, those embryos with low scores (<1.5) poorly correlated with ongoing pregnancy outcome, predicting the chance of ongoing pregnancy of 35.7% or lower. In unsuccessful pregnancies, the tool was able to identify embryos from the same cycle with higher scores in comparison to the embryo transferred. This suggests that relying on BESST in these cases could have resulted in an implanted embryo and an ongoing pregnancy.

CONCLUSIONS: We have successfully implemented a fast scoring system for embryo selection that can be applied in any fertility clinic immediately prior to transfer. We further demonstrated that the integration of this workflow on current practices in fertility clinics may provide advantageous information that increases the chances of successful embryo implantation and ongoing pregnancy.
included patients undergoing IVF or intracytoplasmic sperm injection. All study participants provided informed consent and the study design was approved by the ethics committee of the IVF Nagata Clinic, Fukuoka, Japan.

MATERIALS AND METHODS: We analyzed 1,242 DC embryos with normal fertilization using a conventional-method (CM); we compared blastocyst formation rates between 3- and 4-cell groups during the first division. Ex.2: The two groups from Ex.1 were classified using ETME methods. The blastocyst formation rates of each group were compared. Embryos were evaluated for EC at 27 hours after insemination and morphology was scored on day 2 (poor, ≥ 4 cells with ≥ 50% frag.; fair, ≥ 4 cells with < 50% and ≥ 20% frag.; good, ≥ 4 cells with < 20% frag. and equal blastomere).

RESULTS: Ex.1: Among the 1,242 DC embryos, 669 were in the 3-cell group and 573 were in the 4→2-cell group. The blastocyst and high-quality blastocyst formation rates were significantly higher (p < 0.01) in the 3-cell group than in the 4→2-cell group (53.5% vs. 32.7%, 28.0% vs. 14.1%, respectively). Ex.2: Among the 669 embryos in the 3-cell group, 211 were in the EC-fair embryos, 141 were in the EC-poor embryos, 75 were in the late cleavage (LC)-fair embryos, and 242 were in the LC-poor embryos. Among the 573 4-cell group, 102 were in the EC-fair embryos, 127 were in the EC-poor embryos, 90 were in the LC-fair embryos, and 254 were in the LC-poor embryos. The blastomeres of DC embryos were unequal and no embryo was evaluated as normal fertilization using a time-lapse incubator. (TL) that allows the observation of embryos over time could be useful for identifying FC and CW under an inverted microscope. Consequently, such determination of early-rescue ICSI after short-term insemination (ESHRE 2018). However, FC is present for only short durations. In addition, in some eggs it is difficult to identify CW due to cytoplasmic texture. Consequently, such determinations, when based upon one observational time point under an inverted microscope, can sometimes be difficult. Thus, we investigated whether a time-lapse incubator (TL) that allows the observation of embryos over time could be useful for identifying FC and CW.

DESIGN: We analyzed 6,704 mature eggs from 2,212 cycles of 1,438 individuals that were collected and then subjected to IVF between 2014 and 2017. MATERIALS AND METHODS: We performed insemination at 12:00, removed cumulus cells 5 hour after insemination, and then checked for the presence of the second polar body (2PB), FC, and CW under an inverted microscope. We repeated the observation when FC or CW was not identified, even in the presence of 1PB and 2PB. In a conventional-method group, we performed the second and subsequent observations for fertilization signs every 1-hour under an inverted microscope. Meanwhile, in the TL group, we performed observations for fertilization signs every 1-hour using time-lapse imaging. In both groups, we considered the observation of 2PB extrusion, or the observation of either FC or CW, to be a sign of fertilization. When no fertilization sign was identified by 19:00, we conducted rescue ICSI. We then compared the proportions of positive FC and CW identification, as well as differences in the accuracy of determination between the conventional-method and TL groups. A 2PB was observed in 296 cycles in the conventional-method group and 2548 oocytes in the TL group. The proportions of positive fertilization signs by FC were 13.0% and 19.9% in the conventional-method and TL groups, respectively, indicating that the proportion was significantly higher in the TL group. Meanwhile, those by CW were 70.1% and 62.2% in the conventional-method and TL groups, respectively, indicating that the proportion was lower in the TL group. The infertility rates of the embryos determined to have FC and CW were 3.1% and 1.0%, respectively, in the conventional-method group, and 0.2% and 0.1%, respectively, in the TL group; thus, the rate of infertility was significantly reduced in the TL group.

CONCLUSIONS: Observation over time improves the accuracy of diagnosis for FC and CW, which makes time-lapse observation very useful for determining fertilization signs. Reference: None. SUPPORT: None.

P-424 Wednesday, October 16, 2019 6:30 AM
SPERM DNA FRAGMENTATION REDUCES EMBRYO DEVELOPMENT AND ONGOING PREGNANCY IN COUPLES WITH NON-MALE FACTOR INFERTILITY UNDERGOING INTRACYTOPLASMIC SPERM INJECTION CYCLES. Matheus de Castro Azevedo, BSc.a, Bianca Ferrari Zanetti, PhD.b, Daniela Paes de Almeida Ferreira Braga, PhD.c, Amanda Souza Setti, MSc.c, Assumpito Iaconelli Jr., MD.d, Edson Borges Jr., Ph.D.e, Fertility Medical Group, Sao Paulo, Brazil; Sapientiae Institute, Sao Paulo, Brazil; Fertility Medical Group / Sapientiae Institute, Sao Paulo, Brazil.

OBJECTIVE: Nearly 15% of infertile men have semen parameters within normal reference ranges, which underlines that there must be others subcellular or nuclear factors, which are not identifiable by conventional semen analysis, that may contribute to male infertility. The value of SDF testing to improve the determination of the reproductive status of men that has neither altered seminal parameter nor history of male factor infertility still has to be determined. The objective of this study was to investigate the possible implications of sperm DNA fragmentation (SDF) for the outcomes of intracytoplasmic sperm injection (ICSI) in couples with non-male factor infertility. DESIGN: Prospective cohort study.

MATERIALS AND METHODS: This study included data from 475 non-male factor infertility ICSI cycles, performed from June/2016 to June/2017, in a private university-affiliated IVF center. The sample size calculation suggested that 416 cycles would be enough to demonstrate a 20% effect with 80% power and 5% significance level. Semen samples were evaluated for sperm count, motility, morphology and SDF. Sperm DNA Fragmentation was measured using a Sperm Chromatin Dispersion (SCD) test. Cycles were divided according to SDF index into two groups: low fragmentation index (≤ 30% SDF, n = 433) and high fragmentation index (> 30% SDF, n = 42). Laboratory and clinical outcomes were compared between groups using generalized linear models with linear distribution followed by Bonferroni post hoc test, with adjustment for potential confounders.

RESULTS: Fertilization rate was similar between groups (≥ 30% SDF: 85.28±1.06% vs. < 30% SDF: 90.68±3.61%, p = 0.153). Significant lower rates of normal cleavage speed (≥ 30% SDF: 61.12±2.41% vs. < 30% SDF: 72.53±1.24%, p = 0.010), high-quality embryos on day three (≥ 30% SDF: 42.8% vs. < 30% SDF: 56.41±1.53%, p = 0.021), blastocyst formation rate (≥ 30% SDF: 39.09±2.73% vs. < 30% SDF: 58.83±7.59%, p = 0.016) and high-quality blastocyst rate (≥ 30% SDF: 11.97±1.22% vs. < 30% SDF: 30.09±2.39%, p < 0.001) were observed in cycles with higher SDF. Implantation rate was significantly reduced in the SDF ≥ 30% group (33.24±1.66% vs. < 30% SDF: 46.40±4.61%, p = 0.001), despite the similar pregnancy rates (≥ 30% SDF: 30.40% vs. < 30% SDF: 32.40%, p = 0.862). A 2.5-fold increase in the miscarriage rate was observed in cycles with SDF above the established cutoff (≥ 30% SDF: 42.8% vs. < 30% SDF: 16.8%, p = 0.018).

CONCLUSIONS: High SDF index leads to poor embryo development, and reduced implantation and ongoing pregnancy in couples with non-male factor infertility. Sperm DNA fragmentation testing may reveal hidden sperm abnormalities in men who have been categorized into idiopathic infertility based on apparently normal standard sperm parameters, bringing additional information to sperm quality evaluation in men with unknown history of infertility.

Reference: NA. SUPPORT: None.

P-425 Wednesday, October 16, 2019 6:30 AM
EFFECT OF SPERM SELECTION TECHNIQUES ON HUMAN NEONATAL GENDER RATIO IN PATIENTS UNDERGOING ICSI. Khaled Mohamed Elqusi, BSc.a, Khaled Mohamed Hassanen, BSc.a, Hanaa Ahmed Alkhader, MBch.b, Hosam Zaki, MBchb , Msc, FRCOG.c, Ralf Henkel, PhD.d

FERTILITY & STERILITY®
OBJECTIVE: To investigate the effect of commonly used sperm selection techniques, density gradient centrifugation (DGC), physiological ICSI (PICSI), and magnetic activated cell sorting (MACS), on the neonatal gender ratio of ICSI outcome.

DESIGN: Retrospective cohort study comparing the effect of sperm selection on gender ratio in three groups through statistical data analysis. ClinicalTrials.gov Identifier: NCT01922568.

MATERIALS AND METHODS: A total of 529 babies of known gender born out of 388 ICSI cycles between August 2016 and May 2018 at Ganin Fertility Center, Cairo, Egypt, were investigated for the gender ratio and then divided into three groups according to the sperm selection technique used before performing sperm injection: DGC (237 neonates out of 173 ICSI cycles), PICSI (147 neonates out of 109 ICSI cycles), and MACS (145 neonates out of 106 ICSI cycles). In PICSI and MACS groups, the sperm samples were processed by DGC prior to sperm selection. All embryos transferred were at the blastocyst stage. Power analysis was done by comparing the sex ratio of the neonates between DGC, PICSI and MACS. The chi-squared test for independent samples was chosen to perform the power analysis with α=0.05. P values less than 0.05 were considered statistically significant. All statistical calculations were done using IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows.

RESULTS: Sperm selection using DGC, PICSI and MACS leads to different male ratios. The highest male ratio was observed in the MACS group (62.7%) compared to the DGC group (46.4%) (P=0.002) with statistical power of (76.5%). In contrast, there was no difference (P=0.2) between the PICSI group with a male ratio of (53.1%) and the DGC group (46.4%). The PICSI and MACS groups also did not differ significantly (P=0.09). Moreover, there was neither a significant difference in female age (Mean±SD) between DGC (29.9±5.2 yrs.), PICSI (29.9±4.5 yrs.), and MACS (30.6±4.8 yrs.) (P=0.45), nor in the male age of DGC (34.99±6.4 yrs.), PICSI (36.2±6.2 yrs.) and MACS (36.2±7.7 yrs.) (P=0.22).

CONCLUSIONS: The use of MACS as sperm selection technique significantly alters the neonatal sex ratio at birth in favor of male offspring. Further investigations should be made on phospholipid phosphatidylserine externalization which might be a useful marker during MACS sperm separation and it’s possible association with sex chromosome may provide some evidence for an association between semen quality and sex ratio of the offspring. To verify the outcome of higher male ratio in the PICSI group is needed, future studies with larger number of subjects are needed to compare PICSI with DGC.

SUPPORT: N/A.

P-427 Wednesday, October 16, 2019 6:30 AM

DAY 2 ICSI DOES RESULT IN GOOD QUALITY BLASTOCYST DEVELOPMENT AND PREGNANCY.

Rebecca Kile, MS,a Haleigh Silz, MS,a Sue McCormick, BS,a William B. Schoolcraft, MD,a Rebecca L. Krisher, PhD,b Colorado Center for Reproductive Medicine, Lone Tree, CO; bCCRM, Lone Tree, CO.

OBJECTIVE: Poor prognosis patients are often faced with negative IVF cycle outcomes, in which no or very few blastocysts are produced. Utilizing immature eggs recovered at oocyte retrieval may increase their chance of success. The aim of this study was to determine the efficacy of in vitro maturation of immature oocytes recovered in a standard IVF cycle, matured in vitro and fertilized with ICSI (D2, or rescue, ICSI), with respect to good quality blastocyst yield and establishment of pregnancy.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: After oocyte retrieval, cumulus oocyte complexes (COC) were denuded of cumulus cells. Mature oocytes (MII) were fertilized by ICSI (D1); immature oocytes at the germinal vesicle (GV) or metaphase I (MI) stage were placed into Oocyte Handling Medium for Maturation (OHM Mat) and incubated overnight. ICSI (D2) was performed on all oocytes that matured to MI. Zygotes (2PN) were cultured in sequential culture medium for 5-7 days when good quality blastocysts were biopsied for PGT-A and vitrified.

RESULTS: A total of 165 patient IVF cycles in 2018 in which D2 ICSI was performed were reviewed (average age 37.8 yr±SEM, range 27-47). There were 2,101 oocytes retrieved; 1,325 (63.1%) were MII, 363 (17.3%) were MI, and 408 (19.4 %) were GV. After IVM, 527/771 oocytes matured (68.4%). ICSI on D1 resulted in higher (P<0.01) normal fertilization (63.3%) than on D2 (56.5%), and improved (P<0.01) cleavage (D1, 101.2%; D2, 85.9%). In total, 36 patients (21.8%) that underwent D2 ICSI produced a good quality blastocyst from eggs that were immature at retrieval. Total good quality blastocyst (> grade 3BB) development (per 2PN) for Day 2 ICSI was 20.8% across all patients. Within patients that had blastocyst development from D2 ICSI eggs, there was no difference (P>0.05) in total blastocyst production per 2PN between D1 (52.0%) and D2 (53.0%), or in euploid blastocysts (D1, 47.5%; D2, 38.9%). Three D2 ICSI euploid blastocysts have been transferred into three individual patients, resulting in 1 negative hCG, 1 biochemical pregnancy, and one ongoing pregnancy. For two of these patients, no D1 euploid blastocysts were produced.

CONCLUSIONS: Retaining immature oocytes and performing Day 2 ICSI can yield good quality euploid blastocysts capable of supporting a pregnancy, although fertilization and embryo cleavage rates are reduced. Although the percentage of patients that may ultimately benefit from D2 ICSI is low, for poor prognosis patients these rescued immature oocytes may produce the only euploid blastocysts available for FET. Thus, incorporating D2 ICSI into the treatment protocol gives poor prognosis patients the best chance at ART success.

SUPPORT: None.
OBJECTIVE: To determine the effect of sperm selection techniques for abnormal sperm DNA fragmentation (SDF) patients on the blastocyst grading, implantation and pregnancy rates compared to normal SDF.

DESIGN: Retrospective cohort study included 501 couples who underwent ICSI in Ganin Fertility Center from January 2017 to January 2019.

MATERIALS AND METHODS: Cases were assigned to normal SDF (125 couples) using ejaculated sperm processed by density gradient centrifugation (DGC) using Isolate and abnormal SDF group (376 couples) which subdivided to: 70 cases as ejaculated sperm processed by (DGC), 128 cases as physiological ICSI (PICSI) using ejaculated sperm selected by hyaluronan binding PICSI dishes, 107 cases as ejaculated sperm selected by magnetic activated cell sorting columns (MACS) using Annexin V microbead labeling followed by column separation and 71 cases using testicular sperm (TESTI). All included cases reached the blastocyst stage, female age was 37 years old and male with ≥ 5 millions of sperm count. SDF test was done by TUNEL assay and bench-top flow cytometry. Blastocyst morphological assessment was carried out by experienced embryologists, high-quality blast is defined as ≥ 3BB Grade according to Gardner’s criteria. The data were collected and results were analyzed using statistical Software. The difference is considered significant if P value is ≤ 0.05.

RESULTS: There were no significant differences in male age, female age, number of MII oocytes or number of embryos transferred between the groups.

CONCLUSIONS: PICSI and MACS has superiority over TESTI as sperm selection techniques for patients with abnormal SDF and could improve the embryological and clinical parameters to the normal level. These findings should be confirmed by larger prospective randomized studies.

REFERENCES: 1- Itai Gat, Katelynn Tang, Kevin Quach, Valeriy Kuznyetsov, Ran Antes, Melissa Filice, Khaled Zohni, Clifford Librach; Sperm DNA fragmentation index does not correlate with blastocyst aneuploidy or morphological grading, PLoS ONE, 2017.

SUPPORT: None.

<table>
<thead>
<tr>
<th>Normal</th>
<th>SDF %</th>
<th>DGC %</th>
<th>PICSI %</th>
<th>MACS %</th>
<th>TESTI %</th>
<th>P values of Normal vs. DCG</th>
<th>P values of Normal vs. PICSI</th>
<th>P values of Normal vs. MACS</th>
<th>P values of Normal vs. TESTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDF</td>
<td>14.3</td>
<td>28.6</td>
<td>29.3</td>
<td>29.3</td>
<td>29.6</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Fertilization rate</td>
<td>78.5</td>
<td>78.1</td>
<td>75.9</td>
<td>76.5</td>
<td>71.7</td>
<td>0.88</td>
<td>0.07</td>
<td>0.29</td>
<td>0.01</td>
</tr>
<tr>
<td>Blastulation rate</td>
<td>65.6</td>
<td>58.1</td>
<td>59.6</td>
<td>59.3</td>
<td>53</td>
<td>0.01</td>
<td>0.02</td>
<td>0.04</td>
<td>0.00</td>
</tr>
<tr>
<td>High quality blast rate</td>
<td>54.6</td>
<td>48.9</td>
<td>56.1</td>
<td>54</td>
<td>42.6</td>
<td>0.09</td>
<td>0.60</td>
<td>0.85</td>
<td>0.01</td>
</tr>
<tr>
<td>Good TE*</td>
<td>18.9</td>
<td>17.1</td>
<td>21.6</td>
<td>17.3</td>
<td>15.5</td>
<td>0.24</td>
<td>0.73</td>
<td>0.16</td>
<td>0.10</td>
</tr>
<tr>
<td>*Trophoectoderm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fair TE</td>
<td>34.7</td>
<td>30.2</td>
<td>32.1</td>
<td>35.2</td>
<td>24.3</td>
<td>0.09</td>
<td>0.35</td>
<td>0.63</td>
<td>0.00</td>
</tr>
<tr>
<td>Poor TE</td>
<td>7.6</td>
<td>6.3</td>
<td>9.5</td>
<td>8.4</td>
<td>12.4</td>
<td>0.51</td>
<td>0.28</td>
<td>0.84</td>
<td>0.66</td>
</tr>
<tr>
<td>Good ICM*</td>
<td>32.8</td>
<td>30.9</td>
<td>35.1</td>
<td>31.2</td>
<td>29.4</td>
<td>0.21</td>
<td>0.61</td>
<td>0.50</td>
<td>0.18</td>
</tr>
<tr>
<td>*Inner cell mass</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fair ICM</td>
<td>26.5</td>
<td>21.1</td>
<td>27.5</td>
<td>28.2</td>
<td>21.6</td>
<td>0.03</td>
<td>0.97</td>
<td>0.64</td>
<td>0.02</td>
</tr>
<tr>
<td>Poor ICM</td>
<td>1.5</td>
<td>1.7</td>
<td>0.9</td>
<td>1.7</td>
<td>2.2</td>
<td>1.00</td>
<td>0.49</td>
<td>0.21</td>
<td>0.79</td>
</tr>
<tr>
<td>Pregnancy rate</td>
<td>66.3</td>
<td>51.6</td>
<td>61.4</td>
<td>61.1</td>
<td>54.3</td>
<td>0.06</td>
<td>0.46</td>
<td>0.44</td>
<td>0.11</td>
</tr>
<tr>
<td>Ongoing pregnancy rate</td>
<td>62.2</td>
<td>41.9</td>
<td>59.6</td>
<td>58.9</td>
<td>50.0</td>
<td>0.01</td>
<td>0.70</td>
<td>0.63</td>
<td>0.11</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>47.9</td>
<td>33.7</td>
<td>48.0</td>
<td>42.2</td>
<td>38.6</td>
<td>0.02</td>
<td>0.59</td>
<td>0.31</td>
<td>0.14</td>
</tr>
<tr>
<td>Miscarriage rate</td>
<td>2.0</td>
<td>8.1</td>
<td>3.0</td>
<td>2.1</td>
<td>4.3</td>
<td>0.11</td>
<td>1.00</td>
<td>1.00</td>
<td>0.65</td>
</tr>
</tbody>
</table>
OBJECTIVE: To investigate the effectiveness of immobilized acid-solubilized zona pellucida in the selection of spermatozoa for intracytoplasmic sperm injection (ICSI).

DESIGN: A prospective sibling oocytes study.

MATERIALS AND METHODS: In this study were included 113 couples who fulfilled the inclusion criteria: 1) unexplained infertility factor; 2) good quality oocytes; 3) fertilization failure for 3-5 consecutive ICSI procedures; 4) at least one oocyte at germinal vesicle stage (GV) and 5) at least four metaphase II oocytes retrieved during follicular puncture. Zonae pellucidae were isolated from the patient’s own GV. Zonae were acid solubilized and diluted in carbonate buffer (pH 9.6) for air dry immobilization on glass petri dishes. The partner’s semen was washed and placed in the dishes. The spermatozoa that adhered on the immobilized surface were used for ICSI in the half of the retrieved oocytes from each woman. The other half of the oocytes was fertilized by conventional ICSI. In total, 312 oocytes were injected with zona-selected spermatozoa (zona-selection group) and 366 oocytes were injected with conventionally-selected spermatozoa (control group). The resulted embryos from the zona-selection and the control group were used in 43 and 50 single embryo transfers, respectively. Main outcomes were fertilization rate, embryo quality, implantation rate and pregnancy rate. Statistical analysis was performed using SPSS software version 21.

RESULTS: Slightly higher fertilization rate was observed among the oocytes injected with zona-bound spermatozoa in comparison to the conventionally ICSI group (75.6% vs. 72.3%, p = 0.38). Also no significant differences were observed in the embryo quality and in the implantation rates between the zona-selection and the control group (p = 0.24 and p = 0.59, respectively). However, the pregnancy rate was considerably higher in the zona-selection group when compared with the control group (34.8% vs. 16.4%, p = 0.02). Moreover the miscarriage rate also differed significantly (7% in zona-selection vs. 18% in control group, p = 0.03).

CONCLUSIONS: The use of patient’s zona pellucida immobilized proteins in selection of spermatozoa for ICSI increases pregnancy rates and reduces the risk of miscarriage in couples with unexplained infertility and good quality oocytes.

P-430 Wednesday, October 16, 2019 6:30 AM

HIGHER PREGNANCY RATES AFTER ZONA PELLUCIDA SPERM SELECTION. Runmiana Ganeva, MSc., Dimitar Parvanov, PhD., Magdalena Vasileva, MSc., Kristina Nikolova, MSc., Georgi Stamenov Stamenov, MD./PhD. Nadezhdha Women’s Health Hospital, Sofia, Bulgaria.

OBJECTIVE: To investigate the effectiveness of immobilized acid-solubilized zona pellucida in the selection of spermatozoa for intracytoplasmic sperm injection (ICSI).

DESIGN: A prospective sibling oocytes study.

MATERIALS AND METHODS: In this study were included 113 couples who fulfilled the inclusion criteria: 1) unexplained infertility factor; 2) good quality oocytes; 3) fertilization failure for 3-5 consecutive ICSI procedures; 4) at least one oocyte at germinal vesicle stage (GV) and 5) at least four metaphase II oocytes retrieved during follicular puncture. Zonae pellucidae were isolated from the patient’s own GV. Zonae were acid solubilized and diluted in carbonate buffer (pH 9.6) for air dry immobilization on glass petri dishes. The partner’s semen was washed and placed in the dishes. The spermatozoa that adhered on the immobilized surface were used for ICSI in the half of the retrieved oocytes from each woman. The other half of the oocytes was fertilized by conventional ICSI. In total, 312 oocytes were injected with zona-selected spermatozoa (zona-selection group) and 366 oocytes were injected with conventionally-selected spermatozoa (control group). The resulted embryos from the zona-selection and the control group were used in 43 and 50 single embryo transfers, respectively. Main outcomes were fertilization rate, embryo quality, implantation rate and pregnancy rate. Statistical analysis was performed using SPSS software version 21.

RESULTS: Slightly higher fertilization rate was observed among the oocytes injected with zona-bound spermatozoa in comparison to the conventionally ICSI group (75.6% vs. 72.3%, p = 0.38). Also no significant differences were observed in the embryo quality and in the implantation rates between the zona-selection and the control group (p = 0.24 and p = 0.59, respectively). However, the pregnancy rate was considerably higher in the zona-selection group when compared with the control group (34.8% vs. 16.4%, p = 0.02). Moreover the miscarriage rate also differed significantly (7% in zona-selection vs. 18% in control group, p = 0.03).

CONCLUSIONS: The use of patient’s zona pellucida immobilized proteins in selection of spermatozoa for ICSI increases pregnancy rates and reduces the risk of miscarriage in couples with unexplained infertility and good quality oocytes.

P-431 Wednesday, October 16, 2019 6:30 AM

IMPACT OF A MODIFIED ICSI INJECTION PROCEDURE IN ART OUTCOMES: PRELIMINARY FINDINGS. Claudia G. Petersen, Ph.D.,a Ana Lucia Mauri, B.Sc.,b Mariana Mattila, B.Sc.,a Laura D. Vagnini, B.Sc.,a Adriana Renzi, Ph.D.,a Bruna Petersen, B.Sc.,a Andrea Nicoletti, R.N.,b Felipe Dieamant, M.D.,a Joao Batista A. Oliveira,a Laura D. Vagnini, B.Sc.,c Adriana Renzi, Ph.D.,c Bruna Petersen, B.Sc.,a Ana Lucia Mauri, B.Sc.,a Mariana Mattila, B.Sc.,b

OBJECTIVE: The objective of this study was to evaluate if several pushes in oolema membrane at the moment of injection together with the deposition of spermatozoon adhered onto this membrane during hyaluronic acid treatment. The objective was to evaluate if several pushes in oolema membrane at the moment of injection together with the deposition of spermatozoon adhered onto this membrane during hyaluronic acid treatment.

MATERIALS AND METHODS: A total of 178 patients who were submitted to ICSI procedure were included. At the moment of ICSI procedure, two modifications were performed: 1) modified injection procedure included those oocytes in which the injection needle was pushed once against the oocytes and introduced through the zona pellucida, where the spermatozoa was deposited. 2) modified ICSI was performed with a modified injection procedure. Modified injection procedure included those oocytes at the moment of the injection, the injecting needle was pushed at least 3 times against the oocytes and introduced through the zona pellucida, where the spermatozoa was deposited.

The following parameters were evaluated in each group: patient age, number of oocytes in metaphase II retrieved, fertilization rate, number of embryos transferred, implantation rate and pregnancy rate.

RESULTS: Patients who had their oocytes injected by a modified injection procedure showed an adequate fertilization (64.9%), and higher implantation rate (25%), pregnancy rate/cycle (42%) and pregnancy rate/transfer (46%) compared with those patients in which a standard ICSI injection procedure was performed (fertilization rate: 62.2%, implantation: 14.7%, pregnancy rate/cycle: 23%, pregnancy rate/transfer: 26%). A decrease in fertilization failures was also observed in the group 2 (modified ICSI), however not significant. Table 1 shows the results.

CONCLUSIONS: The modified injection ICSI procedure seems to be useful for improve implantation and clinical pregnancy rates, with satisfactory results. Additional date will be important to provide more information.

P-432 Wednesday, October 16, 2019 6:30 AM

CONSIDERATION OF LOW-INVASIVE ICSI (NBP-ICSI) USING A NON BEVEL PIPET. Satoshi Akimoto, Bachelor, Ayumi Hamaki, Bachelor, Wakana Bekku, MD, Jun Matsukawa, MD, Miwa Sato, MD, Shuichiro Haru, MD, PhD, Hiroto Tajima, MD, PhD, Hironori Asada, PhD, Nadezhda Women’s Health Hospital, Sofia, Bulgaria; Dimitar Parvanov, PhD, Magdalena Vasileva, MSc, Magdalena Vasileva, MSc, Magdalena Vasileva, MSc, Magdalena Vasileva, MSc.

OBJECTIVE: During intracytoplasmic sperm injection (ICSI), degeneration of punctured ovum is often encountered due to the high probability of a weakened egg membrane. In response to such cases, low-invasive ICSI using a Non Bevel Pipet (NBP-ICSI) is performed at this hospital. Consequently at this time, achievement of this procedure was considered.

DESIGN: Cases with a history of weakened egg membrane and high rate (10% and higher) of degeneration were divided in two periods, a period when NBP-ICSI was implemented, and a period when conventional-ICSI (C-ICSI) was implemented. Culture achievement between the two groups was retrospectively considered.

MATERIALS AND METHODS: NBP-ICSI: An incision is made into a section of the zona pellucida using a PZD pipet, during hyaluronic acid treatment. During ICSI, a Non Bevel Pipet manufactured for use in PIEZO-ICSI is processed and used. The Non Bevel Pipet is inserted from the slit made in Q, and ICSI is performed.

C-ICSI: ICSI is performed using a regular ICSI pipet.

Evaluating items, including fertilization rate for each ICSI method, degeneration rate after ICSI, blastocyst formation ratio, favorable blastocyst ratio at Day 5, embryo use ratio, were compared and considered.

RESULTS: Regarding culture achievement for NBP-ICSI, fertilization rate: 69.2%(110/159), degeneration rate after ICSI: 7.8%(13/159), blastocyst formation ratio: 49.4%(43/87), favorable blastocyst ratio at Day 5(15/87) 21.8%, and embryo use ratio: 36.4%(40/110) were obtained. Culture achievement for C-ICSI was fertilization rate: 67.0%(126/188), degeneration rate after ICSI: 8.2%(13/159), blastocyst formation ratio: 49.4%(43/87), favorable blastocyst ratio at Day 5(19/87) 21.8%, and embryo use ratio: 36.4%(40/110) were obtained.

From the results, NBP-ICSI showed a significant lower degeneration rate after ICSI. No significant difference was observed in other evaluation items.

CONCLUSIONS: Achievement of low-invasive ICSI using NBP-ICSI showed the same level of achievement as PIEZO-ICSI which has been reported by many facilities, indicating the possibility of reducing the degeneration rate in cases which have a higher degeneration rate after ICSI. However, since no difference was observed for the evaluation items other than the degeneration rate, basic problems during fertilization and development due to a weakened egg membrane in ICSI still remain and are not thought to be resolved even if invasiveness in ICSI is reduced. In the consideration at this time, the fact that this method has lower invasiveness in ICSI could be
clarified, and the same level of achievement as PIEZO-ICSI or even better can be expected. In the future, expanding the application range of this method to cases with normal egg membranes, along with further consideration as to whether NBP-ICSI can improve culture achievement or not, is desired.

ART LAB - SPERM

P-433 Wednesday, October 16, 2019 6:30 AM
WHAT IS THE BEST SPERM SOURCE AND METHOD OF SPERM SELECTION IN CASES WITH ABNORMAL SEMINAL OXIDATION-REDUCTION POTENTIAL (ORP) LEVELS ON THE DAY OF ICSI?
Emam Mohamed Hassanen, BSc, a, b Khaleed Mohamed Elqusi, BSc, a Yasmine sayed Azzour, BSc, a Hanaa Ahmed Alkhader, MBChb, a Hosam Zaki, MBChb, Msc, FRCOG, a Ralf Henkel, PhD, b Ashok Agarwal, PhD, c d

OBJECTIVE: To investigate whether PICSI or TESA is better for the selection of sperm in cases of abnormal seminal ORP levels for ICSI patients.

DESIGN: Prospective randomized trial, which included 74 patients undergoing ICSI at a busy Fertility Clinic, Cairo, Egypt, from January 2018 to January 2019. ClinicalTrials.gov ID: NCT03365026.

MATERIALS AND METHODS: A total of 74 patients with sperm counts of more than 5x10^6/mL and an ORP of more than 1.42 mV/10^6/mL were included in the study. Male partners were examined for infertility and seminal ORP was measured using the MiOXSYS analyser. PICSI dishes (Origio, Knaardrupvej, Denmark) were prepared by hydrating the hyaluronan microdots with medium followed by incubation for sperm binding at 30°C. Sperm were checked for the hyaluronan binding capacity, immobilized and injected into mature oocytes. TESA was done by testicular tissue aspiration followed by sample processing and oocyte injection. Seminal ORP was tested in the same ejaculate that was used for ICSI and patients with abnormal ORP were randomized into two arms, PICSI (n=40) and TESA (n=34). Embryological parameters included: fertilization, cleavage, blastulation and good quality blastocyst rate were recorded. Pregnancy was followed up after 15 days of embryo transfer and pregnancy rate calculated. All statistical calculations were done using SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows.

RESULTS: There were no significant differences in the female age (30.1±4.58 vs. 29.2±4.16 yrs.) (P=0.5369), male age (36.4±5.87 vs. 34.6±6.44 yrs.) (P=0.2041), seminal ORP values (5.8±6.22 vs. 5±7.99 mV/10^6 sperm/ml) (P=0.9808) and the number of mature injected oocytes (15.7±7.8 vs. 16.8±7.7) (P=0.5631) between the PICSI and TESA groups, respectively. The blastulation rates between PICSI and TESA showed a significant difference (60.2% vs. 48.4%; P=0.0114). In contrast no difference in ORP level was seen between PICSI and TESA, for fertilization (79.8% vs. 80.7%), cleavage (73.4% vs. 73.8%), high quality blastocyst (57.2% vs. 51.9%), pregnancy (67.8% vs. 50%), implantation (41.6% vs. 36.6%), and ongoing pregnancy rates (94.7% vs. 84.6%). There were also no correlations between ORP levels and fertilization (P=0.1523 R=-0.1792), cleavage (P=0.1475, R= -0.1724), blastulation (P=0.1763, R=-0.1623), and the percentage of high quality blastocyst formation (P=0.0992, R=-0.2055). The mean ORP level for the pregnant group was 6.36±6.98 mV/10^6 sperm/ml as compared to 6±8.1 mV/10^6 sperm/ml in the non-pregnant group (P=0.9891).

CONCLUSIONS: The use of PICSI as a sperm selection method in patients with abnormal seminal ORP levels may result in better selection of sperm and improved blastulation rate. Thus, contrary to reports in the literature that TESA-retrieved sperm are unexposed to seminal reactive oxygen species, our study failed to show the advantage of TESA over PICSI dishes.

P-434 Wednesday, October 16, 2019 6:30 AM
INVESTIGATION OF DEEP LEARNING BASED DETECTION OF SPERM MORPHOLOGICAL DEFECTS. Hidetoshi Yamashita, M.S., a Nobuko Yausi, M.S., a Nozomi Uchida, M.S., a Yuri Sukenohe, M.S., a Megumi Ibayashi, B.S., a Masato Saito, B.S., a Kenichiro Hirooka, Ph.D, a Kiyotaka Kawai, M.D.Ph.D, a Miraca Research Institute G.K., Hachioji, Japan; b Kameda IVF Clinic Makuhari, Chiba, Japan; c Kameda Medical Center, Kamogawa, Japan.

OBJECTIVE: Sperm selection in intracytoplasmic sperm injection (ICSI) is generally performed by embryologists’ subjective visual inspection, and developing the method of an objective sperm selection and evaluation is necessary. In this study, we focused on the evaluation of sperm morphology and aimed to investigate the method to detect morphological abnormalities by computer analysis using deep learning models and to evaluate their performances.

DESIGN: We extracted still images of sperm from the videos, which were recorded during ICSI, and embryologists inspected the sperm morphology. We constructed models from these still images and embryologists’ inspection results. We evaluated the accuracy to detect morphological defects and visualized the important region for prediction of abnormality by these models.

MATERIALS AND METHODS: We used a set of 1,095 images of morphologically normal sperms, which succeeded in fertilization, and another set of 475 images of morphologically abnormal sperms, which were not used for ICSI. Embryologists visually inspected these sperms and identified their morphologically abnormal sites. We conducted 2 kinds of classification. The first is whether the sperm has morphological defects. The second is which portion has morphological defects among 3 classes of the head only, both head and neck, and none. These images were analyzed with 2 kinds of convolutional neural network (deep learning) models, which were a simple model with 9 hidden layers and the VGG16 model with 22 hidden layers and pre-trained parameters in the important layers. We compared these model performances and examined the accuracy improvement in image size and class weight adjustment in inverse proportion to imbalanced data.

RESULTS: The discrimination accuracy on the morphological abnormality of the sperm in the VGG16 model was 95.6% (AUC 0.988) in 224 pixels square images, and this was better than that of the 9 hidden layers model (Accuracy 83.2%, AUC 0.959). The abnormal site classification accuracy in the VGG16 model was 87.1% (AUC 0.958). The class weight adjustment could improve the accuracy in neither the VGG16 model nor the 9 hidden layers model. On the other hand, we got similar accuracy using 64 pixels square images but we found that the models learned background noises in images through visualization of the important region.

CONCLUSIONS: We confirmed that the deep learning models on sperm morphology can properly identify morphological defects at high accuracy. This suggested that these models will be able to support in selecting objectively morphologically normal sperm in the future. Our models could work well even in class-imbalanced data, and the class weight adjustment was not necessary for imbalanced data. However, if the image resolution is insufficient for appropriate learning, these models could not learn well even if the accuracy of the model was high. Therefore, the visualization of important region is needed for validation of learning models. In this study, the number of samples is limited at a single facility, and we are going to add much more samples in multiple facilities to validate our method.

SUPPORT: Miraca Research Institute G.K.
OBJECTIVE: Semen analysis (SA) fails to evaluate fertilizing ability and best identifies extreme infertility cases. Cap-Score™ functionally assesses sperm capacituation/male fertility and prospectively predicts pregnancy. Here, we examine the association of SA, Cap-Score, and Cap-Score’s relationship with the probability of generating pregnancy in 3 cycles (PGP; Schinfeld et al., 2018), in men having fertility exams vs fertile men.

DESIGN: Correlation study: Cap-Score, PGP and SA metrics were compared in 1610 men questioning fertility vs 76 fertile men (pregnant partners or recent father).

MATERIALS AND METHODS: Semen was collected from men having SA because of fertility concerns (9 clinics; 10/2016 to 3/2019). Volume, concentration and motility were assessed (WHO criteria; morphology omitted due to variable methods). Fixed samples were shipped to Androvia for Cap-Score and PGP determination. Fertile men were assessed previously (WIRB 20152233). Table 1 was designed with even PGP bins and evaluated by Chi-square.

RESULTS: 59% (948/1610) of men having SA were normospermic (volume, concentration, motility). Compared to fertile men (p<0.001), more men having fertility exams had Cap-Scores ≤ 31 (PGP bins of ≤ 19, 20-29 and 30-39). Fewer than expected had Cap-Scores ≥ 32 (PGP bins of 40-49, 50-59 and ≥ 60). This distribution revealed a high prevalence of reduced capacitation/fertilizing ability in men having fertility exams. Defects in sperm function were equally prevalent regardless of passing any single or multiple SA metrics, or those having >10 million total motile cells (TMC; p=0.990).

CONCLUSIONS: Of normospermic men having fertility exams, 65% (616/948) had Cap-Scores ≤ 31 (PGP ≤ 39%); in contrast, only 25% of fertile men (19/76) scored in this range. Conversely, only 35% (332/948) of normospermic men questioning their fertility had Cap-Scores ≥ 32, in contrast to 75% of fertile men. These data support reports that reduced sperm function/fertilizing ability is common in men questioning their fertility and cannot be detected by traditional SA, contributing to the high percentage of men diagnosed with idiopathic infertility. In men having fertility exams, reduced Cap-Scores were detected equally in normospermic men vs all men examined. These data show that a test of sperm capacituation offers a powerful complement to traditional SA, capable of identifying normospermic men with reduced sperm fertilizing ability. Reference: Schinfeld et al.Â Cap-Score™ prospectively predicts probability of pregnancy. Molecular Reproduction and Development. 2018; 85 (8-9), 654-664

SUPPORT: Androvia LifeSciences LLC.

P-436 Wednesday, October 16, 2019 6:30 AM

PATERNAL CONTRIBUTION TO EARLY EMBRYONIC DEVELOPMENT IN SEVERE MALE FACTOR PATIENTS. Jenna Friedenthal, MD, a Dmytro Gouko, MA, a Joseph A. Lee, BA, b Christine Briton-Jones, PhD, HCLD, a Alan B. Copperman, MD, c Icahn School of Medicine at Mount Sinai, New York, NY; c Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Current evidence suggests that the paternal genome is primarily responsible for embryonic development during the cleavage stage, at which time, expression of paternal genes occurs along with activation of the embryonic genome [1]. Theoretically, sperm could influence earlier post-fertilization events, since defects in the sperm centrosome have the potential to compromise early cell division. Additionally, sperm DNA damage has been shown to adversely affect embryo quality as early as day 2 of development [2]. Evidence regarding the association between severe male factor infertility and embryonic development, embryonic aneuploidy, or clinical outcomes within in vitro fertilization (IVF) cycles utilizing intracytoplasmic sperm injection (ICSI) is contradictory [3]. Thus, we sought to assess the relationship between severe male factor infertility and early embryonic development in an IVF model that includes ICSI and preimplantation genetic testing for aneuploidy (PGT-A).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Our study included patients at a single academic center who underwent IVF-ICSI-A cycles from 2011 to 2019. ICSI was used in all study cases. Patients were divided into 2 cohorts: severe oligospermia (<5 million/mL), and normal semen analyses (SA) (≥ 5 million/mL). The primary outcome was cleavage rate (CR). Secondary outcomes were fertilization rate (FR), blastulation rate (BR), euploid rate (ER), ongoing pregnancy/live birth rate (OP/LBR), and clinical loss rate (CLR). Student’s t-test, chi-squares, and multivariate logistic regression analyses were used for statistical analysis, with p<0.05 considered significant.

RESULTS: A total of 3,029 patients underwent 3,488 IVF-ICSI-A cycles during the study period, leading to 4,716 single, euploid frozen embryo transfers. In our unadjusted analysis, the FR and CR were significantly lower in the severe oligospermia group compared to the normal SA group (FR 82.30% vs 77.78%, p<0.0001; CR 99.25% vs 98.23%, p = 0.007). There were no significant differences in BR, ER, or clinical pregnancy outcomes between the groups. After performing an adjusted analysis that controlled for confounding factors, a significant difference in CR between the oligospermia group and the normal SA group (β = 0.99, p = 0.03) remained.

CONCLUSIONS: In the largest study to date evaluating the association between the paternal genome and embryonic development, we demonstrated that oligospermic samples are associated with impaired early embryo development. Our results provide new insight into the role of the paternal genome in embryonic development prior to activation of the embryonic genome. Future studies should aim to examine more closely paternally-derived genomic actions, including epigenetic factors such as paternal centrosome function, chromatin packaging, or histone modification, which impact successful cell division and growth prior to the cleavage stage in severe male factor patients. Our findings may lead to a better understanding of the ways in which paternal-paternal genomic interactions drive early embryonic development.


SUPPORT: None.

P-437 Wednesday, October 16, 2019 6:30 AM

DOES THE USE OF MICROFLUIDIC SPERM SORTING FOR THE SPERM SELECTION IMPROVE IVF SUCCESS RATES IN MALE FACTOR INFERTILITY? Pinar Ozcan, MD, Assoc. Prof., a Taha Takmaz, MD, a Melis Gökçe Kocer Yaziçi, MD, b Oya Akcin Alagoz, MD, Assoc. Prof., c Mert Yesildalı, MD, c Cem Neset Fıçıoğlu, MD, c
OBJECTIVE: IVF success rate may improve with the selection of viable, motile, and morphologically intact sperm.

CONCLUSIONS: Microfluidic devices, "labs-on-a-chip," are a disposable, easy to use, and inexpensive method for sperm sorting. Our results show that IVF success rates may improve with the use of a microfluidic sperm-sorting chip.

MATERIALS AND METHODS: We analyzed outcomes of 148 patients with AZFc microdeletions undergoing 205 cycles with ejaculated and testicular sperm, 176 iNOA patients undergoing 265 cycles with ejaculated and testicular sperm and 177 azoospermic patients with AID sperm undergoing 284 cycles between September 2015 and September 2018. Experiment groups: group A, testicular sperms for ICSI in aPAZFcM; group B, ejaculated sperm for ICSI in patients with AZFc microdeletions; group C, testicular sperm for ICSI in iNOA patients; group D, ejaculated sperms for ICSI in iNOA patients. Control group (group E): AID sperm for ICSI in azoospermic patients. The parameters were fertilization rate (FR), 2PN cleavage rate (2PNCR), blastocyst formation rate (BFR), implantation rate (IR), cumulative pregnancy rate (CPR), cumulative live-birth rate (CLBR), cumulative miscarriage rate (CMR) and Cancelled Cycle Rate (CCR). Analysis of categorical variables was evaluated with χ2 or Fisher’s exact tests. A level of P<0.05 was considered statistically significant.

RESULTS: Comparing group A, group B has shown better ICSI outcome with statistically significant differences in FR, BFR, CPR, CLBR and CCR between the two groups (all p values were less than 0.02), while iNOA patients had similar ICSI outcomes either with testicular or ejaculated sperm. The group B, D and E had similar outcomes. The group E has exhibited much better ICSI outcome than group A with statistically significant differences in FR, BFR, IR, CPR, CLBR and CCR between the two groups (all p values were less than 0.005), while it was just little better than group C. The CCR is the highest in group A, and the FR is the highest in group E among all five groups.

TABLE 1. Sperm parameters and cycles characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (n=71)</th>
<th>Group II (n=68)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm count (million/ml)</td>
<td>15.49±17.47</td>
<td>30.94±27.14</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Ejaculate volume (ml)</td>
<td>3.68±1.52</td>
<td>3.92±1.90</td>
<td>0.67</td>
</tr>
<tr>
<td>Morphologically normal spermatozoa (%)</td>
<td>1.08±1.16</td>
<td>2.04±1.65</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>TMSC</td>
<td>5.8±38.45</td>
<td>8.29±74.83</td>
<td>0.05*</td>
</tr>
<tr>
<td>Total dosage of gonadotropins (IU)</td>
<td>3.145±1000</td>
<td>2852±920</td>
<td>0.06</td>
</tr>
<tr>
<td>Maximum estradiol levels (pg/mL)</td>
<td>2074±1154</td>
<td>1979±1375</td>
<td>0.35</td>
</tr>
<tr>
<td>Duration of stimulations (day)</td>
<td>9.5±1.48</td>
<td>9.27±1.61</td>
<td>0.18</td>
</tr>
<tr>
<td>Endometrial thickness on hCG day (mm)</td>
<td>9.8±3.1</td>
<td>10±2.28</td>
<td>0.79</td>
</tr>
<tr>
<td>Total number of oocytes retrieved</td>
<td>9.81±6.46</td>
<td>11.1±6.86</td>
<td>0.23</td>
</tr>
<tr>
<td>Number of mature oocytes retrieved</td>
<td>6.69±4.31</td>
<td>7.76±5.16</td>
<td>0.28</td>
</tr>
<tr>
<td>Number of PN</td>
<td>5.32±3.54</td>
<td>4.38±3.37</td>
<td>0.06</td>
</tr>
<tr>
<td>Pregnancy rate</td>
<td>50.7% (68)</td>
<td>27.9% (19)</td>
<td>&lt;0.01*</td>
</tr>
</tbody>
</table>

P-438 Wednesday, October 16, 2019 6:30 AM

 WHICH IS THE BETTER CHOICE FOR THE AZOOSPERMIC PATIENTS WITH AZFC MICRODELETIONS, TESTICULAR SPERM OR DONOR SEMEN (AID) SPERM? Li Zhang, Ph.D,a Jiaming Mao, MD,b Ping Liu, MD, PhDc Jie Qiao, MD, PhDb aPeking University Third Hospital, Beijing, China; bPeking University Third Hospital, Beijing, China; cPeking University Third Hospital, BeiJing, China.

OBJECTIVE: We performed a retrospective study to investigate either testicular or AID sperm is the best choice for azoospermic patients with AZFc microdeletion.

CONCLUSIONS: Our results suggest that ICSI with ejaculated sperm is a more optimal treatment for patients with AZFc microdeletions while iNOA patients didn’t like that. ICSI with AID sperm is a better treatment for azoospermic patients with AZFc microdeletion.

SUPPORT: No.

P-439 Wednesday, October 16, 2019 6:30 AM

SPERM SELECTION WITH HYALURONIC ACID (PICSI) IMPROVES EFFICIENCY OF IVF CYCLES. Lucia Alegre, PhD,a Irene Hervas, PhD, student,b Lorena Bori Arnal, PhDb Alberto Tejera, Sr., PhDb Thamara Vitoria, PhD,a Jose Alejandro Remohi, MD, PhDb Marcos Meseguer, PhDb aIVIRMA Global, Valencia, Spain; bAffiliation not
provided; 3Embryologist, Valencia, Spain; 4IVIRMA Valencia, Valencia, Spain; 5IVIRMA Global, Valencia, Spain, Tel Aviv, Israel.

OBJECTIVE: Sperm immaturity is linked with sperm anomalies caused by spermatogenesis defects. The sperm selection technique PICSI (physiologic intracytoplasmatic sperm injection) avoids immature spermatozoa selection before microinjection. Our purpose is to demonstrate explicitly the utility of PICSI technique in IVF cycles. We monitored from the first zygote obtained by PICSI technique until the fresh or vitrified embryo transfers derived from the treatment compared with ICSI routine technique.

DESIGN: This is the first reported study, up to now, where all transferred embryos were blastocyst stage and only couples undergoing oocyte donation were included, avoiding the oocyte factor bias. PICSI technique can identify mature spermatozoa from a sperm sample to select through HA (hyaluronic acid) receptors binding ability. Single centre analysis, prospective, randomized and triple-blinded trial were undertaken. In the project a total of 277 infertile couples were recruited, 142 in the PICSI group and 135 in the control.

MATERIALS AND METHODS: Spermatozoa were incubated in AH drops for selection before microinjection in PICSI samples. In both groups, zygotes were cultured in a time- lapse incubator (Geri, Geneva or Embryoscope, Vitrolife). The study involved a total of 3104 mature injected oocytes, 2433 zygotes, 1144 viable embryos obtained (Transferred + Vitrified). 348 embryos were transferred for fresh transfer and 203 for vitrification took place. According to the sperm concentration and motility, 4 groups were created. The possible differences between fresh and vitrified outcomes were taken into account with the cumulative pregnancy rates by performing survival curves analysis.

RESULTS: Blastulation rate was similar for PICSI and ICSI groups. Nevertheless, the proportion of good quality embryos in Day 5-6 was higher in PICSI. Significant differences were found in morphokinetic parameters (in hours after ICSI) between groups: tPNa (8.80h vs. 9.14h), tSB (101.55h vs. 102.60h) and tBH (114.77h vs. 110.91h) PICSI group and Control, respectively. The implantation rate was comparable between PICSI and ICSI group. The pregnancy rate was higher in ICSI group, (but non-significant) 74% vs. 70% PICSI group and Control, respectively. No differences were found comparing PICSI-ICSI in fresh or vitrified transfer cycles. PICSI group showed a higher pregnancy rate (but non-significant) when patients presented lower sperm count. No differences were observed in ongoing pregnancy rate or live birth rates between PICSI-ICSI. However, after 4 cycles of embryo transfers the cumulative pregnancy rate in PICSI was significantly higher 88%, while in ICSI group was 71% (LogRank and Tarone-ware Test <0.05).

CONCLUSIONS: No differences between embryo quality and development potential were found between PICSI and ICSI groups; nevertheless, the global efficiency of PICSI cycles was higher. The use of the PICSI technique could be a competitive advantage for patients undergoing oocyte donation especially in those cases in which pregnancy is not successfully accomplished after first cycle.

SUPPORT: PI14/00523, Spanish Ministry of Economy and Competitiveness. Instituto de Salud Carlos III program.

P-441 Wednesday, October 16, 2019 6:30 AM


OBJECTIVE: To successfully achieve ICSI fertilization in couples with a history of complete fertilization failure due to a lack of sperm cytosolic activating factor.

DESIGN: In a prospective controlled manner, consenting couples (IRB 0712009553) with a history of ICSI fertilization failure were included. Various tests were carried out on the male partners’ ejaculates to confirm sperm-related activation deficiencies. Following the utilization of a proprietary gamete treatment method in a subsequent ICSI cycle, embryology and clinical outcomes were recorded and compared with same-patient history cycles.

MATERIALS AND METHODS: Spermatozoa were assessed by standard semen analysis. According to the initial morphological evaluation, subsequent tests were performed. These included an in-house PLC\textsubscript{2} assay to screen for the presence of sperm cytosolic activating factor, and aniline blue staining to assess protamine content. Transmission electron microscopy (TEM) and mouse oocyte activation test (MOAT) were also used to identify structural and functional deficiencies. A proprietary gamete treatment method was performed with ICSI by pre-treatment of spermatozoa and post-injection oocyte activation.

RESULTS: A total of 22 couples (maternal age, 35.8±5.6 yrs; paternal age, 40.1±6 yrs) were included. Prior to undergoing cycles with gamete treatment, these couples underwent a total of 29 ICSI cycles, resulting in a fertilization rate of 10.6% (23/216). However, no couples received a conceptus resulting in the delivery of two healthy babies, with 71.4% (5/7) still ongoing.

CONCLUSIONS: Dysfunction of the male genital tract increases both single-strand (ss) and double-strand (ds) DNA nicks and breaks, resulting in spermatozoa that impair embryonic development. Because dsDNA breaks in the male gamete can be responsible for embryo aneuploidy, the use of MPFS processing to select spermatozoa with the highest motility and genomic integrity may enhance the chances of obtaining a euploid conceptus for transfer.
and MOAT indicated a lack of sperm cytosolic activating factor and compromised fertilizing aptitude. The aniline blue assay also showed a sperm chromatin condensation deficiency, particularly in the globozoospermic patients, with a sperm chromatin fragmentation of 16.8%, corroborated by a 1.9% FISH aneuploidy.

All couples underwent a total of 37 ICSI cycles with gamete treatment, resulting in a 41.2% (120/291) fertilization rate and a 33.3% (8/24) clinical pregnancy rate (P<0.05). Of the 8 couples who achieved a clinical pregnancy, 4 delivered a healthy baby.

CONCLUSIONS: In couples with recurrent and complete fertilization failure, the application of a battery of biosays can help to assess sperm activating factor dysfunction and compromised fertilizing ability. In these couples, gamete treatment in a subsequent cycle enhances the chances of fertilization and successful pregnancies. The achievement of healthy offspring indicates that gamete treatment to overcome fertilization failure appears safe.

P-442 Wednesday, October 16, 2019 6:30 AM
SECOND EJACULATION: A SIMPLE, COST FREE MECHANISM TO DEAL WITH HIGH SPERM DNA FRAGMENTATION. Michael H. Dahan, MD, Rabea Youcef Khoudja, MD, PhD, Abbie Gagnon, M.Sc., Grace Tan, D. Phil, Seang Lin Tan, MD, MBA, Division of REI, McGill University and OriginElle Fertility Clinic and Women’s Health Centre, Montreal, QC, Canada; OriginElle Fertility Center, Montreal, QC, Canada.

OBJECTIVE: High sperm DNA fragmentation is a controversial subject. However, many physicians test for DNA fragmentation and feel it is important. If high, methods of dealing with DNA fragmentation include testicular sperm aspiration, Anexin sperm wash and ICSI. These procedures add cost, pain after surgery and are of undetermined value. Sperm DNA fragmentation is felt to occur in the epididymis while waiting to be expelled. This study was undertaken to determine if a second ejaculation 3 hours after the first could improve sperm DNA fragmentation, by limiting time in the epididymis.

DESIGN: A prospective cohort study where males were requested to wait 3 days without an ejaculation at which point a semen analysis and DNA fragmentation was performed and repeated 3-hours latter on a 2nd specimen.

MATERIALS AND METHODS: 112 subjects underwent the two semen analysis protocol as part of the fertility evaluation. All ejaculations were performed at the fertility center. DNA fragmentation was evaluated using the halo test. Data was compared by intra-subject t-test. Data is presented as % or mean±SD. Power analysis suggested ≥73 subjects were required for an 80% power and an alpha of 5% with a 2 unit mean difference with SD of 6 units. High DNA fragmentation is >35%.

RESULTS: Male age was 36±7 years (range 29-65). DNA fragmentation decreased from 34.6±19.4 to 23.7±16.0% (p<0.0001) in the 1st and 2nd specimen respectively. Average percentage improvement 23±30%. Among subjects with high fragmentation 22/49 (45%) failed to improve into the normal range. Regarding subjects with initial DNA fragmentation>35%, comparison of 1st and second 2nd fragmented to improve were 52±16% & 36±17% (p<0.0001), respectively. Greatest improvement was 97%-28% DNA fragmentation. 7/112 had worse DNA fragmentation in the second specimen and of those 2 fell above the normal range, both with a first specimen above the normal range as well. Among semen parameters volume went from 3.1±3.3ml to 1.9±0.8ml, p<0.0001, concentration from 41±39 to 32±31 million/ml, p=0.001 & progressive motility increased from 57±21% to 60±21%, p=0.06. In none of the cases where total motile sperm count was greater than 5 million did the quality of the second semen specimen convert the subject to ICSI. The first 10 subjects had both 1st and 2nd DNA fragmentation confirmed with the TUNEL assay and equivalent improvements were seen (t=0.97 p<0.05), this was not continued due to cost assumed by the clinic.

CONCLUSIONS: High DNA sperm fragmentation can often be managed with a second ejaculation 3 hours after the first. Changes in sperm quality are not clinically significant and none of the ICSI specimens from ejaculation 1 would have required ICSI based on the ejaculation 3 hours latter. 55% improve into the normal range. Therefore, a second ejaculation represents a safe, cost free mechanism to deal with this issue in many patients.

SUPPORT: None.

P-443 Wednesday, October 16, 2019 6:30 AM
SPERM-BORNE mRNAs AS A BIOMARKER FOR HUMAN SPERM QUALITY. Yunge Tang, Master degree, Ying Zhang, MD, PhD, Wenzhong Zhao, PhD, Xinzhong Zhang, MD, PhD, Weibing Qin, MD, PhD, Shunmei Deng, MD, Jiabo Wu, BSc, Mengyuan Zhang, PhD, Wei Yan, M.D., Ph.D. "Family Planning Research Institute of Guangdong Province, Guangzhou, China; Affiliation not provided; University of Nevada, Reno School of Medicine, Reno, NV.

OBJECTIVE: Although the World Health Organization (WHO) criteria for semen quality are widely followed, a significant proportion of sperm samples provided by sperm banks around the world fail to lead to successful pregnancies, highlighting the needs for better biomarkers that allow for identification of truly fertile sperm.

DESIGN: Laboratory study using human sperm samples.

MATERIALS AND METHODS: We profiled and compared mRNAs in sperm samples with higher (5 pregnancies out of <20 attempts, >25%; n=10) and lower (<1 pregnancy out of 30 attempts, <3.3%; n=10) pregnancy rates using RNA-Seq. Among numerous differentially expressed genes (DEGs) identified between sperm with high (HPR) and low (LP) pregnancy rates.

RESULTS: We selected 23 spermatogenesis-related genes and 10 energy metabolic genes as potential biomarkers for sperm quality because these showed the greatest difference in abundance in the two groups. Further optimization by examining their expression levels in 30 HPR and 30 LP sperm yielded a list of 9 genes that were selected as biomarkers because they could distinguish sperm samples with extremely high (>40%) or extremely low (<1%) pregnancy rates. We then re-tested all of the 60 samples in a blinded manner, with no sample information provided to the examineer and our results showed that these 9 genes can reliably distinguish the two extreme groups.

CONCLUSIONS: Our data suggest that sperm-borne mRNAs can be excellent biomarkers for predicting the fertility potential of sperm in addition to the current motility- and morphology-based methods. We are exploring other RNA species as well as epigenetic markers as potential biomarkers for human sperm quality.

SUPPORT: This work was granted by the Natural Science Foundation of Guangdong Province (2014A030313798, 2018A030313528) and the Science and Technology Foundation of Guangzhou (201510010188).

P-444 Wednesday, October 16, 2019 6:30 AM
DEEP LEARNING-ENABLED SMARTPHONE-BASED SYSTEM FOR AUTOMATED EMBRYO ASSESSMENTS AND EVALUATION. Manoj Kumar Kanakasabapathy, MS, Prudhvi Thirumalaraju, BS, Charles L. Bormann, PhD, Hemanth Kandula, BS, Sandeep Kota Sai Pavan, BS, Divyank Yarravarapu, BS, Hadi Shafiee, PhD, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; Massachusetts General Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: Traditionally, embryos are visually assessed by embryologists and the selection process has been shown to be highly subjective. Commercially available time-lapse imaging (TLI) systems have provided a standardized imaging platform and they provide automated and uninterrupted continuous imaging of embryos over the course of in-vitro embryo development. Recent reports of artificial intelligence (AI) systems make use of data obtained from such time-lapse systems 1, 2. However, these systems are large and prohibitively expensive. Here, as proof-of-concept, we report for the first time, the development and evaluation of an inexpensive smartphone-based system that can perform embryo evaluations using deep-convolutional neural networks (CNN) on-phone.

DESIGN: We have developed an inexpensive (<$5) smartphone imaging system that can be used to image embryos during in-vitro culture. The smartphone-based system automatically evaluates embryos based on their morphology using an AI algorithm. We used a depthwise convolutional deep neural network and transfer-learnt with retrospective embryo images captured at 113 hours post insemination (hpi) that was annotated by a total of 10 embryologists. We evaluated the system to differentiate 50 embryos based on their blastocyst stage.

MATERIALS AND METHODS: Our device consisted of a 3D-printed housing that contained the objective lenses extracted from DVDs, a light source, and a smartphone. The smartphone-based system automatically evaluates embryos based on their morphology using an AI algorithm. We used a depthwise convolutional neural network and transfer-learned with retrospective embryo images captured at 113 hours post insemination (hpi) that was annotated by a total of 10 embryologists. We evaluated the system to differentiate 50 embryos based on their blastocyst stage.
source, and batteries. A smartphone application was developed which performed the analysis locally. The AI utilized by the application was transferred, trained, and validated with 1790 embryo images. To test our system, 50 embryos donated by patients were imaged using the smartphone system at 3 hours post-insemination. Images were automatically downloaded and analyzed by our developed network without the need for any image processing. Performance metrics were calculated for the smartphone system and the overall performance of the smartphone system with the performance of deep-learning based approach that used Embryoscope data was compared.

RESULTS: The accuracy of such a system in classifying 50 embryos based on their blastocyst status was 96% (CI: 86.29% to 99.51%), its sensitivity and specificity were 93.55% (CI: 78.58% to 99.21%) and 100% (CI: 82.35% to 100%), respectively, while its positive and negative predictive values were 100% and 90.48% (CI: 71.32% to 97.32%), respectively. A chi-squared analysis comparing the performance of an Embryoscope-based deep-learning approach with our smartphone system-based deep-learning approach revealed an insignificant difference of 5.03% (P=0.33, P=0.05).

CONCLUSIONS: The results reported here demonstrate that combined with the use of an AI-powered imaging system, automated embryo analysis is not limited to only expensive time-lapse hardware and inexpensive (<$100) systems can be developed for use at fertility centers without loss in performance. The overall impact of our AI-powered system is significant since it enables integration into clinical practices at resource-limited settings at very minimal costs.


SUPPORT: This work was partially supported by the Brigham Precision Medicine Development Award (Brigham Precision Medicine Program, Brigham and Women’s Hospital) and R01AI18502, R01AI138800, and R21HD092828 (National Institute of Health).

P-445 Wednesday, October 16, 2019 6:30 AM

OBJECTIVE: To characterize the phenomenon of globozoospermia using various biomarkers and analyze reproductive outcomes in afflicted patients.

DESIGN: In 5 consenting men with globozoospermia, we assessed protamine content, sperm chromatin fragmentation (SCF), sperm aneuploidy, ultrastructural details by TEM, and epigenome. ICSI cycles with or without AOA were performed on 3 couples, and outcomes were compared.

MATERIALS AND METHODS: Semen analyses were performed on ejaculates of 5 consenting men. Protamine content was measured by Aniline Blue assay on 200 spermatozoa, with a ≤20% normal threshold. SCF scored by TUNEL assay examined 500 spermatozoa, with a <15% normal threshold. Aneuploidy rate assessed by FISH was performed on 1000 spermatozoa, with a threshold.

RESULTS: Of 173 ROSI babies three had congenital aberrations at birth, which corrected spontaneously (ventricular septa) or after surgery (cleft lip and omphalocele).

No statistical differences with respect to their cognitive development were found, however over a part of the response at 1 year old in the ROSI group was significantly lower than in the natural group. Nevertheless, it should be noted that there was no statistical significant difference of childhood growth between two groups at 24 months of age.

CONCLUSIONS: This study showed that there were no significant differences between ROSI and naturally born babies in either physical or cognitive development during the first two years after birth.

P-446 Wednesday, October 16, 2019 6:30 AM
173 BABIES BORN AFTER ROUND SPERMATID INJECTION INTO OOCYTES: SURVEY OF THEIR DEVELOPMENT FROM FERTILIZATION UP TO 2 YEARS OLD. Atsushi Tanaka, M.D., Ph.D., Motoi Nagayoshi, M.D., Izumi Tanaka, Pharm.B., Takashi Yamaguchi, M.D., Ph.D., Motoharu Ohno, M.D., Saint Mother Hospital, Kitakyushu, Japan.

OBJECTIVE: To compare physical and cognitive development of 173 babies born after round spermatid injection (ROSI) with those born after natural conception.

DESIGN: Physical and cognitive development of ROSI babies recorded by parents in government-issued Mother-Child Handbook was checked and verified by attending pediatricians.

MATERIALS AND METHODS: 967 men participated in ROSI. 173 ROSI babies were followed up 2 years for their physical and cognitive development. Controls were 1818 naturally born babies.

Physical and cognitive development of ROSI babies (e.g., body weight increase, response to parents and understanding and speaking simple language) were comparable to those of naturally born babies.

RESULTS: Of 173 ROSI babies three had congenital aberrations at birth, which corrected spontaneously (ventricular septa) or after surgery (cleft lip and omphalocele).

Body weights at 12 and 18 months of age in ROSI group were significantly lower than those of natural babies. Furthermore, the body mass index at 18 months in the ROSI babies was significantly lower than in the natural group.

No statistical differences with respect to their cognitive development were found, however over a part of the response at 1 year old in the ROSI group was significantly lower than in natural babies.

CONCLUSIONS: This study reported 2 novel genes related to globozoospermia, which can cause spermiogenic abnormality and hinder oocyte activation. We also found that AOA can greatly enhance ICSI fertilization of globozoospermic men and is paramount in those with complete form.
evaluate sperm motility function using a sperm motility analysis system (SMAS).

DESIGN: A prospective quasi-randomized controlled study was performed in a single IVF center between January 2016 and December 2017.

MATERIALS AND METHODS: Patients who underwent c-IVF were randomly allocated to two groups: for the control group, sperm preparation was performed using 80% Percoll solution (Sigma) with Sperm Washing Medium (Irvine Scientific); for the test group, sperm preparation was performed using 80% OG with ORIGIO® Sperm Wash (Origio). Sperm preparation was performed using density gradient centrifugation (25 min at 500 g) with a subsequent swim-up (30 min). We examined 47 cycles of fresh ET and 99 cycles of vitrified-warmed ET. Clinical pregnancy and implantation rates after ET were compared between the two groups. We evaluated the sperm motility function after sperm preparation over time using SMAS (DITECT) between the two groups. We also evaluated the fractal dimension, which is one indicator of hyperactivated spermatozoa.

RESULTS: There were no significant differences in patient characteristics between the two groups. Among the 47 fresh ET cycles, 26 were in the control group and 21 were in the test group. Clinical pregnancy and implantation rates in the test group were higher than in the control group (24% vs. 15%, 18% vs. 12%, respectively). Among the 99 vitrified-warmed ET cycles, 44 were in the control group and 55 were in the test group. Clinical pregnancy and implantation rates in the test group were higher than in the control group (27% vs. 18%, 21% vs. 15%, respectively). There were no significant differences in sperm motility function (straight line velocity, curvilinear velocity, average path velocity, flagellar beat cross frequency, and amplitude of the lateral head) over time between the two groups. The fractal dimension of the test group was significantly higher (p < 0.05) than that of the control group after 5 hours (1.50 ± 0.05 vs. 1.36 ± 0.06, respectively).

CONCLUSIONS: Our results showed that the new sperm preparation selection does not influence the outcomes of ART programs only when a female partner is younger than 30 y.o. Thus, we can speculate that oocytes of younger women have the ability to compensate the spermatozoa damaged DNA.

P-449 Wednesday, October 16, 2019 6:30 AM

YOUNGER FEMALE AGE MAY COMPENSATE THE HIGH SPERM DNA FRAGMENTATION IN THE ART PROGRAMS. Anastasia Kirillova, PhD,a Yulia Kiseleva, PhD.,b Olga Golubeva, PhD, c Tatiana Volodjaja, MSC; Nona Mishieva, PhD; Aydar Abubakirov, PhD; Embryologist, Moscow, Russian Federation; aNational Medical Research Center for Obstetrics, Gynecology and Perinatology named after Academician V. I. Kulakov of Ministry of Healthcare of Russian Federation, Moscow, Russian Federation; bNational Medical Research Center for Obstetrics, Gynecology and Perinatology named after Academician V. I. Kulakov of Ministry of Healthcare of Russian Federation, Moscow, Russian Federation; cEmbryologist, Moscow, Russian Federation; dReproductive endocrinology, Moscow, Russian Federation.

OBJECTIVE: The impact of sperm DNA damage on the outcomes of IVF cycles remains controversial. The aim of our work is to determine if maternal age affects the outcomes of ART programs with high levels of partner’s DNA fragmentation.

DESIGN: This retrospective study included 287 couples, undergoing IVF treatment (n=96), ICSI (n=98), ICSI-PGT-A (n=103) with evaluation of functional semen parameters and sperm DNA fragmentation in 2 years (2016-2018). 287 women enrolled in the study were distributed according to their age as followed: under 30 y.o. (n=78); 31-34 y.o. (n=79); 35-40 y.o. (n=89); older than 40 (n=41).

MATERIALS AND METHODS: Sperm DNA fragmentation was evaluated using the TUNEL assay. Fertilization and embryo culture according to the manufacturers recommendations (COOK, Australia). Array CGH (Agilent, USA) was performed for 24-chromosome embryonic genome analysis. The fertilization rate, rates of blastocyst formation, and implantation rates were evaluated.

RESULTS: Our results showed that there are lower fertilization rates (72.3% vs. 84.3%; p < 0.05) and significantly lower rates of blastocyst formation (31.8% vs. 54.2%; p < 0.05) in the group with high values of sperm DNA fragmentation in comparison with the group with normal values of this parameter. Other results are presented in the table.

Our data demonstrates that for couples with a female partner under 30 there is no significant difference in the clinical pregnancies rates between the group with high values of sperm DNA fragmentation and the group with normal values of this parameter (39% vs. 40% (IVF), 36% vs. 34% (ICSI), 60% vs. 59% (ICSI-PGT) respectively). On the contrary, for couples with female partners older than 31 the clinical pregnancies rates were higher for groups with normal values of sperm DNA fragmentation compared to the groups with high values of this parameter.

CONCLUSIONS: Our study shows that high values of sperm DNA fragmentation do not influence the outcomes of the ART programs only when a female partner is younger than 30 y.o. Thus, we can speculate that oocytes of younger women have the ability to compensate the spermatozoa damaged DNA.

P-449 Wednesday, October 16, 2019 6:30 AM


OBJECTIVE: To select spermatozoa with superior chromatin integrity, capable of increasing implantation and clinical pregnancy rates with ICSI.

DESIGN: From October 2016 to April 2019, semen specimens from consenting men (N=47) with prior ICSI failure due to high DNA fragmentation in their ejaculate were simultaneously processed by density gradient centrifugation (DGC) and microfluidic sperm selection (MFSS). TUNEL was carried out on the raw specimens and on the differentially selected aliquots. In men treated by ICSI with their female partners, clinical outcomes were compared between the two sperm-selection methods.

MATERIALS AND METHODS: Fresh ejaculate specimens from consenting men were analyzed according to WHO 2010 criteria. DGC and MFSS were used to isolate spermatozoa based on cell motility and fluid dynamics. Sperm chromatin fragmentation (SCF) was assessed by TUNEL on at least 500 spermatozoa under a fluorescent microscope utilizing a threshold of ≥15%.

RESULTS: A total of 47 men with an average age of 40±9 years had the following average semen parameters: concentration of 46.9±38 x 10^6/mL, 32.8±14 motility, and 2.3±1% morphology. After DGC or MFSS, the sperm concentration was 33.0±27 and 11.6±12 x10^6/mL, with 62.0±31% and 97.7±2% motility, respectively (P<0.0001).

The morphology of the raw sperm sample improved from 2.3±1% to 3.6±1% after MFSS, while it remained at 2.4±1% after DGC. The average SCF decreased from 24% in raw samples to 15% following DGC, and fell to 1.7% after MFSS processing (P<0.0001).

Couples (n=16) who underwent ICSI had an average SCF in their raw sample of 27.1%, which became 19% after DCG selection and only 1.6% after MFSS (< P<0.0001). These couples (female age, 38±5 years; male age, 40±8 years) underwent 38 cycles with DGS sperm selection, achieving a fertilization rate of 67%. The implantation rate was only 0%. Other results are presented in the table.

TABLE. Rates of clinical pregnancies, %

<table>
<thead>
<tr>
<th>Age of women</th>
<th>IVF (&lt;30)</th>
<th>ICSI (&lt;30)</th>
<th>ICSI-PGT (&lt;30)</th>
<th>IVF (31-34)</th>
<th>ICSI (31-34)</th>
<th>ICSI-PGT (31-34)</th>
<th>IVF (35-40)</th>
<th>ICSI (35-40)</th>
<th>ICSI-PGT (35-40)</th>
<th>IVF (&gt;40)</th>
<th>ICSI (&gt;40)</th>
<th>ICSI-PGT (&gt;40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of DNA fragmentation &lt;15%</td>
<td>39%</td>
<td>36%</td>
<td>60%</td>
<td>34%</td>
<td>33%</td>
<td>52%</td>
<td>29%</td>
<td>31%</td>
<td>33%</td>
<td>11%</td>
<td>14%</td>
<td>23%</td>
</tr>
<tr>
<td>Level of DNA fragmentation &gt;15%</td>
<td>40%</td>
<td>34%</td>
<td>59%</td>
<td>28%</td>
<td>24%</td>
<td>41%</td>
<td>18%</td>
<td>19%</td>
<td>21%</td>
<td>0%</td>
<td>0%</td>
<td>2%</td>
</tr>
</tbody>
</table>
P-450 Wednesday, October 16, 2019 6:30 AM

FROM FERTILIZATION TO BLASTOCYST: A COMPARATIVE STUDY OF TESTICULAR TO EJACULATED SPERM IN INTRACYTOPLASMIC SPERM INJECTION (ICSI) TREATMENT CYCLES. Sophie M. LaBarre, BA, a Shuning Wang, PhD, HCLD, b Richard Hackett, MS, a Carol Wheeler, MD. a Warren Alpert Medical School of Brown University, Providence, RI; b Department of Obstetrics and Gynecology, Warren Alpert Medical School of Brown University, Women & Infants Hospital, Providence, RI.

OBJECTIVE: To explore the effect of sperm source on high quality blastocyst development.

DESIGN: Retrospective case control.

MATERIALS AND METHODS: Data for retrospective analysis was gathered from patients who received In vitro Fertilization (IVF) treatment from January 2007 to May 2017. We examined how many 2-pro-nuclei embryos progressed to high quality blastocyst in 1) ICSI cycles with 132 Testicular biopsy aspiration compared with 2) n= 132 ICSI cycles with ejaculated sperm with an initial Total Motile Count (TMC) >5 million and 3) n= 132 ICSI cycles with ejaculated sperm with a TMC ≥ 5 million using analysis of covariance (ANCOVA) testing. Gardner’s embryo grading scale was used for blastocyst grading. 4BB or better was considered a high quality blastocyst. High quality day 2 embryos were defined as 4-6 cells with ≤ 10% fragmentation. Female age, follicle stimulating hormone, body mass index (BMI), sperm analysis parameters, the number of fertilized 2-pro-nuclei, day 2 embryos, day 5 blastocyst data, and day 6 blastocyst data were compared.

RESULTS: No significant difference was found in regard to maternal age, ovarian reserve and BMI in all groups. Significant baseline differences in the number of 2prons were found when assessing day 2 embryo development (P=0.001). Sperm source was not found to have a significant effect (F(6,361) = 0.53, p=0.64652) on high quality day 2 embryo development; means were 2.9 embryos (SD = 3.0) in the testicular biopsy group, 3.6 embryos (SD = 3.4) in the high TMC ejaculated sperm group and 4.0 embryos (SD= 3.7) in the low TMC ejaculated sperm group. Sperm source was found to have a significant effect on day 5 blastocyst development (F(6,361) = 5.40, p=0.00207); the means were 0.3 blastocysts (SD =0.7) in the testicular biopsy group, 0.5 blastocysts (SD =1.3) in the high TMC ejaculated sperm group, and 0.8 blastocysts (SD =1.9) in the low TMC ejaculated sperm group. When considering the number of baseline 2prons, it was found that the effect was greater on day 5 blastocyst development (F(6,361) = 52.44, p = 0.00). With regard to day 6 blastocyst development, the number of 2prons had the greatest effect (F(6,361) = -1.19 p= 0.2764), and sperm source was not found to have a significant effect (F(6,361) = 75.14, p = 0.00). The means of high quality day 6 blastocyst development were 0.4 blastocysts (SD =0.9) in the testicular biopsy group, 0.8 blastocysts (SD =1.3) in the high TMC ejaculated sperm group and 0.7 blastocysts (SD =1.1) in the low TMC ejaculated sperm group. The testicular biopsy group showed an effect of day 5 blastocyst development when controlling for BMI, FSH levels and maternal age, but no other significant effects were seen on day 2 embryo and day 6 blastocyst development were seen. Differences in the baseline number of 2prons seemed to have the greatest impact.

CONCLUSIONS: This study showed that testicular biopsy sperm produces poorer day 5 blastocyst embryo development when compared to ejaculated sperm ICSI cycles. Male factor infertility may have a negative effect not only on high quality blastocyst development but also the method of sperm production may have an impact as well.


SUPPORT: None.
DESIGN: A prospective cohort study was performed on semen analysis. Males waited 3 days without an ejaculation at which point a DNA fragmentation was performed and was repeated on a 2nd specimen 3 hours later.

MATERIALS AND METHODS: 112 subjects underwent the 2 semen analyses with a 3-h interval. All ejaculations were at the fertility center. Analysis were part of the initial work up. DNA fragmentation was evaluated with the halo test. Data was compared by intrasubject test. Data is presented as % or mean±SD. Power analysis suggested ≥ 73 subjects were required for an 80% power and an alpha of 5% with a 2 unit mean difference with SD of 6 units. Stepwise multivariate logistic regression was used to model predictors of ≥ 30% improvement in DNA fragmentation in the second specimen.

RESULTS: Male age was 36±7 years (range 29-65). DNA fragmentation decreased from 34.6±19.4 to 23.7±16.0% (p<0.0001) in the 1st and 2nd specimen respectively (23%±30%). 58/112 subjects demonstrated a >30% improvement in sperm DNA fragmentation in the 2nd specimen compared to the 1st. 7/112 had worse DNA fragmentation in the 2nd specimen. Two factors predicted at least a 30% improvement in DNA fragmentation in the second specimen; male age (95% CI 0.84-0.99, p=0.03) and use of a multivitamin (95% CI 1.25-19.8, p=0.02). 1st ejaculate volume (CI 0.84-2.65), 2nd volume (CI 0.23-1.39), 1st concentration (CI 0.98-1.005), 2nd concentration (CI 0.99-1.03), 1st motility (CI 0.97-1.03), 2nd motility (CI 0.98-1.04), smoking (CI 0.28-1.57), cannabis use (CI 10.0-2.45) and fathering previous pregnancies (0.19-2.9) failed to predict improvement. Initial DNA fragmentation trended towards being a predictor of improvement (CI 1.0-0.96, p=0.06).

CONCLUSIONS: High DNA sperm fragmentation can often be managed with a 2nd ejaculation 3 hours later. First younger men and those taking a sperm improvement vitamin supplement were more likely to have at least a 30% improvement in DNA fragmentation on the second specimen. All men should be proscribed such a vitamin who will undergo this protocol. Those male with extremely high DNA fragmentation may be less likely to show a 30% improvement, likely due to the greater change in absolute number needed.

SUPPORT: None.

P-453 Wednesday, October 16, 2019 6:30 AM

SPERM DNA FRAGMENTATION INDEX IS NOT ASSOCIATED WITH RECURRENT IVF/ICSI FAILURE. Jordan Best, B.S.,* Premal Patel, MD,* Taylor P. Kohn, MD, MPhil,* Elaine de Quadros, D.H.Sc,† Ranjith Ramasamy, M.D.∗ University of Miami, Miami, FL; †University of Miami Miller School of Medicine, Miami, FL; Department of Preventive Medicine, Johns Hopkins University School of Medicine, Baltimore, MD; Fertility & IVF Center of Miami, Miami, FL.

OBJECTIVE: To assess whether DNA Fragmentation Index (DFI) or High DNA Stainability (HDS) as measured by Sperm Chromatin Structure Assay (SCSA), was predictive of recurrent in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) failure.

DESIGN: We performed a retrospective cohort study of couples undergoing IVF, ICSI and frozen embryo transfer (FET) cycles between 2009 – 2018 performed at a large volume fertility center. SCSA was performed for all males prior to IVF/ICSI cycles.

MATERIALS AND METHODS: All couples between 2009 to 2018 who underwent ≥ 2 IVF/ICSI cycles, with maternal age ≤ 40 were included in our analysis. Patients having undergone prior IVF/ICSI at outside centers were excluded. Recurrent IVF/ICSI failure was defined as ≥ 2 failed IVF/ICSI cycles in couples with maternal age ≤ 40. Success was defined as a cycle that led to live birth.

RESULTS: A total of 393 couples with 1215 cycles were included in the analysis with a pregnancy success of 36.9% and an average live birth of 20.6%. The average (±standard deviation) female age of 34.0 ± 3.6 and an average total motile sperm count of 68.1 ± 76.7 million sperm. DFI and HDS were not predictive for achieving a pregnancy (𝑝=0.76 & 𝑝=0.96 respectively), nor was DFI predictive of spontaneous abortion (𝑝=0.92). However, HDS was found to be predictive of spontaneous abortion, with higher rates of HDS seen in live births vs spontaneous abortion (12.4% vs 9.3%, 𝑝=0.003). DFI and HDS were not associated with recurrent IVF failure (𝑝=0.43, 𝑝=0.14 respectively), nor were they predictive of IVF success, defined as live birth, in those with normal values of DFI and HDS when controlling for female age.

CONCLUSIONS: We found that neither DFI or HDS, as assessed by SCSA, were predictive of recurrent IVF failure in patients with high DFI or HDS when controlling for female age and total motile sperm count. This finding suggests that SCSA does not predict recurrent IVF failure.

P-454

WITHDRAWN

P-455 Wednesday, October 16, 2019 6:30 AM

MULTI-SITE, BLIND PROSPECTIVE TRIAL ASSESSING WHETHER SEMEN OXIDATION REDUCTION POTENTIAL (SORP) ASSESSMENT CAN BE USED TO PREDICT LOW FERTILISATION WITH CONVENTIONAL IVF: INTERIM ANALYSIS. Georgie Pool, MSc,1 Shaun Rogers, BSc,2 Anastasia Mania, MSc,3 Georgia Everett, MSc,4 Alpesh Mahesh Doshi, MSc,5 Sri Srikantaharaja, BVSc,6 Hasmukh N. Joshi, BSc,7 Martin Wilding, Ph.D.,8 Samuel Bishop, MSc,9 Lourdes Muriel, BSc,9 Walid Maaloul, PhD,9 Cristina Hickman, PhD.9 City Fertility, London, United Kingdom; 1IVF, London, London, United Kingdom; 2Homerton NHS Hospital, London, United Kingdom; 3Homerton Hospital, London, United Kingdom; 4Create Fertility, London, United Kingdom; 5IVI, London, United Kingdom; 6Nottingham University, Nottingham, United Kingdom; 7Imperial College London, London, United Kingdom.

OBJECTIVE: To identify if static oxidation-reduction potential (sORP) can be used clinically at the time of insemination to predict low fertilisation.

DESIGN: Multi-site prospective control blind study involving 6 independent clinics. Interim analysis assessing data from the first 10 patients enrolled in the study. Primary outcome for the interim analysis: rate of low fertilisation (<25% 2PN/MII), normal fertilisation (2PN per MII). Secondary outcomes: overall fertilisation rate (2PN per MII), 1PN and 3PN rates per MII, daily embryo quality, morphokinetic parameters. Inclusion Criteria: patients undergoing IVF with at least 4 follicles ≥10mm, and 4 mature oocytes collected.

RESULTS: Out of the first ten patients (134 mature oocytes), nine had normal sORP (0.12-0.93, 121 oocytes, Control), and one patient had high sORP (1.69, 13 oocytes, Treatment). Interestingly, the only patient with a low fertilisation rate (2/13, 20%) was in the Treatment group, whilst normal fertilisation rates were all normal in the Control group (ranging from 50-100%, overall 88/121=73%). Compared to Control, Treatment group had a lower 2PN rate (Control vs Treatment: 88/121=73% vs 2/13=15%, 𝑝<0.01), higher polyploidy rate (5/121=4% vs 5/13=38%, 𝑝<0.001). Difference in overall fertilisation rate approached significance (93/121=77% vs 7/13=54%, 𝑝=0.07). 1PN rate (7/121=6% vs 0/13, NS), median number of cells on day 2 (4 vs 3, NS) and day 3 (7 vs 6.5, NS), did not differ between Treatment and Control. Cleavage embryos with more day 3 fragmentation were more even (sORP 0.66-0.37) or more unevenness (sORP 0.59-0.36) were associated with higher sORP than embryos with lower day 3 fragmentation (sORP 0.25-0.22 respectively, 𝑝<0.0001) or more evenness (sORP 0.38-0.4, n=25, 𝑝=0.03). However, good embryo quality rate on days 2 (45/88 vs ½, NS), and 3 (32/74 vs ½, NS) did not differ between Treatment and Control. Morphokinetics was not significantly affected by treatment.

CONCLUSIONS: Out of 10 patients undergoing IVF, sORP assessment correctly identified the 1 case where low fertilisation occurred. With 25% of normospermic samples leading to low fertilisation, new diagnostic tools are required to ascertain whether IVF is the correct treatment. This is the first multi-site prospective study assessing whether sORP can be used this way. Although preliminary, our results are encouraging and in line with other single-centre publications.
THE EVALUATION OF SEMINAL OXIDATION REDUCTION POTENTIAL CAN PREDICT NORMAL SPERM PARAMETERS. Mariem BEN Kehlifa, PhD,\textsuperscript{a} Sonia Mnallah, Dr,\textsuperscript{a} Mohamed Khouf, Dr,\textsuperscript{b} Khaled Mahmoud, Dr,\textsuperscript{a} M. E. D. Habib BEN Aribia, Dr,\textsuperscript{a} Hanen Elloumi, Dr,\textsuperscript{a} Fathi Zhioua, Dr,\textsuperscript{a} Khaled Terras, Dr,\textsuperscript{a} clínique la rose, centre FERTIL-LIA, Tunis, Tunisia; \textsuperscript{b}clinique La Rose, Centre FERTILLIA, jardins du lac 2, Tunisia.

OBJECTIVE: The standard semen analysis is the most popular laboratory test in diagnosis of male fertility. However, it is well-known that normal results of semen analysis can not exclude men from the causes of couples infertility. One of the most important parameters of sperm, in its fertilizing potential is Sperm DNA integrity that has direct positive correlation with Assisted Reproductive Techniques (ART). The most common cause of sperm DNA damage is Oxidative Stress (OS). The evaluation of seminal oxidatives stress have a crucial role in the identification of patients who may benefit from treatments. The aim of our study was to use MiOXSYS System to evaluate OS and to correlate this evaluation sperm parameters, DNA fragmentation and chromat decondensation.

DESIGN: This is a prospective comparative study that was performed between January 2018 and March 2019 includes patients with primary or secondary infertility (\( \geq 3 \) years). Human semen samples were obtained from 200 patients performing a complete exploration of semen parameters at a private ART clinic. Sperm parameters were evaluated according to World Health Organization 2010 guidelines. Exclusion criteria included azoospermia and samples with a concentration \(< 1 \times 10^6 \) sperm/mL.

MATERIALS AND METHODS: In each semen sample, in addition to conventional sperm parameters the following parameters were measured:

- (i) Spermatozoa with DNA strand breaks were assessed by TUNEL (cut-off value <30%), (ii) Abnormal chromatin condensation using Aniline Blue assays (cut-off value <20%), (iii) Oxidative stress was measured by MiOXSYS Analyzer. The study subjects were grouped into two groups referring to a cut-off value of 1.36 mV/10\(^6\) sperm/mL.

RESULTS: Comparing to patients of group 1, patients of group 2, had a significantly lower mean sperm count (14.73 vs 64.72 \times 10^6 sperm/mL) progressive motility (24% vs 38%), and vitality (52% vs 68%). Conversely patients of this group had significantly higher levels of DNA fragmentation and chromat decondensation. This results confirm that sORP, DNA fragmentation and chromat decondensation were inversely associated with normal sperm parameters. When subgroups of patients were investigated according to normal or abnormal semen parameters we identified 2 subgroups in each group: a subgroup containing 25% of patients (n=29) of group 1B failed to meet one or more criteria of sperm quality and groups (1B and 2B) failed to meet one or more criteria of sperm quality.

The combination of conventional sperm parameters with the advanced sperm function test should be included in assessment of male infertility because they can have prognostic implications for couples undergoing ART.

USEFULNESS OF A NEW SPERM TRANSPORT CONTAINER “TRANSPORTER-S” FOR INFERTILITY TREATMENT. Toshiyuki Iwahata, MD, PhD,\textsuperscript{a} Takashi Tanaka, BSc,\textsuperscript{a} Akiyoshi Osaka, Bachelor of Medicine,\textsuperscript{a} Atsushi Yamamoto, MD, PhD,\textsuperscript{b} Yoshitomo Kobori, MD, PhD,\textsuperscript{b} Kouhei Sugimoto, MD, PhD,\textsuperscript{b} Hiroshi Okada, MD, PhD.\textsuperscript{b} Dokkyo Medical University Saitama Medical Center, Koshigaya, Japan; \textsuperscript{b}Dokkyo Medical University Saitama Medical Center, Saitama-prefecture Koshigaya-city, Japan.

OBJECTIVE: The container for storage and transport of ejaculated semen is “clean and wide-bore glass or plastic container” in the guidelines in usual, and it is generally used that a cylindrical container with a height of about 8 cm is used. Since this container has a large volume relative to the amount of semen, which is 100 to 200 ml, it is difficult to completely remove it when collecting it for examination. The new container (Transporter-S: TS) is less likely to be exposed to air and has excellent liquid stability and is suitable for storage and transport of ejaculated semen compared with conventional products.

DESIGN: Prospective study.

MATERIALS AND METHODS: <Examination 1> TS is characterized in that stored samples are less susceptible to temperature changes than conventional containers, and the effects of storage environment on samples were compared between TS and conventional containers. As a substitute for semen in TS and conventional containers, put 5 ml of distilled water at 37 °C and leave each container in an environment at room temperature (25°C) and the ambient temperature in winter (estimated at 10°C) for 15 hours. It compared about the temperature change for every minute.

<Examination 2> Sperm tests were performed on each of the 14 healthy volunteers at the same abstinence period. At that time, with respect to sperm parameters and sperm DNA fragmentation index (DFI) in seminal fluid stored in a conventional container and transporter S, place them at room temperature 25°C and change over time (0 hours 2 hours 4 hours 6 hours) Measurement survey.

<Examination 3> The volunteers who provided ejaculated semen were asked about the feeling of using TS and compared with the conventional container.

The contents of the questionnaire were evaluated by comparing the conventional container and TS very good 5, good 4, normal 3, bad 2, very bad 1 of 5 stages.

RESULTS: Compared with conventional containers, TS has a slower change in sample temperature and is less susceptible to low ambient temperature and, it was more difficult to be affected when the outside temperature was low. In semen that was stored using TS, the decline in exercise rate and survival rate over time became slower than in conventional containers. (Motor rate changes are significantly different after 4 hours and 6 hours. Sperm survival rates are also significantly different after 6 hours.) The sequestration using TS became 1 very good, 4 good, 5 normal, 1 bad, 1 bad. The average value of the questionnaire results was 3.07 ± 0.92, which was comparable to conventional containers. We think that TS use is effective in infertility treatment including the use that is not stable in the climatic area and the patient who takes time after preparation.

CONCLUSIONS: It is considered that TS is less likely to be exposed to air and has excellent liquid stability and is suitable for storage and transport of ejaculated semen, as compared with conventional containers. In the future, it is necessary to conduct further examinations by changing semen and storage temperature with relatively poor findings such as OAT cases.

Reference: None.

SUPPORT: None.
THE TIME-COURSE FROM GERMINAL-VESEL BREAK DOWN (GVBD) TO FIRST POLAR BODY EXTRAUCTION (PBE) IN RESCUED IN VITRO MATURATION (r-IVM), A PROSPECTIVE STUDY ON TIME LAPSE IMAGING.

OBJECTIVE: To access the time-course and associated factors of oocyte maturation from GVBD to PBE in r-IVM.

DESIGN: Non-comparative; Prospective.

MATERIALS AND METHODS: Patients underwent intracytoplasmic sperm injection and had at least one GV oocyte after denudation were included. After denudation, GV oocytes were cultured in G-IVF® media and placed into a time-lapse incubator. Images were taken every 10 mins for 144 hours. The GVBD and PBE time were counted. Patient’s age, protocol, base and hCG day luteinizing hormone (LH), base follicle stimulation hormone (FSH), base and hCG day estradiol (E2), immaturity rate, and big follicle acquisition rate (BFA) were recorded for univariable clustered Cox regression [1,2]. Variables (p < 0.3) were chosen for multivariable analysis. Hazard ratio (HR) with 95% confidence interval (95%CI) were reported.

RESULTS: There were 36 patients (79 GV oocytes) recruited. 12 GV oocytes did not mature. The overall time-course was 23.2h (95%CI 21.3-24.4h). The baseline and analysis results are shown in Table I. The BFA <1 means GV oocytes were from big follicles. GV oocytes in group BFA <1 showed shortened time-course in both univariable (HR 2.43, 95%CI 1.49-4.35, p <.001) and multivariable analysis (HR 2.38, 95%CI 1.32-4.35, p =.004). The adjusted chance of maturation in group base E2 concentration ≤45 showed to be twice greater than group (HR 2.00 95%CI 1.06-3.81, p =.034).

CONCLUSIONS: We first demonstrate a precise time-course of GVBD to PBE in stimulated cycles, which can contribute significantly to catching the fertilization window in r-IVM as well as traditional IVM. We found that GV oocytes from big follicles or patient with higher base E2 have higher chance of maturation. These findings give clues for oocyte and follicle development, but further studies are needed to confirm.


### TABLE I.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Baseline</th>
<th>Univariable analysis</th>
<th>Multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HR 95%CI P-value</td>
<td>HR 95%CI P-value</td>
</tr>
<tr>
<td>Age (year)</td>
<td>35.89±3.21</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>≥35 (n [%])</td>
<td>24 (66.67)</td>
<td>0.95 0.83-1.1 0.505</td>
<td>1.16 0.53-2.52 0.715</td>
</tr>
<tr>
<td>&lt;35 (n [%])</td>
<td>12 (33.33)</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Stimulotio protocol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long (n [%])</td>
<td>9 (25.00)</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Antagonist (n [%])</td>
<td>27 (75.00)</td>
<td>0.76 0.46-1.27 0.296</td>
<td>0.66 0.42-1.03 0.068</td>
</tr>
<tr>
<td>Base FSH (IU/l)</td>
<td>6.40 (5.35-7.98)</td>
<td>0.98 0.88-1.1 0.761</td>
<td>NC</td>
</tr>
<tr>
<td>Base LH (IU/l)</td>
<td>4.55 (4.05-6.68)</td>
<td>1.00 0.91-1.11 0.965</td>
<td>NC</td>
</tr>
<tr>
<td>LH on hCG day (IU/l)</td>
<td>3.35 0.98 0.91-1.06 0.655</td>
<td>NC</td>
<td></td>
</tr>
<tr>
<td>Immaturatoin rate (%)</td>
<td>23.41±11.21</td>
<td>0.97 0.96-0.99 0.010</td>
<td>0.98 0.96-1.01 0.198</td>
</tr>
<tr>
<td>Base E2 (pmol/l)</td>
<td>104.2±48.28</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>≤&lt;50 (n [%])</td>
<td>4 (11.10)</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>≥≥50 (n [%])</td>
<td>32 (88.90)</td>
<td>1.37 0.92-2.05 0.124</td>
<td>2.00 1.06-3.81 0.034</td>
</tr>
<tr>
<td>E2 on hCG day (pmol/l)</td>
<td>11550 (8433.50-15167.00)</td>
<td>0.78 0.49-1.26 0.317</td>
<td>NC</td>
</tr>
<tr>
<td>BFA (%)</td>
<td>108.01 (81.77-132.35)</td>
<td>&lt;.001 2.38 1.32-4.35 0.004</td>
<td></td>
</tr>
<tr>
<td>&lt;1 (n [%])</td>
<td>21 (58.30)</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>≥1 (n [%])</td>
<td>15 (41.70)</td>
<td>2.43 1.49-4.35</td>
<td>&lt;.001 2.38 1.32-4.35 0.004</td>
</tr>
</tbody>
</table>

R=Reference.
NC=Not Chosen.
P-460 Wednesday, October 16, 2019 6:30 AM

DAY 2 LASER ASSISTED HATCHING (AH) SIGNIFICANTLY IMPROVES IMPLANTATION RATES IN FRESH BLASTOCYST TRANSFERS, Sarah H. Bjorkman, MD, Stephanie M. Nichols-Burns, PhD, Jonathan Lo, MSc, Nuri Kodaman, PhD, Pinar Kodaman, MD/PhD, Dawn A. Kelk, Ph.D., HCLD, Yale School of Medicine, New Haven, CT.

OBJECTIVE: The efficacy of assisted hatching has been widely debated. The variable results reported for AH are confounded by the numerous methods of performing AH, including mechanical partial zona dissection, acid tyrode’s, and more recently by laser assistance. Assisted hatching has most commonly been performed on Day 3 embryos. This study assesses if Day 2 laser assisted hatching can improve implantation rates for fresh blastocyst transfers.

DESIGN: Prospective observational cohort.

MATERIALS AND METHODS: On the morning of Day 2 of culture, all embryos were sorted into groups (<4-cell, 4-cell and >4-cells). Those in the AH group underwent laser assisted hatching using an Octax laser (4.0ms) on the morning of Day 2 at the time of embryo check. All embryos were then cultured undisturbed until assessment on the morning of Day 5 when the highest quality embryo(s), based on morphology, were selected for embryo transfer. A total of 446 fresh Day 5 transfers between Jan 2016 - Mar 2019 were analyzed (244 transfers with AH and 202 transfers without AH). A total of 682 embryos were transferred in the 446 cycles (363 embryos in the AH group and 319 embryos in the non-AH group). Because 206 of the 446 transfers involved transfer of more than 1 embryo, a mixed model accounting for both fixed and random effects (i.e. repeated measurements) was used, with SAC modeled as a function of the fixed effects assisted hatching (AH), age, and body mass index (BMI).

RESULTS: Day 2 assisted hatching is associated with successful implantation (p=0.036). As expected, age was negatively associated with implantation rate (p<0.0001). BMI was not. The R-square for the model was 0.52, and the variance component of the random effects (owing to multiple embryo transfers) was 0.082 (95% CI [0.046-0.111]).

<table>
<thead>
<tr>
<th>No AH</th>
<th>With AH</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td># Fresh Day 5 Transfers</td>
<td>202</td>
<td>244</td>
</tr>
<tr>
<td>Mean Maternal Age</td>
<td>35.6</td>
<td>34.4</td>
</tr>
<tr>
<td>Mean BMI</td>
<td>26.8</td>
<td>27.0</td>
</tr>
<tr>
<td>Mean # Embryos Transferred</td>
<td>1.58</td>
<td>1.49</td>
</tr>
<tr>
<td># Embryos</td>
<td>319</td>
<td>363</td>
</tr>
<tr>
<td># Sacs</td>
<td>137</td>
<td>194</td>
</tr>
<tr>
<td>Implantation Rate (%)</td>
<td>42.9%</td>
<td>53.4%</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Large data sets such as the SART database do not allow for evaluation of the impact of specific AH techniques. Certainly, any embryo handling and exposure has the potential to be detrimental to blastocyst development and implantation rates. Here, we show that Day 2 laser AH can lead to a significant increase in implantation rates from 42.9% without AH to 53.4% with AH. Day 2 embryos generally have larger perivitelline space which may allow for reduced peripheral laser exposure to the blastomeres. Further studies are needed to confirm if Day 2 laser AH confers benefit over Day 3 laser AH.

P-461 Wednesday, October 16, 2019 6:30 AM

INNOVATIVE HIGH THROUGHPUT SCREEN IN EMBRYONIC STEM CELLS REPORTS STRESS-FORCED IMBALANCED DIFFERENTIATION, IMPORTANT TO ANALYZE STRESS IN IVF AND DRUG DEVELOPMENT: ANALYSES USING BULK AND SINGLE CELL RNASEQ, Elizabeth E. Puscheck, MD, MS, MBA,a Sudipta Dutta, Ph.D.,b Mohammed Abdullahreem Abdullahan, Ph.D.,b Katherine Gurzield, Ph.D.,b Douglas Ruden, Ph.D.,b Daniel Rappolee, Ph.D.,b Wayne State University, Detroit, MI; bReproductive Stress 3M, Inc., Grosse Pointe Farms, MI; cWayne state university, Detroit, MI.

OBJECTIVE: To validate a high throughput Stress Screen (STS), Htx1-promoter- stemness- fluorescent reporter embryonic stem cells (ESC) were tested for stress-forced override in stemness and changes in metabolic, developmental, epigenetic and proliferative states.

DESIGN: Laboratory study.

MATERIALS AND METHODS: ESC were tested by bulk or single cell (sc) RNAseq after 72hr exposures to 0-300mM hyperosmotic sorbitol (with stemness-maintaining Leukemia Inhibitory Factor, LIF) to quantitatively stress-forced differentiation. Controls for normal stemness were LIF+ and normal differentiation were LIF-. RNA was isolated by RNAeasy lysis or 10XGenomics Dropseq. RNA quality was checked by Agilent TapeStation. cDNA was synthesized using Lexogen’s QuantSeq library kit, and barcoded, multiplexed and sequenced by Illumina NovaSeq 6000. Data were demultiplexed by CASANova software and FC expression was compared between conditions. In replicate experiments, significant p-values (p<0.05) were identified affected pathways. Proliferation or death were assayed by Hoechst staining or Trypan blue staining, respectively. Validating studies including qPCR, immunoblot and immunofluorescence.

RESULTS: Stress forces dose-dependent responses; 6 Warburg anabolism/stemness transcripts and proliferation decreased. Compared with normal differentiation, stress-forced, dose-dependent range of highest up- and down-regulated mRNA increased 3.5 fold, but total transcript types decreased 10% in ESC exposed to 0-300mM sorbitol. Stress forced 5FC increases in 8 1st lineage mRNA, but 5FC decreases in 3 2nd lineage transcripts and 85% of later lines transcripts. The most significant effects on later lineage were increased neural toxicity through suppression. Increases occurred in checkpoint genes, genes mediating epigenetic DNA/Histone methylation, stress response/heat shock genes. Genes that would mediate invasion after stress-implantation decreased. All of the effects reported here were significantly higher for FC and low for false discovery rate (FDR)/P value.

CONCLUSIONS: Stress decreases proliferation, stemness, and Warburg anabolism resulting in fewer stem cells. It compensates for the fewer cells with increase essential, prioritized 1st lineage differentiation compared with decreased 2nd and later lineages. This should predict teratogenesis with few predictive values for neurotoxicity. Stress adaptation is mediated by high FC in few transcripts. This HTS assay should identify IVF culture conditions leading to optimal implantation and exposures of new drugs that could harm the implanting embryo and its stem cells.


P-462 Wednesday, October 16, 2019 6:30 AM

AUTOMATED COMPUTER ANALYSIS OF HUMAN BLASTOCYST EXPANSION FROM EMBRYOSCOPE TIME-LAPSE IMAGE FILES, Thomas TF. Huang, PhD,a Brienne C. Walker, MS,a,b M. Y. Harun, BS,a,b Aaron T. Ohira, PhD,a M. A. Rahman, PhD,a Joshua Mellinger, BS,a Willy Chang, BS,a,b University of Hawaii John A Burns School of Medicine, Honolulu, HI; bPacific In Vitro Fertilization Institute, Honolulu, HI; cDepartment of Electrical Engineering, University of Hawaii at Manoa, Honolulu, HI.

OBJECTIVE: To develop a rapid, quantitative, and automated analysis of human blastocyst expansion from Embryoscope time-lapse image files of zona-ablated embryos using artificial intelligence (AI).

DESIGN: A retrospective observational study comparing time-lapse images of blastocyst expansion in zona-ablated embryos measured either manually using Embryoscope software tools versus automatically using a customized neural network to perform semantic segmentation (SegNet) on exported Embryoscope image files.

MATERIALS AND METHODS: Manual expansion measurements of the trophectoderm (TE) enclosed cavity was performed using the Embryoscope's elliptical measurement tool (ET) at 2.0-hr intervals for the first 10.0 hours of expansion after initial blastocyst formation in 46 laser-ablated human blastocysts. Manual measurements (in μm2) were compared to values calculated using deep learning segmentation (SegNet) to file of exported ET time-lapse images/embryo over the same 10.0 hr period. All embryos had been laser-ablated to enable subsequent biopsy; thus, the total area of blastocyst expansion was defined as the sum of 1) the TE-enclosed area within the zona plus 2) the TE-enclosed area herniating irregularly from the ablation slit.

RESULTS: Compared to manual measurement using the Embryoscope’s elliptical tool, the automated approach using SemSeg demonstrated many
advantages. Although the ET could accurately measure the TE within the uniformly elliptical zona pellucida, it less accurately traced the irregular TE cell surfaces herniating from the ablation slit; the final measurements were less consistent or reproducible between operators. In contrast, such irregular cellular outlines were more accurately demarcated by SemSeg with the neural network, which had an accuracy of >99%, even in areas abutting embryo well boundaries. While the average discordance between the two approaches was 3.2-3.4% at both the beginning and end of the assay, some individual embryo measurements varied by more than 10% at 10.0 hours due to the limitations in the elliptical tool’s accuracy at embryo well edges and boundaries. The averaged median initial and final expansion areas were 12,624 μm² (using the ET) versus 13,055 ± 2 and 21439 ± 2 (using SemSeg). Using either approach, subsequent rank ordering of individual embryos within cohorts revealed an enrichment for euploidy among embryos most rapidly expanding. However, the greatest advantage of SemSeg is to enable an automated, objective analysis of large-scale data sets by machine learning platforms.

CONCLUSIONS: This is the first report of the successful application of automated image analysis to the dynamic process of trophectoderm epithelium expansion in the human blastocyst from stock time lapse files in em-

bryos that will undergo biopsy. This approach now enables the inclusion of this important morphokinetic information in machine learning applications aimed at the non-invasive identification of euploidy.

SUPPORT: This work was supported by the Division of Research of Department of Obstetrics and Gynecology and Women’s Health of the John A. Burns School of Medicine and an intramural grant from the Pacific IVF Institute.

ART OFFSPRING

P-463 Wednesday, October 16, 2019 6:30 AM

NEONATAL OUTCOMES OF SINGLETON LIVE BIRTHS WITH VANISHING TWIN SYNDROME FOLLOWING TRANSFER OF DOUBLE EMBRYOS IN ASSISTED REPRODUCTIVE TECHNOLOGY: A RETROSPECTIVE COHORT STUDY.

Junfang Yan, Master, The Third Affiliated Hospital of Zhengzhou University, Zhengzhou, China.

OBJECTIVE: To compare neonatal outcomes in singleton live births be-

tween groups with and without VTs following transfer of double embryos.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Anonymous data on all cycles per-

formed in the China were obtained from the Reproductive medicine depart-

ment of the Third Affiliated Hospital of Zhengzhou University, involving 6220 singleton live births (2772 fresh embryos transfer (ET) cycles and 3448 frozen embryos transfer (FET) cycles). We analyzed the obstetric out-

comes of gestation age, PTB, SGA (small for gestation age), birthweight, LBW, congenital malformation, pediatric admission and NICU admission in cycles of fresh ET and FET. Logistic regression analysis was performed adjusting for confounders, including age of women, BMI, value of AMH, infantile years, current cycle, antral follicles, cause of infertility, number of oocytes retrieved, endometrial thickness at the day of transplantation, numb-

er of high-quality embryos, embryo stage.

RESULTS: In the fresh ET cycles, the birthweight and gestational age in the study group were lower than in the control group. (2962.4±563.1vs. 3104.9±498.5, p=0.000) and (262.8±8.4vs. 268.9±13.9, p=0.000), respec-

tively. There was a significantly higher risk of PTB (adjusted odds ratio(OR) 2.45,95%CI:1.98-3.03)) and LBW (aOR 2.11, 95%CI :1.67-2.65) in the study group and in the control group. There was a higher risk of pediatric admis-
sion (aOR 3.45,95%CI:2.23-5.33) and NICU admission (aOR 1.98,95% CI. 13.2-2.96) in the study group than in the control group, and In the FET cy-

cles, the gestational age and birthweight in the study group were lower than in the control group, (263.0±15.7vs. 273.0±10.5, p=0.000) and (3099.6±622.4vs. 3352±671.5), respectively. There is a significantly higher risk of PTB (aOR 2.45,95%CI: 2.23-5.33) and LBW (aOR 2.67, 95%CI: 2.13-3.34) in the study group than in the control group. And there was a higher risk of pedi-

atric admission (aOR 2.5,95%CI:1.45-4.41) and NICU admission (aOR 2.22,95%CI:1.43,3.46) in the study group than in the control group.

CONCLUSIONS: There was a higher risk of LBW, PTB, pediatric admis-
sion and NICU admission between the study groups and control groups in fresh ET and FET cycles. However, no increased risk of SGA and congenital malformation was observed in singleton live births in both fresh and frozen ART cycles following transferring double embryos.

REFERENCES: 1. Zander-Fox DL, Tremellen K, Lane M. Single blastocyst em-


2. Pandey S, Shetty A, Hamilton M, Bhattacharya S, Maheshwari A. Ob-


3. Templeton A, Morris JK. Reducing the risk of multiple births by transfer of two embryos after in vitro fertilization. The New England journal of med-


A A A7. A Gianaroli L, Racowsky C, Geraedts J, CEDARS M, Makrigianni-


SUPPORT: Not applicable.

P-464 Wednesday, October 16, 2019 6:30 AM

REPRODUCTIVE AND PERINATAL OUTCOMES USING CRYOPRESERVED OOCYTES: AN ANALYSIS OF NATIONAL DATABASE SPANNING OVER A DECADE USING THREE CLINICAL MODELS.

Mariano Mascarenhas, MS (OG), MRCOG, DNB (OG), Post-doctoral fellow in reproductive medicine, a Hazel Mehlawat, Senior School Student, b Harish M. Bhandari, MBBS MD MRCOG, a Meenakshi Choudary, MBBS MD MRCOG PhD. c aLeeds Fertility, Seacroft Affiliated Hospital of Zhengzhou University, Zhengzhou, China.

OBJECTIVE: To compare neonatal outcomes in singleton live births be-

tween groups with and without VTs following transfer of double embryos.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Anonymous data on all cycles per-

formed in the United Kingdom provided by the Human Fertilisation and Embryology Authority.

MATERIALS AND METHODS: Of 988 015 IVF cycles over a period of

>15 years, 26 586 cycles were suitable for analysis. Three clinical models were used to assess the impact of oocyte cryopreservation on live birth and peri-

Singleton birth data was used for calculating perinatal outcomes. Preterm birth (PTB) was defined as live birth before 37 weeks and low birth weight (LBW) was defined as birth weight <2500 gm. 100, 245 and 6537 singleton births were reported following cycles using autologous cryopreserved oocytes, cryo-
preserved donor oocytes, and fresh donor oocytes respectively.

RESULTS: The LB rate was lower in women having IVF cycles using cry-
opreserved donor oocytes than for fresh donor oocytes (30.7% vs 34.7%, p = 0.035 (95% CI 0.724 to 0.962, p=0.013), LB rate was lower in women using autologous cryopreserved oocytes than those using cryopreserved donor oocytes [18.0% vs 30.7%, OR 0.497 (95% CI 0.388 to 0.636, p=0.001)].

The LB rate and LBW rates were not significantly different between cycles using autologous cryopreserved oocytes and cryopreserved donor oocytes or between cryopreserved donor oocytes and fresh donor oocytes.

The live birth rate per embryo transfer was significantly lower following the first cycle of cryopreserved donor oocytes as compared to first cycle of cryopreserved embryos using autologous oocytes (19.3% (177/917) vs 30.1% (98/326), OR 0.556 (95% CI 0.417 to 0.742), p<0.001). Whilst the PTB rate was not significantly different in this model, women using frozen donor oocytes were more likely to have babies with LBW compared to those using cryopreserved embryos from autologous oocytes (17.5% (14/80) vs 5.9% (9/152), OR 0.297 (95% CI 0.122 to 0.720) p=0.005).

REFERENCES: 1. Zander-Fox DL, Tremellen K, Lane M. Single blastocyst em-


2. Pandey S, Shetty A, Hamilton M, Bhattacharya S, Maheshwari A. Ob-


3. Templeton A, Morris JK. Reducing the risk of multiple births by transfer of two embryos after in vitro fertilization. The New England journal of med-

Limitations: Confounders such as BMI, smoking status not known. The age of women were given as a range rather than as continuous data. LB outcomes possible only per cycle rather than per woman except for first cycle outcomes.

CONCLUSIONS: Women having cycles using cryopreserved oocytes have significantly lower live birth rate compared to cycles with fresh donor oocytes or cryopreserved embryos. This suggests the need for proper counselling of women considering elective oocyte freezing or using eggs from frozen donor egg banks.

SUPPORT: No financial support was sought from any funding agency.

P-465 Wednesday, October 16, 2019 6:30 AM

DOES BODY MASS INDEX INFLUENCE THE ODDS OF A GOOD PERINATAL OUTCOME FOLLOWING FRESH AUTOLeGous IN VITRO FERTILIZATION CYCLES AMONG PATIENTS WITH POLYCYSTIC OVARY SYNDROME? A NATIONAL STUDY. Jenna S. Hynes, MD, a Jeremy M. Weber, MS,b Tracy Truong, MS,c Kelly S. Acharya, MD, a Jennifer L. Eaton, MD, MSC.1 Division of Reproductive Endocrinology and Infertility, Duke University Medical Center, Durham, NC; 2Department of Biostatistics & Bioinformatics, Duke University Medical Center, Durham, NC.

OBJECTIVE: To examine the association between body mass index (BMI) and the odds of a term, normal-weight, singleton live birth among women with polycystic ovary syndrome (PCOS) undergoing in vitro fertilization (IVF).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We utilized the 2012-2015 Society for Assisted Reproductive Technologies Clinical Outcomes Reporting System (SART CORS) to identify fresh, autologous IVF cycles among women aged <41 with ovulatory dysfunction. We included only women with anti-Mullerian hormone (AMH) >4.5 ng/mL to more accurately identify patients with PCOS. Patients were assigned to BMI categories based on the World Health Organization guidelines. The primary outcome was a good perinatal outcome, defined as singleton live birth at ≥37 weeks gestation with birth weight ≥2500g and ≤4000g. A multivariable GEE model was used to assess the association between BMI and a good perinatal outcome while accounting for the correlation between repeated IVF cycles and adjusting for age, race, parity, diagnosis, and smoking.

RESULTS: The analysis included 9,611 cycles from 8,431 women. Baseline characteristics were similar among groups. With increasing BMI, patients had fewer oocytes retrieved and embryos cryopreserved despite higher gonadotropin doses (Table). Pregnancy and live birth rates decreased with increasing BMI, while miscarriage rates increased. After adjusting for covariates, women with class III or super obesity were half as likely to have a good perinatal outcome as normal weight women (OR 0.50, 95% CI 0.37-0.68, P<0.001). Univariate analysis indicated that the risk was identical according to sex, higher in multiple births (OR 2.18 [2.08-2.28], if further adjusted for maternal smoking (OR 2.2), and other maternal morbidity (MM) events except diabetes, and congenital malformations are known to be at increased risks of perinatal morbidity and mortality. The frequency of multiple deliveries was 1.68% (48,425), including 13% from IVF. The frequency of premature deliveries was higher in IVF vs non-IVF group, 19.3% vs 6.9% (p<0.0001), as it was for single deliveries (9.0% vs 5.7%, p<0.0001). The SGA rate was increased in IVF compared to non-IVF group, in all neonates, 21.6% vs 12.1%, (p<0.0001); in singletons, 14.9% vs 11.4% (OR = 1.33 [1.29-1.38], p<0.001). Univariate analysis indicated that the risk was identical according to sex, higher in multiple births (OR = 4.8) and premature births (OR = 2.9), if maternal smoking (OR = 2.2), and other maternal morbidity (MM) events except diabetes, and congenital malformations (OR = 1.7). In multivariate analysis, the added risk of SGA in IVF group was 2.1 [2.07-2.016] after adjustment for age, smoking, maternal obesity; 1.37 [1.34-1.40] if adjusted in addition to multiple births: 1.34 [1.30-1.37] if adjusted in addition to MM; 1.33 [1.30-1.36] if further adjusted for prematurity.

CONCLUSIONS: Large observational studies identified that IVF pregnancies are associated with a significant risk of concerns for babies. SGA babies are known to be at increased risks of perinatal morbidity and mortality. The results of this large cohort, whose strength is the completeness of IVF
and controls neonates data, provide evidence that the proportion of SGA birth post-IVF, including singletons, is increased compared to general population in multivariate analysis, after adjustment for age, smoking, maternal obesity, multiple births, maternal morbidity and prematurity. This is important to inform without worrying candidates for IVF, and understand possible concerns in IVF-children development. Further studies should allow to define more or less at-risk subgroups.

**SUPPORT:** None.

**P-467** Wednesday, October 16, 2019 6:30 AM

**OBSTETRIC, NEONATAL AND LONG-TERM OUTCOMES OF CHILDREN CONCEIVED FROM IN VITRO MATUERED OOCYTES.** Eun Jeong Yu, MD,1 Tae Ki Yoon, M.D. Ph.D.,2 Woo Sik Lee, M.D. Ph.D.,3 Hannah Kim, MD,4 Chanhong Park, M.D.,5 Jayeon Kim, MD, MPH,6 Cha Seoul Fertility Center, OB&GY, Seoul, Korea, Republic of (South); 6CHA Seoul Fertility Center, Seoul, Korea, Republic of (South); 7Fertility Center of CHA Gangnam Medical Center, Seoul, Korea, Republic of (South); 6Fertility Center of CHA Gangnam Medical Center, SEOUL, Korea, Republic of (South).

**OBJECTIVE:** To investigate the obstetric, neonatal, and long-term outcomes of in vitro maturation (IVM) compared to conventional IVF in women with polycystic ovarian syndrome (PCOS).

**DESIGN:** Matched retrospective case-control study.

**MATERIALS AND METHODS:** One hundred eighty-four patients undergoing IVM were compared with 366 patients undergoing IVF. All had PCOS and matched for patients’ age, gestational age at birth, and the number of fetuses. Only women who had been conceived after fresh embryo transfer in the cycle of oocyte retrieval between January 1999 and December 2015 were included. Pregnancies using preimplantation genetic tests, testicular sperm extraction, or donor gametes were excluded. A questionnaire including pregnancy/neonatal outcomes and childhood medical problems/development was developed and distributed by reproductive specialists and administered via phone interview.

**RESULTS:** Women’s mean age at oocytes retrieval was 32.6 ± 2.9 years. Children’s mean age was 7.5 ± 2.3 years. There were no differences in the frequency of obstetric and neonatal outcomes between the two groups. No difference was found in birthweights between the two groups. However, women undergoing IVM had a significantly higher incidence of hospitalization during childhood. Growth developmental status of both groups was within normal range.

**CONCLUSIONS:** In a matched setting between IVM and IVF babies born from women with PCOS, IVM is not associated with any additional risk compared to IVF after a mean follow-up of 7.5 years.

---

**P-468** Wednesday, October 16, 2019 6:30 AM

**COMPARISON OF BIRTHWEIGHT AND GESTATIONAL AGE AT DELIVERY IN SINGLE FROZEN EMBRYO TRANSFERS (FET) WITH AND WITHOUT PGT-A.** Laura Perez Soriano, B.A.,1 Joshua Stewart, M.D.,2 Steven Spandorfer, M.D.,3 Zev Rosenwaks, M.D.4 The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

**OBJECTIVE:** To compare perinatal outcomes and early hormonal trends between elective single blastocyst FET cycles with PGT-A and without PGT-A.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** All patients undergoing an FET cycle of a single blastocyst between January 2015 and December 2017 were included. Cycles were divided into those with PGT-A and without. For PGT-A cycles, only euploid embryos were included. Inclusion criteria: delivery of a live singleton. Exclusion criteria: use of donor oocytes or multiple gestations. Primary outcomes were incidence of term or preterm delivery, low birth weight (LBW) and very low birth weight (VLBW). Secondary outcomes were early BhCG levels and trends. Groups were stratified by FET protocol, natural cycle, or medicated.

**RESULTS:** 876 cycles met inclusion criteria, 502 with PGT-A and 374 without. Main results summarized in table. There was no difference in mean gestational age (GA), birth weight, or incidence of preterm delivery, LBW, or VLBW between the groups. This equivalence persisted after controlling for maternal age and FET protocol type. In FET cycles with PGT-A, median initial and second BhCG levels were significantly lower in cycles resulting in a LBW or VLBW infant compared to NBW. This difference did not persist in cycles without PGT-A.

**CONCLUSIONS:** Reassuringly, there was no difference in mean GA, birth weight, or incidence of preterm delivery, LBW, or VLBW infants between FETs with PGT-A and without. Initial BhCG levels were significantly lower in pregnancies resulting in LBW or VLBW infants as compared to NBW.
infants. This difference did not persist in cycles without PGT-A. Therefore, in pregnancies achieved by FET with PGT-A, early hCG trends may be a useful prognostic indicator for neonatal birth weight. Further studies will need to elucidate the mechanism behind this difference.

**P-469** Wednesday, October 16, 2019 6:30 AM

**ASSOCIATION BETWEEN EMBRYO QUALITY AND BIRTH WEIGHT AMONG SINGLETONS AND TWINS CONCEIVED THROUGH AUTOLOGOUS FRESH IVF CYCLES.** Mengmeng Li, MSPH MBBS, Valerie L. Baker, MD, a Johns Hopkins Bloomberg School of Public Health, Department of Population, Family and Reproductive Health, Baltimore, MD; Johns Hopkins University School of Medicine, Division of Reproductive Endocrinology and Infertility, Lutherville, OR.

OBJECTIVE: To determine if embryo quality is associated with birth weight for infants conceived via autologous fresh IVF.

DESIGN: Retrospective analysis of fresh autologous IVF cycles reported to SART CORS from 2008-2013.

MATERIALS AND METHODS: All autologous fresh IVF cycles resulting in livebirth with outcome confirmed by review of medical record were eligible for inclusion in the analysis. Cycles were excluded if more than 2 embryos or embryos of different quality were transferred.

The primary predictor was embryo quality (poor, fair, good). This grading system in SART CORS has been validated by Vernon et al (2011)1. Outcomes included continuous (in gram) and dichotomized birth weights (SGA: z-score ≤ -1.88; LGA z-score ≥ 1.88). We adjusted for covariates (maternal age, BMI race, smoking history, miscarriage, parity, infertility, gestational age, infant sex). Separate analyses were performed for singletons and twins, as well as for cleaved and blastocyst transfer. Depending on outcomes, multiple linear or logistic regression and Generalized Estimation Equation modeling were conducted.

RESULTS: There were 5262 (67.86%) singleton births (cleaved: 2089, blastocyst: 3173) and 2492 twin births (cleaved: 950, blastocyst: 1542) included in the analysis.

Among singletons conceived via cleaved embryo transfer, embryo quality was not predictive of birth weight. The difference in birth weight between fair vs. good quality was 33.6g (95% CI: -5.6, 72.8); poor vs. good: 123.7g (-30.1, 277.5). For singletons conceived via blastocyst transfer, fair quality was associated with decreased birth weight comparing with good quality (-38.0g (-74.1, -1.9)). No difference was seen for poor vs. good blastocysts (79.4g (-53.9, 212.7)). Among twins, quality for both cleaved embryos and blastocysts was not predictive of birth weight. The difference in birth weight between fair vs. good quality was 33.6g (95% CI: -5.6, 72.8); poor vs. good: 123.7g (-30.1, 277.5). No difference was seen for poor vs. good blastocysts (79.4g (-53.9, 212.7)).

OBJECTIVE: Altered hCG kinetics have been observed in conceptions after fresh vs. frozen/thawed embryo transfers and following blastomere biopsies in cleavage stage embryos. While preimplantation genetic testing has improved pregnancy rates in some populations, the impact of trophectoderm biopsy on hCG kinetics and subsequent birthweight is unknown. The aim of this study was to determine differences in first trimester hCG kinetics by mode of conception and subsequent risk of small and large for gestational age infants (SGA and LGA). Groups examined include unassisted natural conceptions, pregnancies after fresh embryo transfer (ET), frozen ET, and trophectoderm preimplantation genetic testing for aneuploidy (PGT-A).

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Serial serum hCG measurements were assessed for 598 singleton pregnancies between 10 and 28 days post-conception. All PGT-A subjects were also frozen embryo transfers. Chi-squared tests were used to test differences in the incidence of SGA and LGA by mode of conception. A joint random effects and logistic model was used to evaluate the effect of mode of conception on hCG slope (per day increase in log-transformed hCG) and incidence of SGA/LGA. Models were adjusted for maternal age, body mass index, and parity as appropriate. Odds ratios illustrate the change in risk associated with a one standard deviation increase in hCG slope.

RESULTS: Fresh ET had the highest incidence of SGA (12%) and frozen ET had the highest incidence of LGA (16%). PGT-A had the lowest incidence of each event among the groups observed (4% SGA and 8% LGA). Estimated hCG rise per day by group was as follows: Unassisted (0.41), fresh ET (0.39), frozen ET (0.43), PGT-A (0.45). Significant differences in hCG slope were found for all five pairwise group comparisons tested: PGT-A/unassisted (p < 0.01), PGT-A/frozen ET (p < 0.01), PGT-A/frozen ET (p = 0.02), fresh ET/frozen ET (p < 0.01), fresh ET/unassisted (p = 0.03). Slower hCG rise is associated with SGA (OR = 0.64, p < 0.01) but not with LGA (OR = 1.16, p = 0.33).

CONCLUSIONS: Slower hCG rise is associated with a higher risk of SGA; yet hCG rise does not impact LGA risk. There are differences in expected rate of hCG rise by mode of conception such that PGT-A has the fastest hCG rise, followed by frozen ET, unassisted, and fresh ET. Notably, PGT-A is not associated with abnormal fetal growth phenotypes, supporting the safety of this technology. These findings suggest the super-ovulated environment in fresh ET may predispose to abnormal trophoblast differentiation and early placentation resulting in altered hCG kinetics and fetal growth; yet the mechanisms of LGA in frozen embryo transfer may be mediated by other mechanisms beyond trophoblast function.


**TABLE 1.**

<table>
<thead>
<tr>
<th></th>
<th>Singleton (N=5262)</th>
<th>Twin (N=2492)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cleaved Embryo (N=2089)</td>
<td>Blastocyst (N=3173)</td>
</tr>
<tr>
<td><strong>SGA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good (ref)</td>
<td>aOR (95% CI)</td>
<td>aOR (95% CI)</td>
</tr>
<tr>
<td>Fair</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Poor</td>
<td>0.81 (0.60, 1.10)</td>
<td>1.19 (0.92, 1.52)</td>
</tr>
<tr>
<td><strong>LGA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good (ref)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fair</td>
<td>1.12 (0.78, 1.61)</td>
<td>0.83 (0.60, 1.15)</td>
</tr>
<tr>
<td>Poor</td>
<td>2.25 (0.94, 5.38)</td>
<td>1.41 (0.52, 3.79)</td>
</tr>
</tbody>
</table>

**P-470** Wednesday, October 16, 2019 6:30 AM

**IMPACT OF MODE OF CONCEPTION ON EARLY PREGNANCY HUMAN CHORIONIC GONADOTROPIN RISE AND BIRTHWEIGHT.** Hayley M. Richardson, MS, a Charikleia Kalliora, MD, b Monica Mainigi, MD, c Christos Coutifaris, MD, PhD, b Mary D. Sammel, ScD, b Suneeta Senapati, MD, MSCE. a University of Pennsylvania, Philadelphia, PA; b University of Pennsylvania, Division of Reproductive Endocrinology and Infertility, Philadelphia, PA; c University of Pennsylvania, Philadelphia, PA.

OBJECTIVE: Altered hCG kinetics have been observed in conceptions after fresh vs. frozen/thawed embryo transfers and following blastomere biopsies in cleavage stage embryos. While preimplantation genetic testing has improved pregnancy rates in some populations, the impact of trophectoderm biopsy on hCG kinetics and subsequent birthweight is unknown. The aim of this study was to determine differences in first trimester hCG kinetics by mode of conception and subsequent risk of small and large for gestational age infants (SGA and LGA). Groups examined include unassisted natural conceptions, pregnancies after fresh embryo transfer (ET), frozen ET, and trophectoderm preimplantation genetic testing for aneuploidy (PGT-A).

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Serial serum hCG measurements were assessed for 598 singleton pregnancies between 10 and 28 days post-conception. All PGT-A subjects were also frozen embryo transfers. Chi-squared tests were used to test differences in the incidence of SGA and LGA by mode of conception. A joint random effects and logistic model was used to evaluate the effect of mode of conception on hCG slope (per day increase in log-transformed hCG) and incidence of SGA/LGA. Models were adjusted for maternal age, body mass index, and parity as appropriate. Odds ratios illustrate the change in risk associated with a one standard deviation increase in hCG slope.

RESULTS: Fresh ET had the highest incidence of SGA (12%) and frozen ET had the highest incidence of LGA (16%). PGT-A had the lowest incidence of each event among the groups observed (4% SGA and 8% LGA). Estimated hCG rise per day by group was as follows: Unassisted (0.41), fresh ET (0.39), frozen ET (0.43), PGT-A (0.45). Significant differences in hCG slope were found for all five pairwise group comparisons tested: PGT-A/unassisted (p < 0.01), PGT-A/frozen ET (p < 0.01), PGT-A/frozen ET (p = 0.02), fresh ET/frozen ET (p < 0.01), fresh ET/unassisted (p = 0.03). Slower hCG rise is associated with SGA (OR = 0.64, p < 0.01) but not with LGA (OR = 1.16, p = 0.33).

CONCLUSIONS: Slower hCG rise is associated with a higher risk of SGA; yet hCG rise does not impact LGA risk. There are differences in expected rate of hCG rise by mode of conception such that PGT-A has the fastest hCG rise, followed by frozen ET, unassisted, and fresh ET. Notably, PGT-A is not associated with abnormal fetal growth phenotypes, supporting the safety of this technology. These findings suggest the super-ovulated environment in fresh ET may predispose to abnormal trophoblast differentiation and early placentation resulting in altered hCG kinetics and fetal growth; yet the mechanisms of LGA in frozen embryo transfer may be mediated by other mechanisms beyond trophoblast function.

FIRST TRIMESTER VAGINAL BLEEDING DOES NOT PREDICT SMALL FOR GESTATIONAL AGE NEWBORNS FOLLOWING SINGLE EUPLOID FROZEN EMBRYO TRANSFER. Sydney Chang, MD, a Sass Wodoslawsky, BA, a Lily Ottensoser, BA, a Taranesh Gharib Nazem, MD, a Dmitry Gounko, MA, a Joseph A. Lee, BA, b Alan B. Copperman, MD aIcahn School of Medicine at Mount Sinai, New York, NY; bReproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Newborns that are small for gestational age (SGA) have birth weights below the 10th percentile. Uterine/placental factors associated with SGA neonates include decreased blood flow the uterus and placenta, placental abruption, placenta previa, and uterine infection. A secondary analysis of data from the NCPP MD Fetal Growth Studies suggests that more than one day of vaginal bleeding (VB) in the first trimester was associated with lower infant birth weight. However, it is unclear whether this holds true in pregnancies achieved with the use of assisted reproductive technology treatment. The objective of this study was to determine in an infertile population undergoing in vitro fertilization (IVF) whether first-trimester VB is associated with the likelihood of having an SGA infant.

DESIGN: Retrospective, cohort study.

MATERIALS AND METHODS: The study included patients at an academic ART center who underwent a single euploid FET and experienced a live birth from 2012 to 2019. Natural language processing was performed to identify pregnancies complicated by VB prior to 30 weeks of gestation. Blind review of the database was conducted by two independent reviewers to verify data quality. Incidents of ‘spotty’ or ‘stained’ were excluded from the analysis. Primary outcome was the presence of an SGA infant, which was determined using the sex-specific weights for the 10th percentile of neonatal birth weight. Data were evaluated using T-tests, chi-square tests, and multivariate logistic regression models.

RESULTS: A total of 1611 FET cycles with a live birth outcome from 1528 patients were included in the study. The overall incidence of VB was 17.69% (n = 285). Pregnancies were divided into two groups: (1) pregnancies with VB prior to the 10th week of gestation and (2) pregnancies with no VB. Univariate analysis demonstrated significant differences in BMI, gravidity, and route of progesterone administration between groups. There was no difference in aspirin use, average birth weight, or gestational age at delivery between groups. There were a total of 18 (6.32%) SGA infants in the VB group, and 115 (8.67%) SGA infants in the no VB group. Controlling for BMI, gravidity, and route of progesterone administration, multivariate regression analysis did not demonstrate any significant association between VB and the incidence of SGA newborns.

CONCLUSIONS: In contrast to the study published by Bever et al., patients who experienced first trimester VB did not demonstrate a higher incidence of SGA newborns. Use of natural language processing of electronic medical records enabled us to re-construct first trimester incidents not otherwise easily obtainable, limiting potential recall bias as a confounding variable. A limitation of our study design was the lack of a quantitative method to track quantity and duration of VB. Nevertheless, patients undergoing single euploid FET can be reassured that first trimester VB is not associated with a higher incidence of SGA infants.


SUPPORT: None.

P-472 Wednesday, October 16, 2019 6:30 AM

DELAYED BLASTULATION HAS NO IMPACT ON NEONATAL OUTCOMES IN FROZEN-THAWED SINGLE Blastocyst CYCLE TRANSFERS. Aya Yamato, B.S., a Nanako Ishiki, M.S., a Yuka Miyazaki, M.S., a Hiroshi Matsumoto, M.S., a Satoshi Mizuno, Ph.D., a Ryoko Minekawa, Dr., a Aisaku Fukuda, Dr., a Yoshitomo Harimoto, MD, PhD aTVF Osaka Clinic, Osaka, Japan; Affiliation not provided; bTVF Osaka Clinic; cHORAC Grand Front Osaka clinic, Osaka, Japan.

OBJECTIVE: Blastocysts formed on day 6 (D6BL) are available in ART treatment although they are considered to be suboptimal for transfers due to delayed blastulation. As demonstrated in several reports, D6BLs have more abnormalities in mitotic apparatus, resulting poorer clinical outcomes in transfers as compared with blastocysts formed on day 5 (D5BL). However, im-

pacts of delayed blastulation on prenatal outcomes after blastocyst transfers have not been fully investigated so far. The present study was designed to compare neonatal outcomes between singletons born after transfers of a frozen-thawed single blastocyst formed on Day 5 and Day 6.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 1137 neonates born after transfers of a frozen-thawed single D5BL and 134 neonates after D6BL transfers performed between 2008 and 2016 were analyzed. Blastocysts that reached grade 3 by the Gardner’s score on day 5 or 6 were defined as D5BL and D6BL respectively. The following parameters were statistically analyzed using student’s t-test or chi-square test between singletons born after D5BLs and D6BLs transfers: birth weight, birth height, gestational age at birth, sex ratio and occurrence of congenital abnormalities. Multiple linear regression analysis was performed to investigate the influential parameters on fetal growth among gender, gestational age and day of blastulation.

RESULTS: Birth weight (g), birth height (cm), gestational age (weeks), sex ratio (m/f) and congenital abnormality rates (%) of babies born after transfers of D5BLs vs D6BLs were 3057.3 ± 477.7 vs 3041.2 ± 448.7 (ns), 48.7 ± 2.6 vs 48.7 ± 2.9 (ns), 38.7 ± 2.0 vs 38.5 ± 1.8 (ns), 1.04 vs 1.23 and 3.5 vs. 3.0 (ns), respectively. Multiple linear regression identified gender (p<0.01) and gestational age (p<0.01) as associated parameters with fetal weight. Delayed blastulation, on the other hand, was not related to either birth weight or height.

CONCLUSIONS: Our study showed that neonatal outcomes were not statistically different between babies born after transfers of D5BLs and D6BLs. Based on the results of both univariate and multivariate analyses, delayed blastulation has no influence on the neonatal outcomes, therefore transfer of D6BL is an optional alternative for patients who miss blastocysts on day 5.

Reference: None.

SUPPORT: None.

P-473 Wednesday, October 16, 2019 6:30 AM

IS LOW BIRTH WEIGHT RELATED TO HIGH OOCYTE YIELD DURING FRESH TRANSFER ART CYCLES? RETROSPECTIVE ANALYSIS FROM HOMOLLOGOUS CYCLES. Edelmiro Garza-Padilla, M.D., a Julio C. Rosales, M.D., a S. Alberto Dávila-Garza, M.D., a Karla A. Cantá, M.S.C., a Pasquale Patrizio, M.D., a Mario A. Patrón-Vázquez, M.D., a IECH, Monterrey, NL, Mexico; bYale Fertility Center, New Haven, CT.

OBJECTIVE: To determine if the number of retrieved oocytes correlates with live birth rate (LBR) and incidence of low birth weight (LBW).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All cycles of fresh embryo transfer with the use of homologous oocytes (n = 2216) between 2006–2017 performed at a private fertility center were reviewed and included. Groups were established in relationship to the number of retrieved oocytes (group 1: ≤10, group 2: 11-15, group 3: ≥16) and women age (≤35 and ≥36). Non adjusted comparisons between groups were calculated using t-test and chi-squared distribution. Furthermore, one-way analysis of variance (ANOVA) and Tukey posthoc test, were used to test mean comparisons among the three groups. Pregnancy rates (positive serum hCG) and live birth rates were calculated. Finally, after excluding multiple pregnancy newborns, using the Intergrowth® matrix, each newborn was classified according to its weight (percentiles and z-score) to examine its relationship with the number of retrieved oocytes.

RESULTS: The younger group (≤35yo, n = 1176, 53%) had a pregnancy rate of 41.5% and LBR of 29.7% per cycle. The other group (≥36yo, n = 1040, 47%) had a pregnancy rate of 28.2% and LBR of 16.7%. According to the number of retrieved oocytes, the group 2 and 3 had a statistically significant greater pregnancy rate (41.2% and 42%) than group 1 (29.8%) (p<0.001). However, there was no significant difference in the LBR between groups.

Comparative analysis between the number of retrieved oocytes, live birth rate and incidence of low birth weight (LBW) showed the following weight percentile means: group 1 - 46.84±23.79, group 2 - 43.78±27.38 and group 3 - 52.76±27.29, with no statistical differences found among the groups (p=0.077). No correlation was found after performing a linear regression for weight percentile or z-scores and number of retrieved oocytes for all patients and in the younger patients.

CONCLUSIONS: In homologous fresh embryo transfer with the use of homologous oocytes, higher number of retrieved oocytes was associated with a higher pregnancy rate and incidence of low birth weight (LBW). Further studies are warranted to determine if a subgroup of women may be particularly vulnerable to certain maternal and fetal complications.
OBJECTIVE: Assisted reproduction (ART) has been associated with adverse perinatal outcomes, including extremes of birth weight (BW) and pre-term birth (PTB). We sought to explore the incidence of PTB, low birth weight (LBW), very low birth weight (VLBW), and macrosomia (MS) in GC pregnancies.

DESIGN: Retrospective analysis of all GC deliveries from a single agency from 2008-2019.

MATERIALS AND METHODS: Data from a large surrogate agency that consisted of matched GCs and intended parent (IP) couples for an index GC pregnancy were reviewed. The following was collected for each GC pregnancy: BW, number delivered, and gestational age (GA) at delivery. For each GC, history of PTB and history of multiple gestation were also collected. Definitions of LBW, VLBW, and MS were as defined by World Health Organization criteria. PTB was defined as delivery in the GC pregnancy at <37 weeks. Chi-squared was used for dichotomous variables and student’s t-test for continuous variables.

RESULTS: Data show that births from frozen embryos have higher birth percentile when compared to fresh births. As well as 90% of these births presented weight greater than 2500g. We also found a statistical difference that related prematurity with births from fresh transfer. The main results are presented in Table 1.

CONCLUSIONS: Incidence of LBW and VLBW were similar to national averages. Most PTB in index GC pregnancies was in women with a history of PTB, and more likely singleton rather than multiple gestations. In women with prior full term deliveries, carrying multiples did not impart a greater risk of PTB. A GC’s prior obstetric history appears to have the greatest impact on the GA at delivery in the GC pregnancy. These factors should be taken into account when identifying GC candidates and deciding on the number of embryos to transfer.

TABLE 1. Differences between frozen embryo and fresh embryo births regarding birth percentile, gestational age and birth weight stratifications.

<table>
<thead>
<tr>
<th>Percentile*</th>
<th>Gestational age*</th>
<th>Birthweight*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10 10-90</td>
<td>&gt;90</td>
<td>&lt;34 wks 34-37wks &gt;37 wks</td>
</tr>
<tr>
<td>Fresh embryo (n=1443)</td>
<td>219 (15,2) 1117 (77,4) 107 (7,4)</td>
<td>112 (7,8) 263 (18,2) 1067 (74,0)</td>
</tr>
<tr>
<td>Frozen embryo (n=486)</td>
<td>36 (7,4) 376 (77,4) 74 (15,2)</td>
<td>15 (3,1) 51 (10,5) 420 (86,4)</td>
</tr>
<tr>
<td>Total (n=1929)</td>
<td>255 1493 181</td>
<td>127 314 1487</td>
</tr>
</tbody>
</table>

*p<0.001.
ART PREGNANCY RISKS

P-477 Wednesday, October 16, 2019 6:30 AM

OVERVIEW OF 2016 U.S. ASSISTED REPRODUCTIVE TECHNOLOGY (ART) TREATMENT OUTCOMES AND CONTRIBUTION OF ART TO MULTIPLE-BIRTH AND PRETERM INFANTS IN THE UNITED STATES.

Saswati Sunderam, M.A PhD, a Dmitry Kissin, MD, MPH, b Yujia Zhang, PhD, c Sheree Boulet, Dr.PH, c Suzanne G. Folger, PhD, c Lee Warner, PhD, c Wanda D. Barfield, MD, c Centers for Disease Control and Prevention, Chambly, GA; Centers for Disease Control and Prevention (CDC), Atlanta, GA; Centers for Disease Control and Prevention, Atlanta, GA; Centers for Disease Control and Prevention, Atlanta, GA.

OBJECTIVE: To assess national and state-specific ART utilization and outcomes and the contribution of ART to multiple births and prematurity.

DESIGN: Population-based cross-sectional analysis.

MATERIALS AND METHODS: Data for ART procedures and birth outcomes in 2016 were obtained from CDC’s National ART Surveillance System (years 2015 and 2016). Data for all infants born in the U.S. were obtained from 2016 National Vital Statistics System birth data. The number of ART procedures performed per million women 15-44 years of age (ART use), rates of elective single embryo transfers (eSET) among women <35 years, rates of ART preterm and multiple-birth infants, and proportions of ART-conceived infants among all infants, and all multiple-birth and preterm infants were calculated for each reporting area (50 States, District of Columbia, and Puerto Rico), by mother’s state of residence. The proportion of infants who were small for gestational age (SGA) (i.e., born at 37 weeks of gestation or fewer) was considered as subfertile, all others were considered as fertile. The ART pregnancies were additionally categorized by maternal fertility status and infertility diagnosis.

RESULTS: The study population included 1,518,175 pregnancies. A higher proportion of ART infants are multiple and preterm in the U.S compared to all births. Wide variations were observed among reporting areas in the rates of ART utilization and eSET. CONCLUSIONS: A higher proportion of ART infants are multiple and preterm in the U.S compared to all births. Wide variations were observed among reporting areas in the rates of ART utilization and eSET. The proportion of ART-conceived singletons that were SGA was 8.7% for preterm infants, 8.0% for term infants, and 8.1% overall; the corresponding percentages among all singletons were 9.3%, 10.5%, and 9.9%.

CONCLUSIONS: A higher proportion of ART infants are multiple and preterm. Rates of SGA for singletons born preterm, term, and for all gestational ages were lower among ART-conceived infants compared with all infants, possibly indicating better health behaviors and care among ART patients.

SUPPORT: NONE.

FERTILITY & STERILITY®
PUBLICATION OF THE SOCIETY FOR MATERNAL-FETAL MEDICINE

OBJECTIVE: The objective of this large cohort study is to identify by univariate and multivariate analysis whether there is an excess of maternal morbidity (MM) in ongoing pregnancies and deliveries after IVF and fresh transfer techniques, when compared to spontaneous conceptions (SC). DESIGN: This is an observational, exposed-unexposed cohort study comparing pregnancies, deliveries and births following IVF, standard or using Intra Cytoplasmatic injection (ICSI), and fresh transfers to non-IVF controls. The study included all 2,832,578 national deliveries registered between 2013 and 2016 in France, among which 1.5% (43,084) resulted from IVF and immediate fresh transfer.

MATERIALS AND METHODS: Pregnancies and deliveries were analyzed by extracting the Information Systems Medication Program (PMSI) French database. The main identified maternal morbidity indicators for the 43,084 IVF and 2,789,494 non-IVF pregnancies were: venous and arterial thrombosis (VT, AT), gestational diabetes mellitus (GDM), pre-eclampsia (PE), Placenta Previa (PP), placenta abruption (PA) and hemorrhage at delivery (HD). The risks of MM in IVF were estimated in multivariable analysis after adjustment for maternal age, smoking and obesity, and multiple deliveries.

RESULTS: The mean maternal age was 33.9±5.3 years and 29.9 years in the IVF and control groups (p<0.0001). The rate of multiple deliveries was 1.68%, of which 13% if IVF conception. Diabetes and hypertensive disorders during pregnancy were more common in the IVF vs non-IVF group: 1.01% vs 0.9% (p=0.01) and 1.04% vs 0.9% (p<0.001). Tobacco dependence and obesity were less common in the IVF vs non-IVF group (2.2% vs 4.5%, and 3.9% vs 4.3%, p<0.001). The frequency of premature deliveries was higher in IVF vs non-IVF: 19.3% vs 6.9% (p<0.0001), persistent for single pregnancies (9.0% vs 5.7%, p<0.001). The risk of MM (VT, GDM, PE, PP, PA, HD) was higher in IVF vs non-IVF (20.9% vs 14.3%, p<0.0001), even if single pregnancies (19.6% vs 14.1%, p<0.0001) except arterial thrombosis. The risk of MM increased significantly with age for all events except for PE. In multivariate analysis, IVF is a significant risk factor for all MM events except arterial thrombosis. The adjusted risk of the occurrence of at least one concern after IVF is 1.29 [1.26-1.32] at all and 1.32 [1.28-1.35] in single deliveries. This risk is stable over the four years.

CONCLUSIONS: Large observational studies identified that IVF pregnancies are associated with a significant risk of complications, initially attributed to multiple pregnancies, as compared with pregnancies after SC. The strength of this large national exposed-unexposed cohort study lies in the number and completeness of subjects studied. Our data provide in turn evidence for increased adjusted risk of premature delivery and maternal morbidity (VT, GDM, PE, PP, PA, and HD) after IVF, including in single pregnancies. The knowledge of the excess risk is an essential tool for informing without worrying couples candidate for IVF, and analyzing neonatal health of IVF-children. Future developments should allow to refine the knowledge of more or less at-risk subgroups.

SUPPORT: None.

P-480 Wednesday, October 16, 2019 6:30 AM

THE IMPACT OF IVF ON NEONATAL BIRTHWEIGHT FROM 2000 TO 2017: A DRAMATIC REDUCTION OF LOW BIRTHWEIGHT INFANTS. Julia G. Kim, MD, MPH;* Brent M. Hanson, MD;* Andres Reig, MD;* Shelby A. Neal, MD;* Ashley W. Tieg, MD;* Emily K. Osman, MD;* Paul A. Bergh, MD;* Emre Seli, M.D.;* Richard Thomas Scott Jr, MD,* IVF-RLA New Jersey, Basking Ridge, NJ;*Yale University - Bridgeport Hospital, Bridgeport, CT.

OBJECTIVE: IVF is a known risk factor for low birthweights among newborn infants, both multiples and singletons alike. In past decades, new approaches to care such as extended culture, cryo-all cycles, and near comprehensive single embryo transfer (SET) have become increasingly prevalent and have the potential to reduce adverse outcomes and neonatal health risks. This study seeks to determine the change in birthweights over time as these new approaches have been integrated into clinical practice.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Birthweights and demographics of 19,886 IVF pregnancies at a single center from 2000 to 2017 were collected. This cohort included all pregnancies without use of a gestational carrier. These data were compared to annual US statistics reported by the Centers for Disease Control, which reported 72,940,619 pregnancies between 2000 through 2017.

RESULTS: In our IVF population, incidence of low birthweight (LBW) decreased from 36.5% to 21.1%, only slightly higher than the general population of 8.3% the CDC reported for 2017. The dramatically low birthweight (VLBW) was even more dramatic and declined 8% in 2000 to 2.1% in 2017, almost equal to the national risk of 1.4%. Declines in LBW and VLBW births directly correlated with reduced transfer order: the 2017 national rate of twins in similar age groups was 2.4%, on par with our practice’s IVF twin rate of 2.5% the same year. Currently, more than 97% of transfers are eSETs, independent of PGT-A use (~70% of cycles) and includes all age groups/all prior treatment histories.

CONCLUSIONS: Advances in clinical ART have resulted in marked improvements in sustained implantation rates (SIR), providing increased confidence in providers and patients while empowering effective use of eSET. Our prevalence of LBW and VLBW deliveries from IVF pregnancies now
approach that of the general population. This dramatic improvement was accomplished while simultaneously improving SIR such that delivery rates per transfer actually increased. It is now possible to perform SET in all patients without compromising delivery rates and drastically reducing the neonatal risks associated with LBW/VLBW endured by infertile couples and their progeny.

SUPPORT: None.

RESULTS: The didelphus group and the control group were statistically similar with respect to MA, BMI, cause of infertility, infertility type and insemination methods (P > 0.05).

Compared with the control group, the didelphus group had significantly higher rates of preterm delivery (75.0 vs. 42.2%; P = 0.019), very preterm birth (42.9 vs. 8.5%; P = 0.001), low birth weight (89.5 vs. 46.4%; P = 0.001) and perinatal mortality (32.1 vs. 5.1%; P < 0.001), and a significantly lower live birth rate (62.5 vs. 87.5%; P = 0.019); the gestational age at delivery (31.3 ± 5.7 vs. 35.6 ± 3.8 weeks; P = 0.017) and the live birth weight (1944 ± 387 vs. 2455 ± 475 g; P < 0.001) were significantly lower in the didelphus group than those in the control group. Additionally, the miscarriage rate (12.5 vs. 7.8%; P > 0.05) was higher in the didelphus group, but this difference was not significant.

CONCLUSIONS: Twin pregnancy was associated with increased rates of preterm delivery, low birth weight and perinatal mortality in women with a didelphus uterus after IVF-ET.

TABLE. The twin pregnancy outcomes between the didelphus group and the control group

<table>
<thead>
<tr>
<th>Pregnancy outcomes</th>
<th>The didelphus group (n=16)</th>
<th>The control group (n=64)</th>
<th>P-value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscarriage %,(n)</td>
<td>12.5 (2/16)</td>
<td>7.8 (5/64)</td>
<td>NS</td>
<td>1.67 (0.30-9.61)</td>
</tr>
<tr>
<td>Preterm delivery %,(n)</td>
<td>75.0 (12/16)</td>
<td>42.2 (27/64)</td>
<td>0.019</td>
<td>4.11 (1.20-14.14)</td>
</tr>
<tr>
<td>Perinatal mortality %,(n)</td>
<td>32.1 (9/28)</td>
<td>5.1 (6/118)</td>
<td>&lt;0.001</td>
<td>8.84 (2.82-27.70)</td>
</tr>
<tr>
<td>Live birth rate %,(n)</td>
<td>62.5 (10/16)</td>
<td>87.5 (56/64)</td>
<td>0.019</td>
<td>0.240 (0.07-0.84)</td>
</tr>
<tr>
<td>The gestational age at delivery (weeks)</td>
<td>31.3 ± 5.7</td>
<td>35.6 ± 3.8</td>
<td>0.017</td>
<td>8.10 (1.10-32.85)</td>
</tr>
<tr>
<td>&lt; 32 gestational weeks %,(n)</td>
<td>42.9 (6/14)</td>
<td>8.5 (5/59)</td>
<td>0.001</td>
<td>8.10 (1.10-32.85)</td>
</tr>
<tr>
<td>The live birth weight (g)</td>
<td>1944 ± 387</td>
<td>2455 ± 475</td>
<td>&lt;0.001</td>
<td>9.81 (2.16-44.46)</td>
</tr>
<tr>
<td>&lt;2500 g %,(n)</td>
<td>89.5 (17/19)</td>
<td>46.4 (52/112)</td>
<td>0.001</td>
<td>9.81 (2.16-44.46)</td>
</tr>
</tbody>
</table>

OBJECTIVE: To investigate the twin pregnancy outcomes of women with a congenital didelphus uterus after in vitro fertilization-embryo-transfer (IVF-ET).

DESIGN: A retrospective matched case-control study.

MATERIALS AND METHODS: A retrospective 1:4 matched case-control study was conducted of 16 cases of twin pregnancy in women with a congenital didelphus uterus after IVF-ET from January 2004 to December 2017. For each case in the study group, 4 consecutive control twin pregnancies in women with a normal uterus were included. Women in both groups were matched for maternal age (MA), body mass index (BMI), cause of infertility, infertility type and insemination methods. Patients with the monochorionic twins and twins with spontaneous or selective reduction were excluded. The pregnancy and obstetric outcomes between these two groups were compared.

RESULTS: The didelphus group and the control group were statistically similar with respect to MA, BMI, cause of infertility, infertility type and insemination methods (P > 0.05).

Compared with the control group, the didelphus group had significantly higher rates of preterm delivery (75.0 vs. 42.2%; P = 0.019), very preterm birth (42.9 vs. 8.5%; P = 0.001), low birth weight (89.5 vs. 46.4%; P = 0.001) and perinatal mortality (32.1 vs. 5.1%; P < 0.001), and a significantly lower live birth rate (62.5 vs. 87.5%; P = 0.019); the gestational age at delivery (31.3 ± 5.7 vs. 35.6 ± 3.8 weeks; P = 0.017) and the live birth weight (1944 ± 387 vs. 2455 ± 475 g; P < 0.001) were significantly lower in the didelphus group than those in the control group. Additionally, the miscarriage rate (12.5 vs. 7.8%; P > 0.05) was higher in the didelphus group, but this difference was not significant.

CONCLUSIONS: Twin pregnancy was associated with increased rates of preterm delivery, low birth weight and perinatal mortality in women with a didelphus uterus after IVF-ET.
OBJECTIVE: Although elevations in early- to mid-pregnancy blood pressure are related to risk of developing a hypertensive disorder of pregnancy, little is known regarding when this differentiation in blood pressure begins. We evaluated the relationship of preconception and very early pregnancy blood pressure with risk of developing preterm preeclampsia (PE), term PE, and gestational hypertension (GHTN). DESIGN: Prospective cohort study set in the EAGeR trial, which enrolled 1228 couples attempting pregnancy who had a history of pregnancy loss. Women were randomized to receive 81 mg aspirin or placebo for up to 6 menstrual cycles attempting pregnancy and, if they became pregnant, up to 36 weeks' gestation. MATERIALS AND METHODS: Systolic and diastolic blood pressure were measured by trained staff at enrollment prior to conception and at gestational weeks 4, 8, 12, 16 and 20, and were used to derive mean arterial pressure. Hypertensive disorders of pregnancy, including preterm PE, term PE and gestational hypertension, were classified retrospectively from medical record abstraction. We excluded 9 participants with chronic hypertension (blood pressure over 140/90 mmHg and/or anti-hypertensive treatment during preconception or in early pregnancy). Log-binomial models assessed the relationship of blood pressure at preconception and in early- to mid-pregnancy with risk of developing a hypertensive disorder of pregnancy (preterm PE, term PE and GHTN), adjusting for maternal age, pre-pregnancy BMI, parity, and treatment assignment (low-dose aspirin or placebo). We additionally evaluated the interaction of blood pressure with assignment to aspirin due to its efficacy in preventing preeclampsia among high-risk women.

RESULTS: Of 588 women who had a live birth and no chronic hypertension, 10 developed preterm PE, 18 term PE and 24 GHTN. During preconception, systolic blood pressure levels were elevated to similar degrees for women who developed preterm PE, term PE and GHTN compared to women who did not develop hypertension in pregnancy. However, by 4 weeks gestation, those who developed preterm PE had relatively elevated blood pressure (124.8±3.6) compared to those with term PE (117.8±2.7) and GHTN (115.8±2.4), a trend that continued up to 20 weeks' gestation. By as early as 4 weeks gestation, higher mean arterial pressure was associated with higher risk of preterm PE (relative risk [RR] 2.28, 95% confidence interval [CI] 1.01, 5.16 per 10 mmHg) and term PE (RR 1.57, 95% CI 1.02, 2.41 per 10 mmHg). No differences were observed by assignment to low-dose aspirin. CONCLUSIONS: Although preconception blood pressure levels were similarly elevated for women who developed preterm PE, term PE and GHTN as compared to women who did not develop a hypertensive disorder of pregnancy, a differentiation in blood pressure for each condition was observed as early as 4 weeks gestation. This suggests that some of the physiologic changes associated with preterm PE may occur prior to 4 weeks gestation.

SUPPORT: Intramural Research Program, Division of Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development.

P-484 Wednesday, October 16, 2019 6:30 AM

PERCEPTIONS OF MULTIFETAL GESTATION AMONGST PATIENTS BEING TREATED FOR INFERTILITY. Anne Hutchinson, M.D. Seth J. Barishansky, MS; Rafael Confino, BS; Angela K. Lawson, Ph.D.; Mary Ellen Pavone, MD MSCI, Northwestern University, Chicago, IL.

OBJECTIVE: To assess the desire for multifetal gestation in our patient population and understand patient perceptions regarding maternal and fetal risks inherent in these pregnancies.

DESIGN: Cross-Sectional Study.

MATERIALS AND METHODS: We designed a 40-question digital survey based on a previously validated survey and approved by our IRB (Ryan et al, 2004). Between the months of February and April 2019, patients presenting with infertility were approached. After receiving verbal consent, patients were provided with a tablet, preloaded with our survey, which collected de-identified patient demographic information as well as treatment outcomes ranked in order of preference, specifically “no child”, “singleton pregnancy,” “twin pregnancy,” “triplet pregnancy.” Using a series of true/false questions we also assessed knowledge of the complications of multiple births with questions regarding risks to the mother’s health during pregnancy and delivery, risks of cerebral palsy and long-term health problems in the infant and risk of death to the infant as well as knowledge of the financial and psychological risks of multifetal pregnancy.

These questions were then analyzed using chi-squared analysis to compare understanding of maternal and fetal risks of multifetal gestation between groups who identified singleton pregnancy as desired outcome to those who desired twin or triplet pregnancy.

RESULTS: 71 patients completed our survey. 68% reported singleton pregnancy as ideal treatment outcome, 30% reported twin pregnancy as ideal treatment outcome, 2% reported triplet pregnancy as ideal treatment outcome. A chi-squared analysis was used to compare the responses of patients desiring singleton pregnancy to those desiring twin or triplet pregnancy. Both groups showed similar understanding of increased risk of preterm birth in twin (88% vs. 100%) and triplet pregnancies (100% vs. 92%). Similarly, both groups showed similar understanding of the increased risk of triplet pregnancies on maternal health (85% vs. 83%). Patients desiring twin and triplet pregnancies, however, showed less understanding of increased maternal risk in twin pregnancy (77% vs 52%, p<0.05), and increased risk of neonatal morbidity in twin pregnancy (17% vs 44%, p<0.05) and triplet pregnancy (26% vs 54%, p<0.05).

Both groups showed similar understanding of the increased risk of neonatal mortality in twin pregnancies (23% vs 22%) and triplet pregnancies (38% vs 30%).

CONCLUSIONS: A significant number of patients undergoing fertility treatment desire twin and triplet gestation. This desire seems to be associated with an incomplete understanding of maternal and neonatal risks associated with multifetal gestation. We believe that targeted patient education regarding these risks may decrease patient desire for multifetal gestation and help to bring patient and provider goals into better alignment.


P-485 Wednesday, October 16, 2019 6:30 AM

RISK OF ECTOPIC PREGNANCY AFTER DIFFERENT OVARIAN STIMULATION PROTOCOLS IN FRESH SINGLE EMBRYO TRANSFER: ANALYSIS OF 71,831 CYCLES FROM THE JAPANESE ART REGISTRY. Seung Chik Jwa, M.D., Ph.D., M.P.H.; Sachie Seto, M.D., Ph.D.; Masashi Takamura, M.D., Ph.D.; Akira Kuwahara, M.D., Ph.D.; Takeshi Kajihiro, M.D., Ph.D.; Osamu Ishihara, M.D., Ph.D.; Saitama Medical University, Saitama, Japan; Tokushima University, Tokushima, Japan.

OBJECTIVE: To investigate the risk of ectopic pregnancy following different ovarian stimulation protocols in fresh cycles.

DESIGN: Registry-based retrospective cohort study.

MATERIALS AND METHODS: This study included all autologous cycles that resulted in a clinical pregnancy after described ovarian stimulation protocols (natural, clomiphene (CC), clomiphene + gonadotropin, human chorionic gonadotropin (hCG) agonist, and GnRH agonist) in fresh single embryo transfers between 2007 and 2015 in Japan. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using generalized estimating equations adjusted for potential maternal and treatment characteristics.

RESULTS: Among 71,831 clinical pregnancies, 1,049 (1.46%) ectopic pregnancies were reported. Ectopic pregnancy was more frequent for early cleavage stage embryo transfers than blastocyst transfers (1.54% vs. 1.29%, p = 0.008), and assisted hatching (AH) (1.75% in AH group vs. 1.36% in non-AH group, p = 0.003). The highest rate of ectopic pregnancy occurred with CC+gonadotropin (2.06%, 221/10,711), followed by CC alone (1.77%, 160/9,025), GnRH antagonist (1.49%, 216/14,490) and GnRH agonist protocols (1.40%, 415/29,585). The natural cycle had the lowest ectopic pregnancy rate of all ovarian stimulation protocols (0.46%, 376/2,020). Compared with the natural cycle, all other ovarian stimulation protocols were associated with a significantly increased risk of ectopic pregnancy. Ovarian stimulation using CC+gonadotropin had the highest increased risk for ectopic pregnancy (adjusted OR, 4.39, 95% CI, 2.55 to 7.54). In each stimulation protocol, there was no association between the risk of ectopic pregnancy and the number of oocytes retrieved, except with ovarian stimulation using CC.

CONCLUSIONS: Ovarian stimulation protocols were associated with a significantly increased risk for ectopic pregnancy in fresh cycles. These results suggest that ovarian stimulation agents may affect the tubal and intrauterine environment during fresh cycles.

SUPPORT: This study was supported by Health and Labour Sciences Research Grants.
OBSTETRIC AND NEONATAL RISKS IN TERM-SINGLETON ASSISTED REPRODUCTIVE TECHNOLOGY (ART) PREGNANCIES: A SINGLE-CENTER REPORT IN A PERIOD OF 9 YEARS. Satoshi Furuya, MD, Kiyoshi Kubonoya, MD, Ken Kubonoya, MD, Kubonoya Ob/Gyn Clinic, Kashiwa City Chiba Prefecture, Japan.

OBJECTIVE: It is well documented that a singleton pregnancy is safer and healthier than a multiple pregnancy and term (defined as a period from 37 to 41 weeks of gestation) is the optimal timing to give birth for humans. As the number of infertile couples requiring ART is increasing today, pregnancies obtained by ART have often been reported to be associated with a higher risk of poor pregnancy outcomes. This can be accounted for in part by the higher frequency of ART-conceived preterm or multiple births included, and study-design heterogeneity among researches. The aim of our study is to determine whether there is any increase in adverse obstetric and neonatal outcomes in ART pregnancies, compared with naturally conceived pregnancies, even when only term-singleton cases are selected as a base cohort.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We reviewed 14297 consecutive term-singleton labor and delivery cases managed in our facility from January 2010 to March 2019. All information was collected from medical records, including maternal age, parity, details of infertility treatment, pregnancy course and mode of delivery, complications during labor and puerperium, status of the infant at birth, etc. Infertile cases conceived by other than ART (n=676) were excluded from our study subjects in order to assess the effect of ART more precisely. The remaining study population (n=13621) was divided into two groups as follows: cases conceived through ART procedures (Group A: n=750), and cases conceived naturally (Group B: n=12871). We used multivariate logistic regression analysis (shown as odds ratio (OR), maternal medical complications (OR:1.42(1.10 - 1.81), P<0.001), HDP (hyper-tensive disorders of pregnancy; OR:1.64(1.18 - 2.25), P<0.001), forced delivery (i.e., emergency C-section or instrumental delivery; OR:1.52(1.28 - 1.80), P<0.001), abnormal postpartum hemorrhage (OR:2.29(1.77 - 2.94), P<0.001), placenta adherens/accrrete (OR:3.33(1.51 - 8.52), P<0.001), velamentous umbilical cord insertion (OR:7.83(5.03 - 12.11), P<0.001), and heavy-for-date newborn infant (OR:1.71(1.03 - 2.71), P=0.03) was observed in Group A. Difference in the incidence of placental abruption and other neonatal outcomes (Appgar scores, umbilical artery pH value, NICU admission, congenital anomaly) between Group A and B could not be confirmed.

CONCLUSIONS: Among term-singleton pregnancies, cases achieved by ART carry an increased risk for several adverse maternal and neonatal outcomes. In order to secure the safety, obstetricians should recognize term-singleton ART pregnancies as high-risk ones and manage them more cautiously than ever before.

SUPPOT: None.

P-488 Wednesday, October 16, 2019 6:30 AM

AMONG WOMEN WITH CONGENITAL UTERINE ANOMALIES, IS A SHORT CERVIX PREDICTIVE OF PRETERM BIRTH. Amanda Rae Schwartz, MD, Sarah K. Dotters-Katz, MD, Duke University Medical Center, Durham, NC.

OBJECTIVE: Cervical length measurements are used to assess risk for preterm birth in women with normal uterine architecture. The utility of this measurement in women with congenital uterine anomalies is not known. The objective of this study was to describe pregnancy outcomes among women with known congenital uterine anomalies based on cervical length.

DESIGN: A retrospective cohort of pregnant women with a congenital uterine anomaly (CUA) that delivered at a single tertiary academic center and its affiliated community hospital between June 1, 2013 and August 1, 2018 who underwent cervical length screening.

MATERIALS AND METHODS: Women were identified using ICD9 codes for both congenital uterine anomalies as well as for delivery. Prenatal records were reviewed to obtain demographic variables, obstetrics and gynecology history, ultrasound measurement of cervical length (CL) and delivery and neonatal outcomes. Short cervix was defined as a transvaginal cervical length of <25mm. The primary outcome was gestational age at delivery. Secondary outcomes included delivery at <34 weeks, mode of delivery and neonatal death. Women with a short cervix were compared to those with CL ≥ 25mm using Wilcoxon rank sum, Fisher’s exact and chi squared tests.

RESULTS: 95 women with congenital uterine anomalies delivered between June 1, 2013 and August 1, 2018 and were included in analysis. 10 women had a short cervix. Median cervical length in the short cervix group was 17mm (IQR 12.14 - 22mm) as compared to 39mm (IQR 35.42) in the long CL cohort (p<0.001). No significant difference in parity, preterm birth, history of abnormal pap smears, prior cervical surgery, tobacco use or infertility treatment was seen between groups. Women with a short cervix delivered at a median of 28.6 weeks (IQR 21.4, 34.1) as compared to 38.1 weeks (IQR 35.9, 39.4) in the long cervix cohort (p<0.001). Delivery at less than 37 weeks (90% vs 38%, p = 0.002) and less than 34 weeks (70% vs 14%, p<0.001) were also more common among women with a short cervix. Though mode of delivery did not differ, neonatal demise was ten times more common in the short cervix group (40% vs 4.7%, p = 0.004).

CONCLUSIONS: Among women with a CUA, short cervix may portend a more ominous outcome than among women with normal uterine architecture. Larger studies are needed to corroborate this data.

P-489 Wednesday, October 16, 2019 6:30 AM

THE BETTER TRANSFER STRATEGY IN WOMEN WITH A UNICORNUATE UTERUS: SINGLE BLASTOCYST-EMBRYO TRANSFER VERSUS DOUBLE CLEavage-EMBryo TRANSFER. Yuyao Mao, Master, Xihong Li, MD./Ph.D, Yan Ouyang, MD./Ph.D, Jingzi Xiao, Master. Reproductive and Genetic hospital of Citic-Xiangya, Changsha, China.

OBJECTIVE: To investigate the better transfer strategy between single blastocyst-embryo transfer (SBET) and double cleavage-embryo transfer (DCET) in women with a unicorne uterus.

DOES OFFERING A FINANCIAL INCENTIVE FOR ELECTIVE SINGLE EMBRYO TRANSFER DECREASE RATE OF MULTIPLE GESTATION? Channing Burks, MD, Mabel Lee, MD, Valerie Libby, MD, James Goldfarb, MD, MBA, Rachel S. Weinerman, MD, University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH.

OBJECTIVE: The purpose of the study is to assess the impact of offering a financial incentive on the rate of elective single embryo transfer (eSET) at a single IVF center.

DESIGN: Prospective cohort study using historical controls.

MATERIALS AND METHODS: Patients who met the recent ASRM guidelines for eSET who were <38 years old with >1 embryo for transfer who did not have insurance coverage for frozen embryo transfer (FET) were candidates for a financial incentive program offered by a foundation associated with our IVF center to fund a second FET if they did not get pregnant from their initial FET of a single embryo. eSET program was initiated in July 2018. FETs performed in 2017 were used as historical controls. Outcomes included the percent of eSET, multiple gestation and adherence to ASRM guidelines.

RESULTS: There were a total number of 255 FETs performed in 2017 and 193 performed between 7/2018 through 3/2019. Rate of single FET in women of all ages prior to eSET program was 62.5% versus 85.0% after the initiation of the eSET program (p<0.001). Rate of double FET was 34.9% compared to 13.9% (p<0.001). In 2017, there were 132 self-pay cycles, 72 of which would have been eligible for eSET program, compared to 69 eligible cycles after the initiation of eSET program of which 63 participated (54.5% vs. 91.3%, p<0.001). Number of self-pay patients that did not follow ASRM guidelines prior to start of program was significantly higher than after the initiation of eSET program (23.5% vs. 2.9%, p<0.001) Rate of multiple gestation pregnancies was similar before and after initiation of eSET program, (5.4% vs 7.2%, p=0.58).

CONCLUSIONS: There are a significant percentage of patients in our population that do not insurance coverage for IVF. Our eSET incentive program, which provides a financial incentive for patients to transfer a single embryo without the financial burden of paying for an additional transfer if they do not get pregnant demonstrated significantly increased adherence to ASRM guidelines regarding eSET.
TABLE. Reproductive outcomes of SBET and DCET in women with a unicornuate uterus

<table>
<thead>
<tr>
<th>Reproductive outcomes</th>
<th>DCET</th>
<th>SBET</th>
<th>P</th>
<th>aOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>383</td>
<td>156</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Embryos transferred (n)</td>
<td>766</td>
<td>156</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implantation, % (n)</td>
<td>47.9 (367/766)</td>
<td>57.7 (90/156)</td>
<td>0.011</td>
<td>0.628 (0.439-0.899)</td>
</tr>
<tr>
<td>Clinical pregnancy, % (n)</td>
<td>68.1 (261/383)</td>
<td>57.7 (90/156)</td>
<td>0.039</td>
<td>1.522 (1.022-2.267)</td>
</tr>
<tr>
<td>Live birth % (n)</td>
<td>52.0 (199/383)</td>
<td>47.4 (74/156)</td>
<td>&lt;0.001</td>
<td>20.046 (6.132-65.535)</td>
</tr>
<tr>
<td>Multiple pregnancy, % (n)</td>
<td>4.1 (108/261)</td>
<td>3.3 (3/90)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Pregnancy (n)</td>
<td></td>
<td>200</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>Miscarriage, % (n)</td>
<td></td>
<td>19.5 (39/200)</td>
<td>15.1 (13/86)</td>
<td>0.378</td>
</tr>
<tr>
<td>Preterm delivery, % (n)</td>
<td>24.5 (49/200)</td>
<td>12.8 (11/86)</td>
<td>0.028</td>
<td>2.213 (1.088-4.501)</td>
</tr>
<tr>
<td>Term delivery, % (n)</td>
<td>53.0 (106/200)</td>
<td>72.1 (62/86)</td>
<td>0.003</td>
<td>0.437 (0.253-0.754)</td>
</tr>
<tr>
<td>Babies born (n)</td>
<td></td>
<td>199</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Live births (n)</td>
<td></td>
<td>180</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>Perinatal mortality, % (n)</td>
<td>9.5 (19/199)</td>
<td>1.4 (1/73)</td>
<td>0.027</td>
<td>9.900 (1.294-75.734)</td>
</tr>
<tr>
<td>Low birth weight, % (n)</td>
<td>31.7 (57/180)</td>
<td>11.1 (8/72)</td>
<td>0.005</td>
<td>3.163 (1.416-7.062)</td>
</tr>
<tr>
<td>Live birth weight (g)</td>
<td></td>
<td>2750 ± 650</td>
<td>3050 ± 500</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gestational age at delivery (weeks)</td>
<td>36.8±3.9</td>
<td>37.8±2.8</td>
<td>0.029</td>
<td></td>
</tr>
</tbody>
</table>

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: 539 infertile patients with a unicornuate uterus who underwent SBET or DCET from January 2012 to December 2017 were enrolled. SBET and DCET were performed in 156 and 383 patients, respectively. Only the first transfer cycle were considered. The reproductive outcomes were compared between these two groups.

RESULTS: The two groups were statistically similar regarding age, body mass index and cause of infertility (p > 0.05), however, the infertility duration, infertility type and insemination methods were significantly different (p < 0.05). Multivariate regression analysis showed a significantly lower implantation rate (47.9% vs. 57.7%), but markedly higher rates of clinical pregnancy (68.1% vs. 57.7%) and multiple pregnancy (41.4% vs. 3.3%) in the DCET group compared to the SBET group (p < 0.05). While the live birth rate was similar, (52.0% vs. 47.4%, P = 0.451). The DCET group was associated with statistically higher risks of preterm delivery (24.5% vs. 12.8%), low birth weight (31.7% vs. 11.1%), perinatal mortality (9.5% vs. 1.4%) and lower live birth weight (2750 ± 650 vs. 3050 ± 500 g) and gestational age at delivery (36.8 ± 3.9 vs. 37.8 ± 2.8 weeks) compared to the SBET group (p < 0.05). While no significant difference was found in the miscarriage rate (19.5% vs. 15.1%, p = 0.378).

CONCLUSIONS: SBET could increase the implantation rate and decrease the risks of multiple pregnancy, preterm delivery and perinatal mortality, but with the same live birth rate as DCET. So SBET was recommended for women with a unicornuate uterus.

P-490 Wednesday, October 16, 2019 6:30 AM

PREVALENCE, RISK FACTORS AND OBSTETRIC OUTCOMES OF ZYGOTIC SPINDLE TRANSFER AFTER SINGLE EMBRYO TRANSFER CYCLES. Romina Verdura, Physician, Maria Ayelen Demarco, Physician, Mercedes Papayannis, BSc, Jimena Maidana, BSc, Mariana Gomez Peña, BSc, Claudio Bisoli, MSc, Guillermo Terrado Gil, MD, Fabio L. Sobral, Physician, Alejandro Oubiña, Physician, Laura J. Kopcow, Physician, Marcos Horton, Physician, Pregna Medicina Reproductiva, Buenos Aires, Argentina.

OBJECTIVE: To describe the prevalence, main determining factors and obstetric outcomes of multiple pregnancy due to zygotic splitting after single embryo transfer (sET).

DESIGN: We performed a retrospective observational study in 521 clinical pregnancies resulting from cleavage-stage or blastocyst single embryo transfer (sET) following IVF or ICSI cycles with autologous or donated eggs. Fresh and frozen-warmed sET from January 2015 to June 2017 were included, and analyzed for the occurrence of assisted hatching, embryo biopsy for PGT, or inactivation type (IVF vs. ICSI). We also evaluated embryo grading, blastocyst expansion grade, and quality of embryo transfer.

MATERIALS AND METHODS: We retrospectively analysed all pregnancies achieved through single embryo transfers at our center. The population included IVF or ICSI cycles with autologous or donated eggs, and/or their subsequent frozen-thawed cycle. Monozygotic twinning was defined as 2 or more heart beats at 5-6 weeks ultrasound.

RESULTS: We analyzed 521 clinical pregnancies resulting from 1708 single embryo transfers in cleavage-stage (N=674) or blastocyst stage (N=1034). The overall MZT rate 2.87% (15/521), accounting for 0.87 % of cleavage stage derived pregnancies (1/115) and 3.45% of blastocyst stage derived pregnancies (14/406, p = 0.01). The incidence of MZT was higher with ICSI (14/263) compared to conventional IVF (1/153), although not statistically significant (P = 0.08). In the blastocyst transfer group the incidence of MZT was not increased by Assisted Hatching (AH), Preimplantation Genetic Testing (PGT) nor was it affected by type of transfer, (either fresh or frozen) or quality/type of catheter used in the transfer.

Fifteen patients with MZT had 10 term deliveries with no neonatal complications, four of which had vanishing embryos, (one of them triple with a double vanishing embryo). One case had placenta accreta and underwent cesarean hysterectomy. Four patients miscarried, 2 in the first trimester and two in the second trimester (one due to cervical incompetence, and one voluntary interruption, due to a thoracopagus Siamese Twin pregnancy) Finally, one patient delivered at 30 weeks, with twin neonatal demise.

CONCLUSIONS: Although MZT is a rare event associated with ART it cannot be disregarded due to its potentially serious obstetric consequences, especially in a sET blastocyst transfer program. Monozygotic twinning is increased in blastocyst transfers, and special care should be taken to properly inform prospective parents when blastocysts are transferred.

CONTRACEPTION/FAMILY PLANNING

P-491 Wednesday, October 16, 2019 6:30 AM

EFFECT OF SELF-ADMINISTERED LIDOCAINE IN-SITU GEL ON INTRAUTERINE DEVICE INSERTION PAIN: A RANDOMIZED CONTROLLED TRIAL. Ahmed M. Abbas, MD, a Shymaa Ali, MSc, b Noura H. Abd Ellah, PhD, a Omar M. Shaaban, MD, a b 'Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; b Department of Obstetrics and Gynecology, Faculty of Medicine, Suez University, Suez, Egypt. 'Department of Pharmacetics, Faculty of Pharmacy, Assiut University, Assiut, Egypt.

OBJECTIVE: Intrauterine contraceptive device (IUD) is a safe long-acting reversible contraceptive method. However, insertion-related pain presents a barrier to its widespread use in family planning. Our objective is to examine the analgesic effect of a novel self-administered lidocaine vaginal in-situ gel in alleviating pain during IUD insertion compared to placebo among parous women.

DESIGN: Randomized, double-blind, placebo-controlled trial (Clinicaltrials.gov: NCT02943135).

MATERIALS AND METHODS: Reproductive-aged parous women requesting Copper-T 380 A IUD insertion for birth control were counseled to participate. Eligible women based on WHO guidelines were recruited and randomized (1:1) to lidocaine in-situ gel vs. placebo using a permuted
block schedule. Ten minutes before IUD insertion, each participant self-injected the pre-filled syringe with 5 ml lidocaine or placebo in-situ gel vaginally. Neither cervical ripening agents nor analgesics were used before the insertion. The main study outcomes were the participant’s self-rated pain perception utilizing a 10-cm Visual Analogue Scale (VAS) during cervical tenaculum placement, uterine sound and IUD insertion, then 15 minutes post-procedure. A 2 cm difference in VAS score between both arms was considered a clinically significant difference. The secondary outcomes included ease of insertion score, duration of insertion and need for additional analgesia. Mann Whitney and Fisher’s exact tests were utilized for analysis of these outcomes.

RESULTS: One hundred twenty women were enrolled and randomized to lidocaine in-situ gel arm (n=60) or placebo (n=58). Both arms were homogeneous regarding age, parity, BMI, and the prior mode of delivery. Lidocaine group reported significantly lower pain scores during tenaculum placement, uterine sound insertion and IUD insertion, then 15 minutes post-insertion (median[IQR]: 3[2-3] vs 5.4[5-8], p<0.001), IUD insertion (median[IQR]: 3[2-3.75] vs 6[5.5-7], p<0.001) and 15 minutes post-insertion (median[IQR]: 1[1-1.75] vs 2.5[2-3.75], p<0.0001). The ease score of IUD insertion was significantly higher in the lidocaine group (median[IQR]: 8.5[8-9] vs 7.5[6.25-8], p=0.005). Additionally, the IUD insertion in the lidocaine group was associated with less time in comparison to the placebo group (mean±SD: 7.3±1.19 vs. 8.75±1.11 minutes, p=0.048). No difference regarding the need for additional analgesia.

CONCLUSIONS: Self-administration of lidocaine in-situ gel 10 minutes before IUD insertion significantly reduces the induced pain with subsequent easier insertions.


SUPPORT: A fund No. (2016-11) received from The Institutional Grants’ office.

P-492 Wednesday, October 16, 2019 6:30 AM

TREATMENT OF UNFAVORABLE BLEEDING PATTERNS IN CONTRACEPTIVE IMPLANT USERS. Katharine Simmons, MD, MPH, * Bliss Kaneshiro, MD, MPH, † Jennifer Hauschild, CPH, ‡ Kise Bond, BS, ‡ PSM, § Jeffrey T. Jensen, MD, MPH, † Alison Edeleman, MD, MPH, † The Permanente Medical Group, San Leandro, CA, ‡ University of Hawaii, Honolulu, HI; ‡ OHSU, Portland, OR; ‡ Oregon Health & Science University, Portland, OR.

OBJECTIVE: Some users of the etonogestrel (ENG) subdermal contraceptive implant experience unfavorable vaginal bleeding patterns. We evaluated whether a 7-day treatment with oral tamoxifen could reduce the number of bleeding/spotting days in women using an ENG implant who have documented frequent and/or prolonged vaginal bleeding.

DESIGN: Randomized, placebo-controlled, double blind treatment study.

MATERIALS AND METHODS: Subjects started treatment if they experienced ≥3 days of consecutive bleeding/spotting (B/S) and could repeat treatment every 30 days if needed during the 90-day study interval. We collected a daily record of B/S using an interactive text messaging service. The primary outcome was the total number of B/S days in the 30 days following first tamoxifen treatment; secondary outcomes included time to B/S cessation and restart with treatment and number of B/S free days over 90 days.

RESULTS: From January 2017 to November 2018, 112 women enrolled in the study, 107 completed at least 30 days, and 98 completed 90 days. The average subject was 23 years old, white, and had some college education. Women randomized to tamoxifen had more B/S free days in both the first 30 days [20 (SD 7) vs. 15 (SD 7), p = 0.0001] and 90 days [57 (SD 17) vs. 49 (SD 15), p = 0.026]. The tamoxifen group also had faster cessation of B/S with first treatment [6 (SD 4) vs. 8 (SD 5), p = 0.037] and longer time before bleeding restarted [19 (SD 19) vs. 8 (SD 8), p = 0.0001]. Study medications were well tolerated.

CONCLUSIONS: Tamoxifen using the ENG implant with documented frequent and/or prolonged bleeding will have cessation of bleeding within 6 days of starting a short-course of tamoxifen and a longer window of relief from bleeding after one treatment as compared to placebo.

SUPPORT: Grant support for this research was from Merck Women’s Health Investigator Initiated Studies Program and the Oregon Clinical and Translational Research Institute (1 UL1 35RR024140 01) for access and use of REDCap electronic data capture system.

P-493 Wednesday, October 16, 2019 6:30 AM

A NOVEL IN VITRO FLUORESCENT REPORTER PLATFORM FOR IDENTIFYING MALE CONTRACEPTIVES. Krista Maye Symosko, B.S.; a Katherine A. Watkins, B.S.; a E. Rose Lawson, B.S.; a In Ki Cho, Ph.D., M.S.; b Anthony W. S. Chan, DVM, Ph.D.; c Charles A. Easley, IV, Ph.D., M.S.; c University of Georgia, Athens, GA; c Emory School of Medicine, Atlanta, GA.

OBJECTIVE: Due to the challenges surrounding the development of male contraceptives, this study aimed to generate a high throughput testing platform to screen and identify potential male contraceptives.

DESIGN: To date, male forms of oral contraception have largely been ineffective. The current failures in developing male contraceptives stem from the lack of a robust, rapid, and unbiased human spermatogenesis platform. We previously developed a novel in vitro, human pluripotent stem cell model that mimics several aspects of human spermatogenesis.

MATERIALS AND METHODS: In order to address the challenges associated with male contraceptive development, we recently developed a novel in vitro fluorescent reporter platform, Testibow 1.0, that is coupled with our in vitro human spermatogenesis model. Testibow 1.0 is comprised of promoters for spermatogonia driving cytofluorescent protein (cCFP) expression, promoters for primary spermatocytes driving green fluorescent protein (GFP) expression, and promoters for spermatids driving tdTomato expression. Since Testibow 1.0 utilizes fluorescence-based imaging, our model allows for the rapid identification of potential male contraceptives that successfully blocks spermatogenesis, but permits full restoration following treatment cessation.

RESULTS: Testibow 1.0 provides a unique, high content/high throughput imaging platform that can rapidly and efficiently identify novel compounds that could be used as male contraceptives regardless of genetic background. Currently, we are developing a polycistronic version of our fluorescent reporter system, Testibow 2.0, that will express all three of our fluorescent reporters simultaneously in order to begin identifying and characterizing chemical compounds that block spermatogenesis differentiation or meiotic entry. Furthermore, our novel fluorescent reporter platform can be used to begin addressing the safety and efficacy challenges that are hindering male contraceptive development.

CONCLUSIONS: In conclusion, our fluorescent reporter system represents a suitable platform for evaluating the safety and effectiveness of potential male contraceptives prior to clinical trials.

SUPPORT: National Institutes of Health: K22ES025418 (Easley, Charles) and A Bill and Melinda Gates Grand Challenges Exploration Grant (Easley, Charles).

P-494 Wednesday, October 16, 2019 6:30 AM

POLIDOCANOL/DoxyCycline FOAM FOR NONSURGICAL PERMANENT FEMALE CONTRACEPTION: 6 MONTH DATA BABOON CONTRACEPTION STUDY. Jeffrey T. Jensen, MD, MPH, a Carol B. Hanna, Ph.D., b Shan Yao, M.D., c Emily Mishler, MS, a Daniel Choi, DVM, a Nicholas Mukaria Kiulia, MS, d Atunga Nyachiego, PhD, d Ov D. Slagella, PhD a Oregon Health & Science University, Portland, OR; d Oregon National Primate Research Center, Beaverton, OR; e Oregon Oregon National Primate Research Center, BEAVERTON, OR; f Affiliation not provided; g Department of Reproductive Health and Biology, Institute of Primate Research, Nairobi, Kenya; h Professor, Portland, OR.

OBJECTIVE: Our goal is the development of a safe and low cost nonsurgical approach to permanent contraception for women with high efficacy following a single treatment. We previously reported that the addition of doxycycline to polidocanol foam increases the rate of tubal occlusion. Here, we sought to determine if a single transcervical administration of polidocanol/doxycline foam (PDF) would prevent pregnancy in female baboons.

DESIGN: Controlled nonhuman primate cohort study.

MATERIALS AND METHODS: Healthy regularly cycling female baboons underwent laparoscopy with chromoperturbation, for evaluation of...
PRE-REMOVAL PLASMA LEVONORGESTREL LEVEL AND RETURN OF FERTILITY AFTER LEVO-
NORGESTREL 52 MG INTRAUTERINE SYSTEM DISCONTINUATION. Michael A. Thomas, MD, a
Gretchen S. Stuart, MD, MPH, b Carolyn L. Westhoff, MSc, b David L. Eisenberg, MD, MPH, b
Andrea I. Olariu, MD, PhD, b Mitchell D. Creinin, MD. c University of Cincinnati, West Chester, OH; *Affilia-
tion not provided; Columbia University, New York, NY; University of California - Davis, Sacramento, CA.

OBJECTIVE: Evaluate return of fertility after levonorgestrel (LNG) 52 mg intrauterine system (IUS) discontinuation according to pre-removal serum levonorgestrel levels.

DESIGN: Prospective clinical trial.

MATERIALS AND METHODS: Reproductive-aged women who previously delivered only by cesarean section (CS) requesting Multiload-375 Copper IUD per IUD insertion were counseled to participate. Eligible women category 1 or 2 based on WHO guidelines were recruited and randomized (1:1) to lidocaine in-situ gel vs. placebo using a permuted block schedule. Each woman was supplied by a syringe filled with 5 ml lidocaine or placebo in-situ gel to be self-administered vaginally 10 minutes prior to insertion. The primary outcome was the difference in pain scores during IUD insertion using a 10-cm Visual Analog Scale (VAS). A 2 cm difference in VAS score between pain scores was considered statistically significant. Secondary outcome was pregnancy within 6 months of resumption of menses. We plan to follow pregnancy and safety outcomes through 18 months in the PDF-treated animals, and evaluate histologic features of tubal occlusion.

RESULTS: The baseline laparoscopy demonstrated bilateral tubal patency in all of animals selected for the study. All females resumed normal menstrual cycles and mating activity within 3 months of treatment. After 6 months of regular cycles, 11/12 (92%) of control females became pregnant (6/6 MC control, 5/6 untreated control). Significantly fewer (2/12, 16%) pregnancies occurred in PDF-treated females (p < .001, Fisher’s exact test). All of the pregnancies were intrauterine. Both pregnancies in PDF-treated females occurred in nulliparous females - a group considered high-risk for failure. One progressed normally to term and one underwent spontaneous abortion.

CONCLUSIONS: A single transcervical treatment with PDF prevented pregnancy in most baboons. Pregnancy occurred in PDF-treated females considered at high risk of failure due to nulliparity.

SUPPORT: Bill and Melinda Gates Foundation OPP1025233, OPP1191953.
P-497 Wednesday, October 16, 2019 6:30 AM

WOMEN’S SATISFACTION WITH THE MULTIPURPOSE VAGINAL pH-REGULATOR (MVP-R; AMPHORA): RESULTS FROM THE PHASE 3 AMPOWER TRIAL. Michael A. Thomas, MD, a Kelly R. Culwell, MD, MPH, b Clint Dart, MS, c Brandi Howard, PhD, d University of Cincinnati, Cincinnati, OH; e Evofem, Inc., San Diego, CA; f Health Decisions, Durham, NC.

OBJECTIVE: As a multipurpose vaginal pH-regulator, Amphora® is a novel, non-hormonal, woman-controlled, on-demand, contraceptive vaginal gel being investigated for prevention of pregnancy and sexually transmitted diseases. To better understand the treatment experience from the woman’s perspective, the Satisfaction Questionnaire was administered in the phase 3 AMPower trial (NCT03243305).

DESIGN: The phase 3 AMPower trial is a single-arm, open-label study designed to evaluate the efficacy and safety of and women’s satisfaction with Amphora over 7 cycles in sexually active women aged 18-35 years across 112 US sites. The primary efficacy endpoint was the cumulative 7-cycle pregnancy rate. Women’s satisfaction with Amphora was an exploratory endpoint.

MATERIALS AND METHODS: The Satisfaction Questionnaire was given at baseline and the 3 subsequent study visits to assess women’s satisfaction in 4 categories: 1) satisfaction with most recent/study birth control method; and likelihood of 2) recommending this method to others considering a vaginal contraceptive gel, 3) recommending this method to others considering another birth control option, and 4) continuing this method after study termination.

RESULTS: 1330 women were included in the Satisfaction Questionnaire. At Visits 3 (Cycle 2) and 4 (Cycle 5 or 6), more women reported being “very satisfied” or “satisfied” with the study method (85.3% [95/1118] and 89.5% [734/820], respectively), compared with their previous birth control method before enrollment (46.5% [616/1325]). At Visits 3 and 4, 86.6% (968/1118) and 89.8% (736/820) of women, respectively, were “very likely” or “likely” to recommend the study drug as a contraceptive vaginal gel, and as an alternative birth control option (85.7% [958/1118] and 88.2% [723/820], respectively) to others. 82.1% (918/1118) and 81.0% (664/820) of women surveyed at Visits 3 and 4, respectively, were “very likely” or “likely” to continue with Amphora if it were to be available, compared with 2.2% (25/1118) and 3.2% (26/820) of women who were “unlikely” to continue.

CONCLUSIONS: Data from the phase 3 AMPower trial indicate a very high level of satisfaction in women on Amphora compared with their previous birth control method and likelihood of recommending this method to others considering another birth control option, and 4) continuing this method after study termination. Amphora has the potential of fulfilling a vaginal contraceptive gel, 3) recommending this method to others considering another birth control option, and 4) continuing this method after study termination.

SUPPORT: Evofem Inc.

P-498 Wednesday, October 16, 2019 6:30 AM

REPRODUCTIVE AGE WOMEN ARE INTERESTED IN SELF-ADMINISTERED VAGINAL CONTRACEPTIVES THAT PREVENT SEXUALLY TRANSMITTED INFECTIONS. Emily G. Hurley, MD, a Giovanni Pauletti, PhD, b Michael A. Thomas, MD. aUniversity of Cincinnati, West Chester, OH; bUniversity of Cincinnati, Cincinnati, OH.

OBJECTIVE: To develop a better understanding of women’s knowledge of and desire for pregnancy and sexually transmitted infection (STI) prevention. Women’s perspectives may help guide future development of new innovative products.

DESIGN: Questionnaire-based observational study.

MATERIALS AND METHODS: An IRB approved electronic survey investigating women’s opinions on contraceptive choice and STI prevention was distributed at women’s health clinics at the University of Cincinnati. Participation was voluntary and responses remained anonymous. The descriptive data were analyzed using percentages and medians.

RESULTS: One hundred and five surveys were completed. Participants ranged from 18-45 years of age (median 29, IQR 26, 33). The majority of participants were non-Hispanic white (82.9%) and sexually active (86.6%), Approximately 83.7% were sexually attracted to men, while 7.7% were attracted to females and 8.7% were attracted to both. A history of an unintended pregnancy was reported by 26.7% of all participants and 20.0% had previously been diagnosed with an STI. In participants who were sexually attracted to both genders, 94.8% had used some form of contraception, including a hormonal pill (83.5%), barrier method (68.1%) or an intrauterine device (30.8%). Approximately 35.1% reported consistently using a method to prevent STIs, of which, 100% used male condoms. When asked if one felt empowered to choose her desired contraceptive method, 8.2% said no and 7.2% said they were unsure. Approximately 13.4% of participants reported that they feel pressured by their partner to not use contraception and 21.6% feel pressured by their partner to not use protection against STIs.

CONCLUSIONS: In women sexually attracted to men, nearly two-thirds do not routinely use STI prevention and some feel pressured by their partner not to use contraception/condoms. This makes women more vulnerable for unwanted infections and pregnancy. Because of this, there is a role for discretely self-administered female contraceptive products that also prevent STIs.

SUPPORT: University of Cincinnati Office of Research Strategic Collaborative Grants Program.

P-499 Wednesday, October 16, 2019 6:30 AM

THE EFFECT OF DIFFERENT PROGESTOGEN ONLY CONTRACEPTIVE METHODS ON FEMALE SEXUAL FUNCTION IN THE FIRST-TIME USERS: A CROSS-SECTIONAL STUDY. Mohammed Khairy Ali, MD, Ahmed M. Abbas, MD, Ali Shouman, MBBCh, Ahmed M. Abdelmagied, MD, Alaa A. Makkhouf, MSc, Mostafa Nasr Ibrahim, MD, Ahmed Makkhouf, MD Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: The progestin-only contraceptive (POC) methods are used frequently by women in the childbearing period. However; these methods are associated with female sexual dysfunction (FSD) especially injectables. There are potential predictors associated with FSD among POC users which should be put in the consideration during counseling for POC use. Our objective is to assess the female sexual function (FSF) in three POC methods among first-time users.

DESIGN: Cross-sectional study (Clinicaltrial.gov:NCT02579590).

MATERIALS AND METHODS: We included married women between 20-40 years with a heterosexually active relationship lasting for longer than four weeks. They were using one of the POC methods for at least six months for contraception only. Those women were first-time users with regular menstrual pattern, amenorrhea or even with minimal vaginal spotting not affecting the sexual life. The enrolled women were classified into four groups; non-contraceptive users (group I), Depot Medroxyprogesterone Acetate 150 mg (DMPA) injection (group II), etonogestrel 68 mg subdermal implant (group III) and desogestrel 75 µg oral pills (group IV) users for the first time. All participants were asked to complete the Arabic form of the female sexual function index (ArFSFI). A total score of less than or equal to 28.1 points was determined as FSD. The main outcome of the study was to identify the prevalence of FSD among those users. The predictors associated with FSD among POC users were also explored. The data were analyzed using ANOVA, Chi-square test and the logistic regression model.

RESULTS: Four hundred forty-four women consented to participate and divided into two groups; 222 women were non contraceptive users, and 222 women were POC users (88 women were DMPA users, 87 women were etonogestrel implant users and 47 women were desogestrel containing pills users). All groups (non contraceptive users and POC users) were homogeneous in the baseline data. The mean ArFSFI score was significantly lower in POC users than non-contraceptive users (26.92 ± 3.88 Vs 27.42 ± 2.02, p = 0.010; respectively). The mean ArFSFI score was significantly lower in DMPA users in comparison to etonogestrel implant and desogestrel pills users (26.46 ± 1.75, 27.13 ± 1.89, 27.37 ± 1.93, p = 0.010; respectively). Furthermore; the number of women with FSD was significantly higher in DMPA users in comparison to other users (68 women; 77.2%, 44 women; 50.5%, 16 women; 34.0%, p = 0.000; respectively). The baseline characteristics that were revealed from the regression model and significantly associated

FERTILITY & STERILITY®
e307
with a higher likelihood of FSD with POC were circumcision (p = 0.001), parity > 3 times (p = 0.015) and duration of use > 12 months (p = 0.022). A ROC curve analysis in the predictive model demonstrated that circumcision yielded the highest sensitivity (82.84%) while the parity > 3 times had the lowest one (59.76%) and the duration of use > 12 months had a sensitivity of 60.36%.

CONCLUSIONS: There is a high prevalence of FSD in POC users especially DMPA users. The circumcision, parity > 3 times and > 12 months of use are potential significant predictors of FSD in POC users.

SUPPORT: None.

P-500 Wednesday, October 16, 2019 6:30 AM

CHINA FEMALE CONDOM (FC) FUNCTIONALITY STUDY AGAINST AN EQUIVALENT MARKETED FEMALE CONDOM (FC2). Yimin Cheng Sr., M.D., National Research Institute for Family Planning, Beijing, China.

OBJECTIVE: To compare the differences of the rates of total clinical failure and four types of failures (Invagination, Misdirection, Slippage and Breakage) between two kinds of female condoms (FC) [China made FC (FCc) and USA made FC (FC2)] as well as to assess weather every failure of four rates is accord with the standard of WHO.

DESIGN: Prospective, double-blind randomized controlled.

MATERIALS AND METHODS: 300 participants were recruited. A computer-generated randomization sequence was used to assign the 300 participants to one of two groups (1:1). Group A used 5 FCc first, followed by 5 FC2s. Group B used 5 FC2s first, followed by 5 FCcs. The FC2 is made from synthetic nitrate material and is manufactured by the Female Health Company (Chicago, IL, USA). The FCc is made of polyurethane and has a dumbbell shape. It is manufactured by Tianjin CondomBao Medical Polyurethane Tech. Co. (Tianjin, China).

RESULTS: The rate of loss to follow-up was 4.2% for FCc and 2.8% for FC2. The total clinical failure rate of FCc was 0.9% (95% confidence interval 0.5–1.3%) compared to 1.1% (95% confidence interval 0.7–1.5%) for FC2. The upper bound of the one-sided 95% confidence interval for FCc total clinical failure rate, minus the FC2 total clinical failure rate is equal to 0.2% (1.5%–1.3% vs.0.2%). The difference of the total clinical failure rates (1.1% vs.0.9%) between FC2 and FCc was statistically not significant (P > 0.05). No breakage was found both in FCc users and in FC2 users. The failure rates of invagination, misdirection and slippage of FCc were 1.3%, 1.3% and 1.1% respectively. The failure rates of invagination, misdirection and slippage of FC2 were 1.8% , 0.1% and 2.5% respectively. The difference of slippage rates (2.5% vs.1.1%) was statistically not significant (P > 0.05) between FC2 and FCc as well as the slippage rate of FCc was lower than the standard of WHO although the slippage rate of FCc was slightly higher than that of FCc and slightly higher than the standard of WHO. The difference of invagination rates (1.8% vs. 1.3%) was also statistically not significant (P > 0.05) between FC2 and FCc. Although the rate of misdirection for FCc was higher than that for FC2 (1.3% vs. 0.1%) and although the difference of the misdirection rates between two groups was statistically significant, but the rate of misdirection for FCc (1.3%) is lower than that of WHO standard (1.5%).

CONCLUSIONS: (1) The results indicated that the total clinical failure rate of FCc is non-inferior to the total clinical failure rate of FC2; (2) The rates of four types of failure were statistically not significant (P > 0.05) between FC2 and FCc. Although the rate of misdirection for FCc was higher than that for FC2 (1.3% vs. 0.1%) and although the difference of the misdirection rates between two groups was statistically significant, but the rate of misdirection for FCc (1.3%) is lower than that of WHO standard (1.5%).

Youth data were excluded. Other exclusion criteria included requiring in vitro fertilization to conceive prior to the procedure. Patient characteristics analyzed include age, race, marital status, insurance type, and number of children. Univariate and multivariate logistic regression were performed to compare our two cohorts and to assess for factors predictive of post vasectomy compliance.

RESULTS: 1,137 patients underwent vasectomy. The average age was 37.5 years. 89.5% and 88.7% of the patients were White/Caucasian and married, respectively. 27.5% of patients did not follow up for PVSA at any interval. Age was similar between patients who did and did not submit a PVSA (37.8 vs 37.3 years). However race, marital status, and insurance did differ, as patients in the no PVSA cohort were more likely to be African American (8.3% vs 3.7%), single (15.3% vs 9.7%), and have Title 19/Medicaid (2.9% vs 1.2%). On multivariate analysis, single relationship status was independently predictive of failing to present for post vasectomy semen analysis (RR 1.86, p = 0.02). Age (RR 1.02, p = 0.08) and increasing number of children (RR 1.11, p = 0.09) approached significance.

CONCLUSIONS: A significant percentage of patients do not provide a PVSA confirming sterility, with single relationship status being most predictive of noncompliance when controlling for all other preoperative variables. As with all vasectomy patients, counseling these patients that they are not sterile until proven with a PVSA is paramount.


SUPPORT: N/A.

P-502 Wednesday, October 16, 2019 6:30 AM

RETURN TO FERTILITY AFTER 1-YEAR USE OF A SEGESTERONE ACETATE/ETHINYL ESTRADIOL CONTRACEPTIVE VAGINAL SYSTEM USE. Ginger Constantine, MD,a Kurt T. Barnhart, MD, BSCE,b Anne E. Burke, MD, MPH,c Ruth B. Merkatz, PhD,d Shelli Graham, PhD,e Brian Bernick, MD,f Sebastian Mirkin, MD,g Endo-Rheum Consultants, LLC, Malvern, PA;h University of Pennsylvania, Perelman School Of Medicine, Philadelphia, PA;i Johns Hopkins School of Medicine, Baltimore, MD;jPopulation Council, New York, NY;kTherapeuticsMD, Boca Raton, FL.

OBJECTIVE: To assess the return to menses and/or fertility in a subset of women who used a contraceptive vaginal system (CVS; approved by the FDA in August 2018) releasing a daily mean of segesterone acetate (SA) 0.15 mg and ethinyl estradiol (EE) 0.013 mg for up to 13 cycles.

DESIGN: Two multicenter, single-arm, open-label, pivotal, phase 3 studies of the SA/EE CVS; one US-only study (15 US sites) and one international study (5 in the US; 3 in Europe; 3 in Latin America, 1 in Australia).

MATERIALS AND METHODS: Women used the same SA/EE CVS on a 21/7-day in/out regimen for up to 13 cycles. Those who wished to become pregnant or use non-hormonal contraceptives after completing the 13 cycles could participate in a 6-month follow up for return to fertility. Women were instructed to perform a urine pregnancy test within 2-3 weeks following their last visit and then monthly if they experienced pregnancy symptoms and/or did not have a bleeding episode. Women were contacted every 2 months for pregnancy, menses, and contraceptive use information. Women who were pregnant returned to the clinic for pregnancy confirmation and a prenatal care referral. Bleeding <18 days after last CVS use was considered
women's health visits.

Molly Siegel, MD, a looked and under addressed topic in Wednesday, October 16, 2019 6:30 AM sites.

the US study; the US Agency for International Development (USAID; Grant Health and Human Development of the National Institutes of Health not delay or adversely affect return to fertility.

monal contraceptives became pregnant or had a return of menses in the 6 months, 5 at 4 months, and 1 at 6 months.

91.6%) or pregnancy (12 women; 8.4%). Seven pregnancies were reported at 2 months, 5 at 4 months, and 1 at 6 months.

CONCLUSIONS: All women who desired pregnancy or used non-hormonal contraceptives became pregnant or had a return of menses in the 6 months after the last use of the SA/EE CVs, suggesting that the CVs does not delay or adversely affect return to fertility.

SUPPORT: The Eunice Kennedy Shriver National Institute of Child Health and Human Development of the National Institutes of Health (NICHD; Contract Number HHSN27500403372) funded and conducted the US study; the US Agency for International Development (USAID; Grant Number GPO-A-00-04-00019-00) funded the international study, which was conducted by the Population Council; the World Health Organization (WHO) Reproductive Health Research Department funded two international study sites.

P-503 Wednesday, October 16, 2019 6:30 AM

DECLINE IN FERTILITY WITH AGE: AN OVERLOOKED AND UNDER ADDRESSED TOPIC IN WOMEN’S HEALTH VISITS. Molly Siegel, MD, a Sylvia Moses, MD, b Maureen Baldwin, MD MPH, b Maria Rodriguez, MD MPH, b Oregon Health & Science University, Portland, OR, b Affiliation not provided, b Oregon Health and Science University, Portland, OR.

OBJECTIVE: To determine whether women discuss age-related fertility decline with healthcare providers, and women’s response to an educational intervention on the impact of age on fertility.

DESIGN: We conducted a cross-sectional survey of women aged 20-45 visiting public markets in a metropolitan area.

MATERIALS AND METHODS: Participants completed a survey regarding demographics, reproductive life goals, and knowledge and thoughts about age and fertility at baseline and after an educational intervention. Our intervention was a hand out on the impact of age on fertility. We used descriptive statistics to characterize our study population (age, parity, marital, employment and insurance status) and assess responses. We used a multivariable logistic regression model to determine the association between age and learning from the intervention.

TABLE 1. Survey responses regarding age-based fertility prior to and following an educational intervention.

<table>
<thead>
<tr>
<th>Baseline data</th>
<th>Desires future children, % respondents</th>
<th>Childbearing complete, % respondents</th>
<th>Undecided, % respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age-based fertility: Have discussed this with a healthcare provider</td>
<td>16% (17/104)</td>
<td>15% (9/59)</td>
<td>17% (8/46)</td>
</tr>
<tr>
<td>Would like to discuss this*</td>
<td>41% (41/101)</td>
<td>5% (3/59)</td>
<td>32% (15/47)</td>
</tr>
<tr>
<td>Would like more information*</td>
<td>52% (54/103)</td>
<td>7% (4/59)</td>
<td>26% (12/46)</td>
</tr>
<tr>
<td>Following intervention</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Learned something new</td>
<td>71% (72/102)</td>
<td>65% (37/57)</td>
<td>66% (29/44)</td>
</tr>
<tr>
<td>Plan to discuss with partner/family*</td>
<td>46% (47/103)</td>
<td>7% (4/54)</td>
<td>27% (12/44)</td>
</tr>
<tr>
<td>Considering changing reproductive plans*</td>
<td>13% (13/102)</td>
<td>2% (1/55)</td>
<td>23% (10/44)</td>
</tr>
<tr>
<td>Feel it would be helpful to discuss at routine visits*</td>
<td>79% (81/102)</td>
<td>45% (25/56)</td>
<td>73% (32/44)</td>
</tr>
</tbody>
</table>

* = p<0.01

FERTILITY & STERILITY®
OBJECTIVE: Recent studies have suggested that the hyperestrogenic milieu generated during ovarian stimulation may create a suboptimal peri-implantation environment, leading to adverse perinatal outcomes. In this study, we investigate whether supraphysiologic estradiol (E2) impacts early embryonic growth in vitro fertilization (IVF)-embryo transfer (ET) cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Normal responder patients, <40 years old, undergoing fresh IVF/ET cycles resulting in live singleton births were included. Patients with PCOS, multiple births, vanishing twins, or unknown perinatal outcomes were excluded. The primary outcome of interest was crown-rump length (CRL) at 7 to 8 weeks of gestational age. Secondary outcomes recorded were low birth weight (LBW, <2500 grams), pre-term birth (PTB, <37 weeks of gestation) and birth weight. Primary and secondary outcomes were assessed according to peak E2 quartiles. Receiver-operator-characteristic (ROC) curves were constructed for outcomes showing statistical significance.

RESULTS: A total of 4,071 patients with live singleton births were included. The median age, body mass index (BMI), E2 level and birth weight for the study cohort was 36 (33-39) years, 22.3 (20.4-25.0) kg/m2, 1,554 (1,112.7-2,179) pg/mL, and 3,289 (2,920-3,628) grams, respectively. Singletons in the 4th E2 quartile (8.56 mm) had a smaller CRL compared to all other E2 quartiles. The rate of LBW rose from 6.4% (E2 0.001-2,500 pg/mL) to 20.7% (E2 3,501-4,000 pg/mL), without a corresponding rise in the rate of PTB. The odds of term LBW with E2 >2,500 pg/mL were 6.1-7.9 times higher compared to the median E2. Peak E2 level was a weak predictor of LBW (AUC=0.64), but a strong predictor of LBW (AUC=0.86).

CONCLUSIONS: The results of the current study suggest that the hyperestrogenic milieu of ovarian stimulation can adversely impact early embryonic growth and ultimately perinatal outcomes. Our results emphasize the importance of minimizing the supraphysiologic elevations of E2 levels in fresh IVF-ET cycles to optimize the early peri-implantation environment and mitigate adverse perinatal outcomes.

SUPPORT: None.

DOES THE HYPERESTROGENIC MILIEU IN FRESH IN VITRO FERTILIZATION CYCLES IMPACT EARLY EMBRYONIC GROWTH? Nigel Pereira, MD,d Nirali J. Shah, MD,a Isaac Kligman, M.D.,a Zev Rosenwaks, M.D. bRonald O. Perlman and Claudia Cohen Center for Reproductive Medicine, New York, NY; aWeill Cornell Medicine, New York, NY; dThe Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Recent studies have suggested that the hyperestrogenic milieu generated during ovarian stimulation may create a suboptimal peri-implantation environment, leading to adverse perinatal outcomes. In this study, we investigate whether supraphysiologic estradiol (E2) impacts early embryonic growth in vitro fertilization (IVF)-embryo transfer (ET) cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Normal responder patients, <40 years old, undergoing fresh IVF/ET cycles resulting in live singleton births were included. Patients with PCOS, multiple births, vanishing twins, or unknown perinatal outcomes were excluded. The primary outcome of interest was crown-rump length (CRL) at 7 to 8 weeks of gestational age. Secondary outcomes recorded were low birth weight (LBW, <2500 grams), pre-term birth (PTB, <37 weeks of gestation) and birth weight. Primary and secondary outcomes were assessed according to peak E2 quartiles. Receiver-operator-characteristic (ROC) curves were constructed for outcomes showing statistical significance.

RESULTS: A total of 4,071 patients with live singleton births were included. The median age, body mass index (BMI), E2 level and birth weight for the study cohort was 36 (33-39) years, 22.3 (20.4-25.0) kg/m2, 1,554 (1,112.7-2,179) pg/mL, and 3,289 (2,920-3,628) grams, respectively. Singletons in the 4th E2 quartile (8.56 mm) had a smaller CRL compared to all other E2 quartiles. The rate of LBW rose from 6.4% (E2 0.001-2,500 pg/mL) to 20.7% (E2 3,501-4,000 pg/mL), without a corresponding rise in the rate of PTB. The odds of term LBW with E2 >2,500 pg/mL were 6.1-7.9 times higher compared to the median E2. Peak E2 level was a weak predictor of LBW (AUC=0.64), but a strong predictor of LBW (AUC=0.86).

CONCLUSIONS: The results of the current study suggest that the hyperestrogenic milieu of ovarian stimulation can adversely impact early embryonic growth and ultimately perinatal outcomes. Our results emphasize the importance of minimizing the supraphysiologic elevations of E2 levels in fresh IVF-ET cycles to optimize the early peri-implantation environment and mitigate adverse perinatal outcomes.

SUPPORT: None.
diagnostic criteria of an angular pregnancy and followed expectantly. Diagnostic criteria included 1) Nonanomalous uterus; 2) Implantation of the embryo in the lateral angle of the uterine cavity; 3) ≤ 1 cm of myometrial thickness surrounding the gestational sac; 4) Presence of completely circumferential endometrial cavity with no gestational sac, and 5) Lack of an “interstitial line sign.” Maternal and fetal data were gathered from the medical record.

RESULTS: Forty-two cases of angular pregnancy were identified at first-trimester ultrasound. At presentation, 33 patients (78.6%) were asymptomatic, eight (19.0%) had vaginal bleeding, and two (4.8%) had pain. The mean gestational age at diagnosis was 7.4 ± 1.0 weeks, and the mean myometrial thickness was 5.1 ± 1.6 mm (95% CI 4.6-5.6). At initial follow up, 23 cases (54.8%) had resolved, 13 cases (31.0%) persisted as angular pregnancies, and six cases (14.3%) resulted in miscarriage. Three cases (7.1%) of total that persisted had decreased myometrial thickness. At final follow up, 21 (51.2%) deliveries resulted in a live birth, seven (17.1%) in miscarriage, and 13 (31.7%) were continuing gestations. In cases of live birth, 15 (71.4%) were vaginal deliveries, six (28.6%) cesarean sections, 17 (81.0%) term deliveries, and four (19.0%) preterm deliveries. There were no cases of uterine rupture, maternal death, abnormal placentation, or hysterecomy.

CONCLUSIONS: In 42 cases of angular pregnancy diagnosed by first-trimester ultrasound, all but eight resolved with continued follow up. Outcomes were largely positive with a 51.2% live birth rate, 17.1% miscarriage rate, and 31.7% continuing pregnancy rate. Angular pregnancy may represent a clinical entity that more closely resembles a normal, non-ectopic intrauterine pregnancy rather than an ectopic pregnancy. Therefore, most cases can be safely observed, and efforts should be made to expectantly manage gestations while awaiting viability.

P-509 Wednesday, October 16, 2019 6:30 AM
EARLY PLACENTAL GENE EXPRESSION DISCRIMINATES BETWEEN NON-VISUALIZED INTRAUTERINE PREGNANCIES VERSUS TUBAL ECTOPIC PREGNANCY IN UTERINE ASPIRATES. Maureen Baldwin, MD MPH, a Jon D. Hennebold, PhD. b Oregon Health and Science University, Portland, OR; bOregon National Primate Research Center, Division of Reproductive & Developmental Sciences, Beaverton, OR.

OBJECTIVE: All early pregnancies have the potential to be a life-threatening ectopic pregnancy, but there is no reliable diagnostic test to localize a pregnancy until almost two weeks after implantation, when it can be visualized using sonography. We aimed to demonstrate that early placental biomarkers expressed in endometrial samples can discriminate between non-visualized presumed intrauterine pregnancy (IUP) and confirmed ectopic pregnancy (EP).

DESIGN: Case-control.

MATERIALS AND METHODS: We collected uterine aspirates from asymptomatic patients undergoing induced abortion of pregnancy of unknown location (PUL) and those undergoing surgical management of tubal EP. PUL were assumed to be non-visualized IUP if estimated gestation ≥42 days, initial serum human chorionic gonadotropin (hCG) ≥3,000, and hCG declined markedly after uterine aspiration alone (typically defined as >50% in 48 hours). All samples were stored in RNA later® solution and homogenized in TRIzol® (Invitrogen). We performed RNA purification and extraction of 1 mL of homogenate with PureLink® RNA Mini Kit (Ambion®), including on-column DNase treatment with RQ1® RNase-free DNase (Promega®). We performed qRT-PCR (ABI Prism® 7900HT Sequence Detection System: Applied Biosystems) using an RNA-to-Ct™ 1-Step Kit, gene-specific primers, and TaqMan® probes (ThermoFisher) to assess trophoblast-specific chorionic gonadotropin subunit beta (CGb) and RPL10 (endogenous control). Relative expression of CBG and RPL10 to 18S expression.

TABLE. Serial serum hCG trend among non-visualized pregnancies.

<table>
<thead>
<tr>
<th>Estimated gestation (days)</th>
<th>Initial hCG (mIU/mL)</th>
<th>Serial hCG (mIU/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>268</td>
<td>34</td>
</tr>
<tr>
<td>28</td>
<td>336</td>
<td>46</td>
</tr>
<tr>
<td>33</td>
<td>852</td>
<td>137</td>
</tr>
<tr>
<td>37</td>
<td>1621</td>
<td>4*</td>
</tr>
<tr>
<td>38</td>
<td>266</td>
<td>38</td>
</tr>
</tbody>
</table>

All serial hCG trend over 2 days except 12 days for *.
RESULTS: Using quantitative RT-PCR, the mean fold increase in expression of CGB in endometrial samples of non-visualized IUP (n=5) compared to non-pregnant endometrium, was 20.2 (±2.0), which was significantly greater (p<0.01 by t-test) than the 8.0 (±2.8) fold-increase observed in EP.

CONCLUSIONS: The early trophoblast biomarker CGB is detectable in uterine aspirates of non-visualized presumed IUP at a large threshold difference compared to endometrium from EP. This is consistent with localized CGB expression by the invasive syncytiotrophoblast. This preliminary data suggests that molecular targets to specific early placental markers could be utilized for diagnosis of pregnancy location after direct endometrial sampling.

SUPPORT: This work has been supported by the Society of Family Planning Research Fund SFPFRF11-J1 and by the NIH Women’s Reproductive Health Research Program (K12HD085809).

P-510 Wednesday, October 16, 2019 6:30 AM

PREDICTION OF PREGNANCY OUTCOME IN WOMEN WITH FIRST TRIMESTER BLEEDING BY THE DETECTION OF ALPHA-FETOPROTEIN (AFP) IN VAGINAL BLOOD. Amir Mot, MD PhD, Karen Jubanyik, MD, Mursal Gardezi, BSc, Stephanie M. Nichols-Burns, PhD.a Man Zhang, MD PhD.b Ecem Esencan, M.D.a Burcin Simsek, Ph.D.a,b David B. Seifer, MD.a Hugh S. Taylor, M.D.a Yale School of Medicine, New Haven, CT. University of Pittsburgh, Pittsburgh, PA; Yale University, New Haven, CT; Yale University School of Medicine, New Haven, CT.

OBJECTIVE: We previously published that high concentration of alpha-fetoprotein (AFP) in vaginal blood confirms the presence of microscopic embryonic/fetal tissue. Here we attempted to detect the presence of AFP in dried blood collected on pads from women with first trimester bleeding.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: A sample of patients presenting to a fertility center or emergency department with positive pregnancy tests and vaginal bleeding were invited to participate in the study. After informed consent, a hygienic pad was collected from each participant. 1x1 cm² pad patches with dried vaginal blood were placed into 1 ml saline. The dissolved AFP that originated from the vaginal blood (AFPVb) was quantified by an automatic chemiluminescence assay. Two outcomes were evaluated: 1) clinical and/or histopathologic evidence of passage of intrauterine embryonic/fetal tissue (a failed intrauterine pregnancy); 2) a threatened miscarriage with subsequent ongoing clinical pregnancy (heartbeat documented on ultrasound on the day of pad collection or at least once within the subsequent 5 weeks).

RESULTS: To date, 15 women with first trimester bleeding were enrolled. For these women, the median age, gravidity, and parity (with ranges in parenthesis) were 32 (20-51) years, 3 (1-8), and 0 (0-3), respectively. Each woman provided a single pad with dried vaginal blood. Four women passed embryonic/fetal tissue and 11 had an ongoing pregnancy. AFPVb was detected in 5 specimens: 4 from the 4 women passing embryonic/fetal tissue and 1 from a woman with a threatened miscarriage. AFPVb was not detected in the other 10 specimens, all from women with a threatened miscarriage and ongoing pregnancies. The detection of AFP in the vaginal blood was significantly associated with pregnancy loss while its absence was seen exclusively in successful pregnancies (P = 0.004 by Fisher exact test).

CONCLUSIONS: AFP can be extracted and detected in dried blood on pads collected from women with first trimester bleeding. When AFPVb is detected the likelihood of a failed intrauterine pregnancy is 80% whereas this likelihood drops dramatically when AFPVb is undetectable. Measurement of vaginal AFP may help to predict the fate of intrauterine pregnancy in the setting of first trimester bleeding.

SUPPORT: Conacyt A 250768.

P-512 Wednesday, October 16, 2019 6:30 AM

LUTEINIZING HORMONE (LH) SURGE SHOULD REPLACE LAST MENSTRUAL PERIOD (LMP) FOR IMPROVED ACCURACY OF PREGNANCY DATING. James J. Morong, MMBS, MPhil.a Dana B. McQueen, M.D., M.A.S., b Mary D. Stephenson, M.D., M.Sc.a University of Illinois at Chicago, Chicago, IL; aNorthwestern University, Chicago, IL.

OBJECTIVE: To compare the accuracy of pregnancy dating by Luteinizing Hormone (LH) surge versus last menstrual period (LMP).

DESIGN: Observational cohort study of prospectively collected data in two academic RPL Programs from 2005-2018. Inclusion criteria included: women with a history of recurrent early pregnancy loss (REPL), defined as ≥ 2 pregnancy losses <10 weeks; ≥ 1 subsequent pregnancy with a known LMP; documented LH surge, natural conception, and transvaginal ultrasound (TVUS) prior to 8 weeks from LMP, which resulted in a live birth.

MATERIALS AND METHODS: We compared the gestational age (GA) by LH surge (GA_{LH}) and LMP(GA_{LMP}) to the sonographic gestational age (GA_{CRL}), based on the first crown rump length (CRL) of ≥5 mm. Secondary analysis compared the accuracy of pregnancy dating with a measurable CRL ≥5 mm to the conventional CRL ≥ 5 mm. Scatter diagrams were created for the difference between GA_{CRL}-GA_{LH} and GA_{CRL}-GA_{LMP}, paired t-tests were used for analysis. In addition, scatter diagrams were created for CRL vs. GA_{LH} and CRL vs. GA_{LMP}; correlation coefficients for each were compared using Fisher’s z-test. SAS 9.4 was used for statistical analysis, with significance P<0.05. Descriptive statistics were reported as mean, standard deviation and range.

OBJECTIVE: Multifetal pregnancies increase maternal, and perinatal mortality, the presence of each additional fetus increases this risk; moreover, spontaneous loss of the entire pregnancy is 25% for quadruplets, 15% for triplets, and 8% for twins. Several studies showed that the reduction to a lower-order pregnancy (triplet or quadruplet to twin) reduces the risk of medical complications associated with maintaining multiple pregnancies. Multifetal pregnancy reduction is usually scheduled between 11 and 14 weeks of gestation, using chemical substances as adjuvants to help in the embryo reduction success rate. However, these chemical substances present alternative concerns and have been suggested to affect live birth rates. Therefore, we assessed a novel non-chemical-based procedure for fetal reduction performed during early gestation of high order pregnancies.

DESIGN: Single-arm prospective study conducted between December 2013 and September 2018.

MATERIALS AND METHODS: Multifetal pregnancy reduction was carried out between 6 and eight weeks of gestation. The patient was placed in a lithotomy position under general anesthesia. Using the same equipment used for transvaginal ultrasound-guided oocyte recovery, the smallest embryo, located in a position with the easiest access route and preferably the one nearest cervix, was selected for embryo reduction. An echo tipped needle (17 Cook medical ovum aspiration needle) was inserted through the posterior fornix and the posterior uterine wall to the intended gestational sac. Then the needle is inserted in the embryos cardiac area until the absence of fetal heartbeat was seen and confirmed by color and power Doppler. The needle is then extracted, and hemostasis is verified. We avoid aspiration and the use of any chemical substances. We verify the vitality of remaining embryos with color and power Doppler. Patients were followed until delivery, and the baby’s weight was a record as well as any complications.

RESULTS: For the proof of principle, only patient with three gestational sacs were analyzed (n=296). None of the women presented or indicated of any complication due to the surgery. Embryo reduction typically took place during the 7th week (range: 5-10.5 week). After the procedure, 3 patients lost their pregnancy (1.0%); however, 89.9% maintained the remaining 2 gestational sacs and 9.1% for 1 gestational sac. The live birth rates were 94.4% for the 2 gestational sacs (birth weight: 2111±625 grams) and 96.3% for 1 gestational sac (birth weight: 254±1793 grams). There was no difference in the low birth weight rate (2 sacs: 14.5% v 1 sac: 11.5%). The most common for the 2 sacs group was requiring NICU intervention (4.5%), whereas, for the 1 sac group, was restriction of intrauterine growth (14.8%).

CONCLUSIONS: Here, we demonstrate that a non-chemical method can successfully reduce the number of embryos.
RESULTS: A total of 115 women with a history of RPL, with 118 subsequent live births, met inclusion criteria. Subjects were 96% Caucasian and 6% Hispanic. Mean age at delivery was 35.6 years (3.4-26-43). Mean number of prior pregnancy losses <10 weeks was 3.6 (1.8-2-12) and mean number of prior live births was 1.78 (1.41-3.4).

Scatter diagrams of GA\textsubscript{CRL-GALMP} revealed tighter fit around zero vs. GA\textsubscript{CRL-GALH}. Paired T-test revealed a lower mean absolute difference between GA\textsubscript{CRL-GALH} vs. GA\textsubscript{CRL-GALMP} 2.04 vs. 3.08 days, P<0.0001. Fisher’s z-test revealed a greater correlation between GA\textsubscript{CRL-GALH} compared to GA\textsubscript{CRL-GALMP} r=0.77 vs. r=0.62, P=0.0018. This indicates a greater accuracy when using LH surge.

57 subjects had at least one TVUS with a CRL of <5 mm. Scatter diagrams of GA\textsubscript{CRL-LH surge-GALH} revealed a trend towards a tighter fit around zero vs. GA\textsubscript{CRL-LH surge-GALH}. Paired T-test revealed a trend towards a lower mean absolute difference between GA\textsubscript{CRL-LH surge-GALH} vs. GA\textsubscript{CRL-GALH} 1.86 vs. 2.25 days, although this did not reach statistical significance, P=0.33.

CONCLUSIONS: A highly accurate estimated date of delivery (EDD) improves antenatal surveillance and reduces iatrogenic prematurity. Pregnancy is optimally dated in the first trimester and becomes increasingly inaccurate with advancing GA. Numerous publications have concluded that LMP is unreliable for pregnancy dating. Based on the results in this study, LH surge should replace LMP for improved accuracy of dating of pregnancy. There was a trend towards improved accuracy with a CRL <5 mm.

The average GA at time of first ultrasound by all three methods (CRL, LH surge and LMP) was 7 weeks +/- 5 days. Therefore, we propose a new threshold for very early pregnancy dating that supports redating the pregnancy by sonographic CRL if there is a discrepancy of more than 2 days from the LH surge or 3 days from LMP for gestations ≤7 6/7 weeks.


Erin Inman, MD, a Micaela J. Stevenson, BS, b Emily K. Kobernik, MPH, c Molly B. Moravek, MD, MPH, c Samantha B. Schon, MD, MTR d University of Michigan, Ann Arbor, MI; e University of Michigan Medical School, Ann Arbor, MI.

OBJECTIVE: Subchorionic hematoma (SCH) is common, however, is of unknown significance among the infertile population as most studies evaluate women without a history of infertility and with naturally conceived pregnancies. Additionally, 1 small study suggests that SCH is higher among patients undergoing IVF and specifically after frozen embryo transfer (FET). The objective of this study was to identify the prevalence of SCH in the infertile population, as well as risk factors for first trimester miscarriage in affected pregnancies.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: CPT codes were used to identify all obstetric (OB) scans performed at a single infertility clinic from 1/2015-3/2018. All viable intrauterine pregnancies on initial OB scan were included for analysis (n=1254). Chart review was performed to identify the presence of SCH. Data on patient demographics, fertility treatments and pregnancy outcomes were collected. Differences in rate of SCH among fertility treatment cycle were compared using Chi-square test. Bivariate analysis was performed to compare pregnancies with SCH that resulted in first trimester miscarriage (>10 weeks) to those that did not.

RESULTS: SCH prevalence was 11.9% (n=149). SCH rates did not vary significantly when comparing fertility treatment type, specifically by the following groupings: 1) all infertility treatment cycle (ovars, injectables, hybrid, IVF fresh or frozen, donor eggs) v. natural cycle (12.8% v. 9.1%, p = 0.08), 2) oral cycle (clomiphene and letrozole) v. IVF (fresh and frozen) v. natural cycle (10.9% v. 13.7% v. 9.1%, p = 0.12), and 3) IVF Fresh v. IVF Frozen (11.5% v. 13.7% v. p = 0.36). Among pregnancies with SCH, 18.1% (n=27) ended with first trimester miscarriage. Symptoms of vaginal bleeding or cramping were significantly associated with miscarriage (p < 0.008 and p < 0.001 respectively). Age, BMI, infertility diagnosis, medical co-morbidities, and SCH size were not significantly different between these groups. Aspirin use in this population was common at 49.7%, however there was not significantly associated with first trimester miscarriage.

CONCLUSIONS: We found similar rates of SCH and subsequent first trimester miscarriage (0.5-22.6%, 3-29.5% respectively) in our study population to rates reported in the fertile population. Rate of SCH did not vary significantly amongst fertility treatment cycles, including IVF fresh v. frozen cycles, contrary to a prior study. Similar to the fertile population, symptoms are significantly associated with miscarriage. Symptomatic patients should be counseled on increased risk of miscarriage compared to patients with incidentally noted SCH. While prior studies have shown increased rates of SCH in infertile patients taking aspirin, this study is the first to evaluate outcomes and suggest that there is no increased risk of miscarriage with aspirin use in pregnancies affected by early SCH. Future research should further evaluate the effect of aspirin on SCH prevalence and the impact of continuing aspirin use in affected pregnancies.

P-513 Wednesday, October 16, 2019 6:30 AM

CHARACTERIZING TISSUE PROTEOME CHANGES IN THE DECIDUA AND TROPHOBLAST ASSOCIATED WITH VIABILITY AND LOCATION OF PREGNANCY. Lynn A. Beer, B.S., a Kurt T. Barnhart, MD, MSCE, b Mary D. Sammel, ScD, c Suneea Senapati, MD, MSCE, b Courtney A. Schreiber, MD, MPH, d David W. Speicher, Ph.D. d aThe Wistar Institute, Philadelphia, PA; bDepartment of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA; cDepartment of Biostatistics, Epidemiology and Informatics, University of Pennsylvania, Philadelphia, PA.

OBJECTIVE: To compare changes in protein profiles of decidualized endometria and trophoblasts among women with different pregnancy outcomes, specifically a viable intrauterine pregnancy (IUP), ectopic pregnancy (EP), or fetal demise (FD), that identify potential biomarkers and provide insights into cellular pathways affected by fetus viability and location.

DESIGN: An exploratory proteomic profiling study.

MATERIALS AND METHODS: Trophoblast and endometrial tissue was collected from consenting, gestational-age matched women having a viable IUP (n=4), FD (n=4), or EP (n=2). Frozen tissue samples were homogenized, digested with trypsin and analyzed by nanocapillary LC-MS/MS using a Thermo Q-Exactive HF mass spectrometer. Data for each tissue type were processed using label-free quantitation with MaxQuant software. We performed pairwise comparisons of each pregnancy outcome (EP vs IUP, FD vs IUP, and EP vs FD), and protein changes having a fold change ≥ 3 and a Student’s-t-test p-value < 0.05 were considered significant.

RESULTS: A total of 4792 and 4757 high confidence proteins were identified in the decidua and trophoblast proteomes, respectively. The overall protein compositions from all three outcomes were similar with greater than 90% overlap in both tissue types. In the decidua, 125 protein quantities (2.6% of the proteome) were significantly different between EP and IUP, whereas FD and IUP decidua were more similar with only 68 (1.4%) differences. Non-viable pregnancies in different locations (EP vs FD) showed 191 differences (3.9%). A similar depth of analysis and degree of significantly changing proteins was observed in the trophoblast analyses. There are 66 (1.4%) differences between SAB and IUP and 177 (3.7%) differences when EP was compared to FD. However, the largest group of 355 differences (7.2%) was observed between EP and IUP trophoblasts. In both tissue types, proteins associated with ECM remodeling, cell adhesion and metabolic pathways showed decreases in EP specimens compared with MaxQuant software. We performed pairwise comparisons of each pregnancy outcome (EP vs IUP, FD vs IUP, and EP vs FD), and protein changes having a fold change ≥ 3 and a Student’s-t-test p-value < 0.05 were considered significant.

RESULTS: SCH prevalence was 11.9% (n=149). SCH rates did not vary significantly when comparing fertility treatment type, specifically by the following groupings: 1) all infertility treatment cycle (ovars, injectables, hybrid, IVF fresh or frozen, donor eggs) v. natural cycle (12.8% v. 9.1%, p = 0.08), 2) oral cycle (clomiphene and letrozole) v. IVF (fresh and frozen) v. natural cycle (10.9% v. 13.7% v. 9.1%, p = 0.12), and 3) IVF Fresh v. IVF Frozen (11.5% v. 13.7% p = 0.36). Among pregnancies with SCH, 18.1% (n=27) ended with first trimester miscarriage. Symptoms of vaginal bleeding or cramping were significantly associated with miscarriage (p < 0.008 and p < 0.001 respectively). Age, BMI, infertility diagnosis, medical co-morbidities, and SCH size were not significantly different between these groups. Aspirin use in this population was common at 49.7%, however there was not significantly associated with first trimester miscarriage.

CONCLUSIONS: We found similar rates of SCH and subsequent first trimester miscarriage (0.5-22.6%, 3-29.5% respectively) in our study population to rates reported in the fertile population. Rate of SCH did not vary significantly amongst fertility treatment cycles, including IVF fresh v. frozen cycles, contrary to a prior study. Similar to the fertile population, symptoms are significantly associated with miscarriage. Symptomatic patients should be counseled on increased risk of miscarriage compared to patients with incidentally noted SCH. While prior studies have shown increased rates of SCH in infertile patients taking aspirin, this study is the first to evaluate outcomes and suggest that there is no increased risk of miscarriage with aspirin use in pregnancies affected by early SCH. Future research should further evaluate the effect of aspirin on SCH prevalence and the impact of continuing aspirin use in affected pregnancies.
P-515 Wednesday, October 16, 2019 6:30 AM

ISOLATION AND PROFILING OF EXTRACELLULAR VESICLES IN UTERINE FLUID TO DETERMINE NOVEL MARKERS OF ENDOMETRIAL RECEPTIVITY. Tian Tian Li, PhD, Ellen Greenblatt, MD, Crystal Chan, MD, MSc, Susan Luenfeld-Tanenbaum Research Institute, Sinai Health System, Toronto, ON, Canada; 2Mount Sinai Fertility, Sinai Health System, Toronto, ON, Canada.

OBJECTIVE: Uterine fluid contains endometrium-derived extracellular vesicles (EVs), which are membrane-bound cell-cell mediators containing lipids, proteins and nucleic acids. MicroRNAs (miRNA), the small non-coding RNAs molecules directing post-transcriptional gene silencing, are a prominent cargo of EVs. Analysis of the miRNAs in EVs may offer insights into the endometrial secretome and endometrial-embryonic cross-talk around the time of implantation. This study is designed to characterize differentially expressed miRNAs from endometrium-derived EVs during the receptive phase versus pre-receptive phase in both natural and stimulated in-vitro fertilization (IVF) cycles, with the goal to identify novel markers of endometrial receptivity.

DESIGN: Healthy fertile women (Group 1, N=22) with regular menstrual cycles, and women under 40 years of age (Group 2, N=36) undergoing their first or second stimulated IVF cycles were recruited with informed consent. In Group 1, uterine fluid aspiration (UFA) sampling was performed on the day of LH+2 (pre-receptive) and LH+7 (receptive) in natural cycles. In Group 2, UFA sampling was performed on the day of hCG+2 (pre-receptive), day of egg retrieval) and hCG+7 (receptive, day of blastocyst transfer) in IVF cycles.

MATERIALS AND METHODS: Cellular pellet was removed from the aspirated uterine fluid by centrifugation. EVs in the supernatant were then isolated by two steps of ultracentrifugation at 100,000g for 70 minutes. Isolated EVs were characterized by Transmission Electron Microscopy (TEM), Nanoparticle Tracking Analysis (NTA) and flow cytometry. RNAs were extracted from the isolated EVs and profiling of miRNAs was carried out by next-generation sequencing. Resulting sequencing counts were mapped to miRNAs and bioinformatic analysis was performed on all paired samples to determine differentially expressed miRNAs between conditions (adjusted p value < 0.05).

RESULTS: We confirmed the presence of EVs in human uterine fluid, which were characterized as 20-200 nm vesicles with bilayer membranes by TEM. NTA confirmed the high yield of EVs isolated by ultracentrifugation and demonstrated that the majority of these EVs were between 100-200 nm in size. Flow cytometry validated the successful isolation of EVs by their biomarkers CD9 and CD63. Through profiling of the miRNAs in EVs, over 100 miRNAs were found to be differentially expressed (≥2-fold change) between receptive phase and pre-receptive phase in either natural cycles or IVF cycles. Cross-referencing the differentially expressed miRNAs in both cycles, we identified three overlapping miRNAs (hsa-mir-331, hsa-mir-382, hsa-mir-505), all of which were up-regulated during the receptive phase, as potentially important miRNAs related to the establishment of endometrial receptivity.

CONCLUSIONS: This study validates that endometrium-derived EVs can be isolated and characterized from human uterine fluid by ultracentrifugation. It is the first study to comprehensively profile the miRNAs in these EVs and it has identified a small cohort of candidate miRNAs that may be the novel biomarkers of endometrial receptivity.

SUPPORT: The study is supported by the American Society for Reproductive Medicine (ASRM) research grant awarded to Dr. Crystal Chan in 2018.

P-516 Wednesday, October 16, 2019 6:30 AM

EMBRYO ATP PRODUCTION CAN BE MODULATED BY MATERNAL MITOCHONDRIAL DNA SECRETED FROM EXTRACELLULAR VESICLES. David Bolumar, MSc, Alicia Amadoz, PhD, Inmaculada Moreno, PhD, Carlos Simon, MD, PhD, Felipe Vilella, PhD, Ignemomix Foundation/University of Valencia, Paterna, Spain; 2Ignemomix, Paterna, Spain; 3Ignemomix Foundation, Paterna, Spain; 4University of Valencia; 5Institute INCLIV A, Valencia, Spain.

OBJECTIVE: To identify the DNA cargo of extracellular vesicles (EVs) obtained from maternal endometrial fluid and determine whether cargo is incorporated into and thereby affects the embryo energetics regulation in terms of ATP modulation.

DESIGN: DNA cargo identification was performed by sequencing EVs [apoptotic bodies (ABs), microvesicles (MVs), and exosomes (EXOs)] isolated from human endometrial fluid (EF) samples from fertile donors (n=10). EVs populations originating from the same EF sample were evaluated in a paired design. The potential for EVs to transfer DNA to the embryo and to modify embryo energetics through ATP modulation was also investigated.

MATERIALS AND METHODS: EVs from human EF were treated with DNase to remove external DNA. Nextera XT DNA libraries were created and paired-end 300 cycles sequenced. EVs were labelled with 5-ethyl-2'-deoxyuridine (specific DNA label) and incubated with hatching murine embryos (n=600) to investigate EVs DNA transfer into the embryo. Finally, hatching embryos (n=250) were cocultured with EVs, and embryonic ATP levels were quantified (FLASC kit, Sigma) and compared among embryos exposed to the different EV populations. Statistical comparisons were performed using ANOVA.

RESULTS: EVs were the only EV type in which specific DNA cargo was identified. NGS analysis revealed enrichment in mitochondrial DNA comprising the 13 coding genes (11.12±0.53-fold increase). Interestingly, transcription factor binding sites (TFBSs) were also enriched in this EVs population compared to ABs and EXOs (6.9±1.5 and 11.2±2.1-fold change, respectively), most of them mapping throughout the mitochondrial genome. Some of the associated transcription factors (SRF, GABP, E2F4, TR4, FOXA2, FOXA1, CTCF, GATA2, FOX1) are implicated in embryo development, gametogenesis, and cell matrix adhesion. Further, DNA-tagged EV populations were taken up by murine embryos and exhibited different patterns of DNA integration into the cytoplasm and nuclei of the trophectoderm. Interestingly, when embryos were cocultured in the presence of ABs, EVs, or EXOs, those in the presence of EVs maintained their ATP production when compared to EXOs (p<0.001).

CONCLUSIONS: Our results suggest that EVs-derived EVs may act as modulators of embryo energetics. Specifically, EF-conveyed DNA cargo enriched in coding and modulatory mitochondrial DNA and support maintenance of embryonic ATP production. Finally, the ability of EVs to transfer DNA to the embryo suggests that this mode of maternal-embryonic communication may have implications on embryo energetics regulation.

CS & FV contributed equally.

P-517 Wednesday, October 16, 2019 6:30 AM

ENDOMETRIAL EPITHELIAL FOXO1 DIRECTLY MODULATES SIGNALING PATHWAYS NECESSARY FOR UTERINE RECEPTIVITY. Sarah M. Moustafa, MD, Steven L. Young, MD, PhD, Tianyuan Wang, PhD, Steve Wu, PhD, Rong Li, PhD, Xiaojue Wang, PhD, Tom Spencer, PhD, Francesco Demayo, PhD, UNC School of Medicine, Chapel Hill, NC; 2National Institute of Environmental Health Sciences, Research Triangle Park, NC; 3North Carolina State University, Raleigh, NC; 4Affiliation not provided.

OBJECTIVE: We have previously shown that endometrial FOXO1 transcription factor protein expression is indispensable for murine embryo implantation. We also demonstrated that FOXO1 protein expression is concentrated in the uterine epithelial nuclei during the window of receptivity. The objective of this study is to better understand the relevance of FOXO1 in human endometrial receptivity.

DESIGN: Differentially expressed genes (DEGs) from proliferative (non-receptive) versus mid-secretory (receptive) human endometrial epithelium were compared with DEGs of uterine-specific FOXO1KO versus FOXO1F17 mice to determine which FOXO1 gene expression was also regulated during the transition to receptive human endometrium. Ingenuity Pathway Analysis (IPA) identified regulated pathway and FOXO1 ChIP-seq identified the direct role of FOXO1 on the altered pathway.

MATERIALS AND METHODS: Mouse uterine epithelium was isolated by laser capture on day 4.5 of natural pregnancy. The transcriptome of FOXO1 knockout epithelium was compared to that of wildtype mice using RNA sequencing, identifying DEGs defined by at least a 2-fold change. RNA sequencing was also used to generate DEGs from enzymatically separated human endometrial epithelium between non-receptive and receptive by at least a 1.5-fold change. IPA of the FOXO1 altered murine genes conserved in human phase-related DEGs was used to identify altered pathways with known roles in endometrial receptivity. Subsequent comparison of the components of each pathway with FOXO1 ChIP-seq identified the direct role of FOXO1 on the altered pathway.
RESULTS: 1301 RNA species were common to both the mouse and human DEGs. 318 of these genes were directly bound by FOXO1. Pathway analysis identified Wnt/b-catenin signaling (-log(p-value) 4.14, Z score -0.626), estrogen mediated proliferation (-log(p-value) 10, Z score -3.05), and IL-6 signaling (-log(p-value) 4.73, Z score 0.943) as significantly altered by both human cycle phase and murine FOXO1 deletion, strongly suggesting a role of FOXO1 in these critical pathways for normal endometrial function. ChiP-Seq demonstrated direct FOXO1 binding to multiple regulated genes involved in estrogen-mediated proliferation, IL-6 signaling, and Wnt/b-catenin signaling, supporting a direct action of FOXO1 on these essential signaling pathways. FOXO1 was also found to directly bind several upstream regulators critical to endometrial receptivity, including CEBPB and CCND1.

CONCLUSIONS: Epithelial FOXO1 directly regulates key pathways necessary for human uterine receptivity.


P-518 Wednesday, October 16, 2019 6:30 AM

PRESENCE OF P16-POSITIVE SENESENT CELLS IN HUMAN ENDOMETRIUM DURING THE MIDLUTEAL PHASE OF THE MENSTRUAL CYCLE. Dimitar Parvanov, PhD, Dragomira Nikolova, PhD, Rumiana Ganeva, MSc, Nina Vidolova, MSc, Georgi Stamenov Stamenov, MD/PhD. 1Nadezhda Women’s Health Hospita, Sofia, Bulgaria; 2Department of Medical Genetics, Medical Faculty, Medical University – Sofia, Sofia, Bulgaria.

OBJECTIVE: Biomarkers for cellular senescence such as p16ink4a are commonly measured in order to explore the level of senescent in reproductive tissues. It is known that p16ink4a-positive senescent cells in the human endometrium are involved in its receptivity and participate in the acute cellular remodeling at the time of embryo implantation. The objective of the present study was to evaluate and compare the percentage of p16-positive cells in the stromal, glandular and luminal epithelial compartments of the human endometrium.

DESIGN: We measured the percentage of p16ink4a-positive cells by immunohistochemistry in endometrial biopsy samples of 124 women.

MATERIALS AND METHODS: For taxonomic classification, 16S rRNA profiles were obtained using the Ion 16S metagenomics kit and sequenced on the Ion S5 XL system (ThermoFisher Scientific). Functional composition profiles were obtained using the Ion 16S metagenomics kit and sequenced on the NextSeq 500 system (Illumina).

RESULTS: 1301 RNA species were common to both the mouse and human DEGs. 318 of these genes were directly bound by FOXO1. Pathway analysis identified Wnt/b-catenin signaling (-log(p-value) 4.14, Z score -0.626), estrogen mediated proliferation (-log(p-value) 10, Z score -3.05), and IL-6 signaling (-log(p-value) 4.73, Z score 0.943) as significantly altered by both human cycle phase and murine FOXO1 deletion, strongly suggesting a role of FOXO1 in these critical pathways for normal endometrial function. ChiP-Seq demonstrated direct FOXO1 binding to multiple regulated genes involved in estrogen-mediated proliferation, IL-6 signaling, and Wnt/b-catenin signaling, supporting a direct action of FOXO1 on these essential signaling pathways. FOXO1 was also found to directly bind several upstream regulators critical to endometrial receptivity, including CEBPB and CCND1.

CONCLUSIONS: Epithelial FOXO1 directly regulates key pathways necessary for human uterine receptivity.


P-519 Wednesday, October 16, 2019 6:30 AM

THE ENDOMETRIAL MICROBIOME OF CLINICAL MISCARRIAGE, ECTOPIC PREGNANCY AND DURING EARLY PREGNANCY IN A SUCCESSFUL LIVE-BIRTH. Iolanda Garcia Grau, MS, PhD, Inmaculada Moreno, PhD, David Perez-Villaroya, MS, Davide Bau, PhD, Marta Gonzalez-Monfort, BS, Felipe Villela, PhD, Carlos Simon, MD, PhD. 1University of Valencia, Igenomix Foundation-INCLIVA, Valencia, Spain; 2Igenomix Foundation/INCLIVA, Paterna, Spain; 3Igenomix, Paterna, Spain.

OBJECTIVE: Characterize taxonomically and functionally the endometrial microbiome in clinical miscarriage, ectopic pregnancy and successful live-birth.

DESIGN: The endometrial microbiome was analyzed in patients undergoing ART. We describe the results of endometrial fluid samples analyzed prior to embryo transfer with euploid embryos resulting in 2 clinical miscarriages and 1 ectopic pregnancy (Patient 1), and a clinical miscarriage and a 4-week spontaneous successful pregnancy resulting in live birth (Patient 2).

MATERIALS AND METHODS: For taxonomic classification, 16S rRNA profiles were obtained using the Ion 16S metagenomics kit and sequenced on the Ion S5 XL system (ThermoFisher Scientific). Functional composition was assessed by Whole Metagenome Sequencing using the Nextera DNA Flex Library Preparation kit and sequenced on the NextSeq 500 system (Illumina).

RESULTS: The 16S rRNA sequencing of the endometrial fluid collected prior to clinical miscarriages and ectopic pregnancy showed the existence of a pathologic microbiota profile, whereas at 4-weeks of pregnancy had reversed to a normal Lactobacillus-dominated profile.

The functional metagenomics revealed different Lactobacillus species and associated functions between the clinical miscarriage and successful pregnancy. In clinical miscarriage, L. crispatus was detected with the indicated pathogens showing an unstable functional pattern with transposases and insertion elements. Whereas, in the same patient L. iners was the only bacteria present in the uterine cavity at the 4-week in the successful pregnancy, associated with defense mechanisms, energy production and cell division.
FULLYHONIC ANEUPLODY RISK?

Wednesday, October 16, 2019 6:30 AM

CHANGES IN ANTI-MULLERIAN HORMONE AND AMOUNT OF ETHANOL USED DURING ULTRA-
SONIC GUIDED ASPIRATION OF OVARIAN CYST. Lulu Huang, MD,⁎ Ming-Yang Chang, MD,⁎
Yu-Cheng Liu, MD,⁎ Chang Gung Memorial Hospital Linkou Medical Cen-
ter, Taipei, Taiwan; 199 Tun-Hua North Road, 12F Taipei, Taiwan, Taipei,
Taiwan; 1 Affiliation not provided.

OBJECTIVE: To evaluate the effect of transvaginal ultrasound-guided aspiration and ethanol sclerotherapy on ovarian reserve and anti-mullerian hormone (AMH) in patients with ovarian endometriomas. Setting: Teaching hospital affiliated with Chang Gung University, Taipei.

DESIGN: We retrospectively reviewed 124 patients with ovarian endome-
triosmas who underwent trans-vaginal aspiration and sclerotherapy of endo-
metrioma(s) in our hospital. Patients were grouped into minimal amount of ethanol retention, group 1, n = 80, ≤ 5 mL of retention of ethanol, and group 2, n = 44, > 5mL of retention.

MATERIALS AND METHODS: In all of 124 patients, preoperative evalu-
ation included AMH, mid-cycle serum CA-125 level, and color Doppler ul-
trasoundography to exclude possibility of malignancies. Patients underwent ultrasonographic guided transvaginal aspiration and sclerotherapy with 95% ethanol irrigation of the cystic cavity. Patients were grouped into group 1, n = 80, ≤ 5 mL of retention of ethanol, and group 2, n = 44, > 5mL of retention. Ultrasoundography was performed at 3, 6, 9, and 12 months to deter-
mine persistence and size of cysts and AMH level was checked at 6 months after aspiration. Pain scores were evaluated pre- and post-operatively. Pa-
tients were followed up at 1 year for recurrent cysts. Those who were infertile prior to therapy were followed up for subsequent pregnancies (either by as-
sisted reproductive technologies, or by natural conception). All statistics were two-sided and analyses were performed using SPSS software, version 25 (SPSS Inc., Chicago,IL).

RESULTS: The patients age, mean cyst size, bilateralunilaterality in both groups were without significant differences. The mean pre-operative AMH levels for group 1 (≤ 5 mL of ethanol retention) and group 2 (>5mL of ethanol retention) were 3.80 and 3.06 respectively (p>0.05). The AMH at 6-month follow up for group 2 patients was significantly lower than for group 1 patients, with mean decrease of 0.72 (23.6%) and 0.10 (2.7%) respectively (p<0.05). No significant change in CA-125, recurrence rate or pain score was found within 1 year of aspiration.

CONCLUSIONS: Ultrasound-guided sclerotherapy with 95% ethanol is an effective therapy for ovarian endometriomas. The greater the amount of ethanol left in situ during sclerotherapy, the more AMH decreases post-oper-
atively.

P-522 Wednesday, October 16, 2019 6:30 AM

PREOPERATIVE SERUM ANTI-MULLERIAN HORMONE LEVELS IN WOMEN WITH OVARIAN ENDO-
METRIOSIS COMPARED TO WOMEN WITH PERITONEAL ENDOMETRIOSIS. Serin I. Seckin,
MD.⁎ Tamer A. Seckin, MD.⁎ Karli Provost Goldstein, DO.⁎ Icahn School of Medicine at Mount Sinai West/ Luke’s, New York, NY; 1Lenox Hill Hospital/Northwell Health System, New York, NY.

OBJECTIVE: Anti-Mullerian hormone (AMH) is an important serum marker to gauge ovarian reserve and predicted response to number of oocytes retrieved after ovarian stimulation. Patients who have ovarian involvement of endometriosis have clinically demonstrated lower baseline AMH levels. Whether or not patients with peritoneal endometriosis only have lower base-
line AMH levels has not been established. Our aim is to investigate preoper-
ative baseline AMH levels in women who have ovarian endometriosis versus women who have peritoneal endometriosis without ovarian involvement.

DESIGN: Retrospective cross-sectional analysis.

MATERIALS AND METHODS: Pre-operative AMH levels were evalu-
at ed for 111 women aged 19-42 who underwent laparoscopic surgery from January 2017 and July 2018 for suspected endometriosis. Patients were iden-
tified for those who desired future fertility and had preoperative AMH levels done. Patients with a diagnosis of polycystic ovaries or history of prior endometriosis excision surgery and/or ovariectomy were excluded. AMH levels were analyzed according to where endometriosis was anatomically located and confirmed by pathology, comparing women who had peritoneal endometriosis (n=71) without any ovarian involvement versus women with ovarian involvement (n=40). Subanalysis of AMH values was also per-
formed within three different age groups.

RESULTS: Preoperative serum AMH level was not significantly different in the ovarian endometriosis group compared to the peritoneal endometriosis group (3.22 ± 3.07 ng/mL vs 3.94 ± 2.90 ng/mL, P=0.113). Subgroup analy-
sis by age demonstrated significantly lower AMH levels for women with ovarian endometriosis aged 27-35 (2.62 ± 2.28 ng/mL vs 3.85 ± 2.98 ng/
DL, P=0.045). Patients with ovarian endometriosis were significantly more likely to have more endometriotic lesions confirmed on pathology (16.95 ± 8.75 lesions vs 8.97 ± 6.85 lesions, P<0.0001).


CONCLUSIONS: Patients with ovarian endometriosis demonstrate lower serum AMH levels than baseline age-matched populations [1], thus reflecting ovarian function and potential success with oocyte retrieval. These findings indicate that some women with peritoneal endometriosis may be at a similar disadvantage in regards to ovarian reserve compared to women with endometriomas and could benefit from earlier intervention regarding active management of fertility preservation.


P-523 Wednesday, October 16, 2019 6:30 AM
DIENOGEST FOR PAIN AND INTESTINAL SYMPTOMS CAUSED BY RECTOSIGMOID ENDOMETRIOSIS: PROSPECTIVE COHORT STUDY. Simone Ferrero, MD, PhD,¹ Carolina Scala, MD,¹ Valério Gaetano Vellone, MD, PhD,¹ Umberto Leone Roberti Maggiore, MD, PhD,¹ Ennio Biscaldi, MD,¹ Fabio Barra, MD, MD,⁴ DINOGMI, University of Genova, Genova, Italy;¹ Istituto G. Gaslini, Genova, Italy;¹ DISC, University of Genova, Genova, Italy;¹ Department of Gynecologic Oncology, IRCCS National Cancer Institute, Milan, Italy;¹ Department of Radiology, Galliera Hospital, Genova, Italy.

OBJECTIVE: The aim of this study was to evaluate the efficacy of dienogest (DNG) for treating pain and intestinal symptoms in patients with rectosigmoid endometriosis.

DESIGN: 24-month open-label prospective cohort study.

MATERIALS AND METHODS: This study included symptomatic women of reproductive age with rectosigmoid endometriosis. The diagnosis of rectosigmoid endometriosis was performed by transvaginal ultrasonography and confirmed by magnetic resonance imaging. Exclusion criteria for the study were: use of hormonal therapies for endometriosis in the 3 months before study entry (6 months for gonadotropin releasing hormone analogues), previous treatment with DNG, unwillingness to tolerate menstrual changes, undiagnosed vaginal bleeding, obstructive uropathy, complex adnexal cysts at imaging, estimated rectosigmoid stenosis >60%. Eligible women underwent hormonal treatment with DNG (2 mg/day) continuously for 24 months. Consultations were performed every 6 months. The primary endpoint of the study was patient satisfaction. Secondary endpoints were: changes in pain (assessed on a VAS scale) and intestinal symptoms (assessed by a 10-point symptom analogue scale and by the Gastrointestinal Quality of Life Index, GIQLI), changes in quality of life (assessed by the Endometriosis Heath Profile 30, EHP-30), changes in sexual function (assessed by the Female Sexual Function Index, FSFI), tolerability of the therapy, changes in the volume of the rectosigmoid nodules (estimated by using the virtual organ computer-aided analysis, VOCAL).

RESULTS: 132 women were enrolled in the study and 114 (86.4%) completed the 24-months treatment. The mean (±SD) age of the study population was 34.5 ± 4.1 years. 102 patients (77.3%) had already received previous hormonal treatment for treating endometriosis. 56 patients (42.4%) had previously undergone surgery for pelvic endometriosis. All pain symptoms (dysmenorrhea, non-menstrual pelvic pain, deep dyspareunia and painful defecation) significantly improved at 1-year of treatment compared with baseline. The severity of diarrhea, intestinal cramping and passage of mucus significantly improved at 6-, 12- and 24-month assessment compared with baseline. Abdominal bloating improved at 24-month assessment compared with baseline. The GIQLI, the EHP-30 and the FSFI were significantly improved at 24-month follow-up compared with baseline. There was a significant reduction in the volume of the bowel endometriotic nodules between baseline (4.3±0.8 cm³) and 12-month assessment (3.4±1.0 cm³; p<0.001) and between baseline and 24-month assessment (3.1±0.6 cm³, p=0.001). The volume of the nodules did not significantly change between the 12-month and the 24-month assessment. DNG was generally well tolerated, with no reported serious adverse events; the most common adverse effect was headache (8.3%).

CONCLUSIONS: A 2 year-therapy with DNG improves the symptoms caused by rectosigmoid endometriosis with a good safety-profile, proving also a slight reduction of the size of the bowel endometriotic nodules.

P-524 Wednesday, October 16, 2019 6:30 AM
FIBER AND GLUTEN INTAKE AS RISK FACTOR OF LAPAROSCOPICALLY-CONFIRMED ENDOMETRIOSIS. Holly Harris, M.P.H., Sc.D.,¹ Myriam C. Afeiche, Ph.D,¹ Kathryn L. Terry, Sc.D.,¹ Jorge E. Chavarro, MD, Sc.D.,¹ Stacey A. Missmer, Sc.D.² Fred Hutchinson Cancer Research Center, Seattle, WA;¹ Nestlé Research Center, Lausanne, Switzerland;¹ Brigham and Women’s Hospital and Harvard T.H. Chan School of Public Health, Boston, MA;¹ Harvard School of Public Health, Boston, MA;¹ Michigan State and Harvard T.H. Chan SPH, Grand Rapids, MI.

OBJECTIVE: We examined the association between intake of fiber (total fiber, legume, vegetable, cruciferous vegetable, fruit, and cereal fibers) and gluten and diagnosis of laparoscopically-confirmed endometriosis.

DESIGN: A prospective cohort study using data collected from 81,789 premenopausal women from 1991-2013 as part of the Nurses’ Health Study II (NHSII) cohort.

MATERIALS AND METHODS: Diet was assessed with a validated food frequency questionnaire every four years. Multivari一轮 Cox proportional hazards models adjusted for race/ethnicity, menstrual cycle length, parity, age at menarche, body mass index, recent gynecologic/breast exam, and total calories, were used to calculate rate ratios (RR) and 95% confidence intervals (CI).

RESULTS: During 22 years of follow-up, 3793 incident cases of laparoscopically-confirmed endometriosis were reported. Higher intake of fruit fiber was associated with a lower risk of endometriosis diagnosis (RR for 5th quintile vs 1st quintile=0.89; 95% CI=0.80-0.98). A similar association was observed for cereal fiber (RR for 5th quintile vs 1st quintile=0.90; 95% CI=0.81-1.00). In contrast, vegetable fiber intake was associated with a higher risk of endometriosis diagnosis (RR for 5th quintile vs 1st quintile=1.12; 95% CI=1.02-1.24). This association appears to be driven by the association with cruciferous vegetable fiber intake (RR for 5th quintile vs 1st quintile=1.17; 95% CI=1.06-1.30). No significant associations were observed with total fiber or legume fiber. Intake of gluten was associated with a lower risk of endometriosis diagnosis (RR for 5th quintile vs 1st quintile=0.82; 95% CI=0.72-0.93). This association was modified by fertility status. Specifically, the inverse association between gluten intake and endometriosis diagnosis was only apparent among women who had not reported infertility (RR for 5th quintile vs 1st quintile=0.82; 95% CI=0.71-0.95). The corresponding RR for those reporting infertility was 0.94 (95% CI=0.68-1.31).

CONCLUSIONS: Our findings suggest that different types of fiber intake are differentially associated with risk of endometriosis diagnosis. Further analyses are needed to identify whether these associations are driven by consumption of the foods that contribute to fiber intake or due to the fiber content itself. Our finding that gluten intake was associated with a lower risk of endometriosis diagnosis among women who had not reported infertility, and thus were more likely to present with pain symptoms, suggests that gluten intake is unlikely to contribute to heightened endometriosis risk among the general population or exacerbation of pain symptoms among women with endometriosis. The inverse association observed deserves further study in well-designed observational and intervention studies.

P-525 Wednesday, October 16, 2019 6:30 AM
IN UTERO AND EARLY LIFE EXPOSURES IN RELATION TO ODDS OF ENDOMETRIOSIS IN ADOLESCENTS AND YOUNG ADULTS. Naoko Sasamoto, M.D., M.P.H.,¹ Leslie V. Farland, Sc.D.,¹ Allison F. Vitoson, M.S.,¹ Holly Harris, M.P.H., Sc.D.,¹ Amy D. DiVasta, MD, MMSc,¹ Marc R. Lauffer, M.D.,¹ Kathryn L. Terry, Sc.D.,¹ Stacey A. Missmer, Sc.D.¹ Brigham and Women’s Hospital, Boston, MA;¹ University of Arizona, Tucson, AZ;¹ Fred Hutchinson Cancer Research Center, Seattle, WA;¹

FERTILITY & STERILITY®
e317
OBJECTIVE: To investigate the relation between in utero life exposures and endometriosis diagnosis during adolescence and young adulthood.

DESIGN: We conducted a nested case-control study among participants of The Women’s Health Study: From Adolescence to Adulthood (A2A), a longitudinal cohort of adolescents and young women enrolled from 2012-2018.

MATERIALS AND METHODS: Participants (n=604; 295 laparoscopically-confirmed endometriosis cases, 309 population-based controls) in the A2A study (age < 25 yrs at enrollment) completed a modified WERF EPFA questionnaire at baseline. Information on in utero and early life factors were collected, including their mother’s age at delivery, birthweight, gestation length, parents’ smoking status during their pregnancy and/or during infancy, and childhood, and if the participant was breastfed. We calculated odds ratios (OR) and 95% confidence intervals (CI) using logistic regression models, a priori adjusted for age at enrollment, race/ethnicity, maternal endometriosis diagnosis, and age at menarche. Analyses of birthweight were restricted to full term births.

RESULTS: Median age at enrollment was 22 y (range 7-24) in controls and 17 y (range 12-24) in cases, with 68% and 83% non-Hispanic white, respectively. Median age at menarche was 12 y (range 8-15) for both groups. Among cases, 50% had mothers with endometriosis while only 9% of the controls did. The almost all cases (95%) were rASRM stage I or II at diagnostic surgery. Participants who were breastfed had lower odds of endometriosis diagnosis (OR: 0.25) compared to those not breastfed (OR: 0.40). 95% CI: 0.21-0.74). Young women whose mothers smoked during pregnancy (n=13) were four times more likely to be diagnosed with endometriosis < age 25 (OR: 3.93, 95% CI: 0.80-19.43), while those with mothers who smoked during infancy to childhood were 2.5 times more likely to be diagnosed (OR: 2.64, 95% CI: 1.10-6.32). Low birthweight (OR: 0.64, 95% CI: 0.08-4.87) and preterm birth (OR: 1.30, 95% CI: 0.30-5.66) were not associated with endometriosis diagnosis < age 25.

CONCLUSIONS: Among adolescents and young adults, exposure to breastfeeding in early life was associated with lower odds of surgically diagnosed endometriosis. Exposure to maternal smoking during pregnancy and infancy/childhood was associated with greater odds of endometriosis, although the number exposed was small. Further exploration and replication are necessary to draw conclusions regarding risk among those diagnosed during adolescence compared to those diagnosed during adulthood. As these exposures are potentially modifiable, solidifying these associations will form the basis of informative public health messages to prevent endometriosis.

P-526 Wednesday, October 16, 2019 6:30 AM
CUMULATIVE CLINICAL PREGNANCY AFTER SURGICAL TREATMENT OF INFERTILE WOMEN WITH ENDOMETRIOSIS. William Butler, MD, Arshia Rassi, DO, Kristina C. Hawkins, MD, Abdelmoneim Younis, DVM, PhD, Mercer University School of Medicine, MACON, GA; Mercer University School of Medicine, Macon, GA; Affiliation not provided.

OBJECTIVE: Justification for reproductive surgical treatment of endometriosis in infertile women has been questioned given the current success rates with IVF. Although several studies support the use of laparoscopy for surgical treatment, particularly in cases of stage I or II disease, other studies propose either empirical treatment with COH/UI or IVF. This study evaluated pregnancy outcomes in infertile women with endometriosis after surgical treatment.

DESIGN: IRB approved retrospective cohort study of women who presented with a complaint of infertility and were found to have endometriosis at the time of laparoscopic evaluation during 2012-2018. MATERIALS AND METHODS: This study included 374 women, ages 18-44 years, who were found to have normal ovulation, normal male factor and-normal fallopian tubes who chose to undergo laparoscopic evaluation for tubal/peri toneal factors as a potential cause of their infertility versus proceeding with IVF. All patients age 38 or older were encouraged to proceed directly to IVF. The primary reasons given for choosing laparoscopy over IVF involved financial issues and moral/ethical concerns about the IVF process. All surgeries were performed at the Ambulatory Surgery Center by a single endoscopic surgeon using a KTP laser for complete excision/vaporization of all identified endometriotic lesions and adhesions. 252 women were found to have endometriosis at the time of the surgery and their pregnancy data is reported. After surgery, patients were allowed to attempt pregnancy on spontaneous cycles for 3 cycles for age equal to or greater than 35; 6 cycles for age less than 35 yr. If not pregnant, they were allowed a maximum of 3 cycles of COH/UII prior to proceeding with IFV. Clinical pregnancy rates were determined for both spontaneous and COH/UI cycles for each stage of endometriosis found.

RESULTS: Patients with stage I endometriosis had a spontaneous cycle pregnancy rate of 43.9% and an additional pregnancy rate of 36.4% on follow-up COH/UI cycles. Cumulative pregnancy rate was 80.3%. Patients with stage II endometriosis had a spontaneous cycle rate of 28.4% and an additional 15.7% on COH/UI given a cumulative rate of 44.1%. Stage III patients had a spontaneous cycle rate of 18.5% and COH/UI rate of 7.4% giving a cumulative pregnancy rate of 25.9%. Stage IV patients had a spontaneous cycle rate of 19.3% and COH/UI rate of 15.8% giving a cumulative pregnancy rate of 35.0%.

CONCLUSIONS: Laparoscopic surgical treatment of endometriosis in infertile women, particularly in combination with COH/UI, significantly enhances fertility rates. The cumulative pregnancy rate for all patients was 49.6%, compares favorably with prior studies as well as IVF data. Barri, et al reported a 54.2% pregnancy rate surgical treatment of endometriosis. SART 2016 IVF pregnancy data for endometriosis patient showed a pregnancy rate of 46.6% for patients <35 yr and 41.1% for patient’s age 35-37. We believe laparoscopic treatment of endometriosis is an excellent option for these patients, particularly those for whom IVF is not an acceptable treatment option early in life.


P-527 Wednesday, October 16, 2019 6:30 AM
SERUM METABOLOMIC PROFILE AS A NON-INVASIVE ADJUNCT TOOL FOR THE DIAGNOSIS OF ENDOMETRIOSIS-RELATED INFERTILITY. Daniela Antunes Montani, PhD, Daniela Paes de Almeida Ferreira Braga, PhD, Amanda Souza Setti, MSc, Assumpsto Iaconelli, Jr., MD, Diogo Oliveira-Silva, PhD, Edson Borges Jr., PhD, UNIFESP, Diademia, Brazil; Fertility Medical Group / Sapientia Institute, Sao Paulo, Brazil.

OBJECTIVE: Nonsurgical methods for the diagnosis of endometriosis could avoid unnecessary laparoscopies and improve quality of life. We aimed to develop an adjuvant tool for the diagnosis of endometriosis, based on mass spectrometry (MS)-metabolomics.

DESIGN: Case-control study.

MATERIALS AND METHODS: Serum samples from 100 patients undergoing intracytoplasmic sperm injection (ICSI), from January 2017 to December 2017, in a private university-affiliated in vitro fertilization center were collected. Samples were split into two groups according to the cause of infertility: the Endometriosis Group (n = 50), consisting of samples derived from patients with grade III and IV endometriosis, classified according with the American Society for Reproductive Medicine (ASRM), and the Control Group (n = 50), comprising samples derived from patients with isolated male factor infertility. Clinical diagnosis and classification of subjects in the endometriosis group were performed through laparoscopic surgery followed by histology to confirm the presence of endometriotic lesions. The metabolomic profile of each sample was obtained by mass spectrometry. Partial least square discriminant analysis (PLS-DA) was applied to the dataset in order to determine the discriminatory components based upon the combination of variable influence on projection (VIP) values. These variables were used to build a single receiver operating characteristic (ROC) curve. To validate the model, 30 samples from infertile women without any evidence of endometriosis were tested.

RESULTS: Except for the pregnancy rate, which was decreased in the Endometriosis Group (32.0% vs 72.0%, for Endometriosis and Control groups respectively, p=0.007), the patient and cycle characteristics were similar between groups. A total of 429 and 484 ions for the positive and negative ionization modes were analysed, respectively. Considering components one, two and three, the PLS-DA was able to clearly distinguish the Endometriosis-Group from the Control-Group for both positive and negative ionization modes. Ten potential biomarkers were selected based on their importance for model prediction, five in the positive and five in the negative ionization modes. These ions were used to build the ROC curve, which presented an area under the curve (AUC) of 0.904 (CI 95%: 0.796–0.985), indicating the accuracy of the biomarkers for sample classification in the Control.
or Endometriosis groups. Considering these ions as possible biomarkers, the model was able to correctly classify 84% of the patients and, when the validation set was tested, the model was able to correctly classify 86.6% of the samples. Two metabolites were identified by the database. Tricyglycerols and alpha-amino acids were more abundant in serum of positive endometriosis patients, while the other ions were not identified by the currently available database.

CONCLUSIONS: Our evidence suggests that serum metabolomics may be a valuable approach to the diagnosis of endometriosis and may be used as an adjunct tool for the selection of patients who must undergo laparoscopy to obtain a definitive diagnosis.

Reference: NA

SUPPORT: None.

P-528 Wednesday, October 16, 2019 6:30 AM

SYSTEMATIC REVIEW AND CRITICAL APPRAISAL OF CURRENT ENDOMETRIOSIS GUIDELINES INCLUDING 2018 SPANISH ENDOMETRIOSIS GUIDELINE WITH FOUR EVALUATION METHODS.

Maria Carrera, MD, José Antonio Dominguez, MD, PhD, Enrique Perez de la Blanca, MD, Roberto Matorras, Professor, Jose Maria Gris, MD, PhD, Gorka Barrenetxea, Professor, Carmen Maria Segura, MD, Miguel Caballero, MD, PhD, Joaquin Llacer, PhD, Medical Doctor, Gynaecologist, Specialist in Reproductive Medicine, Madrid, Spain; Reproduction specialist, Badajoz, Spain; Hospital Quironsalud. Assisted Reproduction Unit, Malaga, Spain; Basque Country University, Bilbao, Spain; Hospital Vall d’Hebron, Barcelona, Spain; MEDICAL DIRECTOR OF REPRODUCCION BILBAO, BILBAO, Spain; Medical doctor, Madrid, Spain; Gynecologist, Madrid, Spain; Instituto Bernabeu, Alicante, Spain.

OBJECTIVE: To appraise methodological quality of main endometriosis guidelines, including the 2018 Spanish Fertility Society Endometriosis Guideline, with four different evaluation methods: Agree II Instrument, the Right statement, the Australian ICAHE Checklist and the German MiChe, to explore methodological quality differences between them.

DESIGN: Appraisal of main Endometriosis Guidelines with different methodological quality assessment tools to establish differences among them and correlation between evaluation methods.

MATERIALS AND METHODS: Two reviewers (JAD, MCR) performed a systematic research at PubMed, EMBASE, and Web of Science from 2008 to 2019 for endometriosis guidelines, and consensus documents. Inclusion criteria: National or International Guidelines published in English, French or Spanish. The guidelines assessment was performed with the four appraisal tools described above. Nine reviewers (GB, MCR, MCC, JAD, JMG, JLL, RM, EPB, CS) assessed the methodological quality of the guidelines to ensure each guideline was evaluated by at least four different reviewers with each of the four appraisal tools. Guidelines scoring system was calculated for each method and standardising the result of the assessment for comparison. Guidelines were categorised as high quality when they score between 67-100%, moderate quality between 34-66% and low quality between 0-33% of the total score for each appraisal tool.

RESULTS: Ten guidelines along with the Spanish Fertility Society Endometriosis Clinical Guideline (SEF 2018) were included in the review (in chronological order): the Korean Society of Endometriosis Guideline (2018), French Guideline (CNGOF 2018), the National Institute for Health and Care Excellence (NICE 2017), the German Guideline (S2k 2014), the European Society of Human Reproduction and Embryology Endometriosis Guideline (ESHRE 2013), the World Endometriosis Society Montpellier Consensus (WES 2013), the Spanish Health Ministry Guideline (2013), the Australasian Guideline (ACCEPT, 2012), American Society of Reproductive Medicine Endometriosis Committee Opinion (ASRM 2012), and Society of Obstetricians and Gynaecologists of Canada Endometriosis Guideline (SOGC 2010). All of them were assessed by all four methods. Considerable methodological variability was found.

NICE 2017 was the best rated, followed by SEF, 2018 and CNGOF, 2018. According to guideline classification in tertiles, with the Agree II instrument four guidelines reached the upper tertile (high quality) (>67%) NICE 2017, SEF 2018, CNGOF 2018 and ESHRE 2013. All the rest scored as moderate quality (34-66%). With the Right checklist, the classification remained the same. With iCAHE and MiChe appraisal, 4 guidelines moved into the high quality tertile: Canada 2010, ACCPET 2012, WES 2013, and S2K 2014.

CONCLUSIONS: Endometriosis Guidelines have a high degree of methodological variability when appraised by different evaluation tools. Due to this fact, appraisal seems necessary prior to apply recommendations. Guidelines assessment has to be quick and easy so clinicians can perform it themselves in daily practice.

P-529 Wednesday, October 16, 2019 6:30 AM

PRESENCE OF HUMAN HERPESVIRUS 6 (HHV-6) ANTIGENS IN PAIRED SURGICAL SPECIMENS FROM WOMEN EVALUATED FOR ENDOMETRIOSIS: A SURVEY OF NINE PATIENTS.

Kaitlin Doody, MD, Michael C. Doody, MD PhD, Alexander Kusnacko, DO, Konstance Knox, PhD, UT Southwestern, Dallas, TX; The Center for Reproductive Medicine, Knoxville, TN; Coppe Healthcare Solutions, Waukesha, WI.

OBJECTIVE: Endometriosis is a common disease affecting more than 10% of American women of childbearing age, contributing to infertility in 30-50% of those affected. A cause or trigger for the disease has not been identified. Human herpesvirus 6A and 6B (HHV-6) are members of the beta sub-family of herpesviridae that includes cytomegalovirus (CMV) and human herpesvirus 7 (HHV-7). Recent reports have identified the presence of HHV-6 infection within the endometrium in 43% of women with unexplained infertility, but not within the endometrial tissue of fertile women. Examined biopsies from endometrial tissue and endometriosis implants for evidence of active HHV-6 infection to identify a potential association between HHV-6 and endometriosis-associated infertility.

DESIGN: Nine women with known infertility and suspected endometriosis underwent hysterectomy and laparoscopy. With one exception, infertility patients without visually identified endometriosis did not have HHV-6 IHC testing. Endometriosis biopsies were obtained by laser excision and endometrial biopsies were obtained by curettage. Routine histologic evaluation was performed on all collected specimens. Endometriosis was confirmed visually and histologically in eight of the nine patients presented here. One patient had an endometrial polyp without visual evidence of endometriosis.

MATERIALS AND METHODS: Slides from archived formalin fixed paraffin embedded biopsy tissues were assessed by immunohistochemistry with a validated diagnostic assay for late viral proteins of HHV-6.

RESULTS: Of the eight patients with endometriosis, HHV-6 IHC was positive in two, with identification of HHV6 antigens in both endometrium and peritoneal implants. One patient without visually identified endometriosis was found to have HHV-6 IHC in a benign polyp as well as a paired curettage.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age(years)</th>
<th>Duration of infertility</th>
<th>Endometrial biopsy</th>
<th>Peritoneal biopsy(s)</th>
<th>Endometrial polyp</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35</td>
<td>18 mo</td>
<td>Positive</td>
<td>Positive</td>
<td>N/A</td>
</tr>
<tr>
<td>2</td>
<td>33</td>
<td>4 yrs</td>
<td>Negative</td>
<td>Negative</td>
<td>N/A</td>
</tr>
<tr>
<td>3</td>
<td>36</td>
<td>10 mo</td>
<td>Positive</td>
<td>Positive</td>
<td>N/A</td>
</tr>
<tr>
<td>4</td>
<td>27</td>
<td>4 yrs</td>
<td>Negative</td>
<td>Negative</td>
<td>N/A</td>
</tr>
<tr>
<td>5</td>
<td>29</td>
<td>2 yrs</td>
<td>Negative</td>
<td>Negative</td>
<td>N/A</td>
</tr>
<tr>
<td>6</td>
<td>25</td>
<td>20 mo</td>
<td>Negative</td>
<td>Negative</td>
<td>N/A</td>
</tr>
<tr>
<td>7</td>
<td>31</td>
<td>3 yrs</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>8</td>
<td>34</td>
<td>6 yrs</td>
<td>Negative</td>
<td>Negative</td>
<td>N/A</td>
</tr>
<tr>
<td>9</td>
<td>34</td>
<td>2 yrs</td>
<td>Negative</td>
<td>Negative</td>
<td>N/A</td>
</tr>
</tbody>
</table>
specimen. HHV-6 late antigens were located in endometrial epithelial cells and were not seen in stromal or hematopoietic derived cells.

CONCLUSIONS: The presence of reactivated HHV-6 in endometrial epithelial cells and the ability of the virus to up-regulate the expression of cytokines (IL-8, TNFa) and growth factors (VEGF) associated with proliferation, adhesion, and neangiogenesis of endometrial cells, supports further study for a role of HHV-6 in the pathogenesis of endometriosis and associated infertility.


P-530 Wednesday, October 16, 2019 6:30 AM

EFFECTS OF DIENOGEST ON BREAST: MCF CELL LINE DATA. Hyun Jin Kim, M.D., Sung Hoon Kim, M.D., Ph.D. Young Sang Oh, M.S., DeYoung Kim, M.D., Sa Ra Lee, M.D. Ph.D., Hee Dong Chae, M.D., Ph.D., Byung Moon Kang, M.D. Ph.D. University of Ulsan College of Medicine, Asian Medical Center, Seoul, Korea, Republic of (South).

OBJECTIVE: Dienogest (DNG) is a widely used progestin which is safe and effective for long-term management of endometriosis. However, its association to breast cells remains to be elucidated. We performed this study to investigate whether in vitro treatment of DNG can cause any biologic changes on MCF cell line (human estrogen receptor (ER)-positive breast cancer cell line) experiments.

DESIGN: A laboratory study.

MATERIALS AND METHODS: Following in vitro culture of MCF cells, we treated those cells and compared cell viability and the expression of several markers. We also estimated changes in MMP2 activity, PAK4 expression, VEGF (vascular endothelial growth factor) and IL (interleukin) (32)-32 were analyzed by ELISA, and MMP2 (matrix metalloproteinase 2) activity was assessed by zymography.

RESULTS: In vitro treatment of MCF7 cells led to an increased cell viability by estradiol alone and estradiol with DNG. Cell viability was measured utilizing MTT(3,4-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay and the expression of PCNA (proliferating cell nuclear antigen) and PAK4 (p21 activated kinase 4) was measured by western blot analyses. VEGF (vascular endothelial growth factor) and IL (interleukin) were not seen in stromal or hematopoietic derived cells.

CONCLUSIONS: These findings suggest that DNG may have inhibitory effects on carcinomaogenesis of breast cells by suppressing specific biologic changes treated by estradiol. However, further study is necessary using normal human breast cells.

P-531 Wednesday, October 16, 2019 6:30 AM

MAGNETIC RESONANCE WITH GEL ENEMA (MR-e) AND COMPUTED TOMOGRAPHY-BASED VIRTUAL COLONOSCOPY (CTC) FOR DIAGNOSING RECTOSIGMOID ENDOMETRIOSIS. Simone Ferrero, MD, PhD,a Essam R. Othman, MD,b Maha Y. Khashbhab, MSc, c Ibraheem I. Abdelaal, MD,b Ahmad Ab Abo Markeb, PhD,a Ahmad N. Feith, MD,b C. B. Lambalk, MD, PhD.b Amsterdam University Medical Center, location VU, Amsterdam, Netherlands; Academic professor OB-GYN department, Assiut, Egypt; Women’s Health Hospital, Assiut, Egypt; gAssiut University Medical Center, reproductive medicine department, Amsterdam, Netherlands; hAssociate professor, OB-GYN department, Assiut, Egypt, bFaculty of Science, Assiut University, Assiut, Egypt; iAmsterdam University Medical Center, reproductive medicine department, Amsterdam, Netherlands.

OBJECTIVE: Diagnosis of rectosigmoid endometriosis is critical for the clinicians to perform surgical treatment. This study aimed to compare the accuracy of magnetic resonance with gel enema (MR-e) and computed tomography-based virtual colonoscopy (CTC) for diagnosing rectosigmoid endometriosis.

DESIGN: Retrospective analysis of a prospectively collected database.

MATERIALS AND METHODS: This study included patients with pain and/or intestinal symptoms lasting at least 6 months and clinical suspicion of rectosigmoid endometriosis. Exclusion criteria for the study were previous intestinal surgery (with the exception of appendectomy) or previous laparoscopic diagnosis of rectosigmoid endometriosis. Patients underwent both MR-e and CTC. Subsequently they underwent laparoscopy; rectosigmoid nodules were excised by segmental colorectal resection, nodulectomy or biopsy. The surgical specimens were sent to the pathologist in order to be evaluated by standardized criteria.

RESULTS: Out of 90 women included in the study, 44 (48.9; 95% CI, 38.2%-59.7%) had rectosigmoid nodules. Seven patients underwent shaving of the colorectal nodules; 28 patients underwent segmental colorectal resection, in these patients the mean (+ SD) length of the resected bowel specimen was 12.0 ± 2.1 cm. At histology, endometriosis infiltrated only the muscularis propria in 33 patients, the submucosa in 8 patients and the mucosa in 3 patients. There was no significant difference in the accuracy of both radiologic exams for diagnosing the presence of rectosigmoid endometriosis (p = 0.344); in particular, for MR-e, sensitivity was 93.2% (95% CI, 81.3-98.6%), specificity 97.8% (95% CI, 88.5%-99.9%), positive predictive value (PPV) 97.6% (95% CI, 85.5%-99.7%) and negative predictive value (NPV) 93.8% (95% CI, 83.4%-97.9%). For CTC, sensitivity was 88.64% (95% CI, 75.4%-96.21%), specificity 93.48% (95% CI, 82.10%-98.63%), PPV 92.9% (95% CI, 81.2%-97.5%) and NPV 89.6% (95% CI, 80.0%-95.2%). The mean ± (SD) largest diameter of the main endometriotic nodule at histology was 26.8 ± (7.9) mm. The nodule was preoperatively identified by both MR-e and CTC in 37 patients. MR-e was more accurate than CTC in estimating the largest diameter of the main rectosigmoid nodule (p < 0.001). The mean difference in the estimated length of the nodule was 3.1 mm (95% CI, 0.6 to 5.7 mm) at CTC and 2.4 to 3.7 mm (limits of agreement, -0.7 to 6.8 mm) at CTC and 1.6 at MR-e (95% CI, -1.0 to 2.1; limits of agreement, -1.8 to 4.9 mm) when compared with histology. MR-e was more precise than CTC in identifying multifocal disease. Patients complained more discomfort during CTC than during MR-e (p = 0.001).

CONCLUSIONS: This study showed that MR-e and CTC have similar diagnostic accuracy in diagnosing rectosigmoid endometriosis. However, MR-e is more accurate in estimating the largest diameter of the main rectosigmoid nodule, in diagnosing multifocal disease and it is better tolerated than CTC. Moreover, MR-e does not require to administer ionizing radiations.

P-532 Wednesday, October 16, 2019 6:30 AM

MARKERS OF LOCAL AND SYSTEMIC ESTROGEN METABOLISM IN ENDOMETRIOSIS. Velja Mitajovic, M.D., PhD,a Essam R. Othman, MD,b Maha Y. Khashbhab, MSc, c Ibraheem I. Abdelaal, MD,b Ahmad Ab Abo Markeb, PhD,a Ahmad N. Feith, MD,b C. B. Lambalk, MD, PhD.b Amsterdam University Medical Center, location VU, Amsterdam, Netherlands; Associate professor OB-GYN department, Assiut, Egypt; Women’s Health Hospital, Assiut, Egypt; gAssiut University Medical Center, reproductive medicine department, Amsterdam, Netherlands; hFaculty of Science, Assiut University, Assiut, Egypt; iAmsterdam University Medical Center, reproductive medicine department, Amsterdam, Netherlands.

OBJECTIVE: Endometriosis is an estrogen dependent disease. Estrogen metabolites can work independently of their parent hormones. Therefore, we hypothesize that in endometriosis patients estrogen is metabolized along hormonally active pathways to keep a highly estrogenic milieu.

DESIGN: Cross sectional study in which paired urine, endometrial and ectopic endometrial samples were taken from patients with endometriosis and control women and analyzed for estrogen metabolites.

MATERIALS AND METHODS: We recruited 62 Endometriosis cases (disease proven laparoscopically and histologically) and 52 control women (in whom laparoscopy was normal) among patients undergoing laparoscopy for pelvic pain and/or infertility during proliferative phase of cycle. Urine samples were collected preoperatively. At surgery we collected eutopic endometrial samples from endometriosis cases and control women and biopsies from ovarian endometriotic cysts (ectopic endometrium). Estrogen metabolites in urine and endometrial tissue were extracted and determined using Liquid Chromatography-Electrospray Ionization Tandem Mass Spectrometry (LC-ESI-MS/MS). These included:2-hydroxyestrone (2OHE1), 4-hydroxyestrone (4OHE1), 2-hydroxyestradiol (2OHE2), and 4-hydroxyestradiol (4OHE2). Non parametric statistics were used.

RESULTS: Endometriosis cases and control women had similar baseline characteristics. Endometrial estrogen metabolites there was no significant difference among control endometrium, eutopic endometrium of

ASRM Abstracts

Vol. 112, No. 3, Supplement, September 2019
endometriosis patients or ectopic endometrium in levels of 16α OHE1, 20HE1, and 20HE1/16α OHE1 ratio. Eutopic endometrium of endometriosis patients, compared to control endometrium, had significantly higher 40HE1 [30 (30-260)] versus 30 (30-200) ng/g tissue, respectively, P = 0.017]. 20HE1 [146 (3.4-34.6) versus 49 (3-12.8) ng/mg creatinine respectively, P = 0.024] and 20HE1 [107.1 (39.15-15.5) versus 48.1 (1.4-13.7) mg/mg creatinine, respectively, P = 0.018]. All other metabolites did not differ significantly between cases and controls. 

CONCLUSIONS: Eutopic endometrium of endometriosis patients metabolizes estrogen preferentially to estrogenically active (20HE2), and poten-
tially genotoxic (40HE1, 40HE2) metabolites. This adds explanation on endometriosis etiology, provides a link between endometriosis and cancer, and may help in identifying potential endometriosis biomarker of the disease. In urine, a similar pattern could not be identified as ratio of antiproliferative 20HE1 to proliferative 16αOHE1 are similar between cases and controls. 

SUPPORT: Science and Technology Development Fund (STDF) grante # 5525 to E.R.O.

P-533 Wednesday, October 16, 2019 6:30 AM
IMPACT OF GONADOTROPIN-RELEASING HORMONE AGONIST POST-OPERATIVE TREATMENT ON OVARIAN RESERVE CHANGES AFTER LAPAROSCOPIC SURGERY OF OVARIAN ENDOMETRIOMA. Yoo jin Shim, M.D., Jung Ryeol Lee, M.D., Ph.D., Seoul National University Bundang Hospital, Seongnam, Korea, Republic of (South).

OBJECTIVE: Hormonal treatment including gonadotropin-releasing hormone agonist, dienogest and oral contraceptive (OC) has been found to be effective in post-operative recurrence prevention. However, evidence is very limited regarding the change of ovarian reserve following these hormonal treatments. The objective of this study was to compare the impact of dienogest or OC alone versus gonadotropin-releasing hormone agonist (GnRHa) plus dienogest or OC on ovarian reserve.

DESIGN: Retrospective study at university hospital.

MATERIALS AND METHODS: A total of 81 patients undergoing laparoscopic ovarian cystectomy for ovarian endometriosis and subsequent treatment of either at least 2 times of GnRHa plus dienogest/OC (group A, n=46) or dienogest/OC alone (group B, n= 35) between October 2012 and April 2018 were retrospectively analyzed. Main outcome measures included AMH reduction ratio (preoperative – postoperative AMH / preoperative AMH x 100 ), AMH value at 3, 6, and 12 months after operation, CA 125 reduction ratio (preoperative – postoperative CA-125 / preoperative CA-125 x 100) and 12 month recurrence of the 2 groups.

RESULTS: Prior to operation, there were no significant differences between the group A and B in terms of age (33.4 ± 0.6 vs 32.1 ± 5.6, P=0.375), body mass index (21.5 ± 3.3 kg/m² vs 20.9 ± 2.8 kg/m², P=0.365), ARM score (63.6 ± 36.5 vs 69.4 ± 43.2, P=0.520), bilaterality of endometrioma (54.3% in both groups, P=0.996), and pre-operative CA-125 levels (94.6 ± 72.3 U/mL and 91.0 ± 43.1 U/mL, P=0.163).

Pre-operative AMH levels were not different in the two groups (3.9 ± 3.3 mg/mL vs 3.6 ± 1.6 mg/mL, respectively, P=0.820). At 3 and 6 months of treatment, AMH level was more reduced in Group A than Group B, but this difference was not statistically significant. (1.1 ± 0.9 mg/mL vs 1.9 ± 1.8 mg/mL, P=0.311 at 3 months, 1.5 ± 1.8 mg/mL vs 1.8 ± 1.7 mg/mL, P=0.610 at 6 months) The AMH reduction ratio was non-significantly higher in Group A (64 ± 23 % vs 51 ± 25 %, P=0.330 at 3 months, 63 ± 20 % vs 55 ± 30 %, P=0.358 at 6 months). At 12-month follow up, these trends were reversed and the AMH level was higher in group A, but this difference was also statistically not significant (1.95 mg/mL vs 1.64 mg/mL, P=0.615). CA 125 level and reduction ratio at 12 months were not statistically different between the 2 groups. There was no recurrence at 12 months in both groups.

CONCLUSIONS: These results show that, use of GnRHa reduces immediate post-op AMH level more at 3 and 6 months. However, after 12 months this effect is reversed. Long-term effects of GnRHa treatment in ovarian reserve and recurrence could be elucidated with further study with longer follow-up.
P-536 Wednesday, October 16, 2019 6:30 AM
ULTRALONG-TERM CYCLIC USE OF LOW-DOSE MONOPHASIC COMBINED ORAL CONTRACEPTIVE PILLS FOR THE MANAGEMENT OF RECURRENT SEVERE ENDOMETRIOSIS AFTER SECOND-LINE SURGERY. Chung-Hoon Kim, M.D., Ph.D., Jei-Won Moon, M.D., Shin Yong Moon, M.D., Ph.D., Fertility Center, Seoul, Korea, Republic of (South).

OBJECTIVE: We performed this study to evaluate the efficacy of ultra-long-term cyclic administration of low-dose monophasic combined oral contraceptive pills (OCP) for more than 60 months in the resolution of pain and regression of recurrent endometrioma and pseudocyst after second-line surgery for recurrent severe endometriosis.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Twenty-two patients who were prescribed low-dose monophasic combined OCP to be taken with follow-up ultrasonogram (USG) for more than 60 months after January 2001 for the treatment of recurrent severe pain and endometrioma and pseudocyst after second-line surgery were included. All patients included in the present study received cyclic therapy (daily 21 to 35 days followed by 7 day interval) with low-dose monophasic combined OCP (ethinyl estradiol 0.02 mg and desogestrel 0.15 mg daily or ethinyl estradiol 0.02 mg and drospirenone 3 mg daily). Pain and endometrioma and pseudocyst on ultrasonogram (USG) were evaluated. For the evaluation of pain improvement, visual analogue scale (VAS) was used.

RESULTS: In 22 patients included in this study, 6 patients had a unilateral endometrioma while 16 patients had bilateral endometriomas. Sixteen patients and pseudocyst while 6 patients had no visible pseudocyst. Duration of treatment ranged from 64 months to 150 months. Nine patients completed the treatment after complete resolution of dysmenorrhea and complete regression of endometriomas and pseudocysts but 13 patients are currently getting treatment. Pain score by visual analogue scale (VAS) was significantly lower from 12th month of treatment compared with baseline assessment (P < 0.001) and all patients reported complete resolution of dysmenorrhea at 12th month of treatment. Endometrioma size measured at 12th month of treatment significantly decreased compared with baseline size (P < 0.001) and consistently decreased and endometriomas assessed by USG were completely regressed in 20 patients (90.9%) at 60th month of treatment. Pseudocyst size measured by USG was significantly smaller from 12th month of treatment (P = 0.003) and pseudocysts were completely regressed in all patients at 36th month of treatment. Eight patients (36.4%) of 22 patients reported breakthrough vaginal bleeding but bleeding was small and transient and did not cause discontinuations. Except vaginal bleeding, no patients reported any other adverse effects attributed to the ultralong-term use of low-dose monophasic combined OCP.

CONCLUSIONS: Ultralong-term treatment with low-dose monophasic combined OCP is effective without any serious adverse effect in eliminating pain and regressing recurrent endometriomas and pseudocysts in patients with recurrent endometriosis after second-line surgery. Therefore, ultralong-term treatment using low-dose monophasic combined OCP can be an effective strategy in patients with pseudocysts as well as severe pain and recurrent endometriomas despite the second-line surgery. SUPPORT: None.

P-537 Wednesday, October 16, 2019 6:30 AM
THE USE OF DEXTROAMPHETAMINE SULFATE TO ALLEVIATE PELVIC PAIN DOES NOT LOWER DELIVERED PREGNANCY RATES FOLLOWING IN VITRO FERTILIZATION-EMBRYO TRANSFER (IVF-ET) IN YOUNGER WOMEN. Jerome H. Check, M.D., Ph.D., Diane L. Check, BS, MT, Rachael Cohen, D.O., Eric Chang, D.O., Carrie K. Wilson, B.A. 1 Cooper Medical School of Rowan University, Camden, NJ; 2 Cooper Institute for Reproductive Hormonal Disorders, PC, Mt. Laurel, NJ.

OBJECTIVE: Standard medical therapy with oral contraceptives, progestins, gonadotropin releasing hormone (GnRH) agonists or antagonists for pelvic pain syndromes preclude pregnancy while taking the medication, and there is no evidence that such treatment improves subsequent fecundity. Surgical treatment is frequently not effective in relieving pain and can sometimes cause oocyte depletion. Furthermore, it is not clear if surgical removal of endometriosis improves subsequent fecundity, or may have a negative effect related to diminishing oocyte reserve. One of the most effective treatments for pelvic pain is dextroamphetamine which would allow the patient to try to conceive while gaining pain relief. The objective of the present pilot study was to determine if the use of this sympathomimetic amine has any negative effects on pregnancy rates or adverse fetal consequences.

DESIGN: Prospective controlled comparison study.

MATERIALS AND METHODS: Women with moderate to severe dysmenorrhea, who also wanted or needed IVF to become pregnant, were treated with dextroamphetamine sulfate. They were advised that in pharmacologic dosages the drug does not appear to be a teratogen, but its effect on pregnancy rates is not known. Patients were required to be aged ≤35 with normal oocyte reserve (serum anti-mullerian hormone (AMH) level over 1.0 ng/ml). If all embryos on day 3 were abnormal or no embryos were created, the cycle was not counted. The dosage of dextroamphetamine sulfate varied from 9.4mg to 37.6mg. The clinical and live delivered pregnancy rates were compared to historical controls who did not necessarily have pelvic pain.

RESULTS: There were 23 women treated with dextroamphetamine sulfate who had day 3 embryo transfers. All stated their pelvic pain was moderately to markedly improved. There were 197 historical controls having day 3 transfers. The clinical pregnancy rate was 56.5% (13/23) vs. 47.2% (93/197) the live delivered pregnancy rate was 43.5% (10/23) vs. 37.6% (74/197) (p = NS, Chi-square analysis). The implantation rates were 39.5% vs. 32.5%. The average number of embryos transferred was 1.9 for both groups. All babies in the amphetamine treated group were normal.

CONCLUSIONS: Though the study group was small, there does not seem to be any negative effect of using dextroamphetamine sulfate for pelvic pain on pregnancy rates following IVF-ET. Since some believe that endometriosis may have a negative effect on IVF outcome, if there was a bias, it would be against the study group. If anything, there may have been a trend for higher pregnancy rates following IVF-ET. Since some believe that endometriosis may have a negative effect on IVF outcome, if there was a bias, it would be against the study group. If anything, there may have been a trend for higher pregnancy rates in the amphetamine treated group. Based on these data a randomized prospective study is planned comparing pregnancy outcome in women with pelvic pain taking amphetamine vs. no amphetamine who are undergoing IVF-ET to achieve a pregnancy.
DESIGN: A case-control study in University-affiliated infertility center. A total number of 81 women were enrolled in this study. Women who were either undergoing laparoscopic confirmation of endometriosis (n = 23) or were controls (n = 21). Women with endometriosis treated with Gonadotropin-releasing hormone agonist (GnRHa) (n = 31) and 6 follow up women (n = 6).

MATERIALS AND METHODS: Their plasma were collected and detected the metabolic pathways using Bioplex assay, seven metabolic pathways kit (Bio-Rad Laboratories, Hercules, CA) according to the manufacturer's instructions.

RESULTS: We found the AAT, AGP-1 and RBP-4 were increased in endometriosis patients. AAT is a protease inhibitor produced by the liver and beongs to the serpin superfamily of proteins. AAT protects tissue from enzymes secreted by inflammatory cells. AGP-1, also known as orosomucoid, is an acute phase protein produced in the liver. AGP1 acts as a carrier of lipophilic and basic drug, steroids, and protease inhibitors. RBP4 belongs to the lipocalin family and is the specific carrier protein for retinol (Vitamin A), delivering retinol from liver stores to peripheral tissues. To further observe whether AAT, AGP-1 and RBP-4 could be a biomarker of endometriosis, we analyzed the ROC curve. RBP-4 showed high area under the curve (AUC) values of 0.8 (95% confidence interval, 0.6696-0.9276). The AUC of AAT and AGP-1 are 0.71 and 0.68, respectively. With a Plasma RBP-4 level of 15.38 µg/mL as the optimal cutoff value and defined the maximum sensitivity and specificity, RBP-4 showed 79.17% sensitivity and 71.43% specificity. Moreover, AAT and RBP4 levels were significantly decreased in the GnRHa treatment group. Follow up studies also showed that GnRHa treatment decreased plasma AAT and RBP-4 levels in the same endometriosis patient.

CONCLUSIONS: These results found that RBP-4 may be a potential biomarker of endometriosis. AAT and RBP4 levels were significantly decreased in the GnRHa treatment group.

P-539 Wednesday, October 16, 2019 6:30 AM
LONG TERM TREATMENT OF ENDOMETRIOSIS ASSOCIATED PAIN (EAP) WITH LINZAGOLIX: EFFICACY AND SAFETY AFTER 12 MONTHS OF TREATMENT. Robert N. Taylor, MD PhD, Elke Bestel, MD, Jean-Pierre Gotteland, PhD, Veronica Lecomte, Pharm D, Rachel Dubouloz, MSc, Paul Terrill, PhD, Andrew Humberstone, PhD, Ernest Loumaye, MD, PhD. University of Utah Health, Salt Lake City, UT; ObsEva SA, Plan-les-Ouates, Switzerland; Cytel Inc, London, United Kingdom.

OBJECTIVE: To assess safety and maintenance of efficacy of linzagolix with EAP using linzagolix 75 mg once daily alone and 200 mg once daily or increased at 24 and 52 w. These data support Phase 3 trials in women with surgically confirmed endometriosis and moderate to severe EAP. Efficacy was assessed using a daily eDiary as the % of responders (≥ 30% reduction in mean 28-day scores) in overall pelvic pain (OPP), dysmenorrhea (DYS) and non-menstrual pelvic pain (NMPP). Dyspareunia and dyschezia scores were also assessed. Bone mineral density (BMD) of the femur, hip and spine were assessed by dual-energy X-ray absorptiometry (DXA).

RESULTS: At 12 w, there was a significant increase in the % of responders for OPP, DYS and NMPP for doses of 75 mg and above compared to PBO. These effects were generally maintained or increased at 24 and 52 w. At 12 w, there were significant improvements in dyspareunia (200 mg only) and dyschezia scores which were maintained or increased at 24 and 52 weeks. Mean BMD losses (spine) at 24 weeks were <1% at doses of 50 and 75 mg and increased with increasing dose up to 2.6% for 200 mg. A similar pattern was observed at 52 w. BMD changes in femur and hip were similar but generally smaller.

CONCLUSIONS: Linzagolix at daily doses of 75 mg and above significantly improved EAP symptoms at 12 w and these effects were maintained or increased at 24 and 52 w. These data support Phase 3 trials in women with EAP using linzagolix 75 mg once daily alone and 200 mg once daily with low-dose add-back hormonal therapy.

SUPPORT: The study was funded by ObsEva SA.

P-540 Wednesday, October 16, 2019 6:30 AM
DECREASED CLINICAL PREGNANCY AND LIVE BIRTH RATES IN WOMEN WITH ENDOMETRIOSIS, IN THE “eIVF” DATABASE. Kassie Jean Bollig, MD, Henok G. Woldu, PhD, Judy E. Stern, PhD, Albert L. Hsu, MD. Resident Physician, Columbia, MO; Biostatistics and Research Design Unit; University of Missouri, Columbia, MO; Dartmouth-Hitchcock, Lebanon, OR; Department of Reproductive Endocrinology and Infertility; University of Missouri, Columbia, MO.

OBJECTIVE: To determine whether surgically-confirmed endometriosis is associated with decreased implantation, pregnancy, or live birth rates compared with male factor infertility in women undergoing in vitro fertilization (IVF).

DESIGN: Retrospective multivariable analysis of 34,278 fresh IVF cycles in Massachusetts between 2003-2006, from the “eIVF” database.

MATERIALS AND METHODS: IVF cycles in women with surgically-confirmed endometriosis were compared with those in couples with male

| TABLE 1 |
|-------------|-----|-----|-----|-----|
|            | PBO¹ | 50 mg | 75 mg | 100 mg | 200/100 mg² |
| N           |      |      |      |      |             |
| 12 w        | 53   | 49   | 56   | 51   | 56           |
| 24 w        | 40   | 48   | 39   | 44   |              |
| 52 w        | 30   | 36   | 22   | 30   |              |
| % responders OPP | 34.5 | 49.4 | 61.5* | 56.4* | 56.3*        |
| 24 w        | 52.5 | 70.8 | 66.7 | 77.3 |
| 52 w        | 66.7 | 69.2 | 53.8 | 82.4 |
| % responders DYS | 28.5 | 43.3 | 68.2* | 68.6* | 78.9*        |
| 24 w        | 47.5 | 58.3 | 82.1 | 84.1 |
| 52 w        | 50.0 | 69.2 | 64.7 |             |
| % responders NMPP | 37.1 | 46.2 | 58.5* | 61.5* | 47.7         |
| 24 w        | 50.0 | 72.9 | 64.1 | 72.7 |
| 52 w        | 66.7 | 69.2 | 53.8 | 76.5 |
| Dyspareunia Mean (SD) CFB |         |      |      |      |             |
| 12 w        | -0.4 (0.9) | -0.6 (0.7) | -0.7 (0.8) | -0.7 (0.9) | -0.8 (1.1)* |
| 24 w        | -0.7 (0.8) | -0.7 (0.8) | -0.6 (0.8) | -1.0 (1.0) |
| 52 w        | -0.5 (1.1) | -0.9 (1.8) | -0.7 (1.8) | -0.9 (0.9) |
| Dyschezia Mean (SD) CFB |         |      |      |      |             |
| 12 w        | -0.7 (1.7) | -1.4 (1.7) | -2.1 (2.5)* | -2.0 (1.8)* | -1.7 (2.3)* |
| 24 w        | -1.5 (2.1) | -2.2 (2.5) | -2.0 (2.3) | -2.5 (2.6) |
| 52 w        | -2.3 (1.8) | -2.1 (2.9) | -2.9 (3.1) | -2.6 (2.7) |
| BMD spine Mean (95% CI) % CFB |         |      |      |      |             |
| 24 w        | 0.14 (-0.83, 1.11) | -0.80 (-1.57, -0.03) | -1.37 (-2.14, -0.59) | -2.60 (-3.56, -1.65) |
| 52 w        | 0.14 (-1.04, 1.31) | -1.14 (-2.21, -0.07) | -1.40 (-3.35, 0.55) | -2.19 (-3.59, -0.78) |

¹PBO only to 12 w; ²Subjects randomized to 200 mg received 100 mg from 24 to 52 w; *p < 0.05 compared to PBO.
factor infertility; only fresh IVF cycles that resulted in an embryo transfer were analyzed. Couples with both endometriosis and male factor infertility, and women with “suspected endometriosis” (not surgically confirmed), were excluded from analysis. Implantation rates were calculated in two ways: (1) gestational sacs (GS) per embryos transferred (ET), and (2) heartbeats (HB) per ET. Clinical pregnancy and live birth rates per cycle were also calculated. Means were compared using two-sample t-tests; medians were compared with lower max E2 levels. On univariable analysis, fewer women with endometriosis had implantation rates >= 50%, while no differences were found in pregnancy or live birth rates (Table). When adjusting for age and BMI in multivariable analysis, the odds of a clinical pregnancy was 35.5% higher in male factor infertility (OR 1.36, 95% CI [1.07-1.71]), and the odds of a live birth was 33.9% higher in male factor infertility (OR 1.34, 95% CI [1.02-1.76]), compared to women with surgically-confirmed endometriosis.

CONCLUSIONS: Compared with male factor infertility, surgically-confirmed endometriosis is associated with lower odds of implantation, clinical pregnancy and live birth in couples undergoing IVF.

**P-541 Wednesday, October 16, 2019 6:30 AM**

**CIRCULATING PLACENTAL GROWTH FACTOR (PLGF) CONCENTRATION IN PREGNANT WOMEN WITH ENDOMETRIOSIS: A CASE-CONTROL STUDY.** Simone Ferrero, MD, PhD, Fabio Barra, MD, Valerio Gaetano Vellone, MD, PhD, Umberto Leone Roberti Maggiore, MD, PhD, Carolina Scala, MD, *DINOGMI, University of Genova, Genova, Italy; *DISC, University of Genova, Genova, Italy; *Department of Gynecologic Oncology, IRRCS National Cancer Institute, Milan, Italy; *Istituto G. Gaslini, Genova, Italy.

OBJECTIVE: It is widely accepted that angiogenesis is pivotal to the establishment of endometriotic lesions and it is fundamental in the regulation of placental development starting from the early stages of pregnancy. Circulating vascular endothelial growth factor and placental growth factor (PLGF) levels have been reported to be increased in women with endometriosis when compared with controls, conversely decreased levels of PLFG have been reported in pregnant women developing preeclampsia. For this reason, the presence of endometriosis might be a protective factor for the development of early onset preeclampsia during pregnancy, since the increased level of PLGF in these patients might promote placental development. The objective of this study was to assess the first trimester serum concentrations of circulating PLGF in pregnant women with endometriosis compared to those without endometriosis.

DESIGN: Case-control study based on the retrospective analysis of a prospectively collected database.

**P-542 Wednesday, October 16, 2019 6:30 AM**

**PELVIC FLOOR MUSCLE SPASM, COMORBID PAIN AND MENTAL HEALTH CONDITIONS IN WOMEN WITH ENDOMETRIOSIS-ASSOCIATED CHRONIC PELVIC PAIN.** Pamela Stratton, MD, Hannah Tandon, BA, Vy Phan, BS, Ninet Sinai, PhD, MPH, Jay Shah, MD, Margaret Bevans, PhD, RN, Barbara I. Karp, MD, Office of the Clinical Director, Intramural Research Program, National Institute of Neurological Disorders and Stroke, NIH, Bethesda, MD; Rehabilitation Medicine Department, Intramural Research Program, Clinical Center, NIH, Bethesda, MD; Biostatistics & Clinical Epidemiology Service, Intramural Research Program, Clinical Center, NIH, Bethesda, MD; Office of Research in Women’s Health, NIH, Bethesda, MD.

OBJECTIVE: Describe pelvic pain pattern, and pain and mental health comorbidities in women with endometriosis-associated chronic pelvic pain (endo-CPP).

DESIGN: Baseline, cross-sectional data from a prospective, double-masked, placebo-controlled study of botulinum toxin injection for persistent endo-CPP despite optimal pain, surgical and hormonal treatment.

**MATERIALS AND METHODS.** Subjects described headache (including migraine) history and completed standardized questionnaires: Pelvic Pain Questionnaire; Patient-Reported Outcomes Measurement Information System (PROMIS) scales for anxiety, depression, fatigue, and sleep disturbances; Rotterdam Criteria for irritable bowel syndrome (IBS) bowel dysfunction (IBS-D) and IBS with sensitivity norm (IBS-C); Oswestry Disability Index. Patients underwent pelvic exam to confirm pelvic floor spasm and determine pelvic pain pattern. Allo-dynia and hyperalgesia were assessed paraspinally to determine the extent of pelvic (T9-S2) and widespread (C2-S2) spinal segmental sensitization. Ordinal data were analyzed for trends using the Jonckheere-Terpstra Test. Unordered dichotomous variables were compared using Fisher’s exact test.

RESULTS: Women (n=30, age 18-50yr) with endo-CPP (median duration 10.5yr; range 2-20) were evaluated, 22/23 women using hormonal methods (progestin IUD/combined hormonal contraception/depot medroxyprogesterone) had menses suppression; 7 others avoided hormones due to side effects. At pelvic exam, 30/30 had pelvic floor spasm that each identified as a primary focus of endo-CPP. Non-menstrual pelvic pain was reported by 29, dysmenorrhea at their last menses by 27, and dyspareunia by 14/15 who had sex in the last month; 7 others avoided sex because of pelvic pain. Women had widespread and 18 had pelvic spinal segmental sensitization. Most women reported anxiety (18), depression (14), fatigue (23) and sleep disturbances (18). 16 women met criteria for IBS, 22 for PBS, and 17 reported migraine. Moderate disability was reported by 14 women and severe disability by 3. Having either IBS or PBS was associated with depression (p=0.031), anxiety (p=0.003), and fatigue (p=0.029) but not sleep disturbances or disability. Difference was associated with pelvic and widespread sensitization (p=0.025 and p=0.009, respectively), but not PROMIS outcomes.

CONCLUSIONS: Not surprisingly, women with endometriosis-associated chronic pelvic pain persisting despite treatment report non-menstrual pain, dysmenorrhea and dyspareunia. Importantly, they experience significant

<table>
<thead>
<tr>
<th>Surgical Endometriosis (n = 350)</th>
<th>Male Factor Infertility (n = 2824)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>35.4</td>
<td>36.3</td>
</tr>
<tr>
<td>BMI (mean)</td>
<td>25.2</td>
<td>26.5</td>
</tr>
<tr>
<td>AMH (median)</td>
<td>1.58</td>
<td>1.40</td>
</tr>
<tr>
<td>Max FSH (median)</td>
<td>8.03</td>
<td>5.9</td>
</tr>
<tr>
<td>Max E2</td>
<td>1966</td>
<td>2076</td>
</tr>
<tr>
<td>Implantation rate 1 (GS/ET) &gt;= 50%</td>
<td>22.0%</td>
<td>26.9%</td>
</tr>
<tr>
<td>Implantation rate 2 (HB/ET) &gt;= 50%</td>
<td>21.4%</td>
<td>26.4%</td>
</tr>
<tr>
<td>Pregnancy rate</td>
<td>36.9%</td>
<td>41.9%</td>
</tr>
<tr>
<td>Live birth rate</td>
<td>22.3%</td>
<td>25.5%</td>
</tr>
</tbody>
</table>

**MATERIALS AND METHODS:** This study included 40 pregnant women who had histological diagnosis of endometriosis (E) and 40 pregnant women without endometriosis (C). Women included in the control group had no evidence of endometriosis at laparoscopy. Exclusion criteria were previous uterine surgery or uterine malformations, major fetal malformities, alcohol and/or drugs abuse, chronic hypertension disease, known autoimmune diseases, fetal aneuploidy or multiple gestations.

RESULTS: Compared to C women, those with E had no statistically significant difference regarding maternal demographic characteristics (age, BMI, parity, smoking, mode of conception). No statistically significant difference was observed in the first trimester PAPP-A levels, first trimester and mid-pregnancy mean UIA Doppler PI, neonatal birth weight (BW) centiles, SGA fetuses and early onset preeclampsia (<37 weeks of gestation) prevalence. However, women with E had statistically significant higher first trimester concentration of PLGF compared to those without endometriosis (C) (group E: PLGF MoM 1.40; group C: PLGF MoM 1.19; p<0.05).

CONCLUSIONS: First trimester serum concentrations of PLGF are significantly higher in pregnant women with endometriosis compared to those without the disease. The major limitations of this study were that it was retrospective and it had a relatively small sample size. The small number of pregnant women with endometriosis did not allow performing a further subanalysis according to the different forms of endometriosis (peritonal endometriosis, deep endometriosis, ovarian endometriosis).
comorbid pain and mental health conditions. Pelvic muscle spasm and associated sensitization may be a key manifestation of their endometriosis-associated chronic pelvic pain. Comorbid pain conditions and mental health may factor into endo-CPP. These women merit comprehensive assessment and management of their pain patterns.

Clinicaltrials.gov: NCT01553201

SUPPORT: Funded by Intramural Research Program of NINDS, NICHD and the Clinical Center, NIH.

P-543 Wednesday, October 16, 2019 6:30 AM

EFFECT OF ENDOMETRIOSIS ACTIVITY ON PREGNANCY OUTCOME IN PATIENTS WITH REPEATED IMPLANTATION FAILURE. Chenyi Zhong, Master, Liujie Gao, Master, Jingsjn Mao, Master, Yundong Mao, professor "First Affiliated Hospital of Nanjing Medical University, Nanjing, China; Affiliation not provided; OB/GYN, Nanjing, China.

OBJECTIVE: Patients face a problem in IVF/ICSI treatment, repeated implantation failure. In order to explore whether endometriosis affects the implantation of embryo when IVF/ICSI this study compared the pregnancy outcomes of patients with endometriosis who failed to implant repeatedly. So as to explore the appropriate treatment plan for such patients.

DESIGN: Endometriosis patients with repeated implantation failure were grouped according to treatment, and whether down-regulated or not.

MATERIALS AND METHODS: patients who asked for IVF/ICSI treatments in our Reproductive Center. A retrospective cohort study was performed. Endometriosis patients with repeated implantation failure. The differences in pregnancy outcomes were compared. The comparison between quantitative data was tested by analysis of variance. The differences between the classification data were analyzed by Chi-square test.

RESULTS: 1) According to treatment timings, the cumulative delivery rate(according to the numbers of people) was significantly lower than that of the early treatment group (28.17% vs 43.30%, P < 0.05) and the late treatment group (22.27% vs 47.06%, P < 0.01). The available embryo rate (93.56%) and high quality embryo rate (81.84%) in the early treatment group were significantly higher than those in the untreated group (85.20% and 62.93%) and the late treatment group (88.20% and 69.61%), P < 0.01. And the high quality embryo rate in the late treatment group (69.61%) was also significantly higher than that in the untreated group (62.93%), P < 0.05.

2) Kaplan-Meier curve analysis showed that the time required to get a pregnancy live birth for late treatment group was the shortest (12.21±1.05, 13.46±1.08), and the time in the untreated group was longest (21.54±0.49, 22.27±0.45), P < 0.001. 3) Down-regulation increased the clinical pregnancy rate of the untreated group and the late treatment group (41.18% vs 26.32% vs 50.00% vs 24.62%, P < 0.05), and the live birth rate of the treatment group (38.78% vs 17.97% and 41.67% vs 17.69%, P < 0.01). Down-regulation can increase the overall cumulative live birth rate (cycle) (27.78% vs 13.51%, P < 0.05). The available embryo rate (93.56%) and high quality embryo rate (81.84%) in the early treatment group were significantly higher than those in the untreated group (85.20% and 62.93%) and the late treatment group (88.20% and 69.61%), P < 0.01.

3) According to the EMs activity, the clinical pregnancy rate (38.84%) and live birth rate (29.75%) of the EMs-controlled patients were increased compared to the untreated group (26.25% and 18.13%, P < 0.05).

CONCLUSIONS: 1) The treatment of endometriosis will improve the cumulative pregnancy rate and live birth rate of repeated implantation failure; 2) The down-regulation cycle can also improve the pregnancy outcome of endometriosis patients with repeated implantation failure; 3) The control of endometriosis activity can lead to better clinical outcomes in patients with repeated implant failures; 4) It is necessary to control the activity of endometriosis in patients with repeated implantation failures in IVF/ICSI treatment.

P-544 Wednesday, October 16, 2019 6:30 AM

SYMPATHOMIMETIC AMINE THERAPY MAY IMPROVE LIVE DELIVERED PREGNANCY RATES (PR) FOLLOWING IN VITRO FERTILIZATION-EMBRYO TRANSFER (IVF-ET) IN WOMEN OF ADVANCED REPRODUCTIVE AGE – A PILOT STUDY. Jerome H. Check, M.D., Ph.D.1, Rachael Cohen, D.O.2, Diane L. Check, BS, MT3, Eric Chang, D.O.2, 4 Cooper Medical School of Rowan University, Camden, NJ; 5 Cooper Institute for Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ.

OBJECTIVE: A very effective medical therapies for various types of pelvic pain is the use of dextroamphetamine sulfate. The probable mechanism for pain relief seems to be by releasing more dopamine from sympathetic nerve fibers which diminishes cellular permeability. Increased cellular permeability may be the cause of pelvic pain related to increased absorption or irritant chemicals into pelvic tissues leading to excessive inflammation. Increased inflammatory cells, especially natural killer cells, could be a cause of infertility or miscarriage. There have been anecdotal reports of successful pregnancies in patients with repeated failures to successfully conceive despite multiple embryo transfers with this treatment. The objective of the present study was to perform a pilot study to determine if treatment with dextroamphetamine sulfate could improve the chance of a successful pregnancy following IVF-ET, in a poor prognosis group, i.e., women of advanced reproductive age.

DESIGN: Prospective patient option controlled study.

MATERIALS AND METHODS: Women age 40–42 with normal oocyte reserve as evidenced by a day 3 serum FSH ≤11 mIU/mL and a serum anti-mullerian hormone (AMH) level >1.06 ng/mL with a history of moderate to severe dysmenorrhea, dyspareunia, mittelschmerz, or chronic pelvic pain who requested or required IVF-ET were given the option of being treated with dextroamphetamine sulfate during the IVF cycle and the first trimester of pregnancy. They were advised of the theoretical benefit, but the lack of hard data, just anecdotal reports. The IVF would not be started until the dosage that best corrected the pain with acceptable side effects was achieved. The starting dosage was 9.4mg extended release capsules. The maximum dosage was 37.6 mg. All embryo transfers were performed on day 3.

RESULTS: There were 12 couples recruited (grp A) and 11 made it to ET. These results were compared to 77 historical controls (grp B). The historical control group did not have to have a history of pelvic pain. The average number of embryos transferred were 2 vs. 2.1 for grp A and B. The clinical PR per transfer was 27.3% (3/11) vs. 18.2 (17/77). The live delivered PR was 27.3% vs. 11.7% (9/77). The implantation rates were 18.2% and 11.8%. All 11 grp A women had marked improvement of their pelvic pain. The 3 babies born in grp A were full-term and healthy. The small pilot study group precluded meaningful statistical evaluation.

CONCLUSIONS: This pilot study showed sufficient benefit to improving fecundity in this poor prognosis group that we plan to submit a proposal to the IRB for a larger randomized control trial. Many of these grp A women may have had endometriosis. The advantage of dextroamphetamine sulfate over other medical therapies for pelvic pain is that it allows the patient to conceive while receiving pain relief.

ENDOMETRIOSIS - BASIC

P-545 Wednesday, October 16, 2019 6:30 AM

OVEREXPRESSION OF CD44v6 IS INVOLVED IN THE DEVELOPMENT OF THE EARLY ENDOMETRIOTIC LESION IN A XENOGRAFT MODEL. Jennifer Knudtson, MD,1 Jessica E. McLaughlin, MD,2 Marlen Tellez Santos, BS, MS,3 Robert Schenken, MD, # University of Texas Health Science Center San Antonio, San Antonio, TX; University of Incarnate Word, San Antonio, TX.

OBJECTIVE: We previously showed decreased development of endometriotic lesions in CD44 knockout mice compared to control.1 CD44 has 10 different variants and a standard form. Menstrual endometrial cells (MECs) from women with endometriosis have increased adhesion and also express higher levels of CD44 variant 6 (v6), but not v3, compared to MECs from women without endometriosis.2 Here, we assessed the effects of CD44 standard (CD44s), CD44v3 and CD44v6 overexpression (OE) on immortalized human endometrial epithelial (iEECs) and stroma cells (hESCs) in vivo attachment in a nude mouse xenograft model.

DESIGN: In vivo xenograft model.

MATERIALS AND METHODS: OE of CD44s, CD44v3 and CD44v6 was carried out using lipofectamine and their expression verified with qRT-PCR in iEEC and hESCs. Nude mice, 8–10 week old, were injected with estrogen 1 week prior to injection of iEECs and hESCs (n=7 per group). The cells were counted after transfection and plated at 300,000 iEECs and 100,000 hESCs were injected per mouse. Transfected cells were tagged with cell tracker red (iEECs) and green (hESCs). Mice were sacrificed 48 hours after injection into the xenograft. Cells were counted using fluorescent stereo microscopy (FSM). The number of cells visualized by FSM divided by the number of cells counted after transfection and at least 300,000 iEECs and 300,000 hESCs were visualized in each graft. The number of cells visualized by FSM divided by the number of cells counted after transfection and at least 300,000 iEECs and 300,000 hESCs was counted after transfection and at least 300,000 iEECs and 300,000 hESCs were visualized in each graft. The number of cells visualized by FSM divided by the number of cells counted after transfection and at least 300,000 iEECs and 300,000 hESCs was counted after transfection and at least 300,000 iEECs and 300,000 hESCs were visualized in each graft. The number of cells visualized by FSM divided by the number of cells counted after transfection and at least 300,000 iEECs and 300,000 hESCs was counted after transfection and at least 300,000 iEECs and 300,000 hESCs were visualized in each graft. The number of cells visualized by FSM divided by the number of cells counted after transfection and at least 300,000 iEECs and 300,000 hESCs was counted after transfection and at least 300,000 iEECs and 300,000 hESCs.
RESULTS: Expression of mRNA and protein confirmed appropriate OE of CD44s, CD44v3 and CD44v6 in the different cell types. CD44v6 OE did slightly induce CD44v6 expression. At necropsy, the majority of cells attached to the peritoneum. CD44v6 OE increased attachment of hESCs compared to control (p<0.03). CD44v6 OE did not change attachment of iEECs. There was no difference in attachment in iEECs or hESCs with OE of CD44s or CD44v3.

CONCLUSIONS: Overexpression of CD44v6 increases attachment of ESCs to PMCs in an in vitro xenograft model. Mesenchymal endometrial cell type and CD44 variants play a complex role in the development of the early endometriotic lesion.


SUPPORT: KL2 TR001118 (JK), American Society of Reproductive Medicine (JK).

P-546 Wednesday, October 16, 2019 6:30 AM

ABERRANT EXPRESSIONS OF CHLORIDE CO-TRANSPORTERS IN ENDOMETRIOSIS. Inha Lee, M.D.,* Young Bin Won, M.D.,* Heeyon Kim, M.D.,* Jae Hoon Lee, M.D.,* Bo Hyon Yun, M.D.,* Seok Kyo Seo, M.D.,* Young Sik Choi, M.D., Ph.D.,* Byung Seok Lee, M.D., Ph.D.,* SiHyun Cho, M.D., Ph.D.* Yonsei University College of Medicine, Seoul, Korea, Republic of (South); Yonsei University College of Medicine, Gangnam Severance Hospital, Seoul, Korea, Republic of (South).

OBJECTIVE: Recent studies have shown that cell membrane ion channels play an important role in cell migration, also shown in the context of cancer development and metastasis. Although endometriosis is a benign gynecological disease, endometriosis shows a behavior similar to cancer in terms of migration and invasion of nearby tissues and organs. However, there are only few studies on cell membrane ion channels and their association with endometriosis. The aim of this study was to investigate the effect of these ion channels on endometriosis.

DESIGN: Experimental study using human endometrial tissue and human endometrial stromal cell.

MATERIALS AND METHODS: In the endometriosis group (n=21), eutopic endometrial tissue and ectopic endometrial tissue were obtained from the patients who had undergone laparoscopic ovarian cyst enucleation for benign ovarian causes other than endometriosis. Quantitative real time PCR (qRT-PCR) and western blot were performed to quantify ion channel-related NKCC1, NKCC2 and CLC3 mRNA expressions and protein concentrations in endometrial tissue. Furthermore, to test the influence of ion channels on endometriosis, migration of endometrial stromal cells, siRNA transfection and migration assay of eutopic endometrial cell of endometriosis patients. RESULTS: mRNA expression of NKCC1, NKCC2 and CLC3 in ectopic endometrial tissue from endometriosis patients was significantly higher than in eutopic endometrium for both endometriosis and control group (p<0.05). The mRNA expression of eutopic endometrium from endometriosis patients was higher than the control group, but the difference was not statistically significant. Western blot showed an increased expression of NKCC1, NKCC2 and CLC3 in both the eutopic and ectopic endometrium of endometriosis group, compared to the expression in eutopic endometrium of control group (p<0.05). After siRNA transfection, qRT-PCR showed a decreased expression of MMP2 and MMP9. Migration assay further suggested a decreased migratory potential of the eutopic endometrial cells. Additional analysis showed that the magnitude of expression of NKCC1, CLC3 and the size of endometriotic ovarian cyst were positively correlated.

CONCLUSIONS: The expression of NKCC1, NKCC2 and CLC3 associated with plasma membrane ion channels is increased in endometriosis patients, which may be implicated in the increased cell migration potential in endometriosis.

P-548 Wednesday, October 16, 2019 6:30 AM

ENDOMETRIOSIS INCREASED ATHEROSCLEROSIS IN A MURINE MODEL. Ramanahia Mamillapalli, PhD,* Nikoletta Toffoloni, BA,* Joshua Huttler, BA,* Yan Zhang, MD, PhD,* Peng Chen, MD, PhD,* Nina Stachenfeld, PhD,* Hugh S. Taylor, M.D.* Yale University School of Medicine, New Haven, CT; *The John B. Pierce Laboratory.

OBJECTIVE: Epidemiologic studies have identified an association between endometriosis and subsequent development of cardiovascular disease. Here we used an animal model to determine if endometriosis caused atherosclerosis. Further, identifying the molecular mechanisms responsible for atherosclerosis in women with endometriosis is necessary to develop targeted treatment strategies to reduce cardiovascular risk in women with endometriosis. The primary aim to determine if endometriosis increases aortic plaque formation in a murine model and explores the conditions that are mechanistically responsible for the observed changes.

DESIGN: Experimental endometriosis was induced in mice to identify changes related to atherosclerosis and cardiovascular disease. Oil Red O (ORO) staining, biochemical assays and qRT-PCR were performed to measure the degree of atherosclerotic plaque development, lipid levels, and the differential gene expression of inflammation mediators.

P-547 Wednesday, October 16, 2019 6:30 AM

PROPRANOLOL INHIBITS CATECHOLESTROGEN-INDUCED HUMAN ENDOMETRIAL STROMAL CELL SURVIVAL MEDIATED BY p38 MAPK SIGNALING: POTENTIAL THERAPY FOR ENDOMETRIOSIS. Rachel Grimes Sprague, MD, Young Woul Kim, PhD, Asli Ozmen, PhD, Xiaofeng Guo, MD, Anthony N. Imudia, MD, Charles J. Lockwood, MD, MHCM, Ronald R. Magness, PhD, Umit A. Kayisli, PhD. Department of Obstetrics and Gynecology, Morsani College of Medicine, University of South Florida, Tampa, FL.

OBJECTIVE: Catecholestrogens (CCCs), 2-Hydroxyestradiol (OHE2) and 4-OHE2, are biologically active metabolites of 17β-estradiol (E2). Studies indicate that local increases in E2 production as well as aberrant expression of E2 metabolizing enzymes enhance local generation of CCCs in women with endometriosis. CCCs have low binding affinity to estrogen receptors whereas CCCs display high binding affinity to β-arrestin receptor (AR), which induce uterine endothelial cell proliferation during gestation. Our recent data demonstrated β2-AR expression in eutopic and ectopic endometrial tissue. In addition, binding of CCCs to β-AR enhances human endometrial stromal cell (HESC) viability, suggesting contribution of CCCs to the pathogenesis of endometriosis. Thus, we tested the hypothesis that the mechanism of CCE-enhanced HESC viability involves alterations in either proliferation or apoptosis mediated by β-AR-induced common intracellular signaling pathways, i.e. AKT, MAPK and/or NFκB.

DESIGN: BrdU, Apoptotic Cell Detection ELISA, q-PCR, Western blot and XTT analyses were performed on cultured HESCs derived from endometrial biopsies.

MATERIALS AND METHODS: Cultured HESCs treated with 10^(-8) M E2 or 2-OHE2 or 4-OHE2, were measured by BrdU for proliferation and ELISA for apoptosis (n=3 with quadruplicate). Total RNA from E2-treated HESCs was isolated and pro-apoptotic, anti-apoptotic, and proliferation markers were evaluated by q-PCR (n=5 with duplicate). Total and phosphorylated AKT, p38 and ERK1/2 MAPKs, and NFκB levels were detected in lysates of cultured HESCs (n=3 with triplicate) treated for 10 min with vehicle (control) or 10^(-8) M E2 or 2-OHE2; or 4-OHE2 ± 2x10^(-5) M non-specific β-antagonist (propranolol). Subsequently, XTT assays were conducted with p38 MAPK inhibitor to assess the role of p38 MAPK on CCE-induced HESC viability (n=4 with triplicate). Results were analyzed by One-way ANOVA and post hoc Tukey test.

RESULTS: An increased HESC proliferation index by E2 and 4-OHE2 (P<0.05 and P<0.05, respectively) and decreased apoptosis were detected in HESCs treated with 2-OHE2 and 4-OHE2 vs. control (P<0.01 and P<0.01, respectively). Analysis of apoptotic markers by q-PCR revealed a significant decrease in Bax mRNA expression in response to 2-OHE2 treatment vs. control (P<0.01). Among the several intracellular signaling cascades analyzed, only phosphorylation levels of p38 MAPK were increased by either treatment with 2-OHE2; or 4-OHE2 (P<0.05 and P<0.05 vs. control, respectively), but not with E2, β-AR antagonism with propranolol mitigated this increased phosphorylation in p38 MAPK levels (P<0.05 and P<0.01, respectively) and inhibition of p38 MAPK by SB203580 blocked CCC-induced HESC survival (P<0.05 and P<0.001, respectively).

CONCLUSIONS: These data indicate that induction of endometrial stromal cell viability by CCE-β-AR interactions results from an imbalance in both proliferation and anti-apoptotic mechanisms and is specifically mediated by the activation of p38 MAPK signaling. These data also suggest that inhibition of β-ARs with propranolol may be a novel treatment option in endometriosis.
MATERIALS AND METHODS: Endometriosis was induced in 9-week-old female ApoE<sup>−/−</sup> C57BL/6 mice by suturing donor uterine tissue to the walls of the peritoneal cavity. A sham control group was also created using no uterine tissue. After 23 weeks post-surgery, mice were euthanized and serum was collected from the blood. Biochemical assays were carried out for lipid profile at the Yale Core Center. Total RNA was extracted from the serum using Trizol reagent and used for qRT-PCR to analyze the gene expression of inflammatory mediators. Whole aortas were dissected and stored in DPBS at 4°C until being subjected to ORO staining. The degree of staining was quantified using Imaged software. The total area of each longitudinally-opened aorta was measured and the percent of red stain was then calculated using the same red threshold for all samples.

RESULTS: The mice in the endometriosis group showed noticeable bilateral arteriosclerotic lesions, while no lesions were found in the corresponding location in the control mice. ORO staining of the aorta indicated minimal plaque formation in the control mice and a significant increase in plaque development in the endometriosis group. The difference in average percent stain between the groups was 4.75% indicating that the endometriosis group showed significantly more staining than the control group: control, 3.13 ± 0.95, n=5; endometriosis, 7.89 ± 1.56, n=5, (mean ± SEM; P=0.03, unpaired t-test). Biochemical assays from serum showed no significant difference between the control and the endometriosis groups with respect to total cholesterol, HDL, LDL, TG, and glucose levels. However, serum inflammation markers associated with cardiovascular disease such as TNF-α, C-Reactive Protein, and CRP were altered by endometriosis in the mouse model.

OBJECTIVE: Catecholestrogens (CCCs), 2-Hydroxyestradiol (OHE<sub>2</sub>) and 4-OHE<sub>2</sub>, are biologically active metabolites of 17β-estradiol (E<sub>2</sub>). Local increases in E<sub>2</sub> production as well as aberrant expression of E<sub>2</sub> metabolizing enzymes enhance generation of CCCs in women with endometriosis. During gestation CCCs bind adrenergic receptors (ARs) to mediate uterine endothelial cell proliferation. Our recent data demonstrated that compared to the basilar layer of the endometrium, the functionalis layer displayed increased β2-AR expression in women with endometriosis. Moreover, binding of CCCs to β-ARs enhanced human endometrial stromal cell (HESC) viability in culture, suggesting a modulatory role for CCE-β-AR binding in retrograde menstruation that contributes to endometriosis development. It is unknown if, in addition to β-ARs, α-ARs also have a role in this process. We, therefore, tested the hypothesis that ectopic endometrial tissue expresses α1D-AR and that 2-OHE<sub>2</sub> and 4-OHE<sub>2</sub> will potentiate HESC viability via α-ARs.

RESULTS: Immunohistochemistry was performed on paired eutopic/eutopic endometrial tissue and XTT analysis was conducted on cultured CCE-treated HESCs derived from endometriotic biopsies.

MATERIALS AND METHODS: Paired eutopic/eutopic endometrial sections from women with endometriosis in the proliferative (n=5) or secretory (n=4) phases were immunostained using α1D-AR antibody and evaluated semi-quantitatively by HSCORE. Confluent HESCs derived from endometrial biopsies at time of surgery for benign reasons were cultured in 96-well plates (5x10<sup>3</sup> cells/well) and treated with vehicle (control) or 10<sup>−8</sup> M E<sub>2</sub> or 2-OHE<sub>2</sub> or 4-OHE<sub>2</sub> (nonspecific α-AR inhibitor (phentolamine) for 48h. XTT assays measured cell viability. Experiments (n=4) were performed in duplicate and statistical analysis were analyzed by One-way ANOVA and Dunnet's post hoc. T-test.

RESULTS: Immunohistochemistry analysis revealed overall weak to moderate α1D-AR staining in endometrial epithelial cells and weak staining in endometrial stromal cells with no significant difference between eutopic and ectopic endometrial tissues in either phase. Compared to the basalis layer, both stromal and epithelial cells in the functionalis layer of eutopic endometrium displayed stronger α1D-AR staining. In vitro XTT assays revealed that phentolamine partially inhibited (P<0.05 and P<0.001, respectively) 2-OHE<sub>2</sub> and 4-OHE<sub>2</sub>-enhanced HESC survival vs control (P<0.05 and P<0.05, respectively). This inhibitory effect of phentolamine was specific to CCEs since E<sub>2</sub>-enhanced HESC survival was not inhibited by phentolamine.

CONCLUSIONS: Immunostaining with α1D-AR showed similar expression patterns as β2-AR in that there was increased staining to the functionalis layer of the endometrium; albeit, α1D-AR staining was overall weaker in both eutopic and ectopic tissue. Our in vivo and in vitro results indicate that induction of HESC viability by CCE-α-AR binding may contribute to the propagation of endometriosis. Future studies into different α-AR isoform expressions in endometriotic lesions are warranted.

FERTILITY & STERILITY®
OBJECTIVE: Endometriosis is a debilitating gynecologic disease characterized by aberrant inflammation. We have previously demonstrated differential expression of several microRNAs (miRNAs) in endometriosis, and dysregulated expression of several inflammatory cytokines. Altered miRNA expression may modulate the inflammatory response, ultimately increasing severity of disease. Nuclear factor-kappaB (NFkB) is a transcription factor involved in the immune response. It is activated initially by inflammatory cytokines and chronically activated in endometriosis, thus capable of promoting a chronic inflammatory state and altered progesterone response. We hypothesize that miRNAs (Let-7b, 3613-5p, and 125b) alter expression of NFkB1, NFkB2, and progesterone receptor gene (Pgr) in women with endometriosis.

DESIGN: In vitro human primary cell culture.

MATERIALS AND METHODS: Primary eutopic endometrial cells from 6 subjects were cultured in six-well plates (1x10^5 cells). Once cells reached 70% confluence they were transfected with miRNA Let-7b, 3613-5p, or 125b miRNA mimic or each respective miRNA inhibitor. Each transfection was carried out with respective controls and in duplicate. Total RNA was extracted 48 hours post-transfection. Quantitative RT-PCR was performed for genes of interest (NFkB1, NFkB2 and Pgr). Relative expression was calculated using the \(2^{-\Delta \Delta C(T)}\) method. Student’s t-test was used for statistical analysis.

RESULTS: Cells transfected with miRNA Let-7b Mimic demonstrated a 2.25-fold decrease in NFkB2 expression (\(p = 0.04\); there was no significant change in NFkB2 expression in cells treated with Let-7b inhibitor. There was no difference in NFkB2 expression in cells transfected with miRNAs 3613-5p or 125-5p mimic or inhibitor. There was no significant effect on expression of NFkB1 or Pgr when cells were transfected with miRNAs Let-7b, 3613-5p, or 125-5p (mimic or inhibitor).

CONCLUSIONS: Endometriosis sequela are in large part due to the inflammatory nature of the disease. As NFkB2 is a key mediator in the inflammatory response, aberrant miRNA levels can mediate inflammation and aggressiveness of disease through regulation of NFkB2 expression. Here we demonstrate that low Let-7b levels that we have previously reported in endometriosis lead to increased NFkB2 expression and increased inflammation. Let-7b regulation in endometriosis is a key endogenous regulator of inflammation. miRNA Let-7b and NFkB2 represent novel, non-hormonal targets for treating endometriosis.

Support: NIH U54 HD052668.

P-553 Wednesday, October 16, 2019 6:30 AM

INCREASED EXPRESSION OF YAP (YES-ASSOCIATED PROTEIN) IS ASSOCIATED WITH THE DECREASED CELL AUTOPHAGY IN THE EUTOPIC ENDOMETRIAL STROMAL CELLS OF WOMEN WITH ENDOMETRIOSIS. Wei Huang, Ph.D., M.D., a Tianjiao Pei, M.D., a Xin Huang, M. M. Candidate, b Yujing Li, M.D., a West China Second University Hospital of Sichuan University, Chengdu, China; c Department of Obstetrics and Gynecology, West China Second University Hospital of Sichuan University, Chengdu, China; d Affiliation not provided.

OBJECTIVE: To explore the role of Yes-associated protein (YAP) in the regulation of cell autophagy in the eutopic endometrial stromal cells (ESCs) from a subset of women with endometriosis.

<table>
<thead>
<tr>
<th>miRNAs selected</th>
<th>Discovery Study</th>
<th>Hormone users (42 cases, 84 controls)</th>
<th>Not on Hormones (12 cases, 24 controls)</th>
<th>All (adjusted for hormone use) (54 cases, 108 controls)</th>
</tr>
</thead>
<tbody>
<tr>
<td>slnhsa_mir_376b_3p</td>
<td>Hormone Users</td>
<td>0.38 (0.18, 0.81) 0.01</td>
<td>0.41 (0.13, 1.25) 0.12</td>
<td></td>
</tr>
<tr>
<td>slnhsa_mir_1908_5p</td>
<td>Adult Literature</td>
<td>0.26 (0.08, 0.86) 0.03</td>
<td>0.20 (0.75, 0.86, 0.83)</td>
<td></td>
</tr>
<tr>
<td>slnhsa_mir_542_3p</td>
<td>Hormone Users</td>
<td>0.67 (0.37, 1.19) 0.17</td>
<td>1.72 (1.08, 2.75) 0.02</td>
<td></td>
</tr>
<tr>
<td>slnhsa_letra_7p_3p</td>
<td>Adult Literature</td>
<td>2.09 (1.01, 4.34) 0.05</td>
<td>1.55 (0.84, 2.83) 0.16</td>
<td></td>
</tr>
<tr>
<td>slnhsa_mir_296_3p</td>
<td>Not on Hormones</td>
<td>15.8 (1.10, 227.6) 0.04</td>
<td>0.61 (0.35, 1.07) 0.08</td>
<td></td>
</tr>
<tr>
<td>slnhsa_mir_154_5p</td>
<td>Hormone Users</td>
<td>2.65 (0.76, 9.20) 0.12</td>
<td>0.61 (0.35, 1.07) 0.08</td>
<td></td>
</tr>
<tr>
<td>slnhsa_mir_219a_5p</td>
<td>Both Horm Groups</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>slnhsa_mir_124_3p</td>
<td>Hormone Users</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>slnhsa_mir_23b_3p</td>
<td>Hormone Users</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
DESIGN: Experimental study using primary cell culture, quantitative real-time PCR (qRT-PCR), Western blotting, drug interference, and transfection in isolated ESCs.

MATERIALS AND METHODS: Endometrial samples were collected during hysterectomy, including eight patients diagnosed with endometriosis by laparoscopy and six women laparoscopically diagnosed endometriosis-free as controls. The expressions of YAP pathway and cell autophagy markers (mTOR, LC-3) in ESCs of women with or without endometriosis were validated by qRT-PCR and Western blotting. The protein levels of autophagy markers were detected in the eutopic ESCs after verteporfin and rapamycin treatments and the transfection with YAP-knockdown vector in ESCs, respectively. Student’s t test was used for comparisons between two groups after assessing the normality and homogeneity of variance.

RESULTS: The mRNA levels of YAP, TEAD, mTOR were all increased in the eutopic ECs of women with endometriosis compared with controls, but no statistically difference (P > 0.05). The protein levels of YAP (P < 0.05) and mTOR (P < 0.05) were significantly increased in the eutopic ECs of women with endometriosis compared with controls, whereas the ratio of the autophagy marker protein LC3-II/LC3-I (P < 0.05) was significantly decreased in the eutopic ECs of women with endometriosis compared with controls. Moreover, verteporfin treatment interfered the YAP function and led to an increase trend of cell autophagy level, but it had no effect on mTOR expression; rapamycin treatment and YAP knockdown in the eutopic ESCs both inhibited the expression of YAP and increased the level of cell autophagy significantly with an increased ratio of LC3-II/LC3-I (P < 0.05). Moreover, verteporfin treatment interfered the YAP function and led to an increase trend of cell autophagy level, but it had no effect on mTOR expression; rapamycin treatment and YAP knockdown in the eutopic ESCs both inhibited the expression of YAP and increased the level of cell autophagy significantly with an increased ratio of LC3-II/LC3-I (P < 0.05). Moreover, verteporfin and heparin treatments and the transfection with YAP-knockdown vector in ESCs, thereby increasing the degree of lesions in ectopic lesions.

CONCLUSIONS: Estrogen promoted the chemotactic migration of BMSC to a appropriate microenvironment and differentiation into endometrial cells forming endometriosis.

SUPPORT: This research was supported by the Grant from the Science and Technology Bureau of Sichuan (2018SZ0124) (to Wei Huang).

P-554 Wednesday, October 16, 2019 6:30 AM

CD4 AND CD8 BUT NOT DN MUCOSA-ASSOCIATED INVARIANT T CELLS FOSTER THE DEVELOPMENT OF ENDOMETRIOSIS: A PILOT STUDY

Huanhuan Jiang, Doctor, Kaihuan Bi, Bachelor’s, Zhimin Lu, Bachelor’s, Caihua Li, Doctor, Peipei Guo, Graduate, Yunxia Cao, Doctor, The First Affiliated Hospital of Anhui Medical University, Hefei, China.

OBJECTIVE: Our study aims to demonstrate the relationship between Mucosa-associated invariant T (MAIT) cells and endometriosis.

DESIGN: Case-control study.

MATERIALS AND METHODS: The study group comprised 32 patients with a diagnosis of endometriosis. 18 women with only ovarian benign cysts or uterine leiomyoma who underwent laparoscopy were recruited as control group. Peritoneal fluid (PF) was collected during laparoscopy. Peripheral blood (PB) was obtained shortly before the surgery. We investigated MAIT cells and their different subpopulations in PB and PF from endometriosis (EMS) and control group (CG). MAIT cells were characterized as CD3⁺CD161⁺Vα24-β7⁻ cells by flow cytometry. Next based on CD4 and CD8, the cells were divided into three subtypes: CD8 MAIT cells, CD4/CD8⁻ (double negative, DN) MAIT cells and CD4 MAIT cells. And IL-8, 12, 18, 17, MPP-9, INF-g from the peritoneal fluid and plasma were analyzed by ELISA kit.

RESULTS: Our results revealed that there were enrichments of MAIT cells, especially CD4 and CD8 MAIT subset. Moreover, CD8 MAIT cells had a greater activation in EMS group as compared to the results from CG patients. In line with the data, EMS patients produced higher level of IL-8/12/17 as compared to these from controls. On the contrary, control patients exhibited a dramatic upregulation of DN MAIT cells, however, these DN MAIT cells from controls showed a higher expression of PD-1. At the end we performed the relevance analysis, and we discovered that accumulation of PB MAIT cells correlated with elevated level of serum CA125 production.

CONCLUSIONS: Our study suggests functional diversities of MAIT cells subsets in the development of endometriosis. CD4 and CD8 MAIT cells could be a promotor in endometriosis, whereas DN MAIT cells might be a protector for the host.

P-555 Wednesday, October 16, 2019 6:30 AM

ESTROGEN PROMOTES THE CHEMOTACTIC MIGRATION AND DIFFERENTIATION OF BONE MARROW MESENCHYAL STEM CELLS IN ENDOMETRIOSIS.

Wenbi Zhang, doctor,a Lu Li, professorb, Xiaoxi Sun, professorb Obstetrics and Gynecology Hospital of Fudan University, Shanghai, China;bAffiliation not provided; bObs/Gyn hospita of fudan university, shanghai, China.

OBJECTIVE: To confirm the theory of endometriosis (EMT) stem cell origin and to investigate the role of estrogen on the process of bone marrow mesenchymal stem cell (BMSC) chemotactic migration and differentiation.

DESIGN: To illustrate this hypothesis, we employed 17β-estradiol for the co-culture of BMSC and endometrial stromal cells (ESC) in vitro and established BMSC in vitro model.

MATERIALS AND METHODS: Primary cultured BMSCs and ESCs were identified by flow cytometry and immunohistochemical analysis. BMSCs and ESCs were co-cultured and divided into four groups: BMSC group, BMSC + 17β estradiol treatment group, BMSC + ESC group, BMSC + ESC + 17β estradiol treatment group. After 5 days of culture, the chemotaxis of 17β-estradiol was observed through Transwell experiments, and the chip technique was used to analyze the expression of chemokines in the culture medium. Mouse EMT model was established and HE staining was performed. BMSCs were injected through the tail vein into the EMT mice. The mice were divided into two groups according to BMSC 17β-estradiol pretreated or not. The immunofluorescence was used to detect the expression of protein B-cell lymphoma-2 (BCL-2), proliferating Cell Nuclear Antigen (PCNA), Matrix metalloproteinase (MMP-1) in ESC after one month.

RESULTS: We showed that the migration of BMSC promoted by ESC, and the migration ability of BMSC was enhanced after the treatment of 17β-estradiol. Through gene chip detection, 17β-estradiol may accelerate the secretion of chemokines by ESC, which can promote the expression of 25 chemokines, especially for stromal cell derived factor-1a as the main target. Furthermore, the immunofluorescence results in animal experiments showed that the expression of BCL-2, PCNA, MMP-1 in 17β-estradiol pre-treated group was higher than control group. It confirmed that 17β-estradiol might promote the differentiation, proliferation and apoptosis of ESC in ectopic lesions through the migration, differentiation and proliferation of BMSCs, thereby increasing the degree of lesions in ectopic lesions.

CONCLUSIONS: Estrogen promoted the chemotactic migration of BMSC to a appropriate microenvironment and differentiation into endometrial cells forming endometriosis.

SUPPORT: The National Natural Science Foundation of China (Grant number: 81501234), National Natural Science Foundation of China.

P-556 Wednesday, October 16, 2019 6:30 AM

ENDOMETRIOSIS RISK ALLELE IN WNT4 MAY INTERACT WITH RARE MUTATIONS IN HDAC2 GENE

Kenneth Ward, MD, Rakesh Chettier, MS, Hans M. Albertsen, PhD. Juneau Biosciences, LLC, Salt Lake City, UT.

OBJECTIVE: To discover genes that may interact with the endometriosis risk allele in the WNT Family Member 4 (WNT4) gene.

DESIGN: Endometriosis is a common gynecological condition with complex etiology defined by the presence of endometrial glands and stroma in ectopic locations outside of the uterus. Twin and family studies have shown increased relative risk in families. Multiple genome-wide association studies (GWAS) show that several polymorphisms in the region harboring WNT4 and Cell Division Cycle 42 (CDC42) are associated with endometriosis across multiple ethnicities. In this study, we explored whole exome sequencing (WES) data in women carrying the risk allele T (rs2235529) in the WNT4 gene to see if the risk allele interacts with rare protein altering variants in other genes.

MATERIALS AND METHODS: WES was conducted on 1731 women with a confirmed diagnosis of endometriosis and 774 population controls of Northern European Ancestry. Whole exome sequencing (WES) was performed using Ion Proton Instrument with the AmpliSeq Exome Capture Kit. All nonsense and truncating mutations including stop gain, stop loss, splicing, and frameshifts were considered for downstream analysis. Population frequency of these variants are provided if present in the gnomAD database (n=5,000).

RESULTS: The risk allele T in WNT4 (rs2235529) is present in either homozygous or heterozygous form in 787 subjects (554 endometriosis cases and 233 controls). Eight endometriosis patients and none of the controls had histone deacetylase 2 (HDAC2) protein altering mutations identified. The T risk allele was associated with HDAC2 altering mutation burden [p=1.7E-03, OR=15.4 (95% confidence limits 1.9-125.5)].

CONCLUSIONS: In this study, we found that women with mutation in HDAC2 gene in the background of WNT4 risk allele T are more likely to
be susceptible to endometriosis. It has been reported that the levels of HDAC1 and HDAC2 are deregulated in endometriotic stromal cells. HDAC1 and HDAC2 are key regulators of WNT and β3 pathways. During necrolysis remodeling, the deacetylase complex physically interacts with the WNT4 choratin in an HDAC-dependent manner, leading to suppression of the WNT4 gene and WNT4 dependent morphogenesis. Analyses of the ten other human HDAC genes are underway.

**Support:** Juneau Biosciences, LLC.

**P-557**

**WITHDRAWN**

**ENDOMETRIUM**

**P-558 Wednesday, October 16, 2019 6:30 AM**

**CELL-SPECIFIC EFFECTS OF CLOMID AND E2 ON ENDOMETRIUM: INSIGHTS INTO WNT SIGNALING AND STROMAL-EPITHELIAL INTERACTIONS.** Melanie Evans, MS, MD, a,b Lucy Xi Chen, MD, a,b Ann Word, MD, a,b John Wu, MD, a,b Patrick Keller, BS, a Bruce Carr, MD, a,b Orhan Bukulmez, MD, a,b Parkland/UTSW Resident, Dallas, TX; a bUTSW, Dallas, TX; UT Southwestern Medical Center, Dallas, TX.

**Objective:** Hormonal effects on epithelial cells of endometrium are often mediated through stromal cell receptors. Endometrium from women undergoing IVF using minimal stimulation (MS-IVF) with clomiphene citrate (CC) is characterized by marked atrophy of endometrial glands accompanied by relative increases in stromal cells, despite supraphysiologic levels of E2. Previously, we discovered dramatic stromal cell-specific upregulation of Wnt antagonists (secreted frizzled related proteins 1, 4, SFRP1) in endometrium from MS-IVF. Although SFRPs inhibit Wnta signaling during endometrial decidualization and gland formation in endometrial cancer, physiologic regulation of Wnt signaling in endometrium is not well understood. Our objective was to test the hypothesis that SFRPs are secreted constitutively by stromal cells but regulated in vivo by secretions from endometrial epithelial cells.

**Design:** Epithelial cells (Epi, Ishikawa) and primary human endometrial stromal cells were used alone or in co-culture with transwell cell culture inserts. Stromal cells were pretreated for 48 h in serum free media prior to treatment with vehicle or estradiol (E2, 3.6 nM) ± CC (20nM).

**Results:** E2 treatment of stromal cells increased PR (from 1 ± 0.1 to 6.7 ± 0.4 RU, p < 0.01) and total PR (from 1.0 ± 0.11 to 5.4 ± 0.23 RU, p < 0.01). CC was not an ER antagonist in stromal cells also increasing PR gene expression. In contrast to in vivo results, CC did not alter expression of sFRA1 or sFRA2 in stromal cell cultures. In co-culture, Epi did not alter E2-induced upregulation of PRs in stroma. However, co-culture with Epi downregulated stromal cell SFRP4 (83 ± 3%). The magnitude of sFRA4 suppression was dose-dependent with increasing number of Epi cells (from 10²- 10⁷/cm²). Epi co-culture also decreased stromal sFRA1 to 34 ± 11% and expression of stromal growth factors (FGF-9 and TGF-α) significantly. To investigate physiologic relevance, treatment of tissue explants from ovulatory women with E2 for 72 h (to induce epi growth) resulted in suppression of sFRA4 from (1.44 ± 0.3 to 0.55 ± 0.08 mRNA, p < 0.02).

**Conclusions:** Although CC did not have direct effects on sFRA in stroma, secretions from glandular epithelial cells suppressed Wnt antagonists SFRP1, 2, 4 and 7 in stroma. These results support the hypothesis that CC-induced inhibition of epithelial cell growth results in immature, atrophic glands that are insufficient to suppress Wnt inhibitors in stroma thereby accentuating loss of epithelial differentiation and growth. In the absence of CC, E2 induces epithelial cell growth and suppression of stromal SFRPs culminating in full maturation of the endometrium. Although it is believed that CC exhibits its effects simply as an ER antagonist, these studies indicate that the effects of CC are more complex and involve inhibition of Wnt signaling in cell-specific compartments.


**Support:** This work was supported by the tissue core laboratory of NIH HD087150.

**P-559 Wednesday, October 16, 2019 6:30 AM**

**DOES UNIVERSAL SCREENING FOR CHRONIC ENDOMETRITIS IMPROVE PREGNANCY RATES?** Holly Mehr, MD MSEd, a Mousa Shamokni, MD, a Chunnin Wang, PhD, a Richard Bulyagos, MD, a Gary Hubert, MD, a Molly M. Quinn, MD, a University of California, Los Angeles, Los Angeles, CA; a Fertility and Surgical Associates of California, Thousand Oaks, CA.

**Objective:** A growing body of evidence suggests a link between chronic endometritis (CE) and infertility. We investigated whether the implementation of universal screening for CE at the time of oocyte retrieval was correlated with a change in pregnancy rates after initial single thawed euploid embryo transfer (STEET).

**Design:** Retrospective cohort analysis at a high volume private fertility center.

**Materials and Methods:** The analysis included the initial STEET of all patients undergoing autologous IVF/PGT-A with endometrial biopsy screening (EMB) on day of oocyte retrieval from January 2017 to December 2018 and historic controls without universal EMB from September 2015 to August 2016. Cycles performed in the six-month window surrounding the policy onboarding were excluded. The pathologic diagnosis of CE was established via CD 138 staining of endometrial specimens. Patients found to have CE after biopsy were treated with doxycycline and metronidazole and re-biopsied. If persistent CE was demonstrated, a protocol designated second and third-line treatment algorithms prior to embryo transfer. Patients using a gestational carrier, oocyte or embryo donation, and those who had previous embryo transfer were excluded from the analysis. The CE rate, implantation rates (IR) and ongoing pregnancy rates (OPR) were calculated. Statistical analysis was done with T test, Mann Whitney U, Chi squared tests, and logistic regression where appropriate.

**Results:** A total of 375 initial STEETs were analyzed. The average age of the EMB screened and non-screened population differed (35.7 ± 3.9 vs 36.7 ± 4.1, p = 0.0157). In analyses controlled for age, there was no difference in IR (AOR 1.12, 95% CI 0.77-1.80) or OPR (AOR 1.06, 95% CI 0.69-1.63) between screened and non-screened cohorts. The rate of CE found on day of oocyte retrieval was 14.0% (n = 31). The median number of CD138 cells per 10 high power fields was 11 (IQR 8-15) in the CE positive group and 0 (IQR 0-1) in the CE negative group (p < 0.0001). No difference was seen in the IP (76.3% vs 67.7%, p = 0.31) or OPR (65.5% vs 58.5%, p = 0.80) between the treated, CE positive and CE negative groups in their first embryo transfer. CE cure rate was 81% (n=21). Nineteen percent of CE positive patients (n=6) were not cured after 3 cycles of antibiotics. The non-cured group had an 83% OPR.

**Conclusions:** A universal screening strategy detected a lower baseline CE rate than has been previously reported. No association was demonstrated between universal CE screening and IR or OPR. A larger sample size is needed to confirm these findings.

**P-560 Wednesday, October 16, 2019 6:30 AM**

**GATA BINDING PROTEIN 2 EXPRESSION AT IMPLANTATION WINDOW DIMINISHES IN WOMEN WITH ADENOMYOSIS: IMPLICATIONS FOR IMPAIRED ENDOMETRIAL RECEP TIVITY.** Joung Woul Kim, PhD, a Chih-Feng Yen, MD, PhD, b Rachel Grimes Sprague, MD, a Asli Ozmen, PhD, a Nihan Semerci, MSc, a Charles J. Lockwood, MD, MHCM, a Anthony N. Imudia, MD, a Umit A. Kayisli, PhD, a Department of Obstetrics and Gynecology, Morsani College of Medicine, University of South Florida, Tampa, FL; a Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital at Linkou, Chang Gung University College of Medicine, Kwei-Shan, Taoyuan, Taiwan.

**Objective:** Adenomyosis in reproductive age women has negative impacts on embryo implantation. Impaired progesterone (P4) responsiveness causes female infertility associated with endometrial receptivity. Mice deficient in the transcription factor, GATA binding protein 2 (GATA2), are infertile due to embryo implantation failures associated with defective decidualization and endometrial receptivity. Uterine tissues of GATA2 deficient mice display decreased progesterone receptor (PR) levels and diminished P4 responsiveness. We hypothesize that reduced endometrial GATA2 expression during the window of implantation may contribute to implantation failure seen in women with adenomyosis.

**Design:** This, we evaluated the endometrial expression of GATA2 in patients with adenomyosis.
MATERIALS AND METHODS: Uterine specimens were obtained during the window of implantation (cycle days 18-23) from patients with adenomyosis (n=5, age <45 years) who underwent hysterectomy and from age-matched controls who had no endometriosis or adenomyosis (n=5). The GATA2 expression was detected by immunohistochemistry, quantified by a histologic scoring system (HSCORE) and statistically compared using a t-test.

RESULTS: During the window of implantation, both endometrial and myometrial cells displayed predominantly nuclear immunoreactivity for GATA2 expression. Compared to those in the control group, patients with adenomyosis showed significantly reduced GATA2 expression in endometrial luminal epithelium (Mean ± SEM 103.9 ± 15.5 vs. 55.4 ± 14.1, p = 0.049), stromal cells (128.6 ± 20.7 vs. 53.3 ± 10.6, p = 0.012) and myometrial cells (133.7 ± 12.3 vs. 72.6 ± 15.9, p = 0.016). On the other hand, glandular epithelial cells were weakly GATA2 immunoreactive with no difference between women with or without adenomyosis (85.0 ± 9.9 vs. 55.6 ± 26.3, p = 0.325).

CONCLUSIONS: The significant reduction in human uterine GATA2 expression may impair endometrial receptivity by diminishing P4 responsiveness in patients with adenomyosis and, thereby, contributing to possible mechanism(s) behind the reduced embryo implantation reported in women with adenomyosis.

P-561 Wednesday, October 16, 2019 6:30 AM

DEFINING CHRONIC ENDOMETRITIS: ARE PLASMA CELLS SUFFICIENT? Dana B. McQueen, M.D., M.A.S., Kruti P. Maniar, M.D., Anne Hutchinson, M.D., Rafael Confino, BS, Jared C. Robins, MD, Lia A. Bernardi, MD, Mary Ellen Pavone, MD, MSCI, Northwestern University, Chicago, IL.

OBJECTIVE: There is considerable variability in the diagnostic criteria used for chronic endometritis: including number of plasma cells, immunohistochemistry and inclusion of stromal changes. The objective of this study was to compare the prevalence of chronic endometritis in women with unexplained recurrent pregnancy loss (RPL) using different diagnostic criteria.

DESIGN: Cohort Study.

MATERIALS AND METHODS: IRB approval was obtained. The cohort included women with two or more pregnancy losses, endometrial biopsy (EMB) between 1/2016 and 12/2018. TSH values < 4 mU/L, negative antiphospholipid antibodies and normal uterine anatomy. H&E and CD138 immunohistochemical staining were performed. A single pathologist blinded to patient history recorded the number of plasma cells per 10 HPF and the presence or absence of endometrial stromal changes (spindling, edema, foci of breakdown, inflammatory cells, and pigment deposition).

RESULTS: 50 women were included, with a mean age of 35.2 (SD 4.1) years, BMI of 27.1 (SD 6.3) kg/m² and 3.1 (SD 0.9) prior pregnancy losses. The preceding pregnancy was a mean of 117 (SD 146) days prior to EMB and had a gestational age of 6 weeks (SD 3.2). When chronic endometritis was defined by the presence of plasma cells on H&E alone, 24% (12/50) of the cohort met criteria if ≥ 1 plasma cell was used, 16% (8/50) with ≥ 2 plasma cells and 4% (2/50) with ≥ 5 plasma cells. When stromal changes and plasma cells by CD138 were required, the prevalence was 30% (15/50) with ≥ 1 plasma cells, 28% (14/50) with ≥ 2 plasma cells and 16% (8/50) with ≥ 5 plasma cells.

CONCLUSIONS: Establishing specific diagnostic criteria for chronic endometritis is necessary for both research and evidence based treatment guidelines. The definition of chronic endometritis significantly alters its prevalence. Recruitment of a control cohort is currently ongoing to establish the most appropriate diagnostic criteria for chronic endometritis.

SUPPORT: Prentice Grant.

P-562 Wednesday, October 16, 2019 6:30 AM

IMPROVEMENT OF ENDOMETRIAL RECEPTIVITY THROUGH THE USE OF AUTOLOGOUS PLATELET-DERIVED MICROPARTICLES. Enriqueta Garjio Lopez, OBGYN,; Laura Garcia Bernardo, OBGYN; Federico Galera Fernandez, OBGYN Instituto Madrileño de Fertilidad, Madrid, Spain; Instituto Madrileño de Fertilidad, Madrid, Spain.

OBJECTIVE: The goal of the present trial is to evaluate the effectiveness of the application of platelet-rich plasma (PRP) derived from the patient’s autologous plasma in the basal layer of the endometrium for the treatment of patients with suboptimal endometrium.

DESIGN: This is a single arm trial carried out at the Fertility Institute of Madrid. The trial included eighteen patients which presented a suboptimal endometrium, refractory to estrogen therapy between June 2014 and November 2017.

MATERIALS AND METHODS: The trial included thirteen patients that presented a suboptimal endometrium (<7 mm) and five presented implantation failures (in more than three embryo transfers with high quality embryos). Blood was extracted the same day of the application. The blood was centrifuged at 600G for ten minutes to separate red blood cells from plasma. The PRP was harvested and washed with PBS. The microparticles (60 μm) were isolated from the washed material through a 30 μm filter. The centrally suspended microparticles were used and stored at −80°C until the day of the application.

RESULTS: 21 cycle days were included from November 2017. Patient age is included in the table.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>IVF/OVO</th>
<th>Endometrium before/after</th>
<th>Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>41</td>
<td>OVO</td>
<td>7/8,3mm</td>
<td>yes</td>
</tr>
<tr>
<td>2</td>
<td>36</td>
<td>OVO</td>
<td>6/7,5mm</td>
<td>yes</td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>OVO</td>
<td>7,8,1mm</td>
<td>yes</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
<td>OVO</td>
<td>8/10,6mm</td>
<td>yes</td>
</tr>
<tr>
<td>5</td>
<td>35</td>
<td>FIV</td>
<td>6,2/8mm</td>
<td>yes (miscarriage)</td>
</tr>
<tr>
<td>6</td>
<td>48</td>
<td>OVO</td>
<td>5/6mm</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>42</td>
<td>FIV</td>
<td>5/7,2mm</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>43</td>
<td>OVO</td>
<td>7/8,5mm</td>
<td>yes</td>
</tr>
<tr>
<td>9</td>
<td>39</td>
<td>OVO</td>
<td>6/7,6mm</td>
<td>yes (biochemical pregnancy)</td>
</tr>
<tr>
<td>10</td>
<td>41</td>
<td>OVO</td>
<td>6,7,1mm</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>41</td>
<td>OVO</td>
<td>7/2,8mm</td>
<td>No</td>
</tr>
<tr>
<td>12</td>
<td>46</td>
<td>OVO</td>
<td>8/10mm</td>
<td>yes</td>
</tr>
<tr>
<td>13</td>
<td>46</td>
<td>FIV</td>
<td>6,8/8,2mm</td>
<td>No</td>
</tr>
<tr>
<td>14</td>
<td>48</td>
<td>OVO</td>
<td>6,6,7mm</td>
<td>No</td>
</tr>
<tr>
<td>15</td>
<td>48</td>
<td>OVO</td>
<td>10/12mm</td>
<td>Yes</td>
</tr>
<tr>
<td>16</td>
<td>38</td>
<td>FIV</td>
<td>10/14mm</td>
<td>No</td>
</tr>
<tr>
<td>17</td>
<td>38</td>
<td>OVO</td>
<td>6/4,7,6mm</td>
<td>No</td>
</tr>
<tr>
<td>18</td>
<td>40</td>
<td>OVO</td>
<td>6,6,7,2mm</td>
<td>Yes</td>
</tr>
</tbody>
</table>

FERTILITY & STERILITY® e331
supermatant was separated into three fractions, from low to rich factor concentration. Calcium Chloride were added in order to activate the platelets. A hysterectomy was carried out using saline solution as a distension medium and a puncture needle of 17G and 300mm was introduced through the hysteroscope to guide during menstrual period. Several subendometrial injections were administered using the needle, in the uterine lining, until the entire plasma (15 mL) was injected. After the hysteroscopy, the patients started the replacement treatment with oestradiol valerate with a dosage of 6mg per day. Once the endometrium had a thickness of more than 7mm, 200 mg of progesterone was applied 3 times a day, and the embryo transfer was scheduled.

RESULTS: The thickness of the endometrium increased in all 18 patients. All except for one achieved the minimum 7mm required for the transfer. On average, the endometrium thickness increased by 1.52mm. Ten patients showed positive BHCg thirteen days after the transfer (55%). Two of these ten patients miscarried on the first trimester (20%). The rest of the pregnancies concluded with the birth of a healthy child. No adverse effects have been reported.

CONCLUSIONS: PRP can stimulate the proliferation and regeneration of tissues with a great amount of growth factors and cytokines. This is the first study where PRP are applied via a hysteroscopy and subendometrial injections instead of through intrauterine perfusions with a canula. It is suggested that PRP increase the chances of pregnancy in patients with suboptimal endometrium and recurrent implantation failures. It is necessary to carry out randomised and controlled clinical trials to confirm these results.

P-563 Wednesday, October 16, 2019 6:30 AM

REDUNDANT ENDOMETRIUM AND ENDOMETRIAL POLYPS: IS THERE A LINK? Irene Peregrin Alvarez, MD, Robert Roman, MD, Mary Emily Christiansen, MD, Ghassan Saed, MD, Laura Detti, MD. University of Tennessee Health Science Center, Memphis, TN; Wayne State University School of Medicine, Detroit, MI.

OBJECTIVE: Endometrial polyps (EP) and redundant endometrium (RE) are often detected incidentally during routine transvaginal ultrasonography. Several studies on the expression of hormone receptors, oncoproteins and anti-mitotic proteins have been conducted to elucidate the molecular mechanisms underlying EP, however, no studies have been reported on the biology of RE. We explored whether the expression of different endometrial markers could vary in patients with EP and RE and what is their role the etiology and pathogenesis of endometrial pathology.

DESIGN: Pilot experimental study.

MATERIALS AND METHODS: We examined the expression of estrogen receptor (ER), progesterone receptor (PR), androgen receptor (AR), insulin-like growth factor receptor 1 (IGF-1R), B-cell lymphoma 2 (bcl-2), Ki67, HOXA10 and thyroid receptor beta 1 (TR beta 1) in EP and RE. We obtained endometrial specimens from 16 patients aged 20-45 years, that presented to our center between September 2017 and May 2018 who were undergoing hysteroscopy for benign gynecologic pathology (EP, RE or submucosal fibroids). Fragments of the endometrial samples were processed for real-time RT-PCR analysis and used for the expression of the above-mentioned markers. The main outcome measure was tissue expression of these markers and comparison between EP and RE. We performed ANOVA for analysis among the 3 groups. Our results were summarized as median and quartiles (Q1, Q3) and we used SPSS v25 for Windows (SPSS, Chicago, IL); p<0.05 defined significance.

RESULTS: 8 patients had RE, 5 had EP, 1 RE plus EP 2 had normal endometrium. Compared to EP, RE showed increased bcl2 and Insulin-R but similar Ki67,IGF-R1 and HOXA10 expression. Compared to normal endometrium, RE showed increased bcl2, IGF-R1 and Insulin-R expression, while Ki67 was decreased and HOXA10 unchanged.

CONCLUSIONS: RE showed biochemical characteristics similar to endometrial polyps, both stemming from environmental factors. Cell differentiation seemed more enhanced than replication. Similarly to EP, RE could be detrimental for embryo implantation, especially when extensive. This should be of consideration in women undergoing fertility treatments.

References: (1) Peregrin-Alvarez I, Roman RA, Christiansen ME, Detti A L. Endometrial abnormalities: Correlation between different diagnostic modalities. Presented at the American Institute of Ultrasound in Medicine (AIUM) Annual Convention, April 6-9, 2019, Orlando, FL.


P-564 Wednesday, October 16, 2019 6:30 AM

PREVALENCE OF CHRONIC ENDOMETRITIS IN PATIENTS WITH ENDOMETRIAL POLYPS AND UNEXPLAINED INFERTILITY. Alexander Volodarsky-Perel, M.D., Ahmad Badeghi, M.D., MPH, Guy Shrem, M.D., NaaMa Steiner, M.D., Togas Tulandi, M.D. McGill University Health Centre, Montreal, QC, Canada.

OBJECTIVE: To assess the prevalence of chronic endometritis (CE) in patients with endometrial polyps and unexplained infertility compared to patients without history of infertility.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We evaluated patients underwent hysteroscopic polypectomy in the period of 2015 to 2018. The inclusion criteria were age 25-42 and histologically confirmed endometrial polyps. Patients with cycle day 3-5 FSH > 10 mIU/mL, with intrauterine devices, history of repeated implantation failure and recurrent pregnancy loss, autoimmune diseases, suspected placental residua, endometrial cancer, atypical hyperplasia, previous diagnosis of CE, and received any antibiotic treatment in the period of 3 months before hysteroscopy were excluded. Study group included patients with unexplained infertility. The control group included those with no previous history of infertility, not taking hormone treatment in the past 3 months before hysteroscopy or having spontaneous pregnancy in the previous 3 years before the procedure. The diagnosis of CE was established after hematoxylin and eosin and CD 138 staining and was based on the presence of one or more plasma cells per 10 high-power fields. The primary outcome was the prevalence of CE compared between fertile and fertile patients. The secondary outcomes included clinical pregnancy rate (CPR), live birth rate (LBR) and miscarriage rate (MR) of infertile patients after CE treatment (Doxycline 100 mg twice daily for 14 days) compared to infertile patients without CE. To determine factors significantly associated with CE we used multivariate logistical regression. A sample size of 100 in each group has 80% power of showing a 15% difference in primary outcome with an alpha of 0.05.

RESULTS: A total of 237 patients were included in the analysis. Demography, hysteroscopy cycle day, polyp location and diameter were similar between the groups. The prevalence of CE in group of patients with unexplained infertility (n=137) was significantly higher compared to the control group (n=100) [22.6% vs. 8.6%; P = 0.001]. Cumulative CPR, LBR and MR were similar between women with treated CE (n=31) and patients without CE (n=106). Multivariate logistical model showed that infertility diagnosis was significantly associated with the diagnosis of CE (OR 3.16, 95% CI 1.53 – 6.49).

CONCLUSIONS: In women with endometrial polyps the prevalence of CE is higher in patients with unexplained infertility compared to patients without infertility history. The pregnancy outcome of infertile patients with CE treated with one course of Doxycycline was similar to those without CE.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Redundant Endometrium Median (Q1, Q3)</th>
<th>Polyp Median (Q1, Q3)</th>
<th>Normal Median (Q1, Q3)</th>
<th>p-value RE vs Polyp</th>
<th>p-value RE vs normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCL2 (fg/ug RNA)</td>
<td>0.263 (0.16, 0.32)</td>
<td>0.082 (0.07, 0.09)</td>
<td>0.068 (0.06, 0.07)</td>
<td>0.0271</td>
<td>0.0018</td>
</tr>
<tr>
<td>HOXA-10 (fg/ug RNA)</td>
<td>35.05 (28.8, 43.7)</td>
<td>35.33 (29.2, 48.9)</td>
<td>40.56 (40.4, 41.7)</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Ki67 (fg/ug RNA)</td>
<td>1.45 (1.1, 2.5)</td>
<td>2.51 (2.5, 7.3)</td>
<td>5.72 (4.5, 5.9)</td>
<td>ns</td>
<td>0.0009</td>
</tr>
<tr>
<td>IGF1-R (fg/ug RNA)</td>
<td>6.25 (4.5, 7.0)</td>
<td>4.42 (3.9, 5.8)</td>
<td>2.61 (2.6, 2.8)</td>
<td>ns</td>
<td>0.0184</td>
</tr>
<tr>
<td>Insulin-R (fg/ug RNA)</td>
<td>53.33 (47.6, 58.6)</td>
<td>39.69 (26.8, 44.4)</td>
<td>15.6 (15.4, 16.0)</td>
<td>0.0318</td>
<td>0.0002</td>
</tr>
</tbody>
</table>
WHAT IS THE MOST EFFECTIVE TREATMENT FOR ENDOMETRITIS IN WOMENS UNDERGOING ASSISTED REPRODUCTIVE TECHNOLOGY?

OBJECTIVE: Treatment of chronic endometritis (CE) improves implantation rates in patients undergoing assisted reproductive technology (ART), but causative organisms are difficult to identify and the most effective treatment regimen remains undefined. Our objective was to identify the optimal duration and choice of antimicrobial agent(s) on clearance of CE.

DESIGN: Retrospective cohort study of patients between 1/2017 and 12/2018 at a single academic center with an endometrial biopsy (EBM) showing CE.

MATERIALS AND METHODS: All patients diagnosed with CE (defined as >1 plasma cell/HPF; stained for CD138) on EBM followed by test of cure biopsy (TOC) were included. Antimicrobial agents prescribed and length of course were recorded. Regimens were classified as 14 days or less versus 15 days or more (up to 21 days), and by spectra of coverage: Gram positive, Gram negative, Anaerobe, Atypical and Anti-fungal. Primary outcome was presence or absence of CE on TOC. If a patient remained positive on TOC, subsequent treatment(s) were included as separate course(s) for analysis.

RESULTS: 144 women with an initial EMB positive for CE received a total of 225 treatment courses. 11 TOC results were unavailable, leaving 214 courses of treatment with known TOC outcomes. The most common indication for EMB was failed frozen embryo transfer(s) (FET) (mean 0.98±1.00, range 0-7), euploid pregnancy loss or recurrent pregnancy loss. The mean age of women in the cohort was 36.90±3.93 years (range 27-47). Mean number of courses required for clearance was 1.55±0.88 (range 0-6). All courses included antimicrobials providing gram positive and negative coverage. 62.6% (134/214) of women achieved cure with the first 2 courses included anti-fungals. Including anaerobic coverage did not affect cure rates in patients undergoing a longer course of treatment with known TOC outcomes. The most common indication for EMB was failed FET (mean 0.98±1.00, range 0-7), euploid pregnancy loss or recurrent pregnancy loss. The mean age of women in the cohort was 36.90±3.93 years (range 27-47). Mean number of courses required for clearance was 1.55±0.88 (range 0-6). All courses included antimicrobials providing gram positive and negative coverage. 62.6% (134/214) included anaerobic coverage and 66.3% (142/214) included atypical agent(s).


SUPPORT: None.
COMPARISON OF THE ENDOMETRIAL RECEPTIVITY ARRAY TO ENDOMETRIAL THICKNESS, ESTRADIOL AND PROGESTERONE LEVELS AS A MARKER FOR ENDOMETRIAL RECEPTIVITY PRIOR TO FROZEN EMBRYO TRANSFER. Shannon T. Alexa, DO, Inspira Health Network, Vineland, NJ.

OBJECTIVE: Endometrial thickness (ET), estradiol (E2) and progesterone (P4) levels have been traditionally used as a marker for endometrial receptivity when preparing for frozen embryo transfer (FET) with patients undergoing in vitro fertilization (IVF). We propose that using these known receptivity markers in conjunction with Endometrial Receptivity Array (ERA) results will increase the sensitivity of detecting optimal endometrial receptivity for embryo transfer and implantation.

METHODS: Retrospective Chart Review. MATERIALS AND METHODS: A retrospective chart review of 143 patients who had undergone testing for the ERA at the Reproductive Science Center of New Jersey, Eatontown NJ, between 2016-2019 was done. All of the 143 patients underwent a mock cycle with endometrial biopsy and a subsequent ERA modified cycle with FET. These patients then underwent medical management and evaluation with laboratory testing of their E2 and P4 levels and ultrasounds to evaluate ET and uterine artery blood flow. Data on the patient’s age, body mass index (BMI), ERA Results, ET, E2 levels, P4 levels, Pulsatility Index (PI), Resistance index (RI) and modified cycle pregnancy outcome were collected. Exclusion criteria included chronic endometriosis, congenital uterine abnormalities, endometriosis, and patients who underwent biopsy but whose cycle was not managed by the primary site leaving 91 total patients.

RESULTS: Utilizing SAS pairwise comparisons were made for the 4 ERA results and a T-test was done using a pooled standard error. The 4 ERA results were compared to E2, P4, number of hours of P4 given prior to biopsy/transfer, ET and uterine artery PI and RI. Of these variables only the hours of P4 given during a modified ERA cycle was significant (p < 0.0001). In addition, E2 and number of hours of P4 during the modified cycle were highest for patients with a pre-receptive result (mean 457.1 and 140.3) and BMI was highest in patients with post-receptive results. There were minimal differences in means independent of the ERA result for P4 levels, hours of P4 given prior to biopsy, ET, PI and RI. Despite identification of higher results for some of the variables none of the differences were statistically significant. In addition there was no significant difference in pregnancy outcome of modified cycles for previously receptive vs. non receptive ERA results

CONCLUSIONS: In conclusion only the number of hours of P4 given during a patients modified cycle had a significant effect on the ERA result. Given this, it would appear that no linear relationship between these variables including the ERA result exists and that there is no significant relationship between any ERA result and pregnancy outcome exists suggesting a more multifaceted relationship that warrants further exploration. Further understanding of a cumulative approach that incorporates two specific transcriptomic signatures obtained by microarray technology and 130 biopsies from IVF-patients with a known pregnancy outcome were used for clinical validation.

P-568 Wednesday, October 16, 2019 6:30 AM
PROSPECTIVE EVALUATION OF HUMAN HERPESVIRUS 6 (HHV-6) IN ENDOMETRIAL TISSUES OF WOMEN WITH REPEAT IMPLANTATION FAILURE. Kevin J. Doody, M.D.,1,† Kathleen M. Doody, MD,2 Phillip F. Pratt Jr., PhD,3 Constance Knox, PhD2 CARE Fertility, Bedford, TX,4 Coppe Healthcare Solutions, Waukeisha, WI.

OBJECTIVE: Recent reports have demonstrated active human herpesvirus 6 (HHV-6) infection in the endometrium of >43% of women with unexplained infertility and in 0% of fertile women.1 The studies demonstrated HHV-6 associated alterations in cNK cells and multiple cytokines, and suggested that HHV-6 may perturb the uterine micro-environment and disadvantage embryo implantation and placentation. To assess whether HHV-6 could play a role in embryo implantation we initiated a prospective evaluation of active HHV-6 infection in endometrial biopsies (EB) of women with Repeat Implantation Failure (RIF) following transfer of morphologic high quality or PGF2α tested euploid embryos.

DESIGN: EB taken at LH post 5-9 days or progesterin + 5 days were obtained from 24 patients with a history of two or more failed ET/FET. Pipelle segments were placed in 10% buffered formalin and submitted for formalin fixed paraffin embedding (FFPE) and immunohistochemical (IHC) evaluation.

MATERIALS AND METHODS: IHC analysis for an HHV-6 late protein was performed on the EB. The HHV-6 IHC assay is a validated diagnostic test utilizing a monoclonal (Mab) antibody directed at a late structural protein of the virus paired with an isotopic Mab to control for background staining.2 Fisher’s Exact Test and paired t Test were used to analyze difference between HHV+ and HHV-6 patients.

RESULTS: Of the 24 patients demonstrating 2 or more failed embryo transfers, 12 (50%) were positive for HHV-6 late viral proteins in endometrial epithelial cells and 12 (50%) were negative. There were no significant differences in age or diagnosis of endometriosis or PCOS between groups. The HHV-6 positive group had undergone significantly more failed transfers than the HHV-negative group (p = 0.022).

CONCLUSIONS: The ability of human herpesvirus 6 (HHV-6A/B) to infect and cause disruption or failure of specific organ systems has precedence in hematopoietic stem cell (HSC) transplantation. The presence of HHV-6A/B and disruption of HSC graft function and failure of marrow engraftment has been confirmed.3 The HHV-6 induced factors that cause HSC engraftment interference may be operative in preventing the natural or assisted implantation of human embryos. The data presented here strongly suggests that further studies of HHV-6 in infertility and RIF are warranted.

References:
3 Carrigan D, Knot K. HHV-6 Associated Bone Marrow Suppression in Bone Marrow Transplant Patients. Blood. 84(1994): 3307-3310.
P-570 Wednesday, October 16, 2019 6:30 AM

PROGESTERONE AND ESTRADIOL CONCENTRATIONS IN HUMAN ENDOMETRIUM DURING THE MID-LUTEAL PHASE OF THE MENSTRUAL CYCLE. Dimitar Parvanov, PhD, Rumiana Ganeva, MSc, Nina Vidolova, MSc, Polya Penkova, MD, Teodora Tlhornovida, MD, Georgi Stamenov Stamenov, MD/PhD. Nadezhda Women’s Health Hospital, Sofia, Bulgaria.

OBJECTIVE: The aim of this study was to estimate the local progesterone and estradiol concentrations in the endometrial tissue, to compare them with their serum concentrations and to investigate possible associations between them.

MATERIALS AND METHODS: The concentration of (P4) and estradiol (E2) were investigated in serum and endometrial biopsy samples from 58 women aged between 26 and 41 years during mid-luteal phase (7 days after LH surge). The endometrial samples were weighed and homogenized in a glass homogenizer with a Tefhne pestle in a PBS buffer followed by centrifugation at 12,000 g for 10 minutes at 4°C. The obtained supernatant was used for P4 and E2 measurement by electrochemiluminescence immunoassay (ECLIA) on the Cobas e411 analyser (Roche Diagnostics, Mannheim, Deutschland). Statistical analysis was performed using SPSS v.21 (IBM Corp., Armonk, NY, USA).

RESULTS: The observed endometrial P4 levels ranged from 0.001 to 270.54 ng/mg tissue, with a mean of 23.41 ± 57.63 ng/mg tissue and a median of 0.86 ng/mg tissue. The endometrial E2 concentrations ranged between 0.01 and 0.29 pg/mg tissue with a mean of 0.01±0.06 pg/mg tissue and a median of 0.08 pg/mg tissue. The determined mean P4 concentration in the endometrial tissue was 17.9 times higher than the P4 found in the serum samples, while the mean tissue E2 concentration was 1510 times lower in comparison with the E2 serum levels. As a result, the mean P4/E2 ratio (P4 [ng/mg]/E2 [ng/mg]) in the tissue (18538 ± 16636), was 136 times higher than the corresponding P4/E2 ratio in the serum (136.15 ± 85.30). A significant but relatively low Spearman correlation was found when comparing the endometrial tissue and serum P4 concentrations (R = 0.34; p = 0.01). A similar relation was observed between the E2 levels in the endometrial tissue and in the serum (R = 0.35; p = 0.02). Again, modest but significant relation was present between the P4 and E2 tissue levels (R = 0.35; p = 0.02).

CONCLUSIONS: We conclude that the mid-luteal endometrium contains relatively high levels of P4 and significantly low levels of E2 compared to their serum levels. Endometrial P4 and E2 concentrations are positively correlated with their respective levels in serum.

P-571 Wednesday, October 16, 2019 6:30 AM

LIPID PROFILING OF PERI-IMPLANTATION ENDOMETRIUM IN PATIENTS WITH PREMATURE PROGESTERONE RISE IN LATE FOLLICULAR PHASE. Jingjie Li, M.D., Pan Chen, PhD, Xiaoyan Liang, M.D., the Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; the First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To investigate alterations of lipid profile at the window of implantation in patients with premature progesterone rise.

DESIGN: Lipidomics variation of endometrium was evaluated by ultra-high performance liquid chromatography coupled with electrospray ionization high-resolution mass spectrometry (UHPLC-ESI-HRMS). MATERIALS AND METHODS: 43 patients undergoing IVF/ICSI by the reason of tubal factor or male factor were included in this study. The patients were divided into high progesterone group (≥1.5ng/mL, 15 patients) and control group (<1.5ng/mL, 28 patients) on the day of hCG administration. The endometrium tissues were obtained by pipelle biopsy 7 days after hCG trigger. RESULTS: A total of 1026 ions were identified and 25 lipids were showed significantly up-regulated. The endometrium lipid profile was characterized by significant increase in concentration of phosphatidylcholine (PC), phosphatidylethanolamine (PE), lysophosphatidylcholine (LPC), diacylglycerol (DG), ceramide (Cer), phosphatidylinositol (PI), phosphatidylserine (PS) in patients with premature progesterone rise at the end of the follicular phase. The correlation analysis between progesterone level with the lipids showed stronger negative correlation between PE and PS with progesterone level.

CONCLUSIONS: Premature progesterone elevation disturbs lipid homeostasis of endometrium in the peri-implantation period. The altered lipids may impair endometrial receptivity and early embryo implantation.

P-572 Wednesday, October 16, 2019 6:30 AM

EFFECT OF ESTRACE ON PREGNANCY RATES FOR WOMEN WITH THIN ENDOMETRION LING UNDERGOING INTRAUTERINE INSEMINATION. Jasmyn K. Johal, MD, MSc, Sara J. Vaughn, MD, Lusine Aghajanova, MD PhD. Stanford University School of Medicine, Stanford, CA.

OBJECTIVE: To evaluate the effect of exogenous estradiol on pregnancy rates for women with thin endometrial lining undergoing intrauterine insemination (IUI) as compared to women who did not receive estradiol for endometrial support; we hypothesize that there was no difference in pregnancy rates between the two groups.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: All IUI cycles completed at Stanford University Clinic for Reproductive Medicine from March-December 2017 were reviewed. All monitored IUI cycles were included. Cycles with the addition of exogenous estradiol given vaginally or orally were compared to those without exogenous estradiol. Differences in endometrial parameters, pregnancy rates, miscarriage rates and live birth rates were compared between both groups.

RESULTS: A total of 885 IUI cycles were included. In 85 cycles, exogenous estradiol was initiated for thin endometrium. Baseline characteristics including maternal age, body mass index, ethnicity, number of IUI cycles per patient, type of IUI cycle, and total motile sperm count were similar between the two groups. Mean baseline endometrial lining was thicker in the non-estradiol group, and the non-estradiol group was more likely to have a diagnosis of unexplained infertility whereas the estradiol group was more likely to have a diagnosis of diminished ovarian reserve. Despite initiation of estradiol, the mean endometrial thickness at trigger scan remained significantly thinner in estradiol group as compared to the non-estradiol group (6.4 ± 1.3 cm vs. 8.4 ± 1.9 cm, respectively, p < 0.001), although the change in thickness in the estradiol group from cycle day 1 to trigger scan did increase on average by 2.2 cm. Pregnancy, miscarriage and live birth rates were similar between the estradiol and non-estradiol groups (see Table 1).

CONCLUSIONS: Although there is limited data supporting the use of exogenous estradiol to improve outcomes during IUI cycles, this low risk intervention is often employed in the setting of a thin endometrial lining in the late follicular phase. In women undergoing IUI with exogenous estradiol supplementation due to thin endometrial lining, pregnancy, miscarriage and live birth rates were similar to women undergoing IUI without exogenous estradiol use.

P-573 Wednesday, October 16, 2019 6:30 AM

PREMATURE PROGESTERONE ELEVATION DISTURBS LIPID HOMEOSTASIS DURING THE PERI-IMPLANTATION PERIOD. J. Kotsiou, MD, A. Filippou, MD, E. Kotsiou, MD, D. Parvanov, PhD, M. Varos, MD. The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; the First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To investigate alterations of lipid profile at the window of implantation in patients with premature progesterone rise.

DESIGN: Lipidomics variation of endometrium was evaluated by ultra-high performance liquid chromatography coupled with electrospray ionization high-resolution mass spectrometry (UHPLC-ESI-HRMS). MATERIALS AND METHODS: 43 patients undergoing IVF/ICSI by the reason of tubal factor or male factor were included in this study. The patients were divided into high progesterone group (≥1.5ng/mL, 15 patients) and control group (<1.5ng/mL, 28 patients) on the day of hCG administration. The endometrium tissues were obtained by pipelle biopsy 7 days after hCG trigger.

RESULTS: A total of 1026 ions were identified and 25 lipids were showed significantly up-regulated. The endometrium lipid profile was characterized by significant increase in concentration of phosphatidylcholine (PC), phosphatidylethanolamine (PE), lysophosphatidylcholine (LPC), diacylglycerol (DG), ceramide (Cer), phosphatidylinositol (PI), phosphatidylserine (PS) in patients with premature progesterone rise at the end of the follicular phase. The correlation analysis between progesterone level with the lipids showed stronger negative correlation between PE and PS with progesterone level.

CONCLUSIONS: Premature progesterone elevation disturbs lipid homeostasis of endometrium in the peri-implantation period. The altered lipids may impair endometrial receptivity and early embryo implantation.

SUPPORT: This study was financially supported by the National Natural Science Foundation of China (No. 81601347, 81503156), Natural Science Foundation of Guangdong Province (No. 2014A030310096) and Public Welfare Research and Capacity Building Fund of Guangdong (No. 2016A020218006).

TABLE 1.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Estradiol (n=85)</th>
<th>No Estradiol (n=800)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrial Lining thickness (cm), mean±standard error</td>
<td>4.2±1.3</td>
<td>4.9±1.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Estradiol initiation</td>
<td>4.9±0.8</td>
<td>6.4±1.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Trigger</td>
<td>6.4±1.3</td>
<td>8.4±1.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Pregnancy Rate, n (%)</td>
<td>14 (20%)</td>
<td>81 (10%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Spontaneous</td>
<td>8 (10%)</td>
<td>30 (4%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Abortions, n (%)</td>
<td>5 (10%)</td>
<td>42 (10%)</td>
<td>0.78</td>
</tr>
<tr>
<td>Live births to date, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ENVIRONMENT AND REPRODUCTION

P-573 Wednesday, October 16, 2019 6:30 AM

ACUTE EXPOSURE TO UNHEALTHY AIR QUALITY DURING THE 2018 CAMP FIRE WAS NOT ASSOCIATED WITH ADVERSE LABORATORY OUTCOMES IN PATIENTS WHO UNDERWENT ASSISTED REPRODUCTION TREATMENT. Amy Wijekoon, MD, a Mitchell P. Rosen, MD, HCLD, b Salustiano Ribeiro, MSc, a Phil Marsh, BS, a Marcelle I. Cedars, MD, a Thalia R. Segal, MD, a University of California, San Francisco, San Francisco, CA; UC SF, San Francisco, CA; a University of California - San Francisco, San Francisco, CA; c University of California San Francisco, San Francisco, CA.

OBJECTIVE: The Camp Fire, California’s most destructive wildfire, began on November 8th 2018 and the Bay Area’s air quality index (AQI) rose from Healthy (AQI< 50) to Unhealthy (AQI 150-200), enduring for two weeks. Though devastating, this event presents a unique opportunity to assess the short-term effects of exposure to poor quality air on a fertility population. This study investigates the effects of unhealthy air quality on in vitro fertilization (IVF) outcomes of patients undergoing treatment at the University of California, San Francisco (UCSF) during this period.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Data regarding AQI were obtained directly from the Environmental Protection Agency. A LifeAire System is used for air purification in UCSF’s IVF laboratory. During the fires, there were <10ppb volatile organic compounds and <1 ug/m3 of particles (0.1-10 μm) measurable in the laboratory. Clinical outcome data were collected from exposed patients with oocyte retrievals within a month following the Camp Fire. From November 8th to December 8th, 2018). Data on fertilization, blastocyst, and euploid rate were compared to a control population of patients who had oocyte retrievals at UCSF within the year prior to the Camp Fire. Student’s t-test was used to analyze differences in mean rates for each clinical outcome. Chi squared test was used to compare cycle cancellation rate between groups. Regression analyses with cluster analysis for pairwise comparison were performed on exposed patients with prior unexposed cycles, to assess for differences in clinical outcomes within a patient.

RESULTS: Median AQI in the year prior to the Camp Fire was 37 (IQR 31-52), in comparison to a median AQI of 164 (IQR 151-173) during the two weeks of the Camp Fire (p=0.001). One hundred and twelve patients were exposed during the fire, and 45% of them completed preimplantation genetic screening for aneuploidy (PGT-A). There were 969 patients in the control population, with 45% completing PGT-A. No significant differences were noted in age, body mass index, race, infertility diagnosis, or stimulation protocol between the groups. When comparing control group to fire exposed group, there were no significant differences between the fertilization (79% vs 77%, p=0.44), blastocyst (51% vs 57%, p=0.16), or euploid (40% vs 47%, p=0.14) rates. There were also no differences in cycle cancellation rate. Sixty-six exposed patients had non-exposed cycles with the same or different stimulation protocol. When comparing all non-exposed to exposed cycles within a patient, no differences were noted in fertilization (73% vs 76%, p=0.67), blastocyst (48% vs 41%, p=0.22), or euploid (31% vs 41%, p=0.24) rate.

CONCLUSIONS: Unhealthy AQI during the 2018 Camp Fire was not associated with statistically significant differences in clinical outcomes of patients undergoing IVF treatment in a code complaint laboratory. These findings suggest that acute exposure to unhealthy air does not impact egg or sperm function, however, further studies are needed to assess for impact of long-term exposure on outcomes.

SUPPORT: None.

P-574 Wednesday, October 16, 2019 6:30 AM

EFFECT OF GENISTEIN AND DAIDZEIN LEVELS ON OVARIAN RESPONSE AND EMBRYO QUALITY IN PGT-A CYCLES. Lucia Marin, MSc, a Immaculada Campos-Galindo, PhD, b Francisco Dominguez, PhD, a Ma José de los Santos, PhD, a Carmen Vidal, M.D., Ph.D., a Amparo Mercader, Ph.D, a Carlos Simon, MD, PhD, d Carmen Rubio, PhD. a; 1Igenomix, Valencia, Spain; 2IIVI Foundation - ISSLafeBi Medical Research Institute, Valencia, Spain; 3IVIRMA Valencia, Valencia, Spain; 4University of Valencia; Igenomix Foundation-INCLIVA, Valencia, Spain; 5Igenomix, Paterna (Valencia), Spain.

OBJECTIVE: To evaluate if genistein and daidzein (soy-derived phytoestrogens) levels in urine and follicular fluid (FF) could have an impact on the number of antral follicles, MII oocytes, fertilization, embryo quality on day 3, and aneuploidy rates.

DESIGN: Prospective, observational study including preimplantation genetic testing for aneuploidy (PGT-A) cycles in which urine and FF was collected the day of ovum pick (December 2013 - July 2018).

MATERIALS AND METHODS: A total of 36 PGT-A cycles in women <38 years were analyzed by Next Generation Sequencing (NGS). Indications for PGT-A were recurrent miscarriage or repetitive implantation failure. Genistein and daidzein were measured using Ultra-Performance Liquid Chromatography/Electrospray Mass Spectrometry (UPLC/ESI-MS) and normalized according to creatinine levels. In urine samples genistein and daidzein levels were classified in three categories: <10ng; 10-50ng and >50ng. The number of informative urine samples with levels above the limit of detection was 26 for genistein and 36 for daidzein. In FF, lower levels were detected and were classified as follows: <2ng; 2-5ng and >5ng. The number of informative FF samples with levels above the limit of detection was 13 for genistein and 9 for daidzein. The statistical comparisons among groups were carried out using the GraphPadInStat v. 2.05a package (Graphpad Software, San Diego, CA, USA).

RESULTS: For genistein levels in urine, a significant increase in the mean number of antral follicles was observed in the group with higher concentration (14.9±5.3; 18.2±5.3 and 24.5±9.6; p<0.05). A similar trend was observed for the mean number of MII oocytes and 2PN, but without significant differences. Day 3 embryos showed a significant increase in number of antrumore number (6.6±2.0; 5.9±1.8 and 7.2±1.0; p<0.05), and a decrease in fragmentation degree (8.1±6.9; 8.6±8.5 and 5.0±4.1; p<0.05) in the group with higher urine genistein concentration. Genistein levels in FF were correlated with the levels in urine and significant differences were found for the same variables: mean number of antral follicles (11.2±3.7; 19.5±3.5 and 22.5±14.8; p<0.05); mean blastomere number (6.7±3.3; 6.0±1.9 and 7.5±0.7; p<0.05) and fragmentation degree (6.7±5.8; 11.0±8.2 and 2.5±3.5; p<0.05). Aneuploidy rates were significantly decreased in urine genistein levels >50ng (60.8% vs. 42.3%; p<0.05), and a similar trend was observed for FF >5ng, but without reaching statistical significance (69.7% vs. 47.1%). For daidzein levels in urine and FF, no clear correlation was observed with ovarian response and embryo quality.

CONCLUSIONS: In PGT-A couples, genistein, a soy-derived phytoestrogen, appears to enhance ovarian response, embryo quality and euploidy rates. A protective effect of a soy-diet has been previously described in a mouse model (Muhlhauser et al., 2009). In ART patients, soy isoflavones intake has been positively related to live births (Venegas et al., 2015). Therefore, a soy-enriched diet could be beneficial for women undergoing ART, and more specifically in PGT-A cycles.


SUPPORT: Merck research grant 2015-2018.

P-575 Wednesday, October 16, 2019 6:30 AM

THE ASSOCIATION BETWEEN SEASON AT CYCLE START AND CLINICAL PREGNANCY FOLLOWING FRESH EMBRYO TRANSFER. Leslie V. Farland, Sc.D. a, Katherine Corrhea, PhD, a Stacey A. Missmer, Sc.D. b, Catherine Racowsky, PhD. c

aUniversity of Arizona, Tucson, AZ; cAmherst College, Amherst, MA; cMichigan State and Harvard T.H. Chan SPH, Grand Rapids, MI; cBrigham & Women’s Hospital, Boston, MA.

OBJECTIVE: Improvements in laboratory techniques and clinical protocols have led to increasing live birth rates from in vitro fertilization (IVF). Despite this impact, the reproductive potential of patients remains a primary determinant of success. It is therefore of interest to investigate any environmental factors that may influence this potential. As delivery rates from spontaneous conception vary according to season, outcomes from IVF may also be season-dependent. The present study was designed to test the hypothesis that there is an association between season at IVF cycle start and clinical pregnancy. DESIGN: Retrospective cohort of 5,878 fresh embryo transfers.

MATERIALS AND METHODS: Start dates for all autologous cycles resulting in fresh cleavage or blastocyst stage transfers performed in our IVF program between January 2012-December 2017 were categorized by season
and Co might have significant inverse effects on AHM, which also showed between infertile women living in the Eastern China and Southern China. Fe levels were determined in FF and serum by inductively coupled plasma mass spectrometry (ICP-MS), and serum cadmium, tin, antimony, barium, titanium, and mercury) were analyzed in the included patients. FF samples during the oocyte retrieval were analyzed by the included patients. FF samples during the oocyte retrieval were analyzed.

RESULTS: Patient characteristics were similar among seasons. As expected, temperature and day-length varied by season. When compared with cycles started during Winter, there was no difference in clinical pregnancy rate in Spring (OR: 1.08, 95% CI: 0.94-1.25), Summer (OR: 1.10, 0.95-1.27), or Fall (OR: 1.02, 0.88-1.19). Comparisons of clinical pregnancy by month of cycle started revealed that cycles started in June (45.6%) and July (45.1%) had 38% greater odds of clinical pregnancy compared to cycles that started in January (37.5%) (OR: 1.38, 1.08-1.77 for June; OR: 1.38, 1.08-1.76 for July). No other comparisons by month reached statistical or clinical significance. There was a positive linear trend between day-length and clinical pregnancy (P-value, test for linear trend=0.05) but no association with average temperature (P-value, test for linear trend=0.52).

CONCLUSIONS: Our results do not support the hypothesis that clinical pregnancy after fresh transfer is associated with season at cycle start. However, our more detailed analyses found greater odds of clinical pregnancy for cycles started in June and July compared with January and a positive linear trend between clinical pregnancy and day-length, but not temperature. Together, these findings suggest an association between maternal light exposure and outcomes from IVF. The exact mechanism underlying this association is not known but may implicate a role of melatonin and/or Vitamin D on improved oocyte quality and/or endometrial receptivity.

REGIONAL DIFFERENCE OF METAL LEVELS IN FOLLICULAR FLUID AND SERUM AMH LEVEL BETWEEN INFERTILE WOMEN FROM EASTERN CHINA AND SOUTHERN CHINA. Jinxin Xu, MD, a Yanyun Ying, B.S.Med, a Jianpeng Chen, MD, a Dan Li, MD, a Dan Zhang, MD, PhD; b Key Laboratory of Reproductive Genetics (Ministry of Education) and Department of Reproductive Endocrinology, Hangzhou, Zhejiang, China; c Women’s Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China; d Key Laboratory of Reproductive Genetics (Ministry of Education) and Department of Reproductive Endocrinology, Hangzhou, China.

OBJECTIVE: The metal exposure can result in different bioaccumulation in the reproductive tissues as well as diverse disturbance of the reproductive outcomes in different regions, which requires additional researches on regional effects on environmental exposure and reproductive toxicity. Therefore, the study aims to assess the regional difference of metal levels in follicular fluids and serum Anti-muller test tube hormone (AMH) of infertile women from Eastern China and Southern China.

DESIGN: A cross sectional study was approved by the Institutional Review Board Committee, and was conducted between September 2017 and December 2017 in infertility ward in Women’s Hospital, Zhejiang University School of Medicine. 648 female patients diagnosed with unexplained infertility from Eastern China and Southern China were included.

MATERIALS AND METHODS: After informed written consent signed by the included patients, FF samples during the oocyte retrieval were collected. Nineteen elements (vanadium, chromium, manganese, iron, cobalt, nickel, copper, zinc, arsenic, selenium, strontium, molybdenum, silver, cadmium, tin, antimony, barium, titanium, and mercury) were analyzed in FFs by inductively coupled plasma mass spectrometry (ICP-MS), and serum AMH levels are tested. The places of residence were collected from the electronic medical record of the hospital. The associations of metal levels between two AMH levels were adjusted by age, BMI and reproductive hormones (follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), progesterone (P), testosterone (T) and prolactin (PRL)).

RESULTS: We observed that iron (Fe) levels and Cobalt (Co) levels in FFs were both inversely related to serum AMH level (P < 0.5, respectively). Inertile women living in the Eastern China have a significant higher level of Fe and Co in FFs (P < 0.5, respectively) with a significant lower AMH level (P < 0.05, respectively) compared to infertile women from Southern China.

CONCLUSIONS: Bioaccumulations of Fe and Co were quite different between infertile women living in the Eastern China and Southern China. Fe and Co might have significant inverse effects on AHM, which also showed significant regional differences between Eastern China and Southern China.

Tobacco smoke exposure induces epigenetic changes in sperm. Further, studies in our laboratory have shown that pre-conception paternal cigarette smoke exposure induces epigenetic changes in sperm. Further, studies in offspring suggest that pre-conception paternal smoking status impacts neurobehavioral epigenetic and gene expression status in a consistent manner. Parallel studies performed in Nrf-/- mice provide strong evidence for oxidative stress alterations to sperm and the offspring of smoke-exposed sires. Lastly, recovery following a longer recovery period was not observed, indicating potential long-term effects following smoking cessation.

CONCLUSIONS: The current study provides abundant evidence that cigarette smoke exposure induces epigenetic changes to sperm as well as the offspring of smoke-exposed mice. The changes in DNA methylation patterns associated with smoking status. Remarkably, the changes in sperm DNA methylation were largely recapitulated in Nrf-/- mice independent of season. The assessment of heritable effects revealed changes in DNA methylation patterns as well as gene expression in the offspring of mice exposed to cigarette smoke, and strikingly the epigenetic and transcriptional changes identified in the offspring of smoke-exposed mice were also observed in Nrf-/- offspring irrespective of paternal smoking status. Recovery experiments indicated that about half of differentially methylated regions returned to normal within 28 days of removal from smoke, however additional recovery following a longer recovery period was not observed, indicating potential long-term effects following smoking cessation.

CONCLUSIONS: The current study provides abundant evidence that cigarette smoke exposure induces epigenetic changes to sperm as well as the offspring of smoke-exposed mice. The changes in DNA methylation patterns associated with smoking status. Remarkably, the changes in sperm DNA methylation were largely recapitulated in Nrf-/- mice independent of season. The assessment of heritable effects revealed changes in DNA methylation patterns as well as gene expression in the offspring of mice exposed to cigarette smoke, and strikingly the epigenetic and transcriptional changes identified in the offspring of smoke-exposed mice were also observed in Nrf-/- offspring irrespective of paternal smoking status. Recovery experiments indicated that about half of differentially methylated regions returned to normal within 28 days of removal from smoke, however additional recovery following a longer recovery period was not observed, indicating potential long-term effects following smoking cessation.

CONCLUSIONS: The current study provides abundant evidence that cigarette smoke exposure induces epigenetic changes to sperm as well as the offspring of smoke-exposed mice. The changes in DNA methylation patterns associated with smoking status. Remarkably, the changes in sperm DNA methylation were largely recapitulated in Nrf-/- mice independent of season. The assessment of heritable effects revealed changes in DNA methylation patterns as well as gene expression in the offspring of mice exposed to cigarette smoke, and strikingly the epigenetic and transcriptional changes identified in the offspring of smoke-exposed mice were also observed in Nrf-/- offspring irrespective of paternal smoking status. Recovery experiments indicated that about half of differentially methylated regions returned to normal within 28 days of removal from smoke, however additional recovery following a longer recovery period was not observed, indicating potential long-term effects following smoking cessation.
OBJECTIVE: To assess the impact of higher ambient temperature on the risk of stillbirth during the warm season. Extreme ambient temperature events are becoming more prevalent and changes in ambient temperature represent an understudied but potentially modifiable stillbirth risk factor.

DESIGN: Retrospective cohort study based on hospital delivery admission electronic records from 19 hospitals for all deliveries 20 weeks gestation or later.

MATERIALS AND METHODS: We identified the first stillbirth case per mother (n = 498) among singleton deliveries in the NICHD Consecutive Pregnancy Studies (Utah, 2002-2010). Ambient temperature was derived from the Weather Research and Forecasting model and air pollution data were based on modified Community Multiscale Air Quality models. We conducted a case-crossover analysis to estimate the hazard ratio (HR) and 95% confidence interval (95% CI) for the risk of stillbirth for each increase of 1°F Celsius during the warm season (May – September). Risk periods included day of delivery and each of the 7 days prior to delivery as well as the average temperature for the week prior to delivery. Two control periods were selected: two weeks prior to delivery and two weeks after delivery. Women serve as their own controls in this analysis and all non-time-varying factors are controlled by design. Models were adjusted for time-varying relative humidity, ozone, and particulate matter <2.5 microns.

RESULTS: During the week prior to delivery, daily risk of stillbirth significantly increased by 5.1% for each 1°F Celsius increase in temperature beginning 2 days prior to delivery (HR=1.05; 95% CI: 1.00-1.09) with the highest risk observed at 7 days prior to delivery (HR=1.11; 95% CI: 1.06-1.17). Point estimates for the day of delivery, the day immediately preceding delivery and average temperature in the week prior to delivery were elevated but not significantly associated with stillbirth.

CONCLUSIONS: Our findings suggest temperature may be a modifiable risk factor for stillbirth. Notably, the risks we observe beginning 2 days prior to delivery appear consistent with the fact that most stillbirths occur 48-72 hours prior to delivery. High temperature can induce physiologic stress including increased heart rate and inflammatory processes, but the specific underlying biologic mechanisms related to stillbirth remain to be explored. Stillbirth risk associated with ambient temperature merits attention given anticipated increases in ambient temperature over time.

<table>
<thead>
<tr>
<th>Time prior to delivery</th>
<th>Hazard Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day of delivery</td>
<td>1.02</td>
<td>0.98 - 1.06</td>
</tr>
<tr>
<td>1 day</td>
<td>1.04</td>
<td>0.99 - 1.08</td>
</tr>
<tr>
<td>2 days</td>
<td>1.05</td>
<td>1.00 - 1.09</td>
</tr>
<tr>
<td>3 days</td>
<td>1.07</td>
<td>1.02 - 1.11</td>
</tr>
<tr>
<td>4 days</td>
<td>1.06</td>
<td>1.02 - 1.11</td>
</tr>
<tr>
<td>5 days</td>
<td>1.06</td>
<td>1.01 - 1.10</td>
</tr>
<tr>
<td>6 days</td>
<td>1.09</td>
<td>1.04 - 1.14</td>
</tr>
<tr>
<td>7 days</td>
<td>1.11</td>
<td>1.06 - 1.17</td>
</tr>
<tr>
<td>Average for the week prior</td>
<td>1.04</td>
<td>1.00 - 1.08</td>
</tr>
</tbody>
</table>

SUPPORT: This research was supported by the Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

P-580 Wednesday, October 16, 2019 6:30 AM

PROXIMITY TO NEAREST MAJOR ROAD AND FECUNDABILITY IN AN HISTORICAL COHORT

Nina Hatch, MPH, MEM, PhD; Nicole Cardello Deziel, PhD, MPH; D. Robert McConnaughey, PhD; Donna D. Baird, PhD; Allen J. Wilcox, MD, PhD; Clarice R. Weinberg, PhD; Anne Marie Jukic, PhD; Business for Social Responsibility, New York, NY; Yale School of Public Health, New Haven, CT; Westat, Durham, NC; National Institute of Environmental Health Sciences, Durham, NC.

OBJECTIVE: To examine the relationship between distance to major roadway, a proxy for traffic-related air pollution, and fecundability.

DESIGN: Our analysis was conducted within the North Carolina Early Pregnancy Study (n=221) a prospective time-to-pregnancy cohort.

MATERIALS AND METHODS: Pregnancy attempt time, which allows estimation of the per cycle probability of conception, was calculated as the number of oocytes from conception, or no conception, if no conception occurred. Our primary definition of conception included all detected conceptions, including early pregnancy loss, clinical pregnancy loss, and singleton or twin deliveries. In a secondary analysis, conception was defined as clinical pregnancy only. Residences were geolocated for each participant using ArcGIS and roadway information from the U.S. Census Bureau and a 1980 Official Highway Map from the North Carolina Department of Transportation. Residential proximity to nearest major road...
was calculated for each participant. We used generalized linear regression models to estimate fecundability ratios (FR). We also used a logistic regression to estimate the odds ratios (OR) for early pregnancy loss.

RESULTS: In our primary analysis, fecundability was higher for couples living near a major road, but the confidence interval included the null (FR < 0.95, 1.00) (Table). For clinical pregnancies, fecundability ratio was not associated with fecundability (Table). Odds of early pregnancy loss was higher in women who lived < 200 meters from a major road (OR: 2.08, 95% CI: 0.85, 5.09) or who lived 200 - <500 meters away from a major road (OR: 1.82, 95% CI: 0.78, 4.24), but numbers were small (47 losses).

CONCLUSIONS: Living near a major roadway was not associated with reduced fecundability. Proximity to major roads may be associated with early pregnancy loss, but this should be investigated in a cohort with a larger number of early losses. Planned analyses of existing data in this cohort include implantation timing and characteristics of early loss in relation to proximity.

P-581 Wednesday, October 16, 2019 6:30 AM

WOMEN'S KNOWLEDGE ABOUT THE IMPACT OF FEMALE AND MALE AGE, WEIGHT, AND SMOKING ON FERTILITY: RESULTS FROM A NATIONAL SURVEY. Amber K. Worthington, PhD.† Erin E. Burke, PhD.‡ Carly Leathy, BA.§ Penn State University, University Park, PA; †Modern Fertility, San Francisco, CA.

OBJECTIVE: Women’s misconceptions about the impact of female and male age, weight, and smoking on a couple’s fertility likely lead to uninformed decisions regarding reproductive health and family planning; however, little research has examined women’s fertility knowledge. The goal of this study was to provide a large-scale assessment of women’s knowledge about the impact of risk factors on female and male fertility.

DESIGN: A national, cross-sectional survey.

MATERIALS AND METHODS: 327 women were recruited through an e-newsletter in March 2019; no incentive was provided. Eligible participants were aged 18 to 59, identified as women, lived in the USA and provided informed consent. Participants completed an online survey that assessed their knowledge about the impact of female and male age, weight, and smoking on fertility. The data were analyzed using descriptive statistics and dependent sample t-tests; the power was excellent (.99).

RESULTS: Participants ranged in age from 18 to 59 (M = 34.11, SD = 6.64) and the majority identified as heterosexual (95%) and had a partner (81%). 3 items assessed knowledge about the impact of age on female fertility, and 3 items assessed knowledge about the impact of age on male fertility (e.g., “female fertility significantly declines between the ages of 35 and 39” (T); “male fertility significantly declines between the ages of 45 and 49” (T)). Participant responses on all 6 items were coded as correct or incorrect. 87% answered both items about female weight and smoking correctly; 49% answered both about males correctly. A dependent samples t-test revealed that women were less knowledgeable about the impact of male weight and smoking on fertility (M = 1.41, SD = 0.64, range = 0 - 2) than female weight and smoking on fertility (M = 1.86, SD = 0.38, range = 0 - 2); t(326) = 13.13, p < .001.

CONCLUSIONS: These results suggest that women are relatively informed about the impact of their own age, weight, and smoking on fertility but less informed about the impact of male age, weight, and smoking on fertility. These misconceptions may disproportionately assign responsibility for preconception health to women. Providers should be aware of these misconceptions in order to educate patients on the role of male fertility risk factors. Correcting these misconceptions may be a critical step towards decreasing infertility by changing unhealthy behaviors and alleviating the emotional load on opposite-sex coupled women.

SUPPORT: This research was funded by Modern Health, Inc.

P-582 Wednesday, October 16, 2019 6:30 AM

THE DEGRADATION OF VITAMIN D ACROSS TIME: AN ISSUE LEADING TO UNRELIABLE RESULTS IN REPRODUCTIVE RESEARCH. Evelin E. Lara-Molina, MD.† Jason M. Fransasiak, MD.‡ Almudena Devesa-Peiro, MSc.§ Marina Lopez-Nogueroles, PhD.¶ Mireia Florensa, MSc.¶ Marta Martín, MSc.¶ Agustín Ballesteros, PhD.¶ Antonio Pellicer, MD, PhD.¶ Patricia Diaz-Gimeno, PhD.¶ IVI RMA Barcelona, Barcelona, Spain; ¶IVI-RMA New Jersey, Basking Ridge, NJ; ¶IVI Foundation IVIRMA Global, Biomedical Research Institute La Fe, Valencia, Spain; ¶Health Research Institute La Fe, Valencia, Spain; ¶IVIRMA ROMA, Roma, Italy.

OBJECTIVE: Vitamin D deficiency is widely reported with significant impact on many health processes, including reproduction. However, many studies evaluate the impact of Vitamin D utilizing banked samples, and the stability of vitamin D after a prolonged storage is often not taken into account. We aimed to determine if 25-hydroxyvitamin D (25(OH)D3) and its main catabolite 24,25-dihydroxyvitamin D (24,25(OH)2D3) in serum and follicular fluid, are stable across time in frozen samples.

DESIGN: Prospective, non-interventional study.

MATERIALS AND METHODS: Controlled ovarian stimulation was performed in thirty-five egg donors using an antagonist protocol and standard doses of subcutaneous FSH. After 36 hours of a GnRH agonist bolus, the oocytes retrieval was performed. Serum samples and pooled follicular fluid from mature follicles were collected during pick-up for 24,25(OH)2D3 and 25(OH)D3 measurements via LC-MS/MS using a UPLC-TQ-S Xevo Waters system with a Waters Acuity BEH C18 (1.7μm, 2.1x100 mm) column. A baseline Vitamin D analysis and a second one after seven months of storage at -80°C were performed. After testing the normal distribution of metabolites concentration with Shapiro-Wilcoxon, a t-test (when normal distribution) or a Wilcoxon test (for non-normal distribution) was performed in order to contrast mean differences before and after storage.

RESULTS: A significant decrease in 25(OH)D3 concentrations after 7 months of storage was found in serum (from 91.56 ± 39.01 nM to 62.235 ± 24.09 nM, p-value=2.68e-11) and follicular fluid (from 58.13 ± 19.55 to 3.68 ± 11.54 nM, p-value=2.00e-4).

TABLE. Fecundability Ratios for roadway proximity.

<table>
<thead>
<tr>
<th>Roadway proximity (m)</th>
<th>Conception1 yes, 170 cycles no, 438 cycles</th>
<th>Clinical Pregnancy2 yes, 150 cycles no, 545 cycles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per 100m increase</td>
<td>Adjusted3 cycles</td>
<td>Adjusted3 cycles</td>
</tr>
<tr>
<td>0 - &lt;200</td>
<td>FR 95%CI</td>
<td>FR 95%CI</td>
</tr>
<tr>
<td>&lt;200</td>
<td>0.99 (0.98, 1.01)</td>
<td>0.38 (0.36, 0.40)</td>
</tr>
<tr>
<td>200 - &lt;500</td>
<td>1.42 (0.94, 2.14)</td>
<td>1.07 (0.68, 1.68)</td>
</tr>
<tr>
<td>500 - &lt;1000</td>
<td>1.11 (0.77, 1.60)</td>
<td>0.80 (0.53, 1.21)</td>
</tr>
<tr>
<td>&gt;1000</td>
<td>1.18 (0.83, 1.67)</td>
<td>1.10 (0.76, 1.59)</td>
</tr>
</tbody>
</table>

3. Adjusted for: female age, male age, education, income, occupation.

FERTILITY & STERILITY®
ART.
Wednesday, October 16, 2019 6:30 AM

with a reduced chance of implantation following IVF. However, conventional insemination or fertilization check or D3 embryo check, were associated seen when comparing low to high TVOC groups. 

¼ a significantly reduced implantation rate (57.7% vs 37.3%, P

(64.1% vs 65.0%, P

¼ [0.277-3.704], P

0.013). Number of oocytes retrieved, normal versus abnormal fertilization, embryo development, and pregnancy outcome were analyzed. Further, pregnancy outcomes were evaluated based on month of retrieval to examine season in environments related to agricultural practices of the region. Statistical significance was determined using statistical package for social sciences (SPSS) to run two-way ANOVA, Tukey, and one-way statistics.

RESULTS: Men who lived in rural environments had significantly lower pre-wash sperm concentrations (p<0.05) than men who lived in urban environments; however there was no difference in pre-wash semen volume (p=0.54). Women who lived in rural environments had lower numbers of embryos retrieved (p<0.05), lower numbers of atretic embryos (p<0.05), and lower numbers of healthy embryos (p=0.05) compared to women from urban environments. However, fertilization rates, embryo development, and pregnancy outcome did not differ (p=0.45). While not statistically significant due to not reaching power, pregnancy outcomes based on season appear to correlate with decreased success in months with intensive agricultural activity with success rates ranging from 8.3%-34.8% in March, April, September, and October while in months during the growing season and post-harvest, ART success rates range from 41.7%-69.2%.

CONCLUSIONS: Semen parameters vary between urban and rural populations, as demonstrated in previous research. Pre-fertilization parameters are different between women from urban and rural environments. However, embryo development and pregnancy outcomes are not different. Pregnancy outcomes from assisted reproductive technologies may be affected by season and corresponding environmental factors. There appears to be a change in success of ART procedures during various times of year that could be caused by agricultural activity, but further research is needed to determine if and how environmental factors affect gamete production and ART outcomes.

SUPPORT: None.

THE USE OF PRESCRIPTION DRUGS AMONGST MEN AND WOMEN UNDERGOING ASSISTED REPRODUCTIVE TECHNOLOGY (ART) PROCEDURES. Edmond W. M. Rostand, Medical Student. Suhair Ibrahim, MBBS MRCP. Abigail Sharpe, MBBS, MRes. Mariano Mecareñan, MS (OG), MRCP, DNB (OG), Post-doctoral fellow in reproductive medicine. Harish M. Bhandari, MBBS MD MRCP. "School of Medicine, University of Leeds, Leeds, United Kingdom; "Leeds Fertility, Seacroft Hospital, Leeds, United Kingdom.

OBJECTIVE: A pilot study aiming to determine the trends of prescription medication amongst men and women undergoing ART and the associated live birth rates.

DESIGN: This was a retrospective cohort study of heterosexual couples undergoing ART between October 2016 and November 2017 in a tertiary reproductive medicine unit. This pilot study was conducted as an undergraduate medical student project.

MATERIALS AND METHODS: A predefined proforma was used to extract data manually from each patient record for couples who had undergone ART in the defined time period. Information obtained included the drug history of both partners as well as smoking status and units of alcohol consumed each week. The outcome of the ART cycle was recorded. This data was then entered electronically into a spreadsheet and prevalence and

P-582 Wednesday, October 16, 2019 6:30 AM

IMPACT OF AMBIENT TOTAL VOLATILE ORGANIC COMPOUND (TVOC) DURING IN VITRO FERTILIZATION (IVF) LABORATORY PROCEDURES UPON SUBSEQUENT EMBRYO IMPLANTATION: A RETRO- SPECTIVE STUDY. Yanthe Liu, PhD a, Lie Mang, MSc b, Xiaoling Wang, MSc b, Zhang Li, PhD b, Yuying Jiang, MD a, Xue Yan, MD b, Chunyan Wen, MD a, Phillip Matson, PhD a, Masoud Afman a, Tianjin United Family Hospital, Tianjin, China; bEdith Cowan University, Joondalup, WA, Australia.

OBJECTIVE: To investigate the associations between laboratory TVOC levels measured during in vitro manipulation of human oocytes/embryos and subsequent implantation.

DESIGN: Retrospective cohort study in a private IVF center.

MATERIALS AND METHODS: Consecutive IVF cycles (n=103; female age 35.9±4.5 yr) performed at Reproductive Medicine Center, Tianjin United Family Hospital, between August 2018 and April 2019 were included. Intracytoplasmic sperm injection (ICSI) cycles were excluded due to the confounding effect of extra exposure of oocytes during sperm injection. Ambient TVOC readings were continuously logged at 6-minute intervals by a specialized designed device (HuChuang, China) at a fixed position in the embryology laboratory. The readings were retrieved at the closest time point to 4 procedures where embryos were exposed to the ambient environment, namely egg collection, insemination, fertilization check, and D3 embryo check. Embryos were cultured in Mlnc incubators (Cook) at 37°C perfused with clean cylinder gas (6% CO 2,5 %O 2, and balance N 2) post in-line VOC removal. One or two embryos ranked the highest from the cohort were transferred on either D3 or D5, depending on the prognosis of individual patients. Implantation detected by rising hCG was evaluated via multiple variable logistic regression against cycle characteristics, embryology parameters and TVOC levels, expressed by odds ratio (OR) and 95% confidence interval (CI). Proportional embryology parameters were compared using the χ2 analysis.

RESULTS: TVOC levels ranged from 0.15 to 1.98 ppm despite extensive filtration of laboratory air (in-situ HEPA filters, stand-alone IQAir and Coda Tower), reflecting the influence of outside atmospheric conditions. Multiple variable logistic regression showed statistically significant associations between implantation and female age (OR=0.817[0.723-0.924], P=0.001), D3 embryo transfer (or=12.078[1.105-13.202], P=0.041), and the TVOC levels at egg collection (OR=0.171[0.035-0.835], P=0.029).

No effect was seen on the number of previous attempts (1.240[0.725-2.120], P=0.432), stimulation protocol (1.269[0.486-3.316], P=0.627), number of eggs collected (0.954[0.828-1.098], P=0.509), number of embryos transferred (8.954[0.871-9.021, P=0.065), TVOC levels at insemination (1.782[0.162-19.664], P=0.637), at fertilization check (1.013[0.277-3.704], P=0.984) and at D3 embryo check (1.401[0.563-3.489], P=0.468). Using a cut-off at the median TVOC reading (0.64 ppm) at egg collection, there were no significant differences in the fertilization rates (64.1% vs 65.0%, P=0.776), D3 good quality embryo rates (65.5% vs 65.1%, P=1) and embryo utilization rates (50.5% vs 50.6%, P=0.61). However, a significantly reduced implantation rate (57.7% vs 37.3%, P=0.038) was seen when comparing low to high TVOC groups.

CONCLUSIONS: High levels of TVOC at egg collection, rather than at insemination or fertilization check or D3 embryo check, were associated with a reduced chance of implantation following IVF. However, conventional embryology parameters were not adversely affected.
trends of prescription medication use were analysed. Since the sample size was insufficient for reliable statistical analysis, a descriptive report of the prescription drug utilisation patterns was created.

RESULTS: • MATERNAL MEDICATION

Out of 400, there were 22 (5.5%) women taking prescription medications and 44 (11%) on no medications. There were 266 (66.5%) women on folic acid and/or vitamin D alone. The live birth rate of the women on prescription medications was 32.2% (n=29). The live birth rate of the 44 women on no medications was 29.5% (n=13). The live birth rate of the women on folic acid and/or vitamin D was 33.5% (n=89).

There were a total of 60 different medications at an average of 1.4 per patient.

The most common medications were asthma medications (n=22), levothyroxine (n=12), selective serotonin re-uptake inhibitors (SSRIs) (n=10), ferrous sulphate (n=8), and diabetic medications (n=7).


• PATERNAL MEDICATION

Out of 400, 88 male partners were on prescription medication (22%). The live birth rate for those on medication was 30.7% (n=27) compared to those not on medication 33.0% (n=103).

• SMOKING

Female: out of 376, 19 smoked (5.1%) averaging 6.1 per day (Standard Deviation (SD) 4.47). Live birth rate in the smokers was 21.1% (n=4) compared to non-smokers, 30.5% (n=109).

Male: Out of 316 male patients, 44 smoked (13.9%) averaging 8.3 per day (SD 6.9). The live birth rate in smokers was 27.3% (n=12) compared to 32.0% (n=101).

• ALCOHOL

Female: out of 275, 178 drank alcohol (47.5%), averaging 5.8 units per week (SD 5.6). The live birth rate in drinkers was 28.1% (n=50) compared to 36.5% (n=72)

Male: out of 375, 240 drank alcohol (64%), averaging 9.1 units per week (SD 8.2). The live birth rate in drinkers was 33.8% (n=81) compared to 30.4% (n=41).

CONCLUSIONS: The study found that a large number of women are prescribed category C, D or X drugs when attempting ART. The effect these drugs have on the success of ART is unclear. More information is required in order to expand these results and help counsel couples on prescription drug use, smoking and alcohol consumption.

SUPPORT: None.

P-586 Wednesday, October 16, 2019 6:30 AM

DIETARY CADMIUM INTAKE AND FECUNDABILITY IN A NORTH AMERICAN PRECONCEPTION COHORT STUDY. Tommaso Filippini, M.D., a, b, c Sydney K. Willis, M.P.H. a, b, c, Neha Singhal, M.P.H. a, b, c, Katharine L. Rich, Ph.D. a, b, c, Kenneth J. Rothman, Dr.P.H., a, b, c, Marco Vinceti, M.D., Ph.D., a, b, c Lauren A. Wise, Sc.D. a, b, c, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; bBoston University School of Public Health, Boston, MA; cRollins School of Public Health, Emory University School of Medicine, Department of Gynecology and Obstetrics, Atlanta, GA; dRollins School of Public Health, Emory University, Atlanta, GA; eRollins School of Public Health, Department of Epidemiology, Atlanta, GA.

OBJECTIVE: To evaluate the association between dietary cadmium intake (D-Cd) and fecundability. Diet is one of the main sources of cadmium, and D-Cd is often used as indicator of cadmium exposure, particularly in non-smokers.

MATERIALS AND METHODS: Pregnancy Online Study (PRESTO) is a North American prospective preconception cohort of pregnancy planners. At baseline, female participants aged 21-45 years completed a web-based questionnaire on demographic, lifestyle, medical and reproductive factors. Ten months or until reported pregnancy, whichever came first. The analysis was materially by age (<30 vs. ≥30 years), BMI (<30 vs. ≥30 kg/m2), maternal smoking, and couple fecundity, the LIFE Study, Chemosphere. 2012 Jun;87(11):1201-7. https://doi.org/10.1016/j.chemosphere.2012.01.017. Epub 2012 Feb 4. PubMed PMID: 22309709; PubMed Central PMCID: PMC3327819.

SUPPORT: NIH/NICHD grant: R01HD086742.

P-587 Wednesday, October 16, 2019 6:30 AM

ACCURACY OF SELF-REPORTED MENSTRUAL CYCLE CHARACTERISTICS AND INFERTILITY IN A COHORT HIGHLY EXPOSED TO ENDOCRINE-DISRUPTING COMPOUNDS (EDCs). Victoria S. Jiang, MD, a Sarah W. Curtis, BS, a Sabrina A. Gerkowicz, MD, a Jessica B. Spencer, MD, MSc,b Mettrea L. Terrell, MSPh,c Michael F. Nebllett, II, MD, a Michele Marcus, PhD, d Alicia K. Smith, PhD, d Emory University School of Medicine, Department of Gynecology and Obstetrics, Atlanta, GA; bLaney Graduate School, Genetics and Molecular Biology Program, Atlanta, GA; cRollins School of Public Health, Department of Epidemiology, Atlanta, GA.

OBJECTIVE: To determine whether reproductive health outcomes are associated with changes in menstrual function among women within the Michigan Polybrominated Biphenyl (PBB) Registry.

DESIGN: Cross-sectional survey of women in the Michigan PBB Registry. MATERIALS AND METHODS: In 1973, accidental contamination of livestock feed with PBB led to the Michigan Health Department establishing a registry of highly exposed individuals who have been followed for >40 years. Women who were not pregnant, breastfeeding, using hormonal medications, developmentally disabled, diagnosed with cancer, amenorrheic three months, or with prior hysterectomy were recruited into a menstrual function study. 176 women completed a reproductive health survey, obtained daily morning urine samples throughout 4 menstrual cycles, and completed 6 months of daily menstrual cycle diaries. The morning urine samples were analyzed for E13G, Pd3G, and mid-cycle creatinine, and day of luteal transition (DLT). We used a nested mixed linear model to quantify the accuracy of menstrual cycle data and to test for association between endometriosis, infertility, and urinary hormone metabolites.

RESULTS: Women’s self-reported cycle and bleed length correlated accurately with their actual cycle length (p=0.002) and bleed length (p=2.31E-13) from urinary metabolite data. Women with self-reported endometriosis were noted to have higher prevalatory E13G (p=0.001), mid-luteal E13G (p=0.0006), and overall luteal phase E13G (p=0.033) levels. Women with self-reported infertility were noted to have higher mid-luteal E13G (p=0.05), and overall luteal phase E13G (p=0.008) levels.

CONCLUSIONS: Women with self-reported diagnoses of endometriosis and infertility showed statistically significant changes in their menstrual function urinary metabolites. Additionally, this study found that the self-
reported cycle characteristics were positively associated with actual cycle characteristics. Further analyses are required to determine the clinical implications of these menstrual function metabolite changes within this population of women highly exposed to endocrine disrupting compounds.

P-588 Wednesday, October 16, 2019 6:30 AM
IMPACT OF NANOPARTICLES ON MOTILITY OF HUMAN SPERMATOZOA. Hyoeun Kang, MS,a Hyojeong Kwon, MS,b Boyoung Jeon, BS,c Eunjee Lee, MS,d TaiEun Shin, MS,a Jung-Jae Ko, Ph.D.,b Dae Keun Kim, M.D., Ph.D.,c Wojciech Chrzanowski, Ph.D.,d Jae Ho Lee, PhD.e

OBJECTIVE: Nanomaterials, including a large array of nanoparticles are integral components of daily-used products including food, sunscreens, cosmetics and pharmaceuticals. Human and environmental exposure to nanomaterials is commonly occurring, and as the use of nano-enabled products become more widespread, so too will concerns around their safety and impact on human and environmental health. Nanoparticles are reported to be amongst major factors that influence development of various medical conditions including reproductive disorders. But until now, the impact of nanoparticles on sperm motility has not been established. Here we investigate for the first time how nanoparticles affect human sperm motility.

DESIGN: Experimental study with human normal sperm.

MATERIALS AND METHODS: We treated human normal sperm with titanium dioxide (E171) and nanodiamond. Then we performed human sperm motility after incubation with titanium dioxide and nanodiamond particles. Human spermatozoa were incubated with 1 ng, 10 ng, 100 ng and 1000ng of each of the nanoparticle class. Sperm motility profiling was done using computer-aided sperm analysis (CASA) system every 30 min until overnight. We analysis whether nanoparticles were attracted to regions of spermatozoa by electrical microscope. Furthermore, we imaged the surface with electrical microscopy.

RESULTS: Both nanoparticles have shown significantly decreased in sperm motility. Titanium dioxide has been shown 20–30% decrease motility compared with control group. Nanodiamond also reduced 10–20% motility of sperm. In the CASA study, both nanoparticles showed significantly reduction in straight movement pattern compare with control sperm. However, both nanoparticles did not show any significant cytotoxicity to the human sperm up to 1000 ng/ml concentration.

CONCLUSIONS: In this study, we showed that nanogram concentration of nanoparticles decreases motility of human sperm. There is no literature evidence regarding the exposure of human testis and sperm to nanoparticles that are in the blood stream. But these studies suggest that both nanoparticles reduce motility, thus impact negatively on fertilization. Currently titanium dioxide (TiO2) nanoparticles (NPs) are widely used in food, agriculture products, personal care products, cosmetics, sun protection and toothpaste, electronics, and food packaging. Our future research will investigate the mechanism behind the observed effects, because such information would facilitate the production of nanoparticles with increased biosafety.

P-590 Wednesday, October 16, 2019 6:30 AM
BISPHENOL A INDUCES INSULIN RESISTANCE IN SKELETAL MUSCLE BY DOWN-REGULATING THE EXPRESSION OF IRS1 THROUGH ESTRADIOL RECEPTOR. Zhanghong Ke, Doctor,a Binzheng Zheng,b Ph.D.,b 1Fujian Provincial Maternity and Children’s Hospital, Affiliated Hospital of Fujian Medical University, Fuzhou, China; 2Fujian Provincial Maternity and Children’s Hospital, Fuzhou, China.

OBJECTIVE: To investigate the effect of human relevant doses of bisphenol A (BPA), an endocrine disruptor, on insulin resistance and the underlying mechanisms.

DESIGN: Mice were administered with water containing BPA of human relevant doses. C2C12 myocytes were treated with BPA and selective estrogen/androgen receptor down-regulator. Bioinformatic analysis was applied to search for estrogen receptor response element (ERE) in Ir1.

MATERIALS AND METHODS: Mice were administered with water containing BPA of human relevant dose (2.5 μg/L) or higher human relevant dose (25 μg/L) from the day they were born to 8-week-old. The serum levels of fasting glucose and insulin were measured. Differentiated C2C12 myocytes were treated with BPA, and, with or without ICI 182,780 or flutamide. ICI 182,780 and flutamide are selective estrogen and androgen receptor down-regulator. The expression levels of key players in insulin signaling pathway including Atgl, Pnpla3, Dgat1 and Spt, didn’t show significant difference in expression levels between BPA and control groups. Furthermore, key players in lipid metabolism and transportation of skeletal muscle were also measured. Bioinformatic analysis was applied to search for ERE in Ir1.

RESULTS: Mice of 25μg/L group exhibited increased fasting insulin levels and visceral adipose weight compared with control. The expression levels of Ir1 were down-regulated in skeletal muscle of mice from both BPA groups. In contrast, the expression levels of key players in insulin signaling pathway, including Akt2, As160 and Glut4, showed no difference between BPA and control groups. Furthermore, key players in lipid metabolism and transportation of skeletal muscle, including Fatp1, Cd36, Atgl, Pnpa3, Dgat1 and Sp3, didn’t show significant difference in expression levels between groups, either. In conclusion, insulin resistance in skeletal muscle was also measured. Bioinformatic analysis was applied to search for ERE in Ir1.

RESULTS: Mice of 25μg/L group exhibited increased fasting insulin levels and visceral adipose weight compared with control. The expression levels of Ir1 were down-regulated in skeletal muscle of mice from both BPA groups. In contrast, the expression levels of key players in insulin signaling pathway, including Akt2, As160 and Glut4, showed no difference between BPA and control groups. Furthermore, key players in lipid metabolism and transportation of skeletal muscle, including Fatp1, Cd36, Atgl, Pnpa3, Dgat1 and Sp3, didn’t show significant difference in expression levels between groups, either. In conclusion, insulin resistance in skeletal muscle was also measured. Bioinformatic analysis was applied to search for ERE in Ir1.

CONCLUSIONS: Human relevant exposure of BPA induces insulin resistance in young mice. BPA may induce insulin resistance in skeletal muscle by down-regulating the expression of Ir1 through estrogen receptor.
OBJECTIVE: To determine whether the menstrual pictogram super absorbent polymer containing version 3 (MP SAP-c v3) and uterine fibroid daily bleeding diary (UF-DBD) demonstrate reliability, validity, and sensitivity to change and can replace the Alkaline Hematin (AH) method for assessment of efficacy on UF clinical trials.

DESIGN: Post-hoc analysis of vilaprisan phase 2 (ASTEROID 1 and 2) clinical study data in terms of psychometric properties, missing data, and comparability of methods.

MATERIALS AND METHODS: ASTEROID 1 (N=623) study data collected by MP SAP-c v3, UF-DBD, and the AH method were used to assess psychometric properties of the MP SAP-c v3 and UF-DBD, and degree of comparability and extent of missing data with the AH method. Daily scores aggregated over 28 days (monthly) and during bleeding episodes at randomization (RND) and end of treatment (EoT) were analyzed. ASTEROID 2 (N=228) study data were used to confirm ASTEROID 1 findings as appropriate.

RESULTS: ASTEROID 1 data analysis showed that the response distributions in MP SAP-c v3 and UF-DBD appropriately reflected the natural cycle of menstrual bleeding and treatment-related changes. The full range of responses were used to assess bleeding severity. Based on bleeding severity defined by the AH method and overall patient global impression of severity, differences in MP SAP-c v3 and UF-DBD scores between low- and high-severity groups were large and significant (p<0.001). Strong Spearman’s rank correlations were observed between MP SAP-c v3 monthly sum scores and those of both AH (r=0.72 and 0.97) and UF-DBD (r=0.56 and 0.89) at RND and EoT, respectively. Moderate to strong correlations were observed between UF-DBD and AH monthly sum scores at RND (r=0.44) and EoT (r=0.84). Test-retest reliability and sensitivity to changes were also demonstrated. Analyses of ASTEROID 2 data largely confirmed findings from ASTEROID 1.

In ASTEROID 1, details of more sanitary protection items were provided using the MP SAP-c v3 than with the AH method. Fewer days with missing data were observed with the MP SAP-c v3 and UF-DBD than with AH; over the course of the study the mean absolute (relative) number of days with missing values per patient was 16.1 (11.8%) for MP SAP-c v3, 15.5 (11.6%) for UF-DBD and 18.1 (15.9%) for AH.

Both instruments showed good agreement with the AH method in assessments of study eligibility (MP SAP-c v3 and UF-DBD) and treatment response (MP SAP-c v3 and UF-DBD). The positive predictive value (PPV) of MP SAP-c v3 to distinguish women with heavy menstrual bleeding at baseline vs. the AH method (reference standard) was 75.8%. The PPVs of MP SAP-c v3 and UF-DBD for reaching amenorrhea were 100.0% and 99.3%, respectively.

CONCLUSIONS: The MP SAP-c v3 and UF-DBD are valid, reliable, and sensitive measures of menstrual bleeding severity in the UF population. Use of both instruments is more convenient, less burdensome, and associated with greater compliance than the AH method. Coupled with positive results from cognitive interviews and Bland-Altman analyses, these results support the use of MP SAP-c v3 and UF-DBD in UF clinical studies instead of the AH method.

SUPPORT: This study was funded by Bayer AG. Medical writing support provided by Huntsworth Health was funded by Bayer.


SUPPORT: This study was funded by Bayer AG. Medical writing support provided by Huntsworth Health was funded by Bayer.

P-592 Wednesday, October 16, 2019 6:30 AM

VALIDATION OF A MENSTRUAL PICTOGRAM AND A DAILY BLEEDING DIARY AS ALTERNATIVES TO THE ALKALINE HEMATIN (AH) METHOD FOR ASSESSMENT OF EFFICACY OF TREATMENTS FOR UTERINE FIBROIDS (UF) IN CLINICAL STUDIES.

Claudia Haberland, PhD, MSc, Anna Filonenko, PhD, Christian Seitz, MD, Matthias Bömer, Dr, Christoph Gerlinger, PhD, Helen Ann Doll, DPhil, Dorothée Wessiepe, MSc Bayer AG, Berlin, Germany.

OBJECTIVE: To determine whether the menstrual pictogram super absorbent polymer containing version 3 (MP SAP-c v3) and uterine fibroid daily bleeding diary (UF-DBD) demonstrate reliability, validity, and sensitivity to change and can replace the Alkaline Hematin (AH) method for assessment of efficacy on UF clinical trials.

DESIGN: A phenome-wide association study (PheWAS) tests disease diagenes across a patient’s clinical record for association with a specific outcome. We conducted a PheWAS of uterine fibroids utilizing diagnoses from electronic health records (EHRs) of patients at Vanderbilt University Medical Center (VUMC) in Nashville, TN.

MATERIALS AND METHODS: Fibroid cases and controls were identified using a previously validated phenotyping algorithm. We conducted PheWAS analyses with logistic regression models adjusted for body mass index.
P-594 Wednesday, October 16, 2019 6:30 AM

PATIENT-REPORTED OUTCOMES OF A PHASE 1 CLINICAL TRIAL OF INJECTABLE COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (EN3835) FOR TREATMENT OF UTERINE FIBROIDS. Bhuchita Singh, M.D., MPH, MS.a Irene Trueheart, RN, BSN, MA,b Holly Sims, RN, BSN,b Jean-Marie Soma, MS.c Rosina Dixon, M.D., M.P.H., Ph.D, Ms. Gayane Yenokyan, Ph.D,b James Segars, M.D.c Johns Hopkins School of Medicine, Baltimore, MD; b BioSpecifics Technologies Corporation, Lynbrook, NY; c Duke Medicine, Durham, NC.

OBJECTIVE: Uterine fibroids may cause a significant reduction in quality of life for affected women. Since fibroids contain an excessive extracellular matrix, we injected fibroids with purified collagenase Clostridium histolyticum (EN3835) under transvaginal ultrasound guidance in women scheduled for fibroid removal. Here we report the impact of the treatment on the fibroid-related symptoms following injection with study drug and before fibroid removal.

DESIGN: Phase 1 clinical trial.

MATERIALS AND METHODS: Changes in subjects’ quality of life and fibroid-related symptoms were assessed at baseline and following injection of study drug. Standardized-validated questionnaires were used to assess the patient-reported outcomes of quality of life and fibroid-associated symptoms. The McGill Pain questionnaire, the Uterine Fibroid Symptom Health-Related Quality of Life (UFS-QoL), and the Visual Analogue Scale (VAS) for pain were utilized. Study subjects were divided into 2 groups. Group 1 had injection followed by surgery at 2-3 days, and subjects in Group 2 had injection followed by surgical removal of fibroids 60-90 days later. Therefore, Group 1 subjects (n=3) completed the post intervention questionnaire at 24-48 hours post-study drug injection. Group 2 subjects (n=9) completed the post intervention questionnaires at 4-8 days and 60-90 days post study drug injection. To compare the changes in patient-reported outcomes, generalized linear mixed effects models with random intercepts for the person and paired t-tests were used; p<0.05 was considered significant.

RESULTS: No clinically significant adverse events related to the study drug were reported. Of note, all subjects reported a decrease in fibroid-related pain on the McGill Pain Questionnaire following study drug injection. Specifically, for Group 1 there was a trend (p=0.195) and for Group 2, the general trend was a decrease in symptom severity both at 4-8 days and 60-90 days post injection. UFS-QoL Part 2: 5 out of 9 subjects reported an improvement in health-related quality of life, for Group 2, 7 out of 9 subjects reported an improvement in health-related quality of life 4-8 days post injection, and 5 of these subjects sustained the increasing trend at 60-90 days post study drug injection.

CONCLUSIONS: Injection of Collagenase Clostridium histolyticum into fibroids was well tolerated by all study participants. Interestingly, fibroid-related pain was reduced and there was a trend of decreasing fibroid-related symptoms improving quality of life. (Clinical Trials.gov number: NCT0288948).

SUPPORT: BioSpecifics Technologies Corporation.
TO STUDY THE EFFECT OF ULIPRISTAL ACETATE (UPA) TREATMENT IN INFERTILE PATIENTS WITH SINGLE TYPE 2-3 FIGO MYOMAS UNDERGOING IVF. Simone Ferrero, MD, PhD.a, Carolina Scala, MD,b Fabio Barra, MD,a* Umberto Leone Roberti Maggiore, MD, PhD.c DINOOGMI, University of Genova, Genova, Italy; bIstituto G. Gaslini, Genova, Italy; aDepartment of Gynecologic Oncology, IRCCS National Cancer Institute, Milan, Italy.

OBJECTIVE: To study the effect of ulipristal acetate (UPA) treatment in infertile patients with single type 2-3 FIGO myomas undergoing IVF.

DESIGN: Prospective study.

MATERIALS AND METHODS: This study included infertile women of reproductive age who had single type 2 or 3 FIGO myoma and had to undergo IVF. After ovarian stimulation and oocyte retrieval were performed before treating the uterine myomas. All patients underwent transvaginal ultrasonography and hysteroscopy before and after 3-month treatment with UPA (5 mg/day). The largest diameter and volume of uterine myomas (estimated by virtual organ computer-aided analysis, VOCAL) were recorded before and after UPA treatment. Hysteroscopy was performed after UPA treatment to assess if the myoma distorted the uterine cavity. Patients with myomas that were not distorting the uterine cavity underwent embryo transfer; the other patients underwent hysteroscopic or laparoscopic myomectomy. Pregnancy rate was defined as fetal heart beat observed by transvaginal ultrasonography.

RESULTS: 46 women were included in the study. The mean age (±SD) of the study population was 35.6 (±3.8) years. 25 patients had type 2 FIGO myomas and 21 had type 3 FIGO myomas. The mean (±3.8) diameter of the myoma was (±1.7) cm. Three-month UPA treatment was completed by 43 patients (93.5%; 95% C.I. 82.1%-98.6%). After UPA treatment, hysteroscopy showed that the percentage of myomas that were not distorting the uterine cavity was significantly higher in patients with type 3 myomas (n = 9; 42.9%; 95% C.I. 21.8%-66.0%) than in those with type 2 myomas (n = 3; 12%; 95% C.I., 2.5%-31.2%; p = 0.018). These patients underwent frozen-thawed embryo transfer. All patients with myomas distorting the uterine cavity after UPA treatment underwent myomectomy. There was no significant difference in the pregnancy rate per embryo transfer in patients who underwent myomectomy (12/4; 33.3%; 95% C.I. 9.9%-65.1%) and did not undergo surgery (4/12; 35.3%; 95% C.I. 19.7%-53.5%; p = 0.902). The patients underwent a median of two embryo transfer (range, 1-4). There was no significant difference in the pregnancy rate per patient in women who underwent myomectomy (18/34; 52.9%; 95% C.I. 35.1%-70.2%) and in those who did not undergo surgery (7/12; 58.3%; 95% C.I. 27.7%-84.8%; p = 0.104).

CONCLUSIONS: In patients with FIGO type 3 myomas, 3-month treatment with UPA may allow to avoid myomectomy and to immediately perform embryo transfer.
STUDY.

Robert Setton, MD, a Joanna Gao, BS, b Lilli D. Zimmerman, MD, a Zev Rosenwaks, M.D., a Steven Spandorfer, M.D. a aThe Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; bWeill Cornell Medicine, New York, NY.

OBJECTIVE: A recent ASRM guideline highlights that there is insufficient evidence to determine whether non-cavity distorting intramural myomas is associated with a decreased likelihood of achieving pregnancy in patients undergoing fertility treatment. We sought to determine if the presence of non-cavity distorting intramural myomas has an impact on pregnancy outcomes in an ideal study group of patients: patients undergoing either frozen-thawed embryo transfer (FET) of normal euploid embryos or elective single embryo transfer of donor oocytes.

DESIGN: Prospective cohort study, interval analysis.

MATERIALS AND METHODS: Patients who underwent cycles with either autologous FET after preimplantation genetic testing for aneuploidy (PGT-A) or donor egg recipient (DER) cycles were included in this prospective study which began enrollment in September 2018. Patients were stratified based on whether myomas were detected (group A) or no myomas were detected (group B) on pelvic ultrasonography at the time of study enrollment during the patient’s treatment cycle. The FIGO classification system was used and the distance from the endometrial lining to the closest myoma was recorded. The primary outcome was positive pregnancy rate. The secondary outcomes were ongoing pregnancy rate and miscarriage rate. Statistical analysis included Mann-Whitney U test and chi-square test. P<0.05 was deemed statistically significant.

RESULTS: Currently, 53 patients enrolled in the study have completed their ART cycles. 15/53 (28.3%) had a non-cavity distorting intramural myoma. The patients who had myomas were older and had a higher BMI. The peak endometrial thickness was similar between the two groups. Of the patients who had myomas 11/15 conceived, and of the patients without myomas 30/38 conceived. There was no difference in the primary outcome of positive pregnancy rate. There was also no difference for the secondary outcomes of ongoing pregnancy rates and miscarriage rates between the two groups.

CONCLUSIONS: An interval analysis of our ongoing prospective study suggests that non-cavity distorting myomas do not affect positive pregnancy rates, ongoing pregnancy rates, or miscarriage rates in a good-prognosis population with patients undergoing either autologous FET with PGT-A or donor egg recipient cycles. However, this study is ongoing and will continue to evaluate this further.


SUPPORT: None.

FIBROIDS - BASIC

P-600 Wednesday, October 16, 2019 6:30 AM

EFFECT OF SIMVASTATIN ON INTEGRIN-β1 AND ITS DOWNSTREAM MEDIATORS IN HUMAN LEIOMYOMA CELLS. Sadia Afrin, PhD, Md, Soriful Islam, PhD, Szu-Chi Su, MS, Mostafa A. Borahay, MD, PhD. Johns Hopkins University, School of Medicine, Baltimore, MD.

OBJECTIVE: Integrins, extracellular matrix (ECM) receptors, are key mediators of out-in and in-out signaling between a cell and its ECM environment and neighboring cells. Leiomyoma cells were shown to overexpress integrin-β1, which on activation, induces FAK auto-phosphorylation of and activates its downstream signaling including ERK, p38 MAPK, PI3K and cyclin D1. In addition, phosphorylated FAK leads to activation of AKAPl3 and RhoA which further recruits ROCK and MLCK activation. Activation of this cascade promotes leiomyoma development by increasing proliferation, cell spreading and ECM deposition. Therefore, integrin-β1 signaling may serve as a therapeutic target for uterine leiomyomata. Our objectives in this study are to examine the effect of simvastatin on integrin-β1 expression and its downstream mediators in human leiomyomata cells.

DESIGN: In vitro laboratory study using human leiomyomata cells.

MATERIALS AND METHODS: Human leiomyoma (hULM) cells were treated with simvastatin (0.001 to 10 μM) for 24 to 72 hours. Anti-proliferative effect of simvastatin was determined by MIT assay. The effect of simvastatin on the expression of integrin-β1 and its downstream mediators p-FAK, AKAPl3 and RhoA was examined using western blotting after 48-hour treatment. Furthermore, the expression of cyclin D1, a downstream marker of FAK signaling, was evaluated. Student’s t-test was used to determine statistically significant differences (P<0.05).

RESULTS: Simvastatin exhibited significant anti-proliferative effects on leiomyoma cells in a dose- and time-dependent manner. At 48 hours, 85% and 51% proliferation inhibition were noted at 0.01 to 1 μM simvastatin, respectively. Simvastatin treatment at 1 μM for 48 hours was associated with 48% decrease in the expression of integrin-β1. The ratio of phosphorylated to total FAK (p-FAK/total FAK ratio) was reduced by 28% at 1 μM of simvastatin and there was a dose-dependent pattern. At 1 and 10 μM of simvastatin, the expression of AKAPl3 was suppressed by 56% to 34% whereas the expression of ROCK1 and MLCK were decreased by 65% to 43% and 63% to 57%, respectively. Additionally, the expression of cyclin D1 demonstrated a 46% to 36% reduction at 1 and 10 μM simvastatin.

CONCLUSIONS: These encouraging results indicate that the simvastatin treatment of uterine leiomyoma might have a significant therapeutic impact on uterine leiomyoma growth through modulating the ECM-integrin-β1 interaction in leiomyoma. Down-regulated p-FAK/FAK, AKAPl3, ROCK1 and MLCK signaling molecules after simvastatin treatment may correct the mechanical signaling, already disordered in leiomyoma. Suppresing integrin-β1 and its downstream mediators after simvastatin treatment may serve as a promising approach for uterine leiomyomata treatment.

SUPPORT: Supported by NIH grant 1R01HD094380-01.

Group A: Non-cavity distorting myoma (n=15) Group B: No non-cavity distorting myoma (n=38) p

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A</th>
<th>Group B</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>41.7 ± 3.2</td>
<td>37.3 ± 5.1</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.5 ± 7.9</td>
<td>22.2 ± 3.3</td>
<td>0.014*</td>
</tr>
<tr>
<td>Gravidity</td>
<td>1.5 ± 1.8</td>
<td>1.5 ± 1.3</td>
<td>0.66</td>
</tr>
<tr>
<td>Parity</td>
<td>0.33 ± 0.05</td>
<td>0.53 ± 0.8</td>
<td>0.53</td>
</tr>
<tr>
<td>Peak Endometrial Stripe (mm)</td>
<td>10.6 ± 2.4</td>
<td>9.4 ± 2.1</td>
<td>0.37</td>
</tr>
<tr>
<td>Positive Pregnancy Rate</td>
<td>0.73</td>
<td>0.79</td>
<td>0.72</td>
</tr>
<tr>
<td>Ongoing Pregnancy Rate</td>
<td>0.67</td>
<td>0.63</td>
<td>1.00</td>
</tr>
<tr>
<td>Miscarriage Rate</td>
<td>0.16</td>
<td>0.16</td>
<td>0.26</td>
</tr>
</tbody>
</table>
SIMVASTATIN INHIBITS RhoA ACTIVATION, COLLAGEN EXPRESSION AND GEL CONTRACTION IN HUMAN LEIOMYOMA CELLS. Sadia Afrin, PhD, Mostafa A. Borahay, MD, PhD Johns Hopkins University, School of Medicine, Baltimore, MD.

OBJECTIVE: There is a strong evidence that altered vascular homeostasis and signaling play a key role in uterine leiomyoma development and growth. Mechanical stress from disordered extracellular matrix (ECM) can initiate the activation of RhoA and its downstream signaling pathways. In turn, activated RhoA contributes to the production of collagen type 1, alters the viscoelastic properties of tissue and contribute to increased ECM stiffness, a key feature of leiomyomas. Therefore, mechanical signaling pathway seems to be a conceivable pharmacological target in leiomyoma. The objective of this study is to examine the effect of simvastatin on: i) RhoA activation; ii) collagen type 1 expression; iii) gel contraction; and iv) cell migration in human leiomyoma cells.

DESIGN: In vitro laboratory study using immortalized human leiomyoma cells.

MATERIALS AND METHODS: Human leiomyoma (huLM) cells were treated with simvastatin (0.001 to 10 μM) for 48 hours. RhoA activation was measured using the Rhokin RBD Agarose beads to selectively isolate and pull-down the active (GTP-bound) form of RhoA, to be quantified by western blot. Simvastatin effect on collagen gel contraction was measured by culturing the leiomyoma cells in three-dimensional (3D) condition. Photographs were taken at the end of treatment. Simvastatin effect on cells migration were observed by wound closure assay and the wound areas were measured by Image J software. Western blot analysis was performed for examining the effect of simvastatin on collagen type 1 expression. Student’s t-test was used to determine statistically significant differences (P<0.05).

RESULTS: Simvastatin significantly decreased RhoA activation (active/total RhoA ratio) at 1 μM by 33% compared to control. Furthermore, simvastatin suppressed collagen type 1 expression by 58% at 10 μM. In addition, simvastatin inhibited 3D collagen gel contraction at low concentrations as 0.001 μM with the higher concentrations of simvastatin (1 and 10 μM) inducing maximal gel relaxations, similar to collagen gel without cells. Finally, simvastatin decreases the migration ability of leiomyoma cells up to 43% compared to control cells.

CONCLUSIONS: Simvastatin has significant attenuating effects on RhoA activation, a key mediator of leiomyoma mechanical signaling that contributes to its development and growth. Also, simvastatin inhibits the expression of type 1 collagen. Additionally, the remarkable gel contraction noted in leiomyoma 3D culture was inhibited by simvastatin, which also reduced the migration ability of leiomyoma cells. These findings indicate the therapeutic efficacy of simvastatin for the treatment of uterine leiomyoma by targeting its disordered mechanical signaling.

SUPPORT. Supported by NIH grant 1R01HD094380-01.

EXPRESSIONS OF VASCULAR ENDOTHELIAL GROWTH FACTOR AND ANGIopoietin-1 IN MED12 MUTATED AND WILD-TYPE UTERINE LEIOMYOMAS. Ryoko Asano, MD, PhD, Mikiko Asai-Sato, MD, PhD, Naoki Naito, MD, PhD, Koichi Nagai, MD, Yohei Miyagi, MD, PhD, Etsuko Miyagi, MD, PhD, Yoko Shichino, MD, PhD, Hiroshi Hori, MD, PhD, Yuko Kato, MD, PhD, and Yoichi Ueno, MD, PhD.

OBJECTIVE: To investigate whether the expressions of vascular endothelial growth factor (VEGF) and angiopoietin-1 (Ang1) in uterine leiomyomas are influenced by the presence MED12 gene mutation. MED12 gene mutation is the most frequent cause of uterine leiomyomas and MED12 wild-type leiomyomas are larger, produce more erythropoietin (EPO), and have mature vessels compared to mutated-type. MED12 mutated and wild-type leiomyomas may also have differences in the expressions of factors effecting tumor angiogenesis that support tumor growth.

DESIGN: Retrospective study of clinical data and gene mutation.

MATERIALS AND METHODS: This study was approved by the Ethical Committee of Yokohama City University and written informed consent was obtained from all subjects. The leiomyoma tissue samples and clinical data of over a hundred of uterine leiomyoma patients who underwent surgery in our hospital were collected. The mutations in MED12 exon 2, the mutation hot-spot of MED12 gene, were analyzed by Sanger sequencing. The mRNA expression levels of VEGF and Ang1 of leiomyoma tissue were measured by qRT-PCR, gene expression in real-time reaction. The relationship between MED12 gene mutation statuses, mRNA expression levels, and clinical backgrounds were analyzed. Mann-Whitney U test or χ2 test for trend were performed for statistical analyses and P-values of less than 0.05 were considered statistically significant.

RESULTS: Fifty-two MED12 mutated and 56 wild-type leiomyomas were included in this study. The MED12 wild-type leiomyomas were confirmed to have significantly larger diameter compared to MED12 mutated leiomyomas. Larger leiomyomas had the trend to be MED12 wild-type (P = 0.004). VEGF mRNA was 1.3-fold higher in MED12 mutated leiomyomas (P = 0.024); however, Ang1 mRNA and other clinical backgrounds did not have difference between MED12 mutated and wild-type leiomyomas.

CONCLUSIONS: Contrary to our expectation, MED12 mutated leiomyomas expressed higher VEGF mRNA levels. We speculate that MED12 wild-type and mutated leiomyomas grow in different mechanisms including angiogenesis and vessel maturation. The growth of MED12 mutated leiomyomas may be supported by the angiogenetic effect of VEGF rather than EPO and MED12 wild-type leiomyomas may have an advantage in increasing tumor size by reinforced vessel maturation due to EPO.

MULTIOMIC ANALYSIS OF UTERINE LEIOMYOMATOSIS AND RECURRENT CANCER PATIENTS. Thomas Conrads, PhD, Christopher Tarney, MD, Nicholas Bateman, PhD, Anthony R. Soltis, PhD, Brian L. Hood, PhD, Clifton L. Dalgaard, PhD, Matthew Wilkerson, PhD, Kathleen M. Darcy, PhD, Yosunni Casablanca, MD, Ayman Al-Hendy, MD PhD, James Segars, MD, George L. Maxwell, MD, Inova Schar Cancer Institute, Annandale, VA; 2Gynecologic Cancer Center of Excellence, Muthra Cancer Center Research Program, Uniformed Services University of the Health Science, Henry M Jackson FDN, Bethesda, MD; 3Gynecologic Cancer Center of Excellence, Muthra Cancer Center Research Program, Uniformed Services University of the Health Science, Henry M Jackson FDN, Ammandale, VA; 4The American Genome Center, Uniformed Services University, Bethesda, MD; 5University of Illinois at Chicago, Chicago, IL; Johns Hopkins University, School of Medicine, Baltimore, MD; 6Department of Obstetrics and Gynecology, Inova Fairfax Hospital, Falls Church, VA.

OBJECTIVE: Mutation in the fumarate hydratase (FH) gene causes hereditary leiomyomatosis and renal cell cancer (HLRCC). Impaired FH activity leads to accumulation of fumarate resulting in widespread post-translational modifications, such as succinated cysteinyl residues. A comprehensive multi-omics analysis was conducted to identify proteogenomic determinants underlying risk of developing leiomyomas in HLRCC patients.

DESIGN: We performed multi-omics analysis of uterine leiomyomas (ULMs) from HLRCC patients to decipher novel mechanistic insights for improved management of ULMs in HLRCC patients.

MATERIALS AND METHODS: ULMs from HLRCC (n = 17) and non-syndromic (n = 12) patients were obtained under IRB consent from a single institution. Tissues were processed for genomic DNA and RNA to support whole genome sequencing (WGS) and total RNA-seq analysis (Illumina HiSeq X/3000), as well as for quantitative proteomics using a comprehensive mass spectrometry-based approach. Proteomic database searches included variable modifications for 2-succinyl-cystine (2SC) residues. Differential expression and functional integrative analyses were performed using commercial and in-house bioinformatic pipelines.

RESULTS: WGS analyses revealed 16 of 17 HLRCC patients harbored recurrent mutations, insertion, or deletion events fumarate hydratase (FH), whereas 8 of 12 non-syndromic ULM cases exhibited mutations in the mediator complex subunit 12 (MED12) gene. Differential analyses identified 504 proteins (LIMMA p < 0.05, LogFC ≥ 0.5) and 1022 genes (edgeR p < 0.05) as significantly altered between HLRCC and non-syndromic ULMs, 51 of which were co-significant and exhibited high quantitative correlation trends (Spearman = 0.866). Pathway analysis suggested marked alteration of mitochondrial activity in HLRCC versus non-syndromic ULMs as reflected by increased expression of electron transport and ATP synthase proteins. Comparison with historic gene expression studies (Vanharanta S, 2006) validated 36 transcripts and 16 genes as significantly altered between HLRCC and non-syndromic ULMs. Furthermore, 358 of 364 FH-modified peptides corresponding to 239 protein targets were identified, 47 of which have been
previously described as being modified by 2SC in FH-mutated cancer cell lines (Ternette N, 2013 and Yang M, 2014). Pathway analysis of 2SC-modified proteins revealed altered regulation of cytoskeletal organization, cell death and cell migration signaling in HLRC ULMs. Quantitative analyses revealed 63 unique 2SC-labeled peptides were 2.45 (± 0.03)-fold elevated in HLRC versus non-syndromic patients. These candidates included a peptide modified on C106 of Parkin 7 (PARK7), a potent cellular deglycase and sensor of oxidative stress.

CONCLUSIONS: Multi-omic revealed protein alterations and post-translational modifications impacting mitochondrial and oxidative stress signaling in HLRC versus non-syndromic ULMs. These findings define proteogenomic alterations that may better support the treatment of ULMs in HLRC patients.

P-604 Wednesday, October 16, 2019 6:30 AM

REPROGRAMMING OF ESTROGEN SIGNALING BY MLL1 LINKS DEVELOPMENTAL EXPOSURE TO THE RISK OF UTERINE FIBROIDS. Mohamed Ali B Pharm, MSc, Ayman Al-Hendy, MD PhD, Qiwei Yang, PhD.

University of Illinois at Chicago, Chicago, IL; University of Illinois College of Medicine, Chicago, IL; University of Illinois at Chicago (UIC), Chicago, IL.

OBJECTIVE: Environmental exposure to endocrine disrupting chemicals (EDCs) reprograms developmental organs, which leads to their predisposition to tumorigenesis later in life. Uterine fibroids (UFs) are monoclonal tumors arising from aberrant stem cells (SCs) in the myometrium (MM). We have previously demonstrated that MMSCs are the targets for epigenome reprogramming, and the expression of estrogen responsive genes (ERGs) was altered in response to early life exposure to EDCs. However, the mechanism responsible for initiation of this persistent EDCs-induced epigenetic alteration is unknown.

DESIGN: Laboratory research studies using Eker rat fibroid model MM tissues as well as MMSCs.

MATERIALS AND METHODS: Female newborn rats were treated S.C. with vehicle (VEH) or 10 μg/kg of diethylstilbestrol (DES-a tool compound of environmental EDCs) on postnatal days 10-12, a key period of uterine development. MMSCs were isolated from 5 month adult MM tissue (N=5 for each group) using Stro-1 and CD44 surface markers. To determine the role of MLL1 for changes in H3K4me3 in response to DES, knockdown (KD) of Tasp1 (Taspl) was performed using 3 lentiviral particles. To identify targets of epigenomic reprogramming in MMSCs, whole genome RNA-sequencing and ChIP-sequencing (using H3K4me3 antibody) was performed in DES- and VEH-MMSCs. Protein and gene expressions have been measured using Western blot (WB), immunofluorescence (IF) and qRT-PCR. Prime-PCR array of estrogen receptor (ER) signaling has been used. Ingenuity Pathway Analysis (IPA) software was used.

RESULTS: Our previous findings showed that DES exposure increased the expression of ERGs via epigenetic active marker H3K4me3. In this study, IPA analysis of RNA-seq data demonstrated that β-estradiol and ESR1 upstream regulators were highly activated, which was tightly correlated to the diseases of endocrine and reproductive systems . Also, ER signaling involving 47 molecules was activated in DES- MMSCs. By WB and IF analyses, the expression levels of H3K4me3 and activated form of MLL1 were increased in DES- vs. VEH-MMSCs. To identify that MLL1 is the methyltransferase responsible for H3K4me3 mediated reprogramming, we inactivated MLL1 by KD of the Tasp1 protease, which is required to generate the C- and N-terminal fragments that form the active MLL1 heterodimer. WB demonstrated KD of Tasp1 by 90% vs. scramble particle (P<0.05). Taspl KD abrogated the increase in expression of H3K4me3-reprogrammed genes Esr1, Prg3, Cdx2, Cxcl12, Ar, and Tgm2 in DES-MMSCs (P<0.05). To determine the additional estrogen pathway related molecules, which can be altered by MLL1-1, Prime-PCR array of ER signaling was performed in Taspl KD and scramble DES-MMSCs. The data showed that the c-terminal fragment from MLL1 cleaved by Taspl is responsible for regulating ER signaling via direct and indirect epigenetic mechanism.

CONCLUSIONS: Our data demonstrate novel findings that MLL1 activation is required for H3K4me3 regulated ER expression that are vulnerable to disruption by environmental exposures. Taspl KD reverses the DES exposure-induced ER reprogramming and modulates the ER signaling.


SUPPORT: NIH grants: RO1 ES028615, U54 MD070602.

P-605 Wednesday, October 16, 2019 6:30 AM

SINGLE CELL RNASEQ ANALYSES OF UTERINE FIBROIDS AND FIBROID-FREE MYOMETRIA REVEAL PREVIOUSLY UNIDENTIFIED CELL TYPE AND STATE. Waxin Wang, PhD, candidate, Aymana Mas, PhD, Javier Monleón, MD, Stephen Quake, DPhil, Carlos Simon, MD, PhD. Stanford University, Stanford, CA; Igenomix Foundation, Valencia, Spain; Servicio de Ginecologia, Hospital Universitario y Politécnico La Fe, Valencia, Spain; Stanford University; Chanzucker Biohub, Stanford; San Francisco, CA; University of Valencia; Igenomix Foundation-INCLIVA, Valencia, Spain.

OBJECTIVE: Whole tissue studies of uterine fibroids provided information on transcriptomic and genomic signatures of the tumor, but were limited in providing mechanistic and therapeutic insights due to the undefined intra- and inter-tumor heterogeneity. We performed single-cell RNA-seq analyses on uterine fibroids (UF) and fibroid-free myometria (UM) at both expression and mutation level to better understand the molecular and cellular origin of the tumor and to identify targets for less invasive treatments.

DESIGN: Single cell RNAseq analyses on both expression and mutation level were performed on 5582 single cells from UF and matched UM from 6 patients with UF diagnosed, as well as UM from patients with no UF diagnosed.

MATERIALS AND METHODS: UF and UM were dissected after hysterectomy and dissociated separately into single cell suspension. Single cells were index- sorted into 384 well plates containing lysis buffer and ERCC. Single-length RNA was reverse transcribed and amplified (23 cycles) following an adapted SmartSeq2 protocol. Dual-indexed cDNA libraries were sequenced on a NovaSeq to ~1e06 reads/cell. Mutations were called using an adapted GATK pipeline. Downstream analyses such as quality control, dimension reduction, and differential expression were performed using custom R scripts. Cell type and state validation was performed via RNA FISH.

RESULTS: UF and UM consist of cell types and states that are more complex than previously known. While both are composed of the primary hierarchy of smooth muscle cells, fibroblasts, blood vascular endothelia, and immune cells, in UF we identified previously unreported lymphatic vascular endothelia as well as further heterogeneity in fibroblasts and immune cells that does not exist in UM. For UM we report a previously uncharacterized ion-responding cell state. In addition, we observe an overall inflammatory ion-responding cell state. In addition, we observe an overall inflammatory

CONCLUSIONS: Our comprehensive single cell delineation of the cellular hierarchy of UF and UM provides previously unidentified cell type and state for both. The difference in the cellular hierarchy between the two and the differentially expressed genes in cell types that are common to both provide cellular and molecular targets for less invasive treatment for the tumor.

**P-606** Wednesday, October 16, 2019 6:30 AM

**VITAMIN D3 AND ITS ANALOGUE PARICALCITOL REVERSE DNA DAMAGE IN HUMAN UTERINE FIBROID STEM CELLS: MECHANISM FOR POTENTIAL PREVENTIVE THERAPY.** Mohamed Ali B Pharm, M.Sc., Laurens Prusinski Fernung, PhD, Ayman Al-Hendy, MD, PhD, Qiwei Yang, PhD.

*University of Illinois at Chicago, Chicago, IL; *Medical College of Georgia at Augusta University, Augusta, GA.

**OBJECTIVE:** The prevailing model for Uterine Fibroids (UFs) pathogenesis invokes the genetic transformation of a single myometrial stem cell (MMSC) into a tumor-initiating cell (UFSC) that seeds and sustains clonal tumor growth. UFs are known to have higher prevalence in African American (AA) women, which is related in part to their vitamin D deficiency, yet its exact preventive mechanism of action has not been fully revealed yet. Growing body of evidence showed chemopreventive effect of vitamin D. We have recently demonstrated increased DNA repair defect in UFSCs compared to MMSCs. Collectively, we hypothesize that vitamin D3 or its potent analogues, through reparation of an impaired DNA damage response, will provide therapeutic benefits for UFs.

**DESIGN:** Laboratory research studies using Stro-1+/CD44+ MMSCs and UFSCs.

**MATERIALS AND METHODS:** Surgically removed fresh human UF and adjacent MM tissues were collected from two AA patients, and subjected to MM and UFSC isolation using dual Stro-1 and CD44 surface markers. Human UFSCs were treated with concentration ranges (10 nM-1000 nM) of 1, 25 dihydroxyvitamin D3 and its three analogues (Paricalcitol, Doxercalciferol and Eocalcitol). The growth inhibitory effect was determined by MTT assay after 24, 48, and 72 hr. To determine the role of vitamin D and Paricalcitol on DNA damage repair system, UF SCs from 2 AA patients were treated with 100 nM of 1, 25 dihydroxyvitamin D3 or Paricalcitol for 3 days. Total RNA was extracted and DNA damage signaling pathway was examined using Prime-PCR array including 84 genes. The expression levels of 6 DNA double strand breaks repair genes including BRCA1, CHECK1, RAD50, RAD51, NBS1 and MRE11 were validated using RT-qPCR. In addition, protein lysates were extracted from treated and untreated cells and expression levels of DNA damage marker γH2AX as well as RAD51, NBS1 and MRE11 were measured by Western Blot (WB). Unpaired Student t-test was used to measure statistical significance. (P<0.05) was considered significant.

**RESULTS:** Using MTT assay, Vitamin D3 and its analogues treatment showed a potent significant anti-proliferative effect on human UFSCs in a concentration and time dependent manner (P<0.05). Using Prime-PCR array of DNA damage signaling, Vitamin D induced upregulation of 67 DNA repair genes while seven were downregulated and one was unchanged. Paricalcitol showed similar results by inducing the expression of several DNA related genes. Using RT-qPCR, expression of BRCA1, CHECK1, RAD50, RAD51, NBS1, and MRE11 were validated in response to Vitamin D3 and paricalcitol treatment in favor of significant upregulation as compared to untreated control. WB analysis showed that both treatments significantly decreased protein expression of γH2AX while increased the protein levels of DNA damage repair members including RAD51, NBS1 and MRE11. **CONCLUSIONS:** Our studies demonstrate a tight link between DNA damage and vitamin D in UFSCs. Vitamin D3 and its analogue(s) suppress the UF phenotype via targeting DNA damage repair pathway, therefore providing a novel mechanistic insight into clinical effectiveness of Vitamin D3 and analogues on UFSCs.

**SUPPORT:** National Institutes of Health grants R01 HD089553-01 and U54 MD007602.

---

**P-607** Wednesday, October 16, 2019 6:30 AM

**VERTEPORFIN INHIBITS FIBROSIS, INFLAMMATION AND ANGIOSIS RELATED GENES IN UTERINE FIBROID CELLS.** Md Soriful Islam, PhD, Jacqueline Yano Maher, MD, MA, Sadia Afrin, PhD, Szu-Chi Su, MS, James Segars, MD, Johns Hopkins University, School of Medicine, Baltimore, MD.

**OBJECTIVE:** Uterine fibroids are characterized by aberrant cell proliferation and apoptosis, leading to excessive growth and secretion of an altered extracellular matrix (ECM). A key signaling pathway controlling cell proliferation and apoptosis is the Salvador/Warts/Hippo pathway. Hippo signaling is mediated by the TEA domain family member V(E Cad)/Yes-associated protein (YAP)/transcriptional co-activator with PDZ-binding motif (TAZ) tran-
P-609 Wednesday, October 16, 2019 6:30 AM
IL6 AND STAT-3 PATHWAY HIGHLIGHT THE DIFFERENCES IN MOLECULAR RESPONSES IN MYOMETRIUM AND UTERINE FIBROIDS. Minnie Malik, Ph.D., Joy L. Britten, M.D., William Catherino, M.D., Ph.D., Uniformed Services University of the Health Sciences, Bethesda, MD.

OBJECTIVE: Human fibroids are highly prevalent and symptomatic uterine tumors. Phenotypically, they are different from normal myometrium because of massive production of extracellular matrix (ECM), which is a hallmark of these benign tumors resulting in symptoms including abnormal bleeding and pain. Dysregulated production of inflammatory cytokine, IL6 and its regulated JAK/STAT-3 pathway are known to contribute to the fibrotic process. Our objective was to understand the effect of IL6 on fibroid and myometrium cells and the role of JAK/STAT pathway in production of matrix proteins that play a major role in fibroid pathogenesis.

DESIGN: Laboratory study.

MATERIALS AND METHODS: Leiomyoma and patient-matched myometrium cell lines exposed to different concentrations of IL6 and JAK/STAT-3 modulators for various exposure time periods, in a 2D culture model system. Changes in expression of ECM proteins and regulating pathways were assessed using western blot.

RESULTS: In leiomyoma cells, IL6 activation of STAT-3 peaked (2.32+/−0.21 fold) as early as 1.5hr of continuous exposure, and was 1.4+/−0.0 fold increased at end of 3hr of exposure. The maximum increase (1.9+/−0.07 fold) was observed in the ECM structural collagen-1 after continuous exposure to IL6 (3hr) in leiomyoma cells. No significant effect of IL6 was observed in myometrium cells. Collagen-1 protein was increased 3.7+/−1.5 fold on use of JAK/STAT-3 modulators in both pathways in leiomyoma cells exposed to different concentrations of IL6 and JAK/STAT-3 modulators. An increase of 2.21+/−0.05 fold was observed on direct activation of STAT-3 modulators. An increase of 2.7+/-0.05 fold was observed on continuous exposure to IL6 (24hr) in leiomyoma cells. No significant effect of IL6 was observed in myometrium cells. Collagen-1 protein was elevated 2-3 fold in leiomyoma compared to myometrium. IL6 is associated with F-actin and actin tethering, providing a novel target for compounds that regulate the cytoskeleton.

CONCLUSIONS: NA V2, a member of the neuron navigator family, is elevated 2-3 fold in leiomyoma compared to myometrium. NA V2 is associated with F-actin and actin tethering, providing a novel target for compounds that regulate the cytoskeleton.

P-610 Wednesday, October 16, 2019 6:30 AM
OFFERING UNIVERSAL CARRIER SCREENING TO WOMEN OF REPRODUCTIVE AGE SEEKING ROUTINE GYNECOLOGIC CARE. Carleigh B. Nesbit, DO, Ivy Wilkinson-Ryan, MD, Elisabeth D. Erekson, MD MPH, Valerie H. Lacroix, MSc LGC, Devin M. Applebee, MS LGC, Amy W. Bosco, MS LGC, Catherine C. Pollock, BS, Rebecca H. Evans, MD Dartmouth Hitchcock Medical Center, Lebanon, NH.

OBJECTIVE: To investigate differences in demographic and clinical characteristics of reproductive age women who express interest in carrier screening consultation with genetic counseling offered as part of routine gynecologic care and those who do not.

DESIGN: Cross-sectional implementation study at a tertiary care gynecology practice.

MATERIALS AND METHODS: Women ages 18-40 years presenting for routine gynecologic care were eligible for participation. Women were given a packet with information about the benefits of genetic evaluation and assessment prior to conception and offered referral for genetic counseling consultation with the possibility of opting for carrier screening. Interested women were scheduled for comprehensive genetic counseling appointments which included evaluation, assessment, and discussion of available testing options. Demographic and clinical characteristics were obtained by review of the electronic medical record and a survey completed by women at the time of gynecologic visit. The electronic medical record was also reviewed to obtain information on the genetic counseling appointment, type of testing ordered, and test results. Statistical analysis were performed as appropriate with p < 0.05 to compare relevant characteristics.

RESULTS: From October 2018 to March 2019, 131 women were screened for participation. 105 women consented to participate, of which 4 were excluded due to participant or partner having undergone permanent surgical sterilization. Of the 101 women included in this study, 41 expressed interest in genetic counseling referral. Women most likely to express interest were those presenting for infertility evaluation (75.0%) and those presenting for preconception counseling (66.7%). Women presenting for other visit types were less likely to express interest (33.3% for annual exams, 28.6% for problems, 26.7% for contraceptive counseling, p < 0.05). Nulliparous women were more likely than multiparous women to express interest (49.3% vs 16.3%, p < 0.05). Women of higher level of education were also more likely to express interest with least likely groups being those with high school degree or equivalent (30.7%) or associate’s degree (14.3%) and most likely groups being those with a master’s degree (88.9%) or professional degree/doctorate (60.0%) (p < 0.05). No significant differences were seen between differing age, race, ethnicity, employment status, marital status, insurance type, or past history of carrier screening. Of women who expressed interest, 13 (31.7%) attended their scheduled genetic counseling visit and 7 (53.8%) opted to undergo carrier screening.

CONCLUSIONS: After a brief introduction to genetic counseling services during routine gynecologic care in a single tertiary care clinic, nearly half of reproductive age women expressed interest in referral with possibility of carrier screening prior to conception. Nulliparous women, women of higher level of education, and women presenting for infertility evaluation or preconception counseling may be more likely to express interest in these services.

SUPPORT: None.
RESULTS: A total of 1449 embryos were biopsied, 995 for Day 5 and 454 for Day 6. The aneuploidy rates for Day 5 and six biopsies were not significantly different (22.2% and 22.7%, respectively). Independent of the sperm source, there was an observable trend between embryo aneuploidy rate and partner status. The trend was significant (odds ratio=1.02, 95%CI: 1.003-1.040, p=0.022). Interestingly, higher TMPN levels were associated with lower aneuploidy rates, but there was no significant association. When the cohort was separated by sperm characteristics, normospermia presented with similar aneuploidy rates (22%) as terato- (22%), oligo- (27%), crypto- (22%), and a-zoospermia (15%); however, asthenozoospermia samples presented with a higher aneuploidy rate (56%). Lastly, sperm quality how no effect on fertilization rates, blastocyst formation, or implantation rates.

CONCLUSIONS: Here, the poor semen quality did not affect the IVF outcomes. However, we show that the spousal’s age is associated with the aneuploidy rate, whereas donor sperm does not. Therefore, it would be prudent to perform PGT when the sperm donor is of advanced age.

SUPPORT: Conacyt# 231793.

P-612 Wednesday, October 16, 2019 6:30 AM

EXPANDED CARRIER SCREENING FOR RECESSIONALLY INHERITED GENETIC DISORDERS: FACTORS IN DECISION-MAKING WHEN ONE INDIVIDUAL IN A COUPLE IS IDENTIFIED AS A CARRIER. Alice J. Shapiro, M.D., a Molly M. Quinn, MD, b David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA; aUniversity of California, Los Angeles, Los Angeles, CA.

OBJECTIVE: Expanded carrier screening (ECS) is a method of identifying individuals that are carriers for recessively-inherited genetic disorders with the goal of reducing the risk of having a child affected by a genetic disease. While some couples are screened in tandem, others may be screened sequentially to reduce need for a second individual’s test if a partner is found not to carry any mutations. However, it is unknown how often partners of individuals found to be carriers complete the recommended testing with a sequential approach. The goal of this study was to determine the frequency with which the partner of an individual identified as a carrier chooses to undergo testing and what factors may influence that decision.

DESIGN: Retrospective cohort chart review.

MATERIALS AND METHODS: All individuals at a university-affiliated reproductive endocrinology and infertility practice identified to be carriers of a recessively inherited mutation using the Counsyl/Foresight ECS between 9/1/2013 and 4/1/2019 were included. Conditions were categorized by severity (profound, severe and moderate) according to the classification system previously described by Lazarin et al. If an individual screened positive for more than one condition the category corresponding to the more severe condition was used.

RESULTS: A total of 2,061 patients were screened. 760 (36.9%) screened positive as carriers of one or more recessively-inherited disorders. Of these, 577 (75.9%) had reproductive partners listed in the medical record. One-hundred and fifty six (27%) of positively-screened individuals with reproductive partners did not have their partner undergo screening. When compared to those who had a profound mutation, those with a moderate mutation had a trend towards a reduced odds for having their partner screened (OR 0.36 95% CI 0.12-1.05, p=0.06). However, those with a severe mutation did not demonstrate a reduction in odds for having their partner screened when compared to those who had a profound mutation (OR 0.60, 95% CI 0.21-1.74 p=0.35). Number of conditions a patient screened positive for was not predictive of subsequent partner screening (OR 0.95, 95% CI 0.72-1.25, p=0.72).

CONCLUSIONS: Though the greatest utility of ECS is when the carrier status of both reproductive partners is known, not all patients that carry recessively-inherited genetic disorders choose to have their reproductive partner screened. Patients found to be carrier of more debilitating genetic disorders may be more likely to screen their reproductive partners. The emphasizes the importance of the role of the provider in counseling patients prior to performing ECS, as well as genetic counseling after results are received.


P-613 Wednesday, October 16, 2019 6:30 AM


OBJECTIVE: Aging leads to both a decrease in embryo yield and euploid embryo frequency. With increasing utilization of PGT-A technologies, the ability to counsel patients as to the number of expected cycles required to produce a euploid embryo is an important tool. This study aims to provide such a counseling tool utilizing retrospective outcomes data.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 614 IVF cycles with intent for PGT-A from January 1, 2015 to March 15, 2019 at a single institution were reviewed. All cycles proceeding to oocyte retrieval were included, even if no embryos were available to biopsy. Patients who had an oocyte thaw with subsequent embryo biopsy were excluded. Cycles were analyzed to determine number of embryos biopsied, number of euploid embryos, and number of cycles with at least one euploid embryo. These data were utilized to obtain number of euploid embryos per cycle and calculate the estimated number of cycles required to attain at least one euploid blastocyst.

RESULTS: A total of 544 cycles proceeded to biopsy with 2573 embryo biopsies. Of those, 368 (67.6%) cycles had at least one euploid embryo per cycle. Four patients had a transfer and biopsied remaining embryos within the same cycle. The percentage of cycles with euploid embryos decreased by age group from 86.1% of cycles in women less than 35 years old to 23.4% of cycles in women over age 42. Extrapolating data from the number of euploid embryos per cycle by age group, the estimated number of cycles to achieve at least one euploid blast increase from one cycle for women less than age 35 to five cycles for those greater than 42 years of age.

CONCLUSIONS: Managing patient expectations during IVF treatment is critical. Clinicians and patients alike frequently underestimate the likelihood of not having embryos available for biopsy as well as the chance of having a euploid embryo with each cycle. With increasing utilization of PGT-A technology, a tool for estimating the number of cycles anticipated to achieve at least one euploid blastocyst can prove useful to set expectations with preparation for the possibility of multiple cycles.

TABLE 1. Cycle characteristics and biopsy results by patient age

<table>
<thead>
<tr>
<th>Age Group</th>
<th>&lt;35</th>
<th>35-37</th>
<th>38-40</th>
<th>41-42</th>
<th>&gt;42</th>
<th>All Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Number of Cycles (%)</td>
<td>115 (19)</td>
<td>111 (18)</td>
<td>194 (32)</td>
<td>117 (19)</td>
<td>77 (13)</td>
<td>614 (100)</td>
</tr>
<tr>
<td>Cycles with No Biopsy (%)</td>
<td>8 (7)</td>
<td>10 (9)</td>
<td>17 (9)</td>
<td>21 (18)</td>
<td>14 (18)</td>
<td>70 (11)</td>
</tr>
<tr>
<td>Number Embryos Biopsied</td>
<td>702</td>
<td>553</td>
<td>736</td>
<td>404</td>
<td>178</td>
<td>2573</td>
</tr>
<tr>
<td>Number Euploid Embryos (%)</td>
<td>299 (43)</td>
<td>180 (33)</td>
<td>198 (27)</td>
<td>85 (21)</td>
<td>22 (12)</td>
<td>784 (30)</td>
</tr>
<tr>
<td>Cycles with At Least One Euploid per Cycle (%)</td>
<td>29 (66)</td>
<td>79 (71)</td>
<td>37 (60)</td>
<td>57 (49)</td>
<td>18 (23)</td>
<td>270 (60)</td>
</tr>
<tr>
<td>Number of Embryos Biopsied per Cycle</td>
<td>6.10</td>
<td>4.98</td>
<td>3.79</td>
<td>3.45</td>
<td>2.31</td>
<td>4.19</td>
</tr>
<tr>
<td>Number Euploid Embryos per Cycle</td>
<td>2.60</td>
<td>1.62</td>
<td>1.02</td>
<td>0.73</td>
<td>0.29</td>
<td>1.28</td>
</tr>
<tr>
<td>Number of Cycles to Euploid</td>
<td>1.16</td>
<td>1.41</td>
<td>1.66</td>
<td>2.05</td>
<td>4.28</td>
<td>1.66</td>
</tr>
</tbody>
</table>
IMPORTANCE OF EXPANDED CARRIER SCREENING IN THE ASHKENAZI JEWISH POPULATION.

Shelley N. Dolitsky, MD.1 Shama Khan, MPH, MS, LGC.1 Elena Ashkinadze, MS, LGCC.2 Robert Wood Johnson School of Medicine, New Brunswick, NJ; 2Rutgers- Robert Wood Johnson Medical School, New Brunswick, NJ.

OBJECTIVE: Compared to the general population, patients of Ashkenazi Jewish descent have an increased risk of being genetic carriers for certain diseases, with an overall carrier rate ranging from 1 in 4 to 1 in 5. Therefore, the American College of Obstetricians and Gynecologists (ACOG) strongly recommends this population be offered carrier screening for four conditions: Tay Sachs, Cystic Fibrosis, Familial Dysautonomia, and Canavan Disease. Some experts have advocated for a more comprehensive screening panel, and subsequently, ACOG’s Committee on Genetics for the following Jewish Genetic Diseases can be offered to patients: Bloom syndrome, Familial hyperinsulinism, Fanconi anemia, Gaucher disease, Glycogen storage disease type I, Joubert syndrome, Maple syrup urine disease, Mucolipidosis type IV, Niemann-Pick disease, and Usher syndrome. Given the genetic risks inherent in this population, carrier screening programs have been created to test for these founder mutations and have been successful in significantly decreasing the incidence of certain autosomal recessive conditions. Recently, however, with the advent of pan-ethnic, expanded carrier screening, we have the means to identify carriers for a broader array of conditions beyond the fourteen aforementioned. The objective of this study is to assess whether the current screening recommendations are sufficient in diagnosing carrier status in the Ashkenazi Jewish population.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This was a retrospective chart review. Students at a single institution underwent genetic testing with expanded carrier screening through an outreach program at Rutgers University Hillel in October 2015. All the students were of Jewish descent. The genetic conditions tested in the expanded carrier screening were grouped into the following three categories based on ACOG’s 2017 committee opinion regarding carrier screening: the four strongly recommended genetic conditions, the fourteen aforementioned genetic conditions that can be offered, and the genetic diseases that are not specifically mentioned for screening in this population. The results were then divided according to this categorization.

RESULTS: A total of 81 patients were screened. Of these, 36 (44.4%) were found to be carriers of at least one disease. Out of the 36 patients, 28 were found to be a carrier for one disease, 7 for two diseases, and 1 for three diseases, representing 45 total identified mutations. The carrier rate was 7/45 (15.6%) for the four recommended Jewish Genetic Diseases, 20/45 (44.4%) for the fourteen offered conditions, and 25/45 (55.6%) for genetic diseases that were not recommended in this population.

CONCLUSIONS: If carrier screening for the Ashkenazi Jewish population was limited to only founder Jewish mutations in fourteen disorders, 44.4% of carriers would not have been identified. Our data supports that individuals of Ashkenazi descent should be offered pan-ethnic, expanded carrier screening. The likelihood that a donor will have a positive result is substantially more common than in the general population carrier frequencies. The large volume of requests for common genetic testing on gamete donors. Ten cases were performed in 4 cases and galactosemia in 6 cases.

INFORMED CONSENT FOR GENETIC TESTING ON GAMETE DONORS.

P-616 Wednesday, October 16, 2019 6:30 AM

P-615 Wednesday, October 16, 2019 6:30 AM

REPRODUCTIVE ENDOCRINOLOGISTS’ UTILIZATION OF GENETIC COUNSELORS AND THEIR SERVICES: IS THERE AN UNMET NEED?

Meaghan Dwan, BA1 Rachel Gannaway, MS2 Richard S. Lucidi, MD.3 Ana F. Jewell, MS.3 *Virginia Commonwealth University, Richmond, VA; 2Department of Human and Molecular Genetics, VCU Health, Richmond, VA.

OBJECTIVE: Use of genetic testing options is now routine for patients utilizing assisted reproductive technologies (ART) under the care of reproductive endocrinologists (REs). Carrier screening, and often expanded carrier screening, and preimplantation genetic screening including preimplantation genetic diagnosis (PGD) and preimplantation testing for aneuploidy (PGT-A) have become popular options within this patient population. Research suggests that patients utilizing these technologies have found genetic counseling regarding these tests and their results to be beneficial, but limited research has been conducted to examine current practices for genetic counseling in the assisted reproduction setting. The objective of this study was to assess current practices for providing genetic counseling in the ART setting and assess whether there is a need for additional genetic counselor involvement in this medical subspecialty.

DESIGN: Research study conducted via web-based survey.

MATERIALS AND METHODS: REs practicing in the United States were identified using the American Society of Reproductive Medicine (ASRM) member directory and invited via e-mail to participate in a survey about their current practices for providing genetic counseling to their patients, including who is currently responsible for providing this service and for what indications patients receive genetic counseling. Participants were also asked whether they currently employ a genetic counselor, their reasons for doing so or not, and about any future plans for adding a genetic counselor to their staff. Demographic information was collected to determine how representative the sample was of the U.S. REI population and to assess any associations between participant characteristics and attitudes regarding the role of genetic counselors in ART. The survey was designed and administered using REDCap, a web-based tool. SAS version 9.4 was used for statistical analysis.

RESULTS: Of the 135 responses included in the data analysis, over a quarter (27.4%, n = 37) of participants said they currently have at least one genetic counselor on their staff. Of those who do have a genetic counselor on staff, over a quarter (27.0%, n = 10) reported that they see a need for additional genetic counselors at their practice. Of those who do not currently have a genetic counselor on their staff, just under half (41.8%, n = 41) reported that they see a need for one. Current individuals providing genetic counseling in ART practices include physicians, nurses and advanced practice nurses, on-staff genetic counselors, outside genetic counselors and in one case, medical assistants. Genetic counseling is currently provided for a variety of indications in these practices, including ordering and discussing genetic testing, obtaining informed consent, eliciting a comprehensive family history, and interpreting genetic testing results and risk.

CONCLUSIONS: This study provides insight into current practices for genetic counseling in ART and suggests increasing involvement of genetic counselors, as well as a need for more genetic counselors, in this medical subspecialty.
OBJECTIVE: Living in a socioeconomically deprived neighborhood has been associated with an increased risk of adverse birth outcomes. However, variation in the effect of socioeconomic deprivation has not been studied in the U.S. population undergoing in vitro fertilization (IVF). In this study, we sought to explore the relationship between neighborhood-level deprivation and clinical pregnancy rate, live birth outcomes, and preterm birth rates.

DESIGN: A retrospective cohort study of 516 women undergoing their first cycle of IVF at a single academic fertility center in St. Louis, MO from January 2015 to December 2018 was conducted.

MATERIALS AND METHODS: The Area Deprivation Index (ADI) has been validated to the neighborhood-level by Dr. Amy Kind at the University of Wisconsin-Madison. It facilitates the rankings of neighborhoods by socioeconomic status disadvantage. Using published ADI maps, neighborhood-level deprivation index was obtained per individual patient (from the 2013 American Community Survey). To construct a model with relevant factors, independent samples t-test were conducted for continuous variables of interest and chi-square analysis carried out for binary variables of interest. Logistic regression analysis was carried out to determine the relationship between clinical pregnancy (CP), live birth (LB), and preterm birth. Covariates included in the original model were: age, BMI, number of oocytes retrieved, intracytoplasmic injection (ICSI), number of 2PN embryos transferred, and anti-mullerian hormone (AMH) level.

RESULTS: Overall, there was no significant difference between the CP rate in the highest national quintile deprivation index group (most deprived) and those in the lowest (least deprived) group. Compared to the least deprived quintile, the OR for CP in second least deprived quintile was 1.345 (95% CI: 1.046, 1.756, p = 0.037) and in the most deprived group (5th quintile: 0.212-1.723, p = 0.347). Factors significantly associated with CP in the studied cohort were: AMH, ICSI, and age at start of treatment. Overall, there was also no significant relationship between ADI and LB rate, with the most deprived group (compared to the least deprived quintile) having an OR of LB of 1.021 (95% CI: 0.343-3.040, p = 0.970). Interestingly, the hazard ratio of preterm birth at < 37 weeks was elevated in the second and third quintiles of deprivation index compared to the areas with the lowest deprivation index; 1.626 (95% CI: 1.26-2.10) and 1.66 (95% CI: 1.25-2.2). Also interestingly, there was a nonsignificant trend in increasing odds ratio of multiple births in the most deprived quintiles compared to the least deprived quintile (OR 1.935, 95% CI: 1.440 to 8.509, p = 0.382).

CONCLUSIONS: We found no significant association between neighborhood deprivation index and probability of CP or LB after IVF. Given that the academic center is in St. Louis, MO and attracts many patients coming from Illinois, a state that mandates fertility coverage, it may be interesting to further investigate whether those in the most deprived ADI groups (and possibly fertility insurance coverage) are more likely to have multiples.

P-619 Wednesday, October 16, 2019 6:30 AM

EXPLORING THE INTERSECTION OF RACE, RELIGION, AND GENDER IN BLACK WOMEN WITH INFERTILITY. Nicolas A. Johnson, B.S., David A. Grainger, M.D., University of Kansas School of Medicine-Wichita, Wichita, KS.

OBJECTIVE: Investigating the cultural and psychosocial factors that affect Black women’s access to fertility treatment; including intraracial differences between infertile women who have accessed fertility treatment compared to women with infertility that have not accessed care.

DESIGN: Qualitative study in a community-based setting.

MATERIALS AND METHODS: The first author of the study consented participants via phone and conducted semi structured interviews with Black women with an ICD9 or ICD10 diagnosis of female factor or unexplained infertility. Interviews were audio recorded, transcribed, and analyzed in NVIVO using phenomenological methods.

RESULTS: Each of the 12 participants were married or partnered, and the mean age of the women was 39 years. Most women were college educated from working middle class households. All participants were insured. Thus, the analysis revealed each woman’s journey to motherhood, challenges navigating the healthcare system, and the value of their religion throughout their experience.

Journey to Motherhood: Participants expressed their experience with pregnancy loss, delayed diagnosis, the anxiety around inheriting trauma from an adopted child, and belief in the motherhood mandate.

Religion: Emerging themes around religion included the belief in accepting God’s plan, using it as a form of solace. This belief did not impact their overall perception of fertility medication or the use of assisted reproductive technologies to build their families.

P-618 Wednesday, October 16, 2019 6:30 AM

ASSOCIATION OF PREGNANCY OUTCOMES WITH AREA DEPRIVATION INDEX. Vinita Alexander, MD,a Jean-Claire “Mandi” Powe Dillon, MD,b Emily S. Junghem, MD, MSCL,b Washington University in St. Louis, St. Louis, MO; aWashington University School of Medicine, St. Louis, MO.

OBJECTIVE: Living in a socioeconomically deprived neighborhood has been associated with an increased risk of adverse birth outcomes. However, variation in the effect of socioeconomic deprivation has not been studied in the U.S. population undergoing in vitro fertilization (IVF). In this study, we sought to explore the relationship between neighborhood-level deprivation and clinical pregnancy rate, live birth outcomes, and preterm birth rates.

DESIGN: A retrospective cohort study of 516 women undergoing their first cycle of IVF at a single academic fertility center in St. Louis, MO from January 2015 to December 2018 was conducted.

MATERIALS AND METHODS: The Area Deprivation Index (ADI) has been validated to the neighborhood-level by Dr. Amy Kind at the University of Wisconsin-Madison. It facilitates the rankings of neighborhoods by socioeconomic status disadvantage. Using published ADI maps, neighborhood-level deprivation index was obtained per individual patient (from the 2013 American Community Survey). To construct a model with relevant factors, independent samples t-test were conducted for continuous variables of interest and chi-square analysis carried out for binary variables of interest. Logistic regression analysis was carried out to determine the relationship between clinical pregnancy (CP), live birth (LB), and preterm birth. Covariates included in the original model were: age, BMI, number of oocytes retrieved, intracytoplasmic injection (ICSI), number of 2PN embryos transferred, and anti-mullerian hormone (AMH) level.

RESULTS: Overall, there was no significant difference between the CP rate in the highest national quintile deprivation index group (most deprived) and those in the lowest (least deprived) group. Compared to the least deprived quintile, the OR for CP in second least deprived quintile was 1.345 (95% CI: 1.046, 1.756, p = 0.037) and in the most deprived group (5th quintile: 0.212-1.723, p = 0.347). Factors significantly associated with CP in the studied cohort were: AMH, ICSI, and age at start of treatment. Overall, there was also no significant relationship between ADI and LB rate, with the most deprived group (compared to the least deprived quintile) having an OR of LB of 1.021 (95% CI: 0.343-3.040, p = 0.970). Interestingly, the hazard ratio of preterm birth at < 37 weeks was elevated in the second and third quintiles of deprivation index compared to the areas with the lowest deprivation index; 1.626 (95% CI: 1.26-2.10) and 1.66 (95% CI: 1.25-2.2). Also interestingly, there was a nonsignificant trend in increasing odds ratio of multiple births in the most deprived quintiles compared to the least deprived quintile (OR 1.935, 95% CI: 1.440 to 8.509, p = 0.382).

CONCLUSIONS: We found no significant association between neighborhood deprivation index and probability of CP or LB after IVF. Given that the academic center is in St. Louis, MO and attracts many patients coming from Illinois, a state that mandates fertility coverage, it may be interesting to further investigate whether those in the most deprived ADI groups (and possibly fertility insurance coverage) are more likely to have multiples.
CONCLUSIONS: Black women face unique intersectional challenges in their experience living with infertility. The results of this study may serve as a tool for improving physician-patient interactions and foster a better understanding of modern reproductive health disparities and minority health outcomes.

P-620 Wednesday, October 16, 2019 6:30 AM

LONGITUDINAL PROGNOSIS OF PRIMARY OVARIAN INSUFFICIENCY (POI) IN AN URBAN REPRODUCTIVE ENDOCRINOLOGY (RE) CLINIC. Shweta J. Bhatt, MD,1 Valerie S. O’Besso, BA,2 Nataki C. Douglas, MD, PhD,3 Peter McGovern, MD,3 Jacquelyn Loughlin, MD,4 Sara S. Morelli, MD, PhD,5 Rutgers New Jersey Medical School, Newark, New Jersey, NJ; 4University Reproductive Associates, NJ; 5Rutgers New Jersey Medical School, Newark, New Jersey, NJ.

OBJECTIVE: Prompt recognition of symptoms and subsequent diagnosis of POI are critical given its consequences on quality of life and long-term health. Poor access to care in low-income populations may contribute to delayed diagnosis. We previously demonstrated a dearth of board-certified RE physicians providing care for Medicaid patients in New Jersey (1). Given the adverse effects of prolonged hypoestrogenism, we aimed to evaluate length of time to diagnosis of POI in a low-resource/low-income population presenting to an urban university-based RE clinic.

DESIGN: Case series.

MATERIALS AND METHODS: All new patients seen at the RE clinic at University Hospital in Newark, NJ from June 2014 through June 2018 were included. POI was diagnosed in women with oligo/amenorrhea and menopausal levels of follicle stimulating hormone. The primary outcome was time to diagnosis from onset of symptoms.

RESULTS: Of 524 new patients seen, 19 (3.6%) were diagnosed with POI (Table 1). Mean time to diagnosis of POI from onset of symptoms was 6 years, 17/19 (89.5%) women were Hispanic and/or Black. 13/19 (68.4%) reported reported hypoestrogenic symptoms at time of referral. 21.1% were diagnosed with Turner mosaicism. 14 patients completed DEXA scan, of which 35.7% were diagnosed with low bone mass or osteoporosis. Of those diagnosed prior to referral to RE (9/19, 47.4%), only 4 had initiated hormone therapy.

CONCLUSIONS: Prolonged time to diagnosis of POI has adverse effects, as reflected by hypoestrogenic symptoms and decreased bone mineral density. Our study demonstrates a need for more aggressive evaluation of oligo/amenorrhea in underrepresented minority women. Delayed diagnosis and management of POI may be related to health care disparities facing these women, and warrants action to improve access to care.


P-621 Wednesday, October 16, 2019 6:30 AM

IMPACT OF MATERNAL ETHNICITY ON PREGNANCY OUTCOME IN INFERTILE WOMEN WITH POLYCYSTIC OVARIAN SYNDROME. Fabiola D’Ambrosio, MD, Humberto Scoccia, MD. University of Illinois at Chicago, Chicago, IL.

OBJECTIVE: Polycystic ovarian syndrome (PCOS) is the most prevalent endocrine pathology seen among women of reproductive age. The objective of the study is to investigate the impact that ethnic background has on pregnancy outcomes, including live birth rates in infertile women with PCOS going through IVF compared to women without PCOS.

MATERIALS AND METHODS: This study used a coded REDCap data set of 486 women, 18-45 years of age who underwent IVF and embryo transfer between 1/1/2010 and 12/31/2015 at an academic IVF Center after IRB approval (IRB 2015-0623). Patients underwent their 1st IVF cycle following prophylactic withdrawal (norethindrone acetate) using GnRH agonist or antagonist protocols with mixed gonadotropins and demographic data, including race and ethnicity was obtained. Data collected during the IVF process included peak estradiol, number of mature oocytes, fertilization rate, number of top quality embryos on Day 3 of development, number of embryos transferred, implantation rate, clinical pregnancy rate, live birth rate, clinical miscarriage rate, and ectopic pregnancy rate. In women, whose pregnancy resulted in a live birth, additional maternal and neonatal variables were collected, including estimated gestational age (EGA) at delivery, mode of delivery, and weight at birth. Using R analytics software, data was analyzed using logistic regression and linear models. For logistic regression, the estimated coefficient was the log-odds ratio. A significant p value was considered <0.05.

RESULTS: Of the 486 initial women, 360 women were included in the final analysis. Only women with known/reported ethnicity were included. Not Hispanic is the referent cohort for ethnicity and non-PCOS is the referent group when comparing PCOS status. There was no significant difference found for implantation rate (p=0.53) and pregnancy rate (p=0.99) when comparing women without PCOS with the women with PCOS. When taking into account the ethnicity factor in PCOS and the women who conceived and had a live birth, there was no significant difference between being Hispanic with PCOS and the referent non-Hispanic group. However, when evaluating women who started the IVF cycle, women with PCOS are less likely to have a pregnancy that leads to a live birth compared to women without PCOS (p=0.046). Being Hispanic by itself does not seem to affect live birth (p=0.81). Hispanic women with PCOS have the same probability of having a vaginal delivery compared to the referent group (p=0.935). Women with PCOS are more likely to deliver ~2 weeks earlier than non-PCOS patients (p=0.038). Being Hispanic and having PCOS did not affect the EGA at delivery (p=0.83) or affected fetal weight compared to the referent group (p=0.58).

CONCLUSIONS: This pilot study did not find a significant difference in most of the variables studied comparing Hispanic PCOS women with non-Hispanic women without PCOS. However, further studies with a larger number of subjects are needed to assess the impact of ethnicity and PCOS on IVF pregnancy outcomes.
OBJECTIVE: Tubal abnormalities are found in 30-40% of cases of infertility and evaluation of tubal patency is so crucial in their diagnostic workup. Hysterosalpingography (HSG) is a reliable, simple and cost-effective method for evaluation of tubal patency. Our objective is to investigate the anagelse effect of oral diclofenac potassium in pain alleviation during hysterosalinography (HSG).

DESIGN: A randomized double-blinded controlled trial.

MATERIALS AND METHODS: Reproductive-aged infertile women scheduled for HSG were considered for enrollment. Eligible women were recruited and randomized (1:1) to oral diclofenac or Placebo group. All women received oral 50 mg diclofenac potassium or placebo tablets one hour before HSG. The study outcomes were the participant’s self-rated pain perception using a 10-cm Visual Analogue Scale (VAS) during speculum application, cervical tenaculum application, injection of the dye, 5 minutes and 30 minutes post-procedure. A 2 cm difference in VAS score between both groups was considered a clinically significant difference. Other outcomes included the number of women who need additional analgesics and the adverse effects of the study medications. Mann Whitney test and Fisher’s exact test were used for the analysis of the outcomes.

RESULTS: Two hundred women were enrolled and randomized to diclofenac arm (n=100) or placebo (n=100). No difference between both groups in age, parity, BMI, type, duration of infertility and the prior mode of delivery. Women in the diclofenac group reported lower VAS scores during injection of the dye, 5 minutes and 30 minutes post procedure (median: 3 vs. 5.5, p=0.001; 2 vs. 4, p=0.001; 1.5 vs. 3, p=0.003, respectively). No significant difference was found in VAS scores during speculum or tenaculum application. Additionally, twenty-five women asked for additional analgesics in the placebo group versus nineteen women in the diclofenac group (p=0.062). No difference in the rate of adverse effects.

CONCLUSIONS: Oral diclofenac potassium one hour before HSG significantly alleviates the induced pain during and 30 min after the HSG procedure.

SUPPORT: None.

P-623 Wednesday, October 16, 2019 6:30 AM

UTERINE PERISTALIS DURING IMPLANTATION PERIOD: EXPERIENCE OF 3,672 PATIENTS WITH 3 OR MORE FAIRULE OF EMBRYO TRANSFERS.

Hidehiko Matsuyashia, MD, Kotare Kiitaya, MD, Takumi Takeuchi, MD, PhD, Masakazu Doshida, MD, Kohei Yamaguchi, MD, Tomomoto Ishikawa, MD Reproduction Clinic Osaka, Osaka, Japan.; Reproduction Clinic Tokyo, Tokyo, Japan.

OBJECTIVE: Uterine peristalsis caused by uterine contraction is thought to be one of the risk factor for implantation failure, because the uterus is quiescent at the time of implantation perimenstrual period. Previous studies suggested more than 2 or 3 waves/min may be a threshold for implantation failure. Although those reports focused on frequency and direction of the uterine contraction, as far as we know, there were no reports regarding intensity of uterine peristalsis. Therefore, we investigated intensity and location of the uterine contraction in the largest number of patients with recurrent failure of embryo transfers.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Transvaginal ultrasonography scans of uterine peristalsis were performed at the mid luteal phase (7 days after progesterone administration = P7+ on hormone replacement cycle or 9 days after HCG administration = HCG+ on natural cycle). The transvaginal probe (Logiq V5 Expert, 6 to 10 MHz, GE Healthcare) was introduced into the vagina as gently as possible to avoid stimulating the uterine cervix. After scanning the uterus, the probe was fixed as steady as possible while 3 min, video was recorded simultaneously. The video images were analyzed at 10 time the normal speed using Quick Time Player (Ver. 10.4) by a single observer. Frequency, intensity, location and direction of the uterine contractile activity were recorded and evaluated. Intensity was divided into 3 categories; movement with the whole endometrium (strong), with location of the uterine contraction. Therefore, we investigated intensity, direction, frequency and location of the uterine peristalsis. Although those reports focused on frequency and direction of the uterine contraction, as far as we know, there were no reports regarding intensity of uterine peristalsis. Therefore, we investigated intensity and location of the uterine contraction in the largest number of patients with recurrent failure of embryo transfers.

RESULTS: Of 3671 patients (average age, 37.5), 1936 (52.7%) did not show any uterine peristalsis, 1735 (47.3%) had uterine peristalsis. In the peristalsis group, frequency was 55.2% for 1 to 3 times/3 min, 30.2% for 4 to 6, 10.8% for 7 to 9, and 3.8% for 10 or more. Intensity was almost equal among 3 categories (strong 34.1%, medium 37.4%, weak 28.5%). Most uterine peristalsis was observed in the whole uterine cavity (80.7%), whereas those in the upper, middle and lower part of the uterus were 9.7%, 1.6% and 8.1%, respectively. In terms of direction, about half (49.1%) of uterine peristalsis was observed as “lower→upper→lower”, followed by “upper→lower→upper” (16.9%), “lower→upper” (14.5%), “upper→lower” (14.3%), and unfocused (5.9%). Pregnancy outcome of patients (N=24) who had strong uterine peristalsis with 10 or more times/3 min was retrospectively evaluated after taking piperidate hydrochloride (150mg/day). Patients with live birth or ongoing pregnancy with 22 weeks or more were 11 (45.8%), those with biochemical pregnancy or miscarriage were 6 (25.0%), and those without pregnancy were 7 (29.2%).

CONCLUSIONS: These data suggest that uterine peristalsis was frequently observed in patients with recurrent implantation failure. However, we have to determine the cutoff line that should be treated. Further studies will be required.

Reference: None.

SUPPORT: None.

P-624 Wednesday, October 16, 2019 6:30 AM

TRENDS IN EMERGENCY DEPARTMENT UTILIZATION IN WOMEN AGED 18-50 WITH OVARIAN CYSTS (2006-2014).

Daniel Mirmanian, MD; Emma Giuliani, MD; Nicole Ulrich, MD; Erica E. Marsh, MD; Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI.; Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI.

OBJECTIVE: Ovarian cysts may be functional or non-functional with management ranging from expectant, to medical, or surgical. Clinical concerns regarding ovarian cysts include risk of torsion, rupture, hemorrhage, or underlying malignancy. Pain is often an associated feature prompting women to seek evaluation in the Emergency Department (ED), whereas other times ovarian cysts are identified incidentally. The aim of this study was to examine the frequency, trends, and associated features of women presenting to the ED with a diagnosis of an ovarian cyst.

DESIGN: Retrospective cross-sectional study.

MATERIALS AND METHODS: Data from the Nationwide ED Sample (NEDS) database of Health Cost and Utilization Project (HCUP; Rockville, MD), were queried for all ED visits of women aged 18-50 years old with a primary or secondary diagnosis (ICD-9) of ovarian cysts, between 2006-2014. Variables assessed included age, hospital type, medical insurance, household income quartile and disposition.

RESULTS: Between 2006 and 2014 the estimated number of ED visits for ovarian cysts increased (410,435 in 2006 to 628,425 in 2014). However, the proportion of patients admitted to the hospital for this condition decreased during the same time period (12.1% in 2006 to 7.3% in 2014). This decrease far outpaced the trend of decreased admission rates in age matched women who presented to the ED for all other diagnoses (8.2% in 2006 to 7.4% in 2014). Across the years analyzed, the 20-44 age category more frequently sought ED care for ovarian cysts while the older 45-50 age category was admitted at a higher rate. Overall, women that visited the ED for ovarian cysts were more likely to have private insurance or Medicaid, to live in zip codes of the bottom two income quartiles, to visit metropolitan EDs in areas with population >1M, and to live in the southern states. The most frequently associated secondary diagnoses, when ovarian cyst was the principal diagnosis for that ED visit, included tobacco disorder, abdominal pain and female genital symptoms.

CONCLUSIONS: While the total ED visits of women with a primary or secondary diagnosis of an ovarian cyst increased from 2006 to 2014, the proportion of women admitted during the same time period decreased. This decrease in admission rate may be attributed to a shift away from acute surgical management of ovarian cysts and/or an increased in the number of low-acute cases of ovarian cysts presenting to the ED. A disproportionate number of women evaluated in the ED for ovarian cysts were in the lowest two income quartiles highlighting a potential disparity in healthcare delivery and utilization.

P-625 Wednesday, October 16, 2019 6:30 AM

PREVENTING UNNECESSARY PITUTARY MAGNETIC RESONANCE IMAGING: PROLACTIN TO TESTOSTERONE RATIO PREDICTS PITUITARY ADENOMAS IN MALE PATIENTS WITH MILD HYPERPROLACTINEMIA.

Anup B. Shah, MD, MS; Bryan Douglas Naeltz, BA; Neel Parekh, MD; Betul Hatipoglu, MD; Daniel Shoskes, MD; Sarah C. Vij, MD; Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI.; Cleveland Clinic Foundation, Cleveland, OH.; Cleveland Clinic, Department of Endocrinology, Diabetes and Metabolism, Cleveland, OH.

OBJECTIVE: To determine if the prolactin to testosterone ratio (P+T) can be used to predict the presence of pituitary adenoma in patients with mild hyperprolactinemia.

METHODS: We performed a retrospective chart review of men with mild hyperprolactinemia (P level > 40 ng/mL). P+T was calculated as P level divided by total testosterone level. Pituitary adenoma was defined as a presence of a sellar mass on magnetic resonance imaging (MRI). A pretest probability of pituitary adenoma of 10% or greater was required for further testing.

RESULTS: A total of 35 patients with mean age of 36 ± 11 years were included. The mean P+T was 0.4 ± 0.2. The mean P level was 56 ± 31 and the mean testosterone was 6.7 ± 3 ng/mL. A pituitary adenoma was found in 4 patients (11%). The AUC for P+T was 0.67 (p=0.025). The cut-off point was 0.37 with a sensitivity of 60% and specificity of 85%.

CONCLUSION: P+T may be used as an initial screening test to determine further testing for pituitary adenoma in men with mild hyperprolactinemia.
OBJECTIVE: Serum prolactin (PRL) levels are routinely obtained in men presenting with clinical hypogonadism or infertility with mild hyperprolactinemia, often prompting pituitary magnetic resonance imaging (pitMRI) to assess for adenoma. The utility of obtaining pitMRI in this population has not been adequately evaluated. And no society guidelines exist to inform this decision. We hypothesize that a combination of laboratory findings predicts positive pitMRI findings in patients with mild hyperprolactinemia and, given the high rate of negative pitMRIs among young men with mild hyperprolactinemia, sought to identify patients in whom pitMRI can safely be avoided.

DESIGN: Retrospective, case-control chart review.

MATERIALS AND METHODS: Male patients under the age of 50 with mild hyperprolactinemia (15-55 ng/ml) who presented with erectile dysfunction, low libido, hypogonadism, or infertility who had undergone pitMRI were included. Those with a prior diagnosis of prolactinoma, hormonally or dopaminergic therapy, or incomplete clinical data were excluded. Presenting symptoms, age, PRL, body mass index (BMI), testosterone (T), luteinizing hormone (LH), follicle-stimulating hormone (FSH), creatinine (SCr), all medications, and MRI findings were collected. Means of continuous variables were compared with Fisher Exact or Chi-squared tests. Fitted binomial distributions were used to generate Receiver Operating Characteristics (ROCs) and Area Under the Curve (AUC) calculations.

RESULTS: 62 men met inclusion criteria. Pituitary adenomas were identified in 18 patients (29%) with a mean adenoma size of 5.4 ± 5 mm. Mean PRL differed in men with and without adenomas (37.8 ng/ml vs 24.9 ng/ml, p < 0.001), as did dexamethasone suppression (PRL in adenoma group vs. non-adenoma group < 0.01) with considerable overlap. Age, BMI, LH, FSH, and SCr were not associated with presence of adenoma (p > 0.05).

A novel ratio of PRL (ng/mL) to T (ng/dL) (PRL/T) was superior to PRL or T alone in predicting positive pitMRI findings. PRL/T outperformed PRL or T when PRL < 30 ng/mL (AUC 0.88 vs 0.76, 0.83 respectively) and when T < 300 ng/dL (AUC 0.83 vs 0.80, 0.73).

A PRL/T ratio > 0.1 identified adenomas (p < 0.001) with high sensitivity (89%, 16/18 adenomas identified). 43% of pitMRIs could have been prevented if this metric was applied. No patients had pituitary abnormalities when PRL/T < 0.1 and PRL < 30 ng/mL. A more conservative approach of ordering pitMRI when PRL/T ratio > 0.1 and/or PRL ≥ 30 retains 100% sensitivity for identifying adenomas (18/18, p < 0.01). This more conservative guideline would have prevented 32% of pitMRIs when applied to the study cohort.

CONCLUSIONS: The PRL/T ratio is a superior metric to PRL or T alone in identifying young male hypogonadal patients with mild hyperprolactinemia who have imaging-confirmed pituitary abnormalities. A conservative clinical heuristic of ordering pitMRI in patients with hypogonadism with PRL/T > 0.1 and/or PRL ≥ 30 ng/mL detects adenomas with 100% sensitivity and prevents 32% of pitMRIs without changing clinical management, thereby reducing healthcare costs.

P-626 Wednesday, October 16, 2019 6:30 AM
THE UTILITY OF PELVIC ULTRASOUNDS IN ADOLESCENTS PRESENTING TO THE EMERGENCY DEPARTMENT WITH HEAVY MENSTRUAL BLEEDING
Monica W. Rosen, MD, Sarah D. Rominski, PhD, MPH, Jenny S. George, MD, Victoria L. Stoffers, BS, Charlotte M. Bourdillon, MPH, Christine M. Pennesi, MD, Angela C. Weyand, MD, Elisabeth H. Quint, MD University of Michigan, Ann Arbor, MI.

OBJECTIVE: Unlike in adults, the utility of pelvic ultrasonograms (PUS) for heavy menstrual bleeding (HMB) in adolescents who seek care in the Emergency Department (ED) is not well known; therefore, this study was conducted to analyze both decision-making and data utilization around performing PUS in adolescents.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: Patients between the ages of 11 and 19 years who presented to the ED at a tertiary care hospital from 2006-2018 were identified by ICD-9 and ICD-10 codes for HMB. Patients who had PUS were divided into three groups based on endometrial stripe measurements: EMS: EMS ≤ 5mm (group 1), EMS 6-9mm (group 2), and EMS ≥ 10mm (group 3). Patients were further divided into those admitted to the hospital versus those discharged from the ED. Outcome of treatment was evaluated in admitted patients by progress notes indicating when bleeding resolved. Statistical analysis was performed across all groups with cross tab and Chi-Square test, and logistic and linear regression analysis. Approval of this study was granted by the Institutional Review Board.

RESULTS: Two-hundred fifty-eight adolescent females presented to the ED with HMB during this timeframe, of which 113 (43.8%) had PUS. PUS were more likely to be performed if a patient was seen by gynecology, as opposed to hematology or both specialties together (p<0.001). Additionally, the hormone levels value, the more likely PUS were to be performed (p<0.003). The decision of whether or not to order PUS did not differ based on age (p=0.1) or duration of bleeding (p=0.1). There were no structural abnormalities noted on PUS. Forty-nine patients (43.4%) had an EMS that was ≥ 5mm (group 1), 32 (28.3%) had an EMS between 6-9mm (group 2), and 32 (28.3%) had an EMS ≥ 10mm (group 3). There was no difference between thickness of the EMS and duration of bleeding prior to presentation (p <0.01). Among those who had PUS, 67 (59%) patients were treated with hormonal suppression and 46 (41%) were not. There were no significant differences in treatment choices across all EMS groups: 22, 13, and 16 patients were treated with oral contraceptive pills (OCP); 1, 1, and 4 patients used progesterone only pills (POP); and 3, 0, and 7 patients received IV estrogen in groups 1, 2, and 3 respectively (p<0.061). To compare treatment outcomes, we analyzed the 44 patients who were admitted to the hospital, of which 34 (77.3%) had PUS. The distribution of treatments was evenly spread throughout the three EMS groups (p<0.34). There were no significant differences with respect to the amount of time it took bleeding to either significantly taper down or stop completely after initiating treatment (p<0.227, p<0.211, p<0.229, respectively for OCP, POP, and IV estrogen).

CONCLUSIONS: In adolescents with HMB in the ED, performing a PUS did not affect treatment decisions or outcomes. Providers may want to reconsider ordering PUS in adolescents who present for this purpose, as unlike in adults, structural abnormalities are rare and there does not appear to be utility in treating based on the EMS.
common urogenital sinus opening showed in imaging results. In 11 cases of DSD no vagina was displayed.

CONCLUSIONS: MRI and ultrasonography examination is effective at detection of dysplasia gonads, uterus and vagina, in combination with clinical manifestations, pathology is valuable in improving the diagnosis and treatment of patients with disorder of sex development.

P-628 Wednesday, October 16, 2019 6:30 AM

THE UTILITY OF REPEAT SALINE INFUSION SONO-HYSTEROGRAM (SIS) IN THE INFERTILITY WORKUP. Andrey V. Dolinko, MD,a Valery A. Danilack, PhD, MPH,b Ruben J. Alvero, MD,c Victoria V. Snegovskikh, MD.c Women and Infants Hospital and Warren Alpert Medical School of Brown University, Providence, RI; aStanford University, Palo Alto, CA.

OBJECTIVE: The purpose of this study is to evaluate the utility of repeat SIS prior to fertility treatment cycles (FTC) and to identify risk factors for uterine abnormality recurrence or the development of new abnormalities after initially normal imaging.

DESIGN: Retrospective cohort study of women undergoing initial infertility workup and treatment at a single institution who had at least two imaging studies performed 1/1/2007-12/31/2017.

MATERIALS AND METHODS: Initial imaging included hysterosalpingography and/or SIS, while repeat imaging ≥ 9 months later included only SIS. Patient characteristics, imaging results, and FTC data were abstracted from patient charts and a clinical IVF database. Analysis was stratified by initial imaging result: normal or abnormal. In each stratum, result of repeat SIS was compared to patient characteristics using Chi-square test, t-test, or Wilcoxon Rank Sum test.

RESULTS: Of 1163 patients identified, 436 were eligible for study inclusion. Of these, 318 (72.9%) had normal initial imaging and 118 (27.1%) had abnormal initial imaging. Among the former, 22% had an abnormal repeat SIS; among the latter, 54% had an abnormal repeat SIS (p < 0.0001, RR 2.39 (95% CI 1.83-3.12)). On average, 22.6±13.9 months passed between imaging studies. In both groups, women with abnormal repeat SIS were older than those with normal repeat SIS (p < 0.01). Women with normal initial imaging were more likely to have had a live birth in the interim if their repeat imaging was normal (29.9 vs 6.7%, p < 0.001), an association that did not persist on Image Analysis (p < 0.338). Regardless of initial imaging outcome, there was no association found between repeat imaging outcomes and total number of FTCs [IVF, FET, ovulation induction, or natural cycle (timed intercourse or IUI)] performed, max total gonadotropins used, or maximum peak estradiol level between imaging studies. Finally, there was no difference in the live birth rate among cycles started within one year after repeat SIS across groups.

CONCLUSIONS: Uterine cavity evaluation should continue to be performed as the standard of care. Correction and treatment of uterine abnormalities helps equalize the live birth rate among cycles started within one year after repeat SIS across groups.

P-630 Wednesday, October 16, 2019 6:30 AM

ASSESSMENT OF SPERM RETENTION AFTER INTRUTERINE INSEMINATION (IUI) WITH USE OF CERVICAL DEVICE. Rebekah Wolak, MD,a Barry A. Rikps, MD,b Jake Godwin, BS,c Guinevere Redick, MDc Eglin Air Force Base Medical Group, Eglin Air Force Base, FL; aUniversity of Florida, Pensacola, FL; bAffiliation not provided.

OBJECTIVE: Retention and colonization of sperm in cervical/uterine mucus is a purported mechanism of action for intrauterine insemination (IUI) efficacy. This study was designed to assess whether use of a siliconic device to plug cap the cervix reduces reflux and loss of sperm after intrauterine insemination.

DESIGN: Prospective, assessor-blinded, randomized controlled trial (RCT) for the application of device with an intra-cervical stem and soft external cap designed to be placed and maintained during insemination.

MATERIALS AND METHODS: IRB approval was obtained prior to recruiting subjects presenting for IUI as a planned part of treatment in a single office setting over a period of 17 months. With consent, subjects were assigned to routine IUI or IUI with use of the device by randomized number generation. semen preparation for IUI was a standard dual wash to prepare 0.5 ml sample. A 5 ml vaginal lavage was collected from each subject before and after IUI and processed by lab technicians blinded to assigned study group. The two vaginal washes were processed by centrifugation and re-suspension to 0.5 ml. A Makler chamber was used for total sperm count (motile and non-motile). Primary outcome was proportion of sperm retained after IUI. Secondary outcomes were ease of use, evaluation of device design, patient comfort/satisfaction, incidence of conception and ongoing pregnancy rates. Statistical analysis was performed using Student t-Test analysis (or Wilcoxon Rank Sum).

RESULTS: Sperm retention was evaluated between 50 patients relegated to randomly assigned Group A (n = 26) in which IUI was performed with device in place versus Group B (n = 24) in which IUI without device was performed. Data analysis with the Student t-test was applied. Results failed to show a difference in our primary outcome of retention of sperm between the Group A & Group B demonstrating an insignificant (p = 0.5023). An evaluation of the relationship between time interval of device and proportion of retention within the cases showed the data was significant. A correlation analysis of case subjects with relation to device time interval verified (r = 0.35, with p = 0.0126). In further evaluation of absolute value of sperm number in inseminate of both Case and Control subjects and sperm retention percentage, no demonstrable difference was seen in either group (r = 0.033, and p = 0.81).

INTRATUBERINE INSEMINATION
CONCLUSIONS: Despite overall low fertility rates, IUI remains a common first step in the management of infertility given ease of treatment and low cost. Our device and study design failed to show a significant increase in sperm retention above conventional IUI technique. Notable, and not a surprising finding, is a reduction in measurable sperm reflux (sperm loss) after routine IUI, suggesting further research is warranted to improve IUI efficiency. Guiding future efforts, the finding of a significant correlation of sperm retention with extended device placement suggests a need to place and retain a therapeutic device for a prolonged period. Further, this study design suggests viability of using pre- and post-IUI vaginal washing technique for future studies.


A MULTI-CENTRIC, PROSPECTIVE TEST OF CAP-SCORE’S®ABILITY TO PREDICT A MAN’S PROBABILITY OF GENERATING PREGNANCY. Jay S. Schinfeld, MD, FACOG,1 Randy S. Morris, MD,2 Giampiero D. Palermo, M.D., Ph.D,3 Zev Rosenwaks, M.D.,4 John E. Nichols, Jr., MD,4 Fady I. Sharara, M.D.,4 Eric K. Seaman, MD,4 Cristina Cardona, PhD,5 G Charles Ostermeier, PhD,6 Alexander J. Travis, VMD, PhD,6 Abington Reproductive Medicine, Abington, PA; bIVF1, Naperville, IL; cThe Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; dPiedmont Reproductive Endocrinology Group, Greenville, SC; eVirginia Center for Reproductive Medicine, Reston, VA; New Jersey Urology, Short Hills, NJ; eAndrovia LifeSciences, Mountainside, NJ; fCornell University, Ithaca, NY.

OBJECTIVE: Semen analysis lacks an evaluation of fertilizing ability, and fails to diagnose many cases of male factor infertility. Previously, Cap-Score™, the percentage of sperm that can capacitate, showed strong correlations with male fertility (retrograde and cohort comparison studies), and prospectively identified low versus normal fertility using a simple cut-off. However, male fertility is a continuum; logistic regression based on clinical pregnancy outcomes related Cap-Score to the probability of generating a pregnancy (PGP) in 3 cycles (Schinfeld et al, 2018; n=124; 5 clinics). Here, we prospectively tested the relationship between the predicted PGP and actual intrauterine insemination (IUI) outcomes.

DESIGN: A multicentric prospective test of the PGP model’s ability to predict pregnancy. IUI was used as the experimental model to ensure collection of outcomes and provide control over number and timing of inseminations relative to ovulation. For inclusion, men had to have ≥3 million cells post-wash, and female partners could not have factors precluding IUI, e.g., tubal occlusion, hydroosalpinges.

MATERIALS AND METHODS: Studies approved by Weill Cornell’s IRB (1210013187) or WIRB (20152233). Cap-Score and outcomes were obtained from 6 clinics (n=292). A total of 128 finished treatment (pregnant or ≥3 IUIs). The PGP model was tested in two ways. First, the new outcomes were obtained how Cap-Score relates to the probability of generating a pregnancy (PGP) in 3 cycles (Schinfeld el al, 2018; n=124; 5 clinics). Here, we prospectively tested the relationship between the predicted PGP and actual intrauterine insemination (IUI) outcomes.

RESULTS: Only a slight change (average 2.6%) from the original model (PGP=1/[1+exp[-2.86+0.08*Cap-Score]]; n=124; p<0.01) was noted when new data were added (PGP=1/[1+exp][-2.26+0.06*Cap-Score]]; n=252; p<0.001), and fit improved. When predicted PPGs were compared to observed pregnancies, significant linear relationships were seen for n=5 (y=0.81x+0.10; R²=0.84; p=0.03) and n=6 (y=0.69x+0.14; R²=0.86; p<0.01). The slopes were not different from 1 and intercepts were not different from 0 (p>0.05; t-tests).

CONCLUSIONS: Despite the potential for introducing noise when using cases from diverse settings, there was no significant change upon doubling the data set. A 1:1 relationship was detected between predicted PPGs and the observed proportion of men generating pregnancy. These results further demonstrate the strong association between Cap-Score, sperm function/fertilizing ability, and the ability to generate pregnancy.


A MOL REPRODUCTIVE ISSUES

QUALITY OF LIFE AFTER FERTILITY PRESERVATION AMONG TRANSGENDER PEOPLE. Amanda Adeleye, MD,1 Garrett Michael Reid, BS,2 Yuoo Ha Au, B.S,3 J. A. M. E. S. F. Smith, M.D.4 Evelyn Mok-Lin, MD5 UCSF REI fellow, San Francisco, CA; REI UCSF, Center for Reproductive Health, San Francisco, CA; University of California, San Francisco, San Francisco, CA.

OBJECTIVE: There are limited data on the quality of life among transgender people who sought fertility preservation or family building. This pilot study sought to describe the quality of life among transgender people who sought fertility services through the Gender Expansive Attitudes about Reproductive Health (GEAR) study.

DESIGN: Cross-sectional survey.

MATERIALS AND METHODS: This survey queried transgender people who underwent ovarian stimulation or semen cryopreservation at an academic medical center between January 1, 2015 and March 31, 2019. Enrollment is ongoing. Primary outcomes included the number of healthy days and depressed/anxious days as measured by the CDC health related quality of life survey and whether or not ovarian stimulation or semen cryopreservation was emotionally challenging. Primary outcomes were compared by gender identity and ease of gamete collection using a Fisher’s Exact or Wilcoxon Rank-Sum test where appropriate.

RESULTS: Among 40 transgender people who presented for care, 18 initiated the survey and 16 completed the survey (n=12 transfeminine people, n=4 transmasculine people).

The median number of healthy days for the entire cohort was 21 (IQR 15.5-25.5). Transmasculine people experienced more healthy days than transfeminine participants (p=0.01). There were no associations between gender identity and the number of depressed or anxious days (p=0.09 and 0.14 respectively).

Fourteen participants completed the survey about the ease of gamete collection. The majority of people, 64.3% (n=8 transfeminine women, n=1 transmasculine man) found the process of ovarian stimulation or sperm cryopreservation “not at all difficult” or “neither difficult or easy.” Five participants (n=4 transfeminine women, n=1 transmasculine man) found the process “somewhat difficult” or “very difficult.” The ease or difficulty of fertility preservation was not associated with either gender identity (p=0.604) nor the number of healthy days, depressed days or anxious days (p=0.688, 0.528 and 1.00 respectively).

CONCLUSIONS: In this pilot study, transmasculine people experienced more healthy days compared to transfeminine people. Gender identity was not associated with the number of depressed or anxious days. Whether or not participants found the process of ovarian stimulation or sperm cryopreservation emotionally difficult, was not associated with quality of life metrics.

SUPPORT: None.

A MOL REPRODUCTIVE ISSUES

P-632 Wednesday, October 16, 2019 6:30 AM

QUALITY OF LIFE AFTER FERTILITY PRESERVATION AMONG TRANSGENDER PEOPLE.

A MOL REPRODUCTIVE ISSUES

LGBTQ REPRODUCTIVE ISSUES

P-632 Wednesday, October 16, 2019 6:30 AM
MATERIALS AND METHODS: Transgender and gender diverse individuals assigned female at birth age 18 and older that currently have an IUD participated in an online survey about reproductive history, rationale for IUD choice, unwanted side effects, and satisfaction. RESULTS: Median age was 25.8 (SD 4.7) and 14 (16%) identified as transgender, 70 (82%) as genderqueer or non-binary, and 1 (1%) as agender. The majority (71 (85%) was white and had minimum of a college education (47, 55%). 72 (85%) were sexually active, and 63 (88%) were at risk for pregnancy. 62 (73%) chose a 52mg-Levonorgestrel (LNG) IUD (Mirena®/Liletta®), 5 (6%) the lower dose IUDs (Kyleena®/Skyla®), and 17 (20%) the copper IUD (Paragard®). Menstrual manipulation was the main reason for choosing a 52mg-LNG IUD (35, 56%). Other influential factors included how long the IUD lasted (39, 63%), provider recommendation (28, 45%), and to avoid side effects experienced from other methods of contraception (28, 45%), 24 (39%) experienced unwanted side effects including worsening cramping (8, 33%), pelvic pain (7, 29%), bloating (7, 29%) and weight gain (7, 29%). 6 (25%) reported these side effects within the first 0-6 months. 6 (25%) desired removal. Of those that desired removal, 2 (33%) would opt for another IUD.
The main reasons for choosing the lower dose IUDs were the size of IUD (2, 40%), and lower hormone dose (2, 40%). Other influential factors included insurance coverage (4, 80%), how long the IUD lasted (4, 80%), and menstrual manipulation (3, 60%). 2 (40%) experienced unwanted side effects including heavy bleeding (2, 100%), worsening cramping (2, 100%), and pelvic pain (2, 100%). 5 (100%) stated these side effects within the first 3-6 months. Neither (2, 100%) desired removal.

The majority of participants selecting the copper IUD did so to avoid hormones (12, 71%). Other influential factors included how long the IUD lasted (12, 80%), to avoid side effects experienced by other methods of contraception (9, 60%), and provider recommendation (6, 40%). 10 (67%) stated they were experiencing unwanted side effects including irregular bleeding (7, 70%) and worsening cramping (5, 50%). 4 (40%) reported these side effects in the first 0-6 months. However, only 2 (20%) desired removal, and both would opt for another type of IUD.

CONCLUSIONS: Of the IUD options available, the majority of transgender and gender diverse individuals surveyed opted for a 52mg-LNG IUD and chose this specific IUD type for menstrual manipulation. Although side effects were experienced with all options, many occurred within the first 6 months, and few desired removal. As a result, providers should counsel this population about the benefits of an IUD as well as expected side effects including those that should resolve over time.

P-634 Wednesday, October 16, 2019 6:30 AM FERTILITY PRESERVATION KNOWLEDGE AMONG TRANSGENDER WOMEN: PRELIMINARY FINDINGS FROM THE GEAR STUDY. Amanda Adeleye, MD, Garrett Michael Reid, BS,a Yu Ho Au, B.S.,a J. M. M. E. S. F. Final, B.S.a M. D. Evelyn Look Lin, MD,a aREI UCSF, Center for Reproductive Health, San Francisco, CA; aUniversity of California, San Francisco, SAN FRANCISCO, CA.

OBJECTIVE: The American Society of Reproductive Medicine and the Endocrine society guidelines recommend a discussion about fertility prior to the commencement of gender affirming hormonal therapy (HT). There are limited data about how transgender people obtain this information and their understanding of HT on their fertility. This pilot study sought to describe how transgender patients acquire information about their fertility and the accuracy of their knowledge through the Gender Expansive Attitudes about Fertility (GEAR) study.

DESIGN: Cross sectional survey.

MATERIALS AND METHODS: This survey queried transgender people who sought consultation for ovarian stimulation or semen cryopreservation at an academic medical center between January 1, 2015 and March 31st, 2019. Enrollment is ongoing. Participants were asked about their most helpful resource when learning about fertility or family building options. Transgender women were assessed on whether their knowledge was aligned with clinical practice. A Fisher’s exact test was used to determine whether fertility preservation answers differed by the educational resource used.

RESULTS: Among 40 eligible patients, 12 transgender women completed the survey. Seventy-five percent (n=9) of transgender women cited the internet as their primary source of fertility education. A minority, (n=3) stated their medical team (n=2) or friends (n=1) as their primary source of information. Sixty-six percent of participants (n=8) thought that HT should be discontinued prior to sperm freezing. The source of knowledge (internet vs. medical team or friends) was not associated with responses to whether HT should be discontinued (p=0.24). A minority of participants, 16.7% (n=2) stated that it was not possible to freeze sperm after starting HT. Both participants cited the internet as their most useful resource, however there was no difference in the preferred educational resource and the answer to this question (p=0.545). Although sperm can be retrieved through surgical means when necessary, the majority of participants 83.3% (n=10) believed that ejaculation was required for sperm cryopreservation. There were no differences in participant answers by their preferred educational resource.

CONCLUSIONS: In this pilot study, the majority of transgender women obtained their information about fertility preservation from the internet. A minority of transgender women had misconceptions about their fertility potential after starting HT. Future studies may consider targeting the fertility knowledgebase among transgender women.

SUPPORT: None.

P-635 Wednesday, October 16, 2019 6:30 AM IN VITRO FERTILIZATION (IVF) OUTCOMES IN GAY AND SINGLE WOMEN USING DONOR SPERM. Sara E. Barton, M.D., Sue McCormick, BS, William B. Schoolcraft, MD, Mandy G. Katz-Jaffe, Ph.D., Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: To describe the IVF outcomes in gay and single women using donor sperm.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The first IVF oocyte retrieval in women using donor sperm due to lack of a male partner from January 1, 2016 to December 31, 2018 were reviewed at a single IVF center. Women with ≥3 failed IVF attempts at a previous clinic or >1 failed IVF attempt at our center, oocyte donation, and transfers to a gestational carrier were excluded.

The primary outcome was ongoing pregnancy rate. Secondary outcomes are listed in Table 1. Additionally, we calculated the odds of having no embryo transfer with women with failed blastocyst development or no euploid embryos in cycles where preimplantation genetic testing for aneuploidy (PGT-A) was performed.

RESULTS: 90 women included, 86 women had a freeze-all cycle (84 for PGT-A; 2 for other indications) and the remaining 4 women had a fresh transfer. In the freeze-all group for PGT-A, 21.4% (18/84) had no euploid embryos, and 11.9% (10/84) had no blastocyst development; therefore 32.6% (28/86 freeze all cycles) did not have a transfer. The median maternal age of those with no blastocyst development was 43 (range 40–45) years and no euploid embryos 42.5 (35–47) years, significantly older than women who had an embryo transfer [39 (25–45) years, P<0.05].

CONCLUSIONS: It is unknown that women using IVF for lack of a male partner presented at advanced maternal age. While the outcomes of this study suggest this population may have favorable livebirth rates compared to infertile women of the same age, female age remains a strong predictor of a failed cycle. Women presenting to infertility clinics at advanced reproductive ages should be counseled regarding the negative impact of age on fertility, regardless of previous fertility attempts. These data should be useful to guide counseling in gay and single women pursuing IVF treatment without prior infertility.

REFERENCE: NA

SUPPORT: None.

TABLE 1. Outcome variable

<table>
<thead>
<tr>
<th>N=90</th>
</tr>
</thead>
<tbody>
<tr>
<td># oocytes retrieved</td>
</tr>
<tr>
<td># fertilized oocytes (2PN)</td>
</tr>
<tr>
<td># usable blastocysts</td>
</tr>
<tr>
<td># embryos transferred</td>
</tr>
<tr>
<td>Positive HCG</td>
</tr>
<tr>
<td>Implantation rate (FHT)</td>
</tr>
<tr>
<td>Ongoing pregnancy rate per FET</td>
</tr>
<tr>
<td>Ongoing pregnancy rate per retrieval</td>
</tr>
<tr>
<td>Miscarriage rate</td>
</tr>
</tbody>
</table>

*results displayed as median (range) or odd (%)*
MALE REPRODUCTION AND UROLOGY

P-636 Wednesday, October 16, 2019 6:30 AM

DELTA-9 THC CAN BE DETECTED AND QUANTIFIED IN THE SEMINAL FLUID OF MEN WHO ARE CHRONIC USERS OF INHALED CANNABIS. Malinda S. Lee, MD, MBA; Andrea Lanes, PhD; Elizabeth S. Ginsburg, MD; Janis H. Fox, MD; Brigham and Women’s Hospital, Boston, MA.

OBJECTIVE: To detect whether delta-9 tetrahydrocannabinol (THC) and THC metabolites can be identified and quantified in human seminal fluid.

DESIGN: Proof-of-concept study in which serum, urine and semen testing was conducted in 12 male chronic users of inhaled cannabis.

MATERIALS AND METHODS: Healthy men aged 18-45 years who identified as chronic and heavy users of inhaled cannabis (at least 4 times per week for at least one year) were eligible to participate. Eligibility screening took place via structured phone interviews and preceded a single study visit performed at Brigham and Women’s Hospital, Boston, Massachusetts. Participants were asked to abstain from ejaculation for 48-72 hours prior to their study visit, and to use cannabis within 24 hours of their visit. After informed consent was obtained, participants provided urine, semen and serum samples on site.

Semen analyses were performed as standard practice, using a Hamilton-Thorn IVOS Semen Analyzer. The remaining ejaculate, as well as the urine and serum samples, were frozen and stored at -80 degrees C. Cannabinoid assay testing in all three fluid matrices was performed through high performance liquid chromatography/tandem mass spectrometry by NMS Labs (Wilson, PA). Serum and semen were tested for THC (the primary active component of cannabis), 11-hydroxy delta-9 THC (11-OH THC, the main psychoactive metabolite of THC), and delta-9 carboxy THC (THC-COOH, an inactive metabolite of THC). Urine was tested for THC-COOH, the main metabolite of THC in urine, as well as creatinine to provide a normalized ratio.

RESULTS: The median age and BMI of participants was 27.0 years and 24.7 kg/m2, respectively. Over half the participants were daily users of cannabis and had been using cannabis marijuana for over five years. On average, participants used cannabis 10 hours prior to their study visit and abstained for 53 hours from their last ejaculation. The median sperm concentration, motility and morphology was 75.5 million/mL, 69.5% and 5.5%, respectively. Urinary THC-COOH was detected in all 12 participants, whereas at least one serum THC metabolite was present in 10 of 12 participants. Two semen samples had insufficient volume to be analyzed. Delta-9 THC was above the reporting level of 0.50 ng/mL in the seminal fluid of two of the remaining ten participants. The major downstream THC metabolites were not detected in any of the semen samples. Seminal delta-9 THC was moderately correlated with serum levels of delta-9 THC (r=0.66), serum 11-OH THC (r=0.57), and serum THC-COOH (r=0.67). Seminal delta-9 THC was not correlated with urinary cannabinoid levels or semen analysis parameters.

CONCLUSIONS: This is the first study to report that delta-9 THC can be identified and quantified in human seminal fluid. Seminal delta-9 THC was found to be moderately correlated with serum THC and THC metabolites.

SUPPORT: This study was funded by the Expanding the Boundaries Grant from the Dept. of Obstetrics, Gynecology & Reproductive Biology, Brigham and Women’s Hospital.

P-637 Wednesday, October 16, 2019 6:30 AM


OBJECTIVE: To isolate and characterize exosomes1, extracellular vesicles containing functional biomolecules, from testicular tissue in azoospermic men and to perform gene expression analysis in order to classify exosomes within the testicular germinal epithelium to predict spermatogenesis reserve.

DESIGN: A case and control prospective study.

MATERIALS AND METHODS: A total of 17 surgically retrieved testicular specimens from 17 subjects (13 non-obstructive azoospermia (NOA)); 7 with sperm identified at testicular biopsy and 6 with no sperm identified; 4 obstructive azoospermia (OA), all with retained spermatogenesis) were obtained from consenting men from March 2018 to August 2018. Exosome isolation was performed by a standardized differential ultracentrifugation protocol. Nanoparticle tracking analysis was used for characterization of exosome size and concentration. Protein expression was measured by BCA assay and mass spectrometry proteomics analysis was performed. Gene expression was determined by RNA sequencing. Sequences were queried against the Homo sapiens reference genome and filters of contaminants. The Wald test and ANOVA were used to determine significance.

RESULTS: The total number of isolated exosomes was 71x10^6/µL specimen volume with a mean size of 129 nm. Global transcriptional change in men with OA (retained spermatogenesis) was compared to men with NOA and no sperm identified at the time of testicular biopsy by analysis of 17,571 genes. A single gene (POS) was found to be significantly upregulated in the exosomes of men with retained spermatogenesis as compared to those without sperm identified (log2 fold change: 5.89, p-value 0.049). Paradoxically, within the overall NOA cohort, the majority of genes were significantly upregulated in the testicular exosomes of men that had no sperm identified at the time of biopsy compared to those with sperm identified (1,005 genes significantly upregulated, 147 significantly downregulated, p-value <0.05), including retinoic acid signaling mediators and regulators of the self-renewal capacity of germline cells. Furthermore, both groups within the NOA cohort had unique protein expression profiles with 1,926 proteins specific to men with NOA and retained spermatogenesis as compared to men with no sperm identified at the time of biopsy.

CONCLUSIONS: Investigators have identified many potential biomarkers in male infertility, however, few clinical diagnostic tools are currently2,3 available. We show that the testicular germinal epithelium secretes exosomes, which carry unique gene expression profiles in azoospermic men with and without retained spermatogenesis. Specifically, we identify a single gene (POS) essential for germine specification which is significantly upregulated in the exosomes of men with retained spermatogenesis. These transcripts may serve as a biomarker for spermatogenesis, as well as the functional capacity of spermatozoa. Furthermore, the molecular expression of testicular tissue exosomes indicates that these extracellular vesicles may interact with the germinal epithelium in order to ordain new waves of spermatogenesis.


SUPPORT: None.

P-638 Wednesday, October 16, 2019 6:30 AM

AN AGE-BASED NOMOGRAM BASED ON CUT-OFF VALUES OF SEMEN ANALYSIS RESULTS, FROM 2010 WHO REFERENCE VALUES FOR SEMEN CHARACTERISTICS. Guy Shrem, M.D.; Michael H. Dahan, M.D.; Jacques Balayla, M.D.; Naama Steiner, M.D.; Alexander Volodarsky-Perel, M.D.; Weon-Young Son, Ph.D.; Mali Salmon-Divon, Ph.D.1 McGill University, Montreal, QC, Canada; 2Affiliation not provided; 3McGill University Health Centre, Montreal, QC, Canada; 4Division of Reproductive Endocrinology and Infertility, McGill University Health Care Centre, Montreal, QC, Canada; 5Senior Lecturer, Ariel, Israel.

OBJECTIVE: To create a nomogram for sperm parameters along with the male life.

DESIGN: A retrospective evaluation of all records of Computer-Assisted Semen Analysis (CASA) (and human-verified) performed between January 2009 to December 2018 at a University Health Center.

MATERIALS AND METHODS: We encountered 17,915 CASA at all ages. Samples that did not meet the WHO lower reference limit [1] (concentration ≥ 15 mil/mL, motility ≥ 40%, morphology ≥ 4%) were excluded, leaving 8045 samples.

RESULTS: For concentration, percentiles 25th to 75th of the population had a three-phasic pattern reflecting an increase in sperm concentration until around age 30 years, followed by a plateau in sperm concentration until age 45 years, and then a decrease in sperm concentration begins.

For sperm motility, 50-95 percentiles demonstrate a triphasic distribution with an increase until 30 years of age, a plateau until the age of 40 years and...
then decrease in motility. In the groups of two lowest percentiles (10th and 25th), a modest decrease begins at age 30 years, whereas a steeper slope is seen after the age of 40 years.

For sperm morphology, there are two different phasic trends. The 50th percentile and above exhibit a decrease in normal morphology throughout the twenties, subsequently values stabilize. Opposed to this trend, the groups of two lowest percentiles (10th and 25th) have stable low morphology values up to the 7th decade.

CONCLUSIONS: Males have the best semen parameters from age 30-40 years. This may be acting as a compensatory mechanism to obtain pregnancy with female fertility falling at this age.


P-639 Wednesday, October 16, 2019 6:30 AM

YO® HOME SPERM TEST’S MOTILE SPERM CONCENTRATION AND YO SCORE™ CORRELATES WITH AUTOMATED SEMEN ANALYSIS™

RESULTS. Stan Honig, MD, a Lev Rabinovich, PhD, b Natan Bar-Chama, MD. aYale University, New Haven, CT; bMedical Electronic Systems, Caesarea Industrial Park, Israel; cIcahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: To evaluate the accuracy of the YO® Home Sperm Test (“YO”) motile sperm concentration (MSC) and YO SCORE™ results in the hands of TRAINED professional as compared to the SQA-V automated laboratory sperm analyzer (Medical Electronic Systems).

DESIGN: Multi center, Double-blind prospective study.

MATERIALS AND METHODS: 316 human semen samples were tested by TRAINED professionals at three sites utilizing the YO Home Sperm test kit. In parallel, the same samples were tested on the SQA-V automated semen analyzer (Medical Electronic Systems). Samples were collected, liquefied, split and run in a blinded fashion. TRAINED professionals ran the YO test using the YO device (mini-microscope) on either a Galaxy or iPhone Smartphone following the YO app. instructions. YO automatically reports (a) LOW MSC <6m/mL or MODERATE/NORMAL MSC ≥ 6m/mL, and (b) a YO SCORE displayed as a two-digit integer, from 10 to 90+ MSC centile levels derived from the 2010 WHO 5th edition Table A1-2 of semen parameter centile distribution for recent fathers. The YO MSC results from the TRAINED professional were analyzed statistically vs. the SQA-V based on negative and positive percent agreement (NPA and PPA). The TRAINED professional YO SCORE results were analyzed for accuracy vs. SQA-V semen quality groupings with an allowance of ± one YO SCORE deviation.

RESULTS: The YO device demonstrated high levels of PPA, NPA and accuracy when TRAINED professional MSC levels were compared vs. SQA-V results: 97.6%, 97.0% and 97.3% respectively with inter-site CV ≤ 2%. YO SCORE results obtained by TRAINED professionals demonstrated an overall accuracy of 94.3% for distinguishing between MSC semen quality groupings which were established based on SQA-V MSC.

CONCLUSIONS: Using the YO® Home Sperm Test TRAINED professionals showed a high level of accuracy for motile sperm concentration when compared to the SQA-V automated laboratory sperm analyzer in 316 semen samples. This study also demonstrated that the YO SCORE is a reliable tool for defining different motile sperm concentration categories.

P-640 Wednesday, October 16, 2019 6:30 AM

FERTILITY AND INFERTILITY TREATMENT KNOWLEDGE AMONG MEN AGED 18-50 IN THE U.S.

Parker H. Murray, MS4, a Rashmi Kudesia, MD. aTexas College of Osteopathic Medicine, UNTHSC; Fort Worth, TX; bCCRM Fertility Houston, Houston, TX.

OBJECTIVE: To validate the Fertility and Infertility Treatment Knowledge Scale (FIT-KS) among men aged 18-50 in the United States, and to assess fertility knowledge among men in the general population, with comparison to the female population in the original validation study.

DESIGN: Cross-sectional web-based survey study.

MATERIALS AND METHODS: An online survey with format identical to that previously constructed for the original FIT-KS validation study was administered to English-fluent men aged 18-50 residing in the United States. STATA v15.1 was used to compute descriptive statistics, and conduct analyses, including the Student’s t, Pearson’s χ2, Spearman’s ρ, and Kruskal-Wallis tests, to assess for correlation to demographics and comparison between the male and female cohorts. The study received IRB exemption.

RESULTS: In preliminary analysis, 99 men completed the survey, with median age 30 (28, 37); 50 (50%) were single, with 14 (14.1%) in a relationship, 33 (33.3%) married, 2 (2%) divorced. Most (65.7%) had no children, and identified as White (74.8%), with 9.1% Hispanic or Asian, and 7.1% Black. The majority (89.9%) reported an annual household income at or below $100k, and 60.6% held a college or higher degree.

The mean FIT-KS score was 12.3 +/- 0.34 (out of 29, 42.4% correct). Increasing age was the only significant demographic predictor of higher FIT-KS score (p = 0.002). In item analysis, notable findings include: though 74 (74.8%) knew at which ages women are most fertile, many (48.5%) overestimated age of maximal fertility decline, fecundability at age 30 (63.6%) or age 40 (71.7%), and 74.7% underestimated the spontaneous miscarriage rate. Only 6.1% agreed that men can contribute to a couple’s infertility, though 25.3% acknowledged male age could impact fertility. Only 17.2% knew how long sperm survive in the female reproductive tract. A majority were generally aware of lifestyle issues that impact fertility, though only 31.3% knew about lubricants. When asked about IVF, 19.2% overestimated success rates at female age 35 and 85.9% at age 44. The twin rate was underestimated by 70.7%, and 95% overestimated success rates for oocyte cryopreservation.

When compared to the original validation cohort, men in this sample scored lower than women on total FIT-KS score (12.3 +/- 0.34 vs. 16.2 +/- 0.32), as well as in natural fertility and infertility treatment success sub-sections (all p < 0.0001).

CONCLUSIONS: These preliminary results uphold the conclusion that fertility knowledge in the general population is low. Though the validation analysis for the FIT-KS in men is ongoing, these findings suggest that men also tend to overestimate natural fertility and infertility treatment success rates and underestimate risks and impact of lifestyle. Most surprising, the low rate of acknowledging the male role in infertility suggests a particular need for education in this area. Outreach efforts aimed at educating the public about fertility must target both men and women to sufficiently penetrate the general population and correct gaps in knowledge.

SUPPORT: None.

TABLE I

<table>
<thead>
<tr>
<th>Site Name, Location</th>
<th>N</th>
<th>PPA</th>
<th>NPA</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xytex Corporation, Augusta, GA</td>
<td>82</td>
<td>100.0%</td>
<td>98.2%</td>
<td>99.1%</td>
</tr>
<tr>
<td>Xytex Corporation, New Brunswick, NJ</td>
<td>136</td>
<td>97.0%</td>
<td>97.1%</td>
<td>97.1%</td>
</tr>
<tr>
<td>Medical Electronic Systems, Caesarea, IL</td>
<td>98</td>
<td>96.2%</td>
<td>95.8%</td>
<td>96.0%</td>
</tr>
<tr>
<td>OVERALL</td>
<td>316</td>
<td>97.6%</td>
<td>97.0%</td>
<td>97.3%</td>
</tr>
</tbody>
</table>

Inter-site CV

YO SCORE Agreement TRAINED vs. SQA-V

<table>
<thead>
<tr>
<th>SQA-V Semen Quality Group</th>
<th>SQA-V MSC Range, 10^6/mL</th>
<th>YO SCORE</th>
<th>YO SCORE Accuracy vs. SQA-V</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOW (n = 90)</td>
<td>0 - &lt;6</td>
<td>10 - 30</td>
<td>96.7%</td>
</tr>
<tr>
<td>LOW NORMAL (n = 55)</td>
<td>6 - 32</td>
<td>40 - 60</td>
<td>94.5%</td>
</tr>
<tr>
<td>AVERAGE NORMAL (n = 78)</td>
<td>32 - 63</td>
<td>70 - &gt;90</td>
<td>93.6%</td>
</tr>
<tr>
<td>HIGH NORMAL (n = 93)</td>
<td>63 - &gt;94</td>
<td>70 - &gt;90</td>
<td>92.5%</td>
</tr>
<tr>
<td>OVERALL (n = 316)</td>
<td></td>
<td>70 - &gt;90</td>
<td>94.3%</td>
</tr>
</tbody>
</table>

YO MOSC TEST

Results: TRAINED vs. SQA-V

Support: Medical Electronic Systems.
Efficacy of antioxidant supplementation on conventional and advanced sperm function tests in patients with idiopathic male infertility. Mohamed Arafa, MD, a, Ashok Agarwal, PhD, b Ahmad Majzoub, MD, c Kareim Khalafalla, MD, d Sami Alsaid, MD, d Haitham Elbardissi, MD, d  

Objective: Antioxidants have long been used in the empirical treatment of infertile men. While a positive effect has been reported by a number of studies, others have failed to reproduce any benefit leading to controversy regarding their efficacy in the treatment of infertility. The aim of the present study was to evaluate the effects of antioxidant combination therapy on conventional semen parameters and advanced sperm function tests in men seeking fertility.  

Design: Prospective clinical trial.  

Materials and Methods: 148 patients presenting with male factor infertility to a tertiary medical center with at least one abnormal semen parameter over a period of 6 months were included. Patients with varicocele, leukospermia, history of genitourinary infections, any febrile illness and exposure to chemotherapy were excluded.  

All participants were treated with the antioxidant supplement FH-PRO (1000 mcg B12, 30mg Zinc, 150mg Selenium, 350mg Arginine, 200mg Co-Q10, 120mg Vitamin C, 20IU Vitamin E) (Fairhaven Health, Bellingham, WA) for a period of 3 months. Semen analysis, sperm DNA fragmentation (SDF) (Halsperm kit, Halotech, Madrid, Spain), oxidation reduction potential (ORP) (MiOXSYS, Ayru BioScience, Englewood, CO) and hormones (FSH, LH, prolactin, and testosterone) were performed on all participants initially and following treatment. Numbers (percentages) were used to report categorical values while mean ± SE to report numerical values. Results were compared using Wilcoxon Signed Ranks Test and a p value of <0.05 was considered statistically significant.  

Results: The mean age of study participants was 35.9 ± 0.5 years and body mass index 29.6 ± 0.4 Kg/m². Compared to the pretreatment test results, there was statistically significant improvement in conventional semen parameters including sperm concentration, total and progressive motility and normal morphology after 3 months of treatment with FH-PRO. Furthermore, a significant improvement in advanced sperm function tests (SDF & ORP) was also observed following antioxidant supplementation.  

Conclusions: Treatment of patients with idiopathic male infertility with FH-PRO antioxidant regimen for 3 months resulted in significant improvement in conventional semen parameters and advanced tests of sperm function. It may offer promise to the medical treatment of idiopathic male infertility.  

Table:  

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Semen volume (ml)</td>
<td>3.18 ± 0.12</td>
<td>3.12 ± 0.11</td>
<td>0.058</td>
</tr>
<tr>
<td>Sperm concentration (10⁶/ml)</td>
<td>22.23 ± 2.01</td>
<td>30.57 ± 2.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total motility (%)</td>
<td>34.59 ± 1.43</td>
<td>38.47 ± 1.54</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Progressive motility (%)</td>
<td>4.00 ± 0.61</td>
<td>8.06 ± 0.81</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Normal morphology (%)</td>
<td>2.86 ± 0.19</td>
<td>3.98 ± 0.26</td>
<td>0.017</td>
</tr>
<tr>
<td>SDF (%)</td>
<td>38.63 ± 2.10</td>
<td>32.04 ± 1.82</td>
<td>0.002</td>
</tr>
<tr>
<td>ORP (mV/10⁶ sperm/ml)</td>
<td>10.26 ± 1.29</td>
<td>6.21 ± 1.18</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* P<0.05.
Left scrotal temperature was significantly negatively correlated with sperm concentration (−0.268, p < 0.004), total motility (−0.337, p < 0.001), normal morphology (−0.282, p < 0.003) & left testicular size (−0.292, p = 0.002). While it was significantly positively correlated with ORP (0.374, p = 0.001), left inguinal temperature (0.521, p < 0.001) & right scrotal & inguinal temperatures (0.843, p < 0.001; 0.521, p < 0.001).

CONCLUSIONS: Increased scrotal and inguinal temperatures are detected in patients with testicular dysfunction secondary to clinical varicocele.

P-644 Wednesday, October 16, 2019 6:30 AM

RE-EXAMINING THE INCIDENCE OF KARYOTYPIC ABNORMALITIES AND Y CHROMOSOME MICRODELETIONS IN MALES WITH AZOSPERMIA OR SEVERE OLIGOSPERMIA.

Olivia Carpillo, MD, Jessica A. Marinaro, MD, Micah J. Hill, DO, Alan H. DeCherney, MD, Kate Devine, MD, Rebecca Chason, MD, NIH, Bethesda, MD, MedStar Georgetown University Hospital, Washington, DC; National Institute of Child Health and Human Development, NIH, Bethesda, MD; NIH NICHD, Bethesda, MD; Shady Grove Fertility, Washington D.C., DC; Shady Grove Fertility, Annapolis, MD.

OBJECTIVE: Prior studies evaluating the prevalence of karyotypic abnormalities and Y chromosome microdeletions in males with azoospermia and severe oligospermia are limited by small sample sizes and may differ from those seen in the modern clinical infertility setting. Thus, we set out to evaluate the prevalence of these abnormalities in a large clinical cohort undergoing IVF.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Couples treated with in vitro fertilization (IVF) from January 2014- April 2019, with ‘male factor’ assigned as an infertility diagnosis were screened against inclusion criteria: sperm concentration < 5 million sperm/mL and available results for karyotype and/or Y chromosome microdeletion panel. Patients were included in the analysis whether autologous sperm was available for IVF/ICSI (89.4%) or donor sperm needed to be used. The prevalence of karyotypic abnormalities and Y microdeletions were calculated within this population.

RESULTS: Over 7300 male partners were screened, and 1315 unique male patients met inclusion criteria. When normal variants were excluded, 9.0% of all patients had a karyotypic abnormality or Y microdeletion. Of these, 76 (5.9%) patients had abnormal karyotypes and 42 (4.4%) patients had Y microdeletions. The most common karyotypic abnormalities were Klinefelter Syndrome (38.2%), balanced translocations (17.1%), Robertsonian translocations (15.8%). Chromosome 9 inversions, which are classified as normal variants, were found in 15 patients (1.2%). All Y microdeletions identified were in AZFc, which may be due to better prognosis for obtaining sperm for ICSI among men with AZF deletions relative to AZFa and AZFB microdeletions.

CONCLUSIONS: In a large population of azoospermic and severely oligospermic men whose female partners underwent IVF, the incidence of karyotypic abnormalities was approximately 6%, which is similar to previous reports. Our study population was nearly four-times larger than prior studies. While non-existence of results positive for AZFa and AZFb microdeletions must be taken into account, the low incidence (4.4%) of AZFc microdeletions in our population indicates that Y chromosome microdeletions may be less common in men with azoospermia and severe oligospermia than previously reported.


P-645 Wednesday, October 16, 2019 6:30 AM

IMPACT OF COMMERCIAL SPERM SUPPLEMENTATION ON SEMINAL PARAMETERS. Megan Goodwin, MS, Kaci D. Rogers, MS, Fady I. Sharara, M.D., Virginia Center for Reproductive Medicine, Reston, VA.

OBJECTIVE: Various products on the market to improve seminal parameters, but the impact of such supplements has not been well studied in a clinical setting. We sought to evaluate the effects of a new commercially available supplement on patients with male factor infertility.

DESIGN: Prospective.

MATERIALS AND METHODS: An initial semen analysis (SA) was performed and, if abnormalities were noted, men were started on Androferti (Innovus Pharmaceuticals, San Diego, CA), a commercial supplement in powder form, taken twice daily. Androferti is a blend of nutrients including L-Carnitine, Vitamin C, Selenium, CoQ10, Zinc, Vitamin E, Folate, and Vitamin B12. A second SA was then performed after a minimum of 30 days to evaluate the results of supplementation.

RESULTS: A total of 120 male patients with an abnormal initial SA and at least 30 days of taking Androferti (149.15 ± 146.26 days on average) were prospectively evaluated. Of these patients, 94 had been on Androferti for 60 or more days. There were no differences in average semen volume (2.93 vs 2.80 cc, P=NS) or concentration (46.2 ± 42.1 ×10^6/cc, P=NS) between the first and second SA, but there were significant increases in sperm motility and progression (36.6% vs 40.2%, P=0.023; 2.19 vs 2.35, P=0.034, respectively). The average number of total motile sperm per ejaculate, however, did not differ between the first and second SA (39.6 vs 39.6 Millions, P=NS). There was also a trend towards improved strict sperm morphology after 30 days on Androferti (1.935% vs 2.74%, P=0.061).

CONCLUSIONS: Supplementation with Androferti significantly improved sperm motility and progression, with a trend to improve strict morphology, as early as 30 days after supplementation. Future studies will evaluate whether such supplementation will improve spontaneous conception or IUI success rates.

Reference: None.

SUPPORT: None.

P-646 Wednesday, October 16, 2019 6:30 AM

REPEAT SEMEN ANALYSIS – AN UNNECESSARY DELAY IN UROLOGIC EVALUATION? Lauren Ursillo, MD,a Arielle S. Yeshua, MD,a Christine Mullin, M.D., Avner Hershlag, M.D.,b Weivi Shan, MS Phd,b Baruch Abittan, M.D.,c Sarah Girardi, MD, Randi H. Goldman, M.D.d NYU Winthrop Hospital, Mineola, NY; bNorthwell, Manhasset, NY; cNorthwell Fertility; dNorthwell Health Department of Biostatistics, New Hyde Park, NY; eNorthwell Fertility, Manhasset, NY.

OBJECTIVE: Most conventionally accepted guidelines recommend obtaining a repeat semen analysis (SA) following an abnormal initial test. The objective of this study is to determine if repeating a SA when one or more abnormal values is identified may unnecessarily delay REI referral to a Urologist by determining the likelihood that a patient with an abnormal SA will have an entirely normal SA with subsequent tests.

DESIGN: Retrospective cohort study at a single academic medical center.

MATERIALS AND METHODS: All men who underwent two or more SA (one to six months apart) from January 2016 to December 2018 at one large academic fertility center were included. Semen samples were evaluated manually by trained technicians according to 2010 World Health Organization (WHO) criteria. Normal values included concentration ≥ 15 million/mL, motility ≥ 40%, and Kruger morphology ≥ 4%. Total motile sperm concentration (TSMC) was calculated by multiplying the concentration x volume x motility divided by 100 and considered normal at >20 × 10^6 per ejaculate. SA parameters were sequentially analyzed for differences between the first and any subsequent SA to determine how often an abnormal SA becomes entirely normal with additional tests. We assumed that abnormalities in any SA parameter would result in Urology referral and analyses were performed with and without consideration of morphology defects.

RESULTS: Five hundred fifty first and second SA from 275 men were analyzed, each of whom had at least one defect in the first SA (Table). The most common abnormality was morphology defects. Seventy-nine percent (N=217) of men had at least one abnormality on the second test as well, while the remaining 21% had SA that normalized entirely with a second
SA, including morphology defects. When morphology defects were excluded, approximately 3/4 (73.3%) of men with an initial abnormal SA had persistently abnormal results on a second test, while the remaining 26.7% had a normal second SA. Among patients with at least two initial defects, only 8.1% had a normal second SA; when morphology defects were excluded, this figure increased to 16.4%.

CONCLUSIONS: The majority of men with abnormal semen analyses on initial testing have persistent abnormalities on repeat testing that warrant referral to Urology. Less than 1 in 10 men with two or more defects on initial testing had a normal second SA. These results suggest that referral to a Urologist may be considered after a single abnormal SA to expedite male-factor infertility workup and treatment.

P-647 Wednesday, October 16, 2019 6:30 AM
LONG TERM SAFETY AND EFFICACY OF CLOMIPHENE CITRATE FOR THE TREATMENT OF MALE HYPOGONADISM. Devang Sharma, MD,a Sarah C. Krzastek, MD,b Natasha Abdullah, BA,b Mark I. Sultân, BS,c G Luke Machen, MD,c Jessica L. Wenzel, BS,c Alex M. Ellis, BS,c Xizhao Chen, BS,c Mehraban Kavoussi, BS,c Raymond A. Costabile, MD,c Ryan F. Smith, MD,c Parviz K. Kavoussi, MD,a University of Virginia, Charlottesville, VA; bAffiliation not provided; cYale University School of Public Health, New Haven, CT; dMedical College of Wisconsin, Milwaukee, WI; eUT Austin Dell Medical School, Austin, TX.

OBJECTIVE: The aim of our study was to assess the ability of clomiphene citrate (CC), a selective estrogen receptor modulator, to maintain eugonadal testosterone levels and improve the symptoms of hypogonadism in men being treated with CC for extended periods of time.

DESIGN: A retrospective chart review was performed to identify all patients treated with CC for hypogonadism from two institutions from 2010-2018. Duration of CC therapy, serum testosterone levels, improvement in hypogonadal symptoms, and side effects while on CC were assessed.

MATERIALS AND METHODS: Hypogonadism was defined as a baseline serum testosterone < 300ng/dL. Side effects while on CC were subjectively reported by patients. As the longest duration of CC treatment in the literature to date is 3 years, patients were divided into those on CC treatment for ≤ 3 years, and those on treatment for > 3 years. Unpaired t-test was used to evaluate changes in testosterone and estradiol between groups. Fisher’s exact test was used to compare side effects, symptom improvement, and requirement for anastrozole between groups.

RESULTS: 400 patients were treated with CC from 2010-2018. Mean patient age was 39 ± 11 years. Mean length of CC treatment was 25.5 ± 20.48 months with a range of 0-84 months. 280 patients were treated with CC for ≤ 3 years (mean CC duration 12.75 ± 9.52 months), and 120 patients were treated with CC for > 3 years (mean CC duration 51.93±10.52 months). Following treatment with CC for > 3 years, 106 patients (88%) achieved eugonadal testosterone levels, 92 patients (77%) reported improvement in hypogonadal symptoms, and 10 patients (8%) reported side effects on CC. There was not a statistically significant difference in the results between patients treated > 3 years and patients treated ≤ 3 years. The most common side effects reported by patients treated > 3 years included changes in mood (N=5), blurred vision (N=3), and breast tenderness (N=2). There were no significant adverse events with long term sequelae in any patients treated with CC.

CONCLUSIONS: Testosterone replacement therapy (TRT) has traditionally been the primary treatment for hypogonadism in men. However, exogenous testosterone disrupts the hypothalamic-pituitary-gonadal (HGP) axis and suppresses intratesticular testosterone production and spermatogenesis. CC is commonly used to treat hypogonadism in men desiring to preserve spermatogenesis and fertility, and may be used as an off-label primary treatment for hypogonadism. There is a paucity of long-term data on the efficacy and safety of CC, with no published data with the use of CC in men for durations longer than three years. CC has not historically been offered as a primary treatment for hypogonadism in men who do not desire fertility preservation, perhaps in part due to the lack of data regarding long term safety and efficacy of CC. This data demonstrates that CC is safe and effective with few side effects when used as a long-term treatment for hypogonadism.

P-648 Wednesday, October 16, 2019 6:30 AM
PATERNAL AGE IS A PREDICTOR OF ELEVATED SPERM DNA FRAGMENTATION IN INFERTILE MEN. Julie Sroga Rios, MD,a Robert M. Coward, MD,b Fangbai Sun, MPH,c Heping Zhang, PhD,c Nanette Santoro, M.D., Anne Z. Steiner, MD, MPH,a University of Cincinnati and Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; bUniversity of North Carolina, Chapel Hill, NC; cYale University School of Public Health, New Haven, CT; dUniversity of Colorado Denver, Aurora, CO; eDuke University Medical Center, Durham, NC.

OBJECTIVE: Increased sperm DNA fragmentation (DF) has been associated with reduced embryo quality and pregnancy rates, and increased miscarriage rates. The underlying cause of increased SDF is unknown. Our objective is to examine clinical factors associated with abnormal DF in infertile men.

DESIGN: Cross sectional study.

<table>
<thead>
<tr>
<th>Table 1. Characteristics of males by level of DF</th>
<th>0≤SCSA ≤ 30 % (n=119)</th>
<th>SCSA &gt; 30% (n=28)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sperm concentration (million/ml)</strong></td>
<td>20.0 (11.0, 40.0), n=119</td>
<td>18.0 (12.0, 51.5), n=28</td>
<td>0.624</td>
</tr>
<tr>
<td>Normal morphology (%)</td>
<td>5.0 (3.0, 8.5), n=104</td>
<td>5.0 (2.0, 11.0), n=19</td>
<td>0.666</td>
</tr>
<tr>
<td>Total motility (%)</td>
<td>45.2 ± 15.6, n=119</td>
<td>38.2 ± 20.5, n=28</td>
<td>0.048</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>33.0 (30.0, 36.0), n=119</td>
<td>36.0 (32.5, 40.0), n=28</td>
<td>0.009</td>
</tr>
<tr>
<td>BMI (mg/kg2)</td>
<td>27.7 (24.2, 31.3), n=118</td>
<td>28.0 (24.3, 30.9), n=27</td>
<td>0.994</td>
</tr>
<tr>
<td>History of Smoking</td>
<td>0.748</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>71/119 (59.7)</td>
<td>17/28 (60.7)</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>106/119 (89.1)</td>
<td>2/28 (7.1)</td>
<td></td>
</tr>
<tr>
<td>Former</td>
<td>5/119 (4.2)</td>
<td>9/28 (32.1)</td>
<td></td>
</tr>
<tr>
<td>History of Alcohol Use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>0/8/119 (6.7)</td>
<td>0/28 (0.0)</td>
<td>0.476</td>
</tr>
<tr>
<td>Current</td>
<td>0/106/119 (89.1)</td>
<td>27/28 (96.4)</td>
<td></td>
</tr>
<tr>
<td>Former</td>
<td>5/119 (4.2)</td>
<td>1/28 (3.6)</td>
<td></td>
</tr>
<tr>
<td>Varicocele (self-reported)</td>
<td></td>
<td></td>
<td>1.000</td>
</tr>
<tr>
<td>Yes</td>
<td>11/119 (9.2)</td>
<td>2/28 (7.1)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>100/119 (90.8)</td>
<td>26/28 (92.9)</td>
<td></td>
</tr>
<tr>
<td>Duration of Infertility (months)</td>
<td>24.0 (16.0, 36.0), n=116</td>
<td>24.0 (13.0, 36.0), n=26</td>
<td>0.951</td>
</tr>
</tbody>
</table>

Wilcoxon’s rank-sum test, Chi-square, or Fisher’s exact test were used where appropriate.
MATERIALS AND METHODS: A secondary analysis of 147 infertile males enrolled in the Male, Antioxidant, and Infertility (MOXI) Trial, MOXI participants, who were 18-40 years old with at least one abnormal semen parameter, provided a semen sample and completed questionnaires including baseline demographics, health and lifestyle factors. Semen samples underwent standard semen analysis and DF testing using sperm chromatin structure assay. Abnormal DF was defined as > 30%. Bivariate analysis and subsequent multivariable regression analysis were performed. Variables were introduced to the multivariable regression analysis in a step-wise fashion, using a p-value of <0.10 on the bivariate analysis to enter and a p-value of < 0.05 to remain.

RESULTS: Nineteen percent of subjects had DF >30%. Males with abnormal DF were older and had lower total sperm motility compared to controls (Table 1). No differences were seen in environmental or lifestyle exposures between groups (data not shown). Only male age remained a significant predictor of abnormal DNA fragmentation in the regression model (OR 1.16; 95% CI 1.03,1.32; p=0.02).

CONCLUSIONS: Older male age and lower sperm motility, but not smoking, obesity, or environmental or lifestyle exposures are associated with increased DF among infertile males. Longitudinal studies are needed to confirm causal inference. The role of abnormal DF during infertility treatment as well as optimizing treatment options in men with abnormal DF is worthy of further study.

SUPPORT: R25 HD 075735; U10HD077844, U10HD077680, U10 HD077841, U10HD027049; U10HD038992; and U10HD059525.

P-649 Wednesday, October 16, 2019 6:30 AM
ANTIOXIDANT COMBINATION THERAPY: A NEW HOPE FOR OLIGOATHENOTERATOSPERMIC PATIENTS. Kareim Khalafalla, MD, a Mohamed Arafa, MD, MPH, Chi-Huang Chen, MD, PhD. Taipei Medical University Hospital, Taipei, Taiwan.

OBJECTIVE: Idiopathic oligoathenoteratospermia (ioAT) is a challenging condition often seen in up to 40% of infertile men and has been linked with increased seminal oxidative stress. This study aims at evaluating the effect of antioxidant combination formula (FH PRO) on the semen parameters and advanced sperm function tests in patients with ioAT.

DESIGN: Prospective clinical trial.

MATERIALS AND METHODS: Patients presenting to the Male infertility clinic with semen parameters showing ioAT (sperm concentration > 1 and ≤ 15 million/ml, motility ≤ 40%, normal forms ≤ 0.4%) were included in the study. Patients with clinical varicocele, epididymo-orchitis, irradiation or chemotherapy, history of recent STDs infection, malignancy and recent antioxidant use were excluded. Study subjects received antioxidant formula FH PRO, Fairhaven Health (1000 mcg B12, 30mg Zinc, 140mcg Selenium, 350mg Arginine, 2000mg, 200mg Co-Q10, 120mg Vitamin C, 200IU Vitamin E) (Fairhaven Health, Bellingham, WA) daily for 3 months.

Semen samples were collected before and after treatment and analyzed according to WHO 5th edition guidelines and for oxidation reduction potential (ORP) (MIOXSYS analyzer, Aytu Bioscience, Englewood, USA) and sperm DNA fragmentation (Halosperm kit, Halotech, Madrid, Spain). Numbers (percentages) were used to report categorical values while mean ± SE was used to report numerical values. Results were compared using Kruskal Wallis Test and a p value of <0.05 was considered statistically significant.

RESULTS: 52 infertile patients completed the study with a mean age 35.7±6.6 years and a mean infertility duration 5.9±2.4 years. There was a significant improvement in semen parameters including sperm count (p=0.001), progressive motility (p=0.002) and normal morphology (p=0.001) compared to pre-treatment results. Significant decrease in seminal oxidation reduction potential was observed (p=0.001), as well as significant decrease in sperm DNA fragmentation (p=0.007).

CONCLUSIONS: Medical treatment of infertile men with idiopathic OAT by Fairhaven Pro resulted in a significant improvement in semen parameters, reduction in seminal oxidative stress and sperm DNA fragmentation. We conclude that these changes should lead to improvement in men’s fertility and better outcome in natural conception as well as in assisted reproduction.

P-650 Wednesday, October 16, 2019 6:30 AM
THE VALUE AND USAGE OF DNA BANKING ON SEMEN DONORS. Lauren Isley, M.S., L.C.G.C., Kara Baldwin, M.S., Pamela Callum, M.S., California Cryobank, Los Angeles, CA.

OBJECTIVE: To illustrate the uses and benefits of banked extracted DNA on semen donors based on our experience with genetic evaluation needs after the donor’s initial qualification.

DESIGN: Data was compiled for all additional genetic evaluation needs on California Cryobank (CCB) semen donors from 2017 to 2018 following the donor’s initial qualification. Cases involving stored DNA as the utilized sample type were identified. The data was then evaluated based on the specific indication for the additional testing.

MATERIALS AND METHODS: Not applicable.

RESULTS: Banked extracted DNA was utilized for genetic evaluation purposes in 24 cases involving 19 donors. In the majority of cases (13/24), the additional testing was performed based on a recipient’s request to evaluate the donor’s carrier status for an autosomal recessive condition for which the recipient was a carrier. One case involved a request to perform HLA testing for compatibility purposes. In seven cases, extracted DNA was utilized for preimplantation genetic testing (PGT) assay creation based on recipient need. Three cases involved additional genetic testing on the donor prompted by the report of a genetic condition in a donor-conceived offspring. In 2 of these 3 cases, testing confirmed the donor’s carrier status for an autosomal recessive condition for which he was not previously tested, resulting in restricted distribution of remaining vials and recipient notifications.

CONCLUSIONS: Banking extracted DNA on gameote donors is advantageous both for gamete donor facilities and recipients. Banked DNA is valuable when a donor is unavailable for sample collection and may serve multiple purposes, including additional evaluations to investigate reports of genetic diagnoses in donor-conceived offspring. Given the rapid evolution and availability of genetic testing, gamete donor facilities may consider a uniform approach to DNA banking on donors with careful attention to the initial consent process for DNA collection and re-contacting donors to discuss requests for specific uses of their DNA samples.

SUPPORT: California Cryobank.

P-651 Wednesday, October 16, 2019 6:30 AM
COMPARISON OF SEMEN QUALITY IN NORTHERNTAIWAN BETWEEN 2017 AND 2001-2010. Shang-Yu Tseng, Master, Chii-Ruey Tseng, MD, MPH, Chi-Huang Chen, MD, PhD. Taipei Medical University Hospital, Taipei, Taiwan.

OBJECTIVE: Semen quality is a crucial indicator of male reproductive ability. This study aimed to show the trend of men sperm quality in northern Taiwan in the year of 2017.

DESIGN: We recruited 1125 male samples in 2017 from Center of reproductive Medicine, Taipei Medical University Hospital. The semen data of 2017 were compared to the semen data from 2001 to 2010.

MATERIALS AND METHODS: Semen analysis was performed through standardized methods outlined in the World Health Organization laboratory manual. Furthermore, sperm sample of low quality rate was calculated.

RESULTS: The median of sperm volume, total sperm count, progressive sperm motility and rapid progressive sperm motility in 2017 was decreased by 0.56ml, 2.1710^6/ml, 8% and 3% respectively, compared to the data of 2001-2010. Low quality rate of sperm concentration, volume, total sperm count, progressive motility and rapid progressive motility in 2017 were increased significantly.

CONCLUSIONS: These finding shows the fact that man sperm parameter values were significantly decreased in the year of 2017 in comparison with the data in 2001-2010. Moreover, it was estimated that total sperm count was decreased by 2.85x10^3/ml annually.

FERTILITY & STERILITY®
P-652 Wednesday, October 16, 2019 6:30 AM

PERSISTENT GENDER GAP AND A TREND TOWARDS SUBSPECIALIZATION: CHARACTERISTICS OF SURGEONS PERFORMING VASECTOMY IN THE UNITED STATES. Joshua A. Halpern, MD, MS, a Mary Kate Keeter, MPH, a Alexander J. Tatem, MD, a Katelyn Zumpf, MS, a Leah J. Welty, PhD, a Nelson E. Bennett, Jr., MD, a Robert E. Branigan, MD, a Northwestern University Feinberg School of Medicine, Chicago, IL; bNorthwestern University, Chicago, IL; cMen’s Health Center, Indianapolis, TX.

OBJECTIVE: We sought to characterize trends in the characteristics of urologic surgeons performing vasectomy over time.

DESIGN: Retrospective, cross-sectional study.

MATERIALS AND METHODS: We examined surgeon characteristics for catalogs from American Board of Urology (ABU) certifying urologists between 2004 and 2013, which included information on surgeon age, gender, certification cycle, self-reported subspecialty, and practice area population. We used generalized estimating equations (GEE) with a log link and negative binomial distribution to determine whether the association between a surgeon characteristic, such as gender, and the count of vasectomies, changed over time. Analyses were conducted in R version 3.4.3 and SAS 9.4.

RESULTS: A total of 115,146 vasectomies were performed by 5,415 individual certifying urologists. Mean surgeon age was 43.9 ± 8.3 years, which remained stable throughout the study. The majority of surgeons self-identified as general urologists (80.6%). A small proportion self-identified as andrology and infertility specialists (1.7%), pediatric urologists (1.4%), and other specialists (16.4%). Surgeons were equally distributed across the various certification cycles.

CONCLUSIONS: While the number of vasectomies performed per certifying surgeon during the study period was 12 (interquartile range [IQR] 5-23), ranging from 10 to 12.5 for each individual certifying year. Based on the distribution of vasectomies performed per cycle year, The majority of vasectomies were performed by high-volume surgeons (≥ 23 vasectomies) ranging from 51.5% - 66.0%, whereas the proportion performed by low-volume (≤ 5 vasectomies) surgeons ranged from 4.2% - 6.13%. The maximum number of vasectomies performed by a single certifying surgeon was 1,183. Female surgeons accounted for approximately 7.0% of all certifying urologists. Mean surgeon age was 43.9 ± 8.3 years, which remained stable throughout the study. The majority of surgeons self-identified as general urologists (80.6%). A small proportion self-identified as andrology and infertility specialists (1.7%), pediatric urologists (1.4%), and other specialists (16.4%). Surgeons were equally distributed across the various certification cycles.

P-655 Wednesday, October 16, 2019 6:30 AM

PREDICTIVE BIOMARKER AS MICROBIOMES IN THE SEMINAL PLASMA ASSOCIATED WITH SPERMATOGENESIS STATUS. HyoJeong Kwon, b Boyoung Jeon, b Eunji Lee, b Hyeon Kang, b TaiEun Shin, a Kyu Bum Kwack, Ph.D., a Jung-Jae Ko, Ph.D. a, b Daesun Kim, M.D. Ph.D., a Jae Ho Lee, Ph.D. c aCHA Fertility Center in Seoul, Seoul, Korea, Republic of (South); bDepartment of Biomedical Science, CHA University, Seoul, Korea, Republic of (South); cCHA Fertility Center, Seoul, Korea, Republic of (South).

OBJECTIVE: Whether microbiota in seminal plasma has a specific co-relationship with spermatogenesis status on male fertility or not?

DESIGN: Andrology at the in vitro fertilization center.

MATERIALS AND METHODS: We investigated that whole microbiome screen in the seminal plasma of normal group (4 cases), abnormal group (4 cases; sertoli cell only syndrome (SCO) 2 cases, hypospermatogenesis 2 cases) using next generation sequencing (NGS). We harvested normal semen and azoosperma semen by SCO, Klinefelter’s syndrome, and hypospermatogenesis cases. And we performed microbiome analysis used by NGS for identification of microbiome in the seminal plasma of normal and azoosperma patients. Therefore, we analyzed microbiome’s taxonomic composition of each sample from phylum to genus level.

RESULTS: Based on the metagenomics-NGS, we found that total 638 microbe genome counts in the seminal plasma. Therefore, non-obstructive azoosperma present 437 genomes count number and normal spermatoza present by 384 genomes count of microorganisms. We investigated specific microbiome on the genus level in the azoosperma patient compared to normal group. Azoosperma group present a significantly higher population of Prevotellaceae, Prevotella, Porpyromonas, Streptococcus, and Sutterellaceae compared to normal spermatoza group. In the case of hypospermatogenesis group showed a specifically more abundant Prevotellaceae, Prevotella, Streptococcus than Porpyromonas, Sutterellaceae in the seminal plasma. Normal group revealed more variable microbiota regarding family and genus bacteria compared to azoosperma patients and have no major dominant microbiota.

CONCLUSIONS: Specific microbiome profiling data may be valuable for prediction of normal spermatogenesis. The small sample size used in the present study may be insufficient to clarify the role of microbiota in this preliminary study. However, this data showed possible for the external validation study of seminal plasma microbiota. Male infertility may be associated with the residual bacterial flora as microbiomes microenvironment.

P-656 Wednesday, October 16, 2019 6:30 AM

SUB-FERTILITY AND ITS PSYCHOLOGICAL IMPACT ON MEN. Pranav Dadhich, MD, Garrett K. Berger, PharmD, Peter N. Dietrich, MD, Johnathan Doolittle, MD, Abbey Kruper, PsyD, Jay I. Sandlow, MD. Medical College of Wisconsin, Milwaukee, WI.

OBJECTIVE: Inertility affects an estimated 15% of couples attempting to conceive. Of these couples, male factor etiology is thought to play a part in
MATERIALS AND METHODS: This single-center prospective study utilized a questionnaire containing both narrative questions and a Likert survey to probe overall psychological and emotional domains relevant to the impact of sub-fertility on males. Specifically, the effects of sub-fertility on mood, marital relations and sexual experience were assessed. The Likert survey was utilized to better characterize patient’s abilities to cope with sub-fertility as well as the desire for additional resources in regards to its impact. Data were analyzed using SPSS v24.

RESULTS: One hundred sixty-four men completed the questionnaire. Of those, 83 men (51.6%) reported a negative effect on mood, 40 (24.8%) reported a negative effect on their relationship and 40 (24.8%) described a negative effect on their sexual experience. Approximately one third of men (34.6%) doubted their ability to manage the emotional impact of this pathology. Lastly, around one-fourth of men (25.7%) requested additional resources to aid in coping with these psychological impacts.

CONCLUSIONS: Sub-fertility has a significant impact on the emotional and psychological well-being of men who presented to our infertility clinic. As indicated above, one in four men feel the need for additional resources or treatment to address the psychological impact of this pathology. When encountered in clinic, these particular individuals are provided pamphlets and/or appropriate referrals when indicated. While the medical management of infertility remains paramount, it is important to consider the emotional toll this pathology has on patients and possible need for further resources.

OBJECTIVE: Mammalian semen consists of spermatozoa and accessory glands fluid secretions which promote sperm survival, motility and overall male fertility. A primary component of seminal fluid are prostaglandins (PG), which have a dual role: facilitation of sperm transport within the female reproductive tract, via inducing peristaltic contractions (PGF2α), and induction of sperm motility (PGE1; PGE2). A partial loss or an altered ratio of a reproductive tract, via inducing peristaltic contractions (PGF2α), and induc-

<table>
<thead>
<tr>
<th>TABLE. Demographics, Healthcare Utilization, and Overall Health Status of Fertile and Infertile Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infertile Fertile</td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>Age, years</td>
</tr>
<tr>
<td>Income, % of poverty level</td>
</tr>
<tr>
<td>Religion, %</td>
</tr>
<tr>
<td>No Religion</td>
</tr>
<tr>
<td>Catholic</td>
</tr>
<tr>
<td>Protestant</td>
</tr>
<tr>
<td>Other Religions</td>
</tr>
<tr>
<td>Race, %</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>Black</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Martial Status, %</td>
</tr>
<tr>
<td>Married</td>
</tr>
<tr>
<td>Widowed</td>
</tr>
<tr>
<td>Divorced/Separated</td>
</tr>
<tr>
<td>Never Married</td>
</tr>
<tr>
<td>Education, %</td>
</tr>
<tr>
<td>Less than High School</td>
</tr>
<tr>
<td>High School</td>
</tr>
<tr>
<td>College</td>
</tr>
<tr>
<td>Health Insurance Status %</td>
</tr>
<tr>
<td>Private</td>
</tr>
<tr>
<td>Medicaid</td>
</tr>
<tr>
<td>Military</td>
</tr>
<tr>
<td>Uninsured</td>
</tr>
<tr>
<td>Usual Place for Healthcare, %</td>
</tr>
<tr>
<td>Excellent</td>
</tr>
<tr>
<td>Very Good</td>
</tr>
<tr>
<td>Good</td>
</tr>
<tr>
<td>Fair</td>
</tr>
<tr>
<td>Poor</td>
</tr>
<tr>
<td>Health Status, %</td>
</tr>
</tbody>
</table>

OBJECTIVE: Epidemio-

| Data were analyzed using SPSS v24.
| RESULTS: One hundred sixty-four men completed the questionnaire. Of those, 83 men (51.6%) reported a negative effect on mood, 40 (24.8%) reported a negative effect on their relationship and 40 (24.8%) described a negative effect on their sexual experience. Approximately one third of men (34.6%) doubted their ability to manage the emotional impact of this pathology. Lastly, around one-fourth of men (25.7%) requested additional resources to aid in coping with these psychological impacts.

CONCLUSIONS: Sub-fertility has a significant impact on the emotional and psychological well-being of men who presented to our infertility clinic. As indicated above, one in four men feel the need for additional resources or treatment to address the psychological impact of this pathology. When encountered in clinic, these particular individuals are provided pamphlets and/or appropriate referrals when indicated. While the medical management of infertility remains paramount, it is important to consider the emotional toll this pathology has on patients and possible need for further resources.

OBJECTIVE: Mammalian semen consists of spermatozoa and accessory glands fluid secretions which promote sperm survival, motility and overall male fertility. A primary component of seminal fluid are prostaglandins (PG), which have a dual role: facilitation of sperm transport within the female reproductive tract, via inducing peristaltic contractions (PGF2α), and induction of sperm motility (PGE1; PGE2). A partial loss or an altered ratio of a

<table>
<thead>
<tr>
<th>TABLE. Demographics, Healthcare Utilization, and Overall Health Status of Fertile and Infertile Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infertile Fertile</td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>Age, years</td>
</tr>
<tr>
<td>Income, % of poverty level</td>
</tr>
<tr>
<td>Religion, %</td>
</tr>
<tr>
<td>No Religion</td>
</tr>
<tr>
<td>Catholic</td>
</tr>
<tr>
<td>Protestant</td>
</tr>
<tr>
<td>Other Religions</td>
</tr>
<tr>
<td>Race, %</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>Black</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Martial Status, %</td>
</tr>
<tr>
<td>Married</td>
</tr>
<tr>
<td>Widowed</td>
</tr>
<tr>
<td>Divorced/Separated</td>
</tr>
<tr>
<td>Never Married</td>
</tr>
<tr>
<td>Education, %</td>
</tr>
<tr>
<td>Less than High School</td>
</tr>
<tr>
<td>High School</td>
</tr>
<tr>
<td>College</td>
</tr>
<tr>
<td>Health Insurance Status %</td>
</tr>
<tr>
<td>Private</td>
</tr>
<tr>
<td>Medicaid</td>
</tr>
<tr>
<td>Military</td>
</tr>
<tr>
<td>Uninsured</td>
</tr>
<tr>
<td>Usual Place for Healthcare, %</td>
</tr>
<tr>
<td>Excellent</td>
</tr>
<tr>
<td>Very Good</td>
</tr>
<tr>
<td>Good</td>
</tr>
<tr>
<td>Fair</td>
</tr>
<tr>
<td>Poor</td>
</tr>
<tr>
<td>Health Status, %</td>
</tr>
</tbody>
</table>

OBJECTIVE: Epidemiologic studies have found that a greater degree of comorbidity is associated with worse fertility potential. However, these findings are largely based on retrospective studies of men interacting with the health care system. Our objective was to evaluate the association of fertility and health status in men in the United States using a nationally representative survey.

DESIGN: We compared the demographics, healthcare utilization, and overall health status of fertile and infertile men in the National Survey for Family Growth (NSFG).

MATERIALS AND METHODS: We performed an analysis of the male 2011-2017 cycles of the NSFG, a nationally representative survey of family planning. Infertile men were defined as men who had ever used infertility services or men who self-reported as non-surgically sterile. Men who reported completed pregnancies were considered fertile.

RESULTS: Of the 13,861 men surveyed, 1,071 men were infertile, and 5,661 men were known to be fertile. Projecting to the national population, this translates to 5,205,771 infertile men and 26,577,702 fertile men. Of the total population of sexually active men aged 15-49, roughly 8.5% (95% CI: 7.8-9.3) of men were infertile. Compared to known fertile men, infertile men had significant demographic and healthcare utilization differences (Table). Infertile men were wealthier, better educated, more likely to be white, more likely to be married, and more likely to have private insurance. Importantly, infertile men and fertile men had similar overall health status. On multivariate analysis, differences in income, marital status, and usual healthcare place remained significant.
CONCLUSIONS: While infertile men do have significant demographic and healthcare utilization differences compared to fertile men, the overall health status of both infertile and fertile men appear similar.

P-658 Wednesday, October 16, 2019 6:30 AM

AN EVIDENCE-BASED ANALYSIS OF INGREDIENTS IN POPULAR MALE FERTILITY SUPPLEMENTS. Manish Kuchakulla, B.S., Yash Soni, B.S., Premal Patel, MD, Ranjith Ramasamy, MD University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: To study the level of evidence available for ingredients of popular over-the-counter male fertility supplements.

DESIGN: Systematic review

MATERIALS AND METHODS: We performed a systematic search using the terms “male fertility supplement”, “male sperm supplement”, and “male reproductive supplement”. We identified the top male fertility supplements available from the most commonly used online retailers in the United States: A1 Supplements, Amazon, Vitamin Shoppe, and Walmart. The ingredients of each of these supplements were identified and a systematic review was performed to identify randomized controlled trials studying each ingredient impact on sperm parameters and/or live birth rates using search terms, “Xingredient and sperm,” “Xingredient and male fertility,” and “Xingredient and sperm parameters.” A score was assigned to each ingredient based on its available evidence using The American Heart Association Evidence-Based Scoring System. Subsequently, a composite level of evidence score was calculated for each supplement to assess its overall level of evidence.

RESULTS: Ninety unique ingredients were identified from the top 17 listed male fertility supplements. The most commonly used ingredients were Vitamin E, Folic Acid, Zinc, Vitamin C, Selenium, Vitamin B12, L-Carnitine, and Maca. Only 17% of ingredients had published data showing positive effect on semen parameters, of these, the most studied ingredients are L-Carnitine, Vitamin E, Vitamin C, CoQ10, and Zinc. None of the supplements had any published evidence of their use in a randomized controlled trial. Our scoring system gave an average composite rating of 1.66 (on a scale to 5) for the evidence level of the popular supplements. Evolution 60 and Conception XR had the highest composite scores with 3.6 and 3.5, respectively. Mitamen and Standard Process scored the lowest with 0 and -3.3, respectively.

CONCLUSIONS: Many fertility supplements claim to improve fertility; however, their promises are rarely backed by evidence. Very few ingredients used in popular fertility supplements had positive evidence demonstrated in randomized clinical trials. These findings can help providers counsel men attempting conception about the use of the over the counter supplements.

P-659 Wednesday, October 16, 2019 6:30 AM

ELEVATED BLOOD SUGAR PARAMETERS IN YOUNG INDIAN MEN ATTENDING OUR FERTILITY CLINIC. Madhavi M. Panpalia, MS, a Sujatha Reddy, MD, b Chitra Ishwar, MD, b Meenal Khandeparkar, MS, b Dattatray Naik, MSc, c Suresh Dhumal, MSc, c Prashant Makwana, MSc, c Firuza Rajesh Parikh, MD DNB PhD, d Jashol Hospital and Research Centre, Mumbai, India, e Genexplore Diagnostics and Research Centre Pvt. Ltd., AHMEDABAD, India.

OBJECTIVE: India is considered the diabetic capital of the world (1). This study aims to review the levels of high blood sugar parameters for the incidence of Type 2 Diabetes in young male partners of Indian couples seeking fertility treatment since there is a paucity of studies documenting blood sugar levels in young Indian men.

DESIGN: Retrospective observational study in the young Indian male visiting our Fertility Centre.

MATERIALS AND METHODS: Over a 6 month period, 727 male partners of Indian ethnicity (median age 35 years, range 24 - 45 years) of couples visiting our fertility clinic for the first time were investigated for blood sugar levels with one or more of the following parameters:

- Fasting plasma glucose (FFPG) with no calorie intake for at least 8 hours.
- 2 hours plasma glucose (2 hr PG) during oral glucose tolerance test (OGTT) using a glucose load containing 75 gm glucose.
- Glycosylated Haemoglobin (HbA1C).

Criteria by the American Diabetes Association (ADA) for the diagnosis of Diabetes

<table>
<thead>
<tr>
<th></th>
<th>Fasting plasma glucose (FFPG)</th>
<th>2 hrs plasma glucose in OGTT</th>
<th>HbA1C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic</td>
<td>≥ 126 mg/dl</td>
<td>≥ 200 mg/dl</td>
<td>≥ 6.5 %</td>
</tr>
<tr>
<td>Prediabetic</td>
<td>100 - 125 mg/dl</td>
<td>140 - 199 mg/dl</td>
<td>5.7 - 6.4 %</td>
</tr>
<tr>
<td>Normal</td>
<td>&lt; 100 mg/dl</td>
<td>&lt; 140 mg/dl</td>
<td>&lt; 5.7 %</td>
</tr>
</tbody>
</table>

RESULTS: Of the 727 young male partners, while 62 (8.5 %) were diabetic, 279 (38.4 %) were prediabetic. The remaining 386 (53.1 %) were normal.

CONCLUSIONS: Our study found that Indian men showed deranged blood sugar parameters indicating the prevalence of diabetes in young Indian men. Furthermore it highlights the importance of screening male partners prior to fertility treatment. In India, a trend indicates that there is a rapid increase in the number of individuals becoming diabetic and a decline in the mean age of onset of Type 2 Diabetes. This is a disturbing trend as Type 2 Diabetes is seen in Indian males a decade earlier than in Caucasian males (2).


P-660 Wednesday, October 16, 2019 6:30 AM

HIV/OTHER STD INFECTIONS AMONG 338,432 INFERTILE POPULATIONS SHOULD RECEIVE MORE ATTENTION IN HUNAN, CHINA, 2012-2018: A CROSS-SECTIONAL STUDY. Gang Liu, PhD, a Weina Li, PhD, a Institute of Reproduction and Stem Cell Engineering, Central South University, changsha, China; b Reproductive and Genetic Hospital of CITIC-Xiangya, changsha, China.

OBJECTIVE: Although infertile populations were not at high risk for HIV compared with sex workers and MSM groups, they do not adjust their high risk practices in natural pregnancies for reproduction. However, data regarding HIV/STD testing, infections and coinfections among infertile couples are limited. This study aimed to assess HIV/other STD prevalence among infertile populations in China.

DESIGN: This study was performed as a retrospective survey of 338,432 infertile populations in Hunan, China, from 2012-2018 in our hospital.

MATERIALS AND METHODS: A cross-sectional hospital-based study was conducted to evaluate the prevalence of HIV/other STDs (HBV, HCV, syphilis, Chlamydia trachomatis, Neisseria gonorrhoeae, Mycoplasma genitalium (MG)) among 338,432 infertile populations. We calculated linear trends in prevalence using bivariate linear regression.

RESULTS: The overall prevalence rates of HIV, chlamydia, gonorrhea, MG, syphilis, HBV and HCV antibody positivity in this study were 0.04%, 1.73%, 0.05%, 2.60%, 2.15%, 12.01% and 0.56%, respectively. The predominant infection was HBV, followed by MG, syphilis, and chlamydia. Of those participating, 16.65% (5636/ 338342) had at least one positive test: 0.59% (1999/338432) had more than one positive test. Only 1.13% of participants (382/ 338342) reported STD signs and symptoms suggesting genital tract infection. However, the variation in HIV prevalence was not significant (β=0.000, P(trend)= 0.907) during this period. From 2012-2018, the characteristics of the HIV-infected infertile population had not shifted dramatically: women composed 32.56% of HIV cases in China, and the incidence rate for men was 2 times the rate in women. Concordant infections were found in 4.65% of infertile couples (6/ 129).

The highest incidence of 54.26% (70/129) was found at 30–39 years of age. Overall, 87.60% of the HIV-infected population had a relatively low education. All HIV-positive women discontinued treatment, but 45.98% (40/87) of HIV-positive men continued their assisted reproductive therapy with donor semen.

CONCLUSIONS: Therefore, screening for STDs should be emphasized regardless of symptoms in the clinical setting, and targeted interventions
should focus especially on infertile populations with low income and less education.

P-661 Wednesday, October 16, 2019 6:30 AM

IMPACT OF BODY WEIGHT ON SEMEN PARAMETERS AND REPRODUCTIVE HORMONES OF MEN WITH IDIOPATHIC INFERTILITY. Sami Alsaid, MD, Kareim Khalafalla, MD, Ahmad Majzoub, MD, Mohamed Arafa, MD, Haitham Elbardisi, MD, Hamad Medical Corporation, Doha, Qatar.

OBJECTIVE: Obesity is known to have a detrimental impact on human health including reproductive potential. We aim to evaluate the effect of body weight on semen parameters & reproductive hormones of men with idiopathic infertility

DESIGN: Retrospective Chart review.

MATERIALS AND METHODS: Charts of 6,483 patients who presented to our infertility clinic between 2012 - 2016 were screened. Patients with idiopathic male infertility were included while those with genetic abnormalities, varicocele, genitourinary infections, surgery and history of radiotherapy or chemotherapy were excluded. Demographic & clinical data (semen parameters, hormones & BMI) of the initial visit (before any treatment) was collected.

Patients were grouped according to the WHO BMI classification into underweight, normal, overweight and obese. Kruskal–Wallis one-way analysis of variance test was used to compare the data between them. The different variables were correlated with Spearman correlation.

RESULTS: A total of 2231 patients were included in the study. Their mean age was 36.11 ± 0.17 years & their mean BMI was 28.71 ± 0.61 kg/m². While the means of age differed significantly between the study groups, they belonged to the same age generation.

Spem concentration, progressive motility & normal morphology were highest in patients with normal body weight compared with the other patient groups. A significant increase in estradiol & a decrease in testosterone were noted as BMI increased.

A significant (p<0.001) but weak negative correlation was observed between BMI & sperm concentration (r=-0.135), progressive motility (r=-0.116), normal morphology (r=-0.110) & serum testosterone levels (r=-0.226). While a between BMI & sperm concentration (r=-0.135), progressive motility (r=-0.116), normal morphology (r=-0.110) & serum testosterone levels (r=-0.226). While a

P-662 Wednesday, October 16, 2019 6:30 AM

SIGNIFICANT DELAYS IN EVALUATION OF MALE PARTNER AMONGST INFERTILE COUPLES. Adithya Balasubramanian, BA,1 Nannan Thirumavalavan, M.D.,2 Jenna N. Bates, BS,1 Eric K. Wang, BA,1 Alan Hsieh, MD,2 Ujval S. Pathak, MPH,1 Kelly Payne, B.A.1 Alexander W. Pastuszak, MD, PhD,3 Larry I. Lipshultz, M.D.1 1Baylor College of Medicine, Houston, TX; 2University Hospitals Urology Institute/Cleveland Clinic, Cleveland, OH; 3University of Utah School of Medicine, Salt Lake City, UT.

OBJECTIVE: To characterize the prior evaluation and intervention that infertile couples received prior to male evaluation.

DESIGN: Retrospective review of couples presenting for male infertility evaluation by fellowship trained male reproductive urologists.

MATERIALS AND METHODS: Couples presenting for infertility to a male infertility specialist were identified and charts were reviewed for duration of attempting pregnancy, prior reproductive workup, and prior use of assisted reproductive technology (ART). Variables were compared between couples presenting for primary versus secondary infertility and between couples who had undertaken ART and those who had not. Physical exam findings at evaluation, and subsequent therapeutic interventions were recorded.

RESULTS: A total of 806 patients were included for analysis. The mean age at presentation was 36.2 (range 20–73) years for men, and 32.42 (range 19–53) years for women (p<0.001). 39% (312/799) of couples were first evaluated by a gynecologist only, 25% (200/799) a reproductive endocrinologist (REI) only, 18% (147/799) presented without a female workup, and 18% (140/799) of couples saw both a gynecologist and REI prior to presentation at our clinic. In total, 14% previously attempted ART; 6% (46/776) underwent intrauterine insemination (IUI) (range 1-8 cycles); 6% (43/776) underwent invitro fertilization (IVF) (range 1 to 8 cycles); 3% (20/776) underwent both IUI and IVF. Couples who had undertaken ART were attempting pregnancy for 39 months versus 22 months for those who had not undergone ART (p<0.001). The majority (63%) of females had no abnormality in their workup. 72% (78/109) of men undergoing ART had at least one abnormality diagnosed at examination. Varicocele was the most common abnormality diagnosed amongst these men (Table 1). Varicocele repair (VR) (41%, 45/109) and testicular sperm extraction (11%, 12/109) were the most common interventions pursued following evaluation.

CONCLUSIONS: Our findings highlight that a male workup for infertile couples often lags behind a female workup and sometimes even ART. We

<table>
<thead>
<tr>
<th>Exam Findings</th>
<th>Overall (N=806)</th>
<th>ART Cohort (N=109)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Riding Testicle</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Varicocele (Vx)</td>
<td>54%</td>
<td>57%</td>
</tr>
<tr>
<td>Absence of Vas</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Epididymal Cyst/Granuloma</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Hypospadias</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Interventions Pursued</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (N=806)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vx Repair</td>
<td>28%</td>
<td>41%</td>
</tr>
<tr>
<td>Testicular Sperm Extraction</td>
<td>16%</td>
<td>11%</td>
</tr>
<tr>
<td>Vasal Varicocelectomy</td>
<td>1%</td>
<td>3%</td>
</tr>
<tr>
<td>Microepididymal Sperm Aspiration</td>
<td>4%</td>
<td>2%</td>
</tr>
</tbody>
</table>
identified that undergoing a simple, inexpensive male workup composed of scrotal ultrasound, semen analysis and hormone levels identifies several correctable forms of male infertility and prompt surgical interventions such as VR that can potentially improve outcomes.

SUPPORT: A.W.P. is a National Institutes of Health (NIH) K08 Scholar supported by a Mentored Career Development Award (K08DK115835-01) from the National Institute of Diabetes and Digestive and Kidney Diseases. This work is also supported in part through a Urology Care Foundation Rising Stars in Urology Award (to A.W.P.) and NIH grant K12 DK0083014, the Multidisciplinary K12 Urologic Research (KURe) Career Development Program awarded to D.JL (NT is a K12 Scholar) from the National Institute of Kidney and Digestive Diseases to Dolores J Lamb. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

P-663 Wednesday, October 16, 2019 6:30 AM

MALE MULTIVITAMIN USE AND SEMEN QUALITY. Sydney K. Willis, M.P.H.,* Elizabeth E. Hatch, Ph.D.,* Greg Sommer, PhD, Michael L. Eisenberg, M.D.,* Tanran Wang, MPH,* Lauren A. Wise, Sc.D.,* Boston University School of Public Health, Boston, MA; Sandstone Diagnostics, Livermore, CA; Stanford University, Stanford, CA.

OBJECTIVE: To prospectively evaluate the association between male multivitamin use and semen quality. Male factors contribute up to 50% of couple infertility, but few modifiable factors have been identified. Several studies have examined the influence of male multivitamin use on semen quality, but findings have been inconsistent.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Pregnancy Study Online is a web-based preconception cohort of North American pregnancy planners. At baseline, female participants completed a questionnaire on demographics, lifestyle, and reproductive history, including multivitamin use. Multivitamin use was ascertained by asking “Which of the following vitamins and/or minerals did you take on a regular basis (daily or almost every day)?” with “multivitamins” as a response option. Female participants invited their male partners to complete a similar baseline questionnaire. During October 2015 through April 2019, a subset of male participants from the U.S. whose partners reported regular menstrual cycles were invited to use Trak, an FDA-approved device that measures sperm concentration and semen volume at home. Men were instructed to provide up to two semen tests, with at least 3 days of abstinence time, and upload their results online via self-report and smartphone photo images. We used generalized estimating equations, accounting for within-person correlation, to estimate risk ratios (RR) and 95% confidence intervals (CI) for the association between male multivitamin use and low semen volume (≤ 2 vs >2 ml), low sperm concentration (≤ 20 vs >20 million/ml), and low total sperm count (TSC, ≤ 50 vs >50 million). The analysis included 223 men who provided a total of 375 samples. The median and interquartile range of attempt time for men at study enrollment was 1 (1-3 cycles). We adjusted for abstinence time, age, body mass index (BMI), and lifestyle and socio-demographic factors.

RESULTS: At baseline, 34% of male participants reported taking multivitamins on a regular basis. Nearly 14% of samples had semen volume ≤ 2 ml, 18% had sperm concentration ≤ 20 million/ml, and 14% had TSC ≤ 50 million. Compared with men not taking multivitamins regularly, RRs for men reporting regular multivitamin use were 0.98 (CI: 0.54-1.78) for low semen volume, 0.66 (CI: 0.40-1.09) for low sperm concentration, and 0.74 (CI: 0.42-1.31) for low TSC.

CONCLUSIONS: In a geographically heterogeneous cohort of U.S. men, we observed slight inverse associations between regular multivitamin use and low semen concentration and low TSC; little association was observed for low TSC.

P-665 Wednesday, October 16, 2019 6:30 AM

EFFECT OF MEDICAL COMORBIDITIES OVER SEMINAL PARAMETERS AND SPERM DNA FRAGMENTATION. Cristian R. Alvarez Sedo, PhD, Heydy W. Uriondo Boudri, MSc., Lourdes Correa Brito, BS, Federico Bleckwedel, BS, Carolina Salazar, MD, Natalia Vic, MD, Carlos Sancho Minano, MD FERTILIA, TUCUMAN, Argentina.

OBJECTIVE: Several publications have been shown that it could be a relationship between male infertility and general health status. The aims of this study were to investigate the prevalence and effect of some medical comorbidities over sperm parameters and DNA fragmentation in an Argentinian population.

DESIGN: Retrospective controlled cohort study.

MATERIALS AND METHODS: Under the approval of the institutional ethics committee, a retrospective study was performed for 1,092 men who were examined due to infertility between August 2017 and April 2019. The initial evaluations were comprised of a complete medical history, a physical examination, endocrine assessment, and at least two semen analyses. Sperm parameters and DNA fragmentation were compared between men with and without medical comorbidities.
RESULTS: Significant medical comorbidities were found in 112 of 1092 (10.3%) men, including 3.6% with hypertension, 2.3% with hypothyroidism, 2% with mental, 2% with diabetes/dyslipemia and 0.6% with respiratory disease. Semen volume, sperm count and progressive motility were significantly lower in men with comorbidities that in men without comorbidities (p=0.045, p=0.036 and p=0.025, respectively). Regarding sperm DNA fragmentation, it was higher in patients with comorbidities (p=0.018). Sperm vitality and strict morphology were not significantly different. Within patients with comorbidities, patients with diabetes/dyslipemia and anxiety disorders presented significantly higher levels of DNA fragmentation (p=0.001).

CONCLUSIONS: After this preliminary study, we can conclude that medical comorbidities are associated with the impairment of sperm production and function. It has been published that obesity and metabolic disorders could be associated with impaired sperm function by altering physical and molecular structure of germ cells. A complete male infertility evaluation, including an exhaustive anamnesis, could offer the possibility of specific therapy in order to improve some semen parameters. We didn’t assess this theoretical benefit, however it would be very interesting to evaluate if that therapy, despite the improvement of the general health status, could improve the spermatogenesis.

MALE REPRODUCTION AND UROLOGY - BASIC

P-666 Wednesday, October 16, 2019 6:30 AM

ROLE OF LEPTIN AS A PARACRINE FACTOR CRITICAL FOR HUMAN LEYDIG STEM CELL FUNCTION AND DIFFERENTIATION. Himanshu Arora, PhD, Ranjith Ramasamy, M.D. University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: Impaired testosterone production as a result of Leydig cell loss or dysfunction can occur in men with testicular failure. Although several testosterone formulations are available, none are capable of replicating the physiological pattern of testosterone secretion. We have shown in our recent study conducted in murine models that, Leydig stem cell transplantation along with peritubular myoid cells and Sertoli cells could be used to physiologically increase serum testosterone thereby potentially minimizing the adverse effects. However, in order to optimize the function of Leydig stem cells, we need to understand the paracrine factors released by myoid and Sertoli cells. In the present study we evaluated the significance of paracrine factors secreted by human peritubular myoid cells and Sertoli cells on Leydig stem cell function.

DESIGN: A total of 8 men with testicular failure underwent testis biopsies for sperm retrieval. Using an IRB approved protocol, about 10mg of testicular tissue from each of these men were processed for Leydig stem cell isolation, culture and characterization.

MATERIALS AND METHODS: The presence of Leydig stem cells (LSCs), Sertoli cells (SCs) and peritubular myoid cells (PMCs) in the harvested adult testes was confirmed by immunohistochemistry and real time PCR (qPCR) using PDGF-α, 3βHSD and Sox-9, PZLF, respectively. After stimulation by Luteinizing hormone (LH), the levels of 3βHSD mRNAs were increased. Additionally, the CD146 (+) cells representing LSCs were sorted using MACS kit and maintained along with unsorted cells in charcoal stripped medium. Condition media was collected from both the cell types and screened for secreted protein using RayBio Human Antibody Array for a total of 80 molecules.

RESULTS: We successfully isolated and cultured LSCs from all 8 testis biopsies. We were able to culture up to 3 million cells/biopsy. Of the cells cultured, up to 70% of the cells were Leydig stem cells and 10% of them were Sertoli-cell in origin on day 14. IF and qPCR data showed as the majority of cell population was up to 70% of the cells were Leydig stem cells and 10% of them were Sertoli-cell in biopsies. We were able to culture up to 3 million cells / biopsy. Of the cells cultured, both the cell types and screened for secreted protein using RayBio Human.

PRESENTATION AND DISCUSSION: Leptin is a specific paracrine factor which is released by Sertoli and myoid cells which could be critical for LSC differentiation and testosterone production. Further studies are ongoing to validate the implications of Leptin in terms of their role in LSCs function, differentiation and survival. Leptin is a specific paracrine factor which is released by Sertoli and myoid cells which could be critical for LSC differentiation and testosterone production. Further studies are ongoing to validate the implications of Leptin in terms of their role in LSCs function, differentiation and survival.

SUPPORT: Supported by the American Urological Association Research Scholar Award and Stanley Glaser Award to RR. J.M.H. is supported by NIH grants IR01 HL137355, IR01 HL107110, IR01 HL134558, SR01 CA136387, 5UM1 HL113460 and Soffer Family Foundation.

P-667 Wednesday, October 16, 2019 6:30 AM

IDENTIFICATION OF TWO NOVEL SEMINAL PEPTIDES, WHICH ACT AS NEUTRAL ENDOPEPTIDASE INHIBITORS AND MODULATE SPERM MOTTILITY. Alexander Kucherov, MD, ’ Kelvin Davies, PhD. ’ Albert Einstein College of Medicine / Montefiore Medical Center, Bronx, NY. ’ Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: Poor sperm motility is highly predictive of male factor infertility. Semenogelins, and their peptide products, are recognized as important determinants of sperm motility; most research suggests they act as inhibitors of sperm motility. Peptidomic analysis of semen identified several semenogelin-derived peptides. Based on sequence analysis, these peptides may act as substrates, and thereby inhibitors, of neutral endopeptidase (NEP). Since inhibition of NEP activity has been associated with increased sperm motility, this raises the intriguing possibility that certain semenogelin-derived peptides may activate sperm motility. The present study determined if two novel seminal semenogelin-derived peptides, (RSIY-15 and SSIIY-15), were indeed NEP inhibitors and if they had a positive effect on sperm motility.

DESIGN: A colorimetric assay was performed using recombinant human NEP enzyme at 0.1 μg/ml and fluorogenic NEP peptide substrate. RSIY-15 and SSIIY-15 were synthesized and the colorimetric assay was performed to evaluate their inhibitory nature and Ki. Sperm analysis was undertaken in order to determine the effects of RSIY-15 and SSIIY-15 on sperm motility.

MATERIALS AND METHODS: 50μL of substrate, at a range of concentrations, was added to 50μL of NEP enzyme followed by 50μL of a range concentrations of RSIY-15 and SSIIY-15. Dixon and Lineweaver Burk plots were generated to evaluate the inhibitory nature of RSIY-15 and SSIIY-15. Semen samples from patients presenting for routine semen analysis were collected; semen from each patient was divided into aliquots and motility analyzed following addition of 1μL of 75μM RSIY-15 or SSIIY-15. Addition of 1μL 75μM RSIY-11 or 200 μM Opiorphin (peptides previously identified as NEP inhibitors) were utilized as positive controls, and vehicle (PBS) was utilized as negative control. Additionally, 1 aliquot was set aside without addition. 2μL of semen was then placed into a 4-chamber microlcell disposable counting chamber slide. Progressive and non-progressive motility was assessed at 0, 30, and 60 minutes after the addition of peptide. Wilcoxon Rank-Sum Tests were used to evaluate differences in sperm motility between groups.

RESULTS: Colorimetric assays indicate that RSIY-15 and SSIIY-15 both act as competitive inhibitors of NEP. Both peptides appear to have Ki similar to RSIY-11 (12.58 ± 3.75 μM and 13.69 ± 5.44 μM, respectively). Semen analysis for 30 patients was undertaken. Compared to PBS controls, the addition of RSIY-15 and SSIIY-15 lead to improved progressive and total sperm motility (p < 0.05).

CONCLUSIONS: The novel seminal semenogelin-derived peptides RSIY-15 and SSIIY-15 act as competitive inhibitors of NEP. Both peptides increased progressive and total sperm motility when added to semen samples. Contrary to the prevailing viewpoint that semenogelin is primarily an inhibitor of sperm motility, our observations demonstrate that semenogelin and its peptide products both activate and inhibit sperm motility. Further studies are underway to investigate the breakdown products of these peptides, and to compare the peptidomic profiles of fertile and infertile men.

SUPPORT: NIH/NIDDK (DK107807 awarded to KD).
**P-670 Wednesday, October 16, 2019 6:30 AM**

**FAM9B WAS ASSOCIATED WITH HUMAN SPERMATOGENESIS AND MALE-SPECIFIC STERILITY.** Xinjie Zhuang Dr, Ping Liu, prof., Reproductive Medicine Center. Department of Obstetrics and Gynecology, Peking University Third Hospital, Beijing, China.

**OBJECTIVE:** Spermatogenesis is the process of gamete formation, which includes mitosis in spermatogonia, meiosis in spermatocytes, and spermiation. A key event is the formation of the synaptonemal complex (SC). Mutations of genes encoding SC components (such as SYCP3, synaptonemal complex protein 3) lead to infertility or subfertility due to germ cell death. Fam9B mapped on the human chromosome X (Xp22.3) was more similar to SYCP3 in their amino acid sequences and expressed in human testis. However, the expression and precise underlying mechanisms of Fam9B have not been clearly in testes during the spermatogenesis and infertility. And Fam9B mutation associated with sterility?

**DESIGN:** This study was an analysis of azoospermia, sertoli cell only syndrome (SCOS) and proven fertile patients, including 162 patients diagnosed with azoospermia, 65 patients diagnosed with SCOS and 10 proven fertile patients at the Reproductive Medical Center of Peking University Third Hospital between January 2015 and January 2019. Fam9B was cloned, expressed and identified. Genome DNA sequencing analysis, RT-PCR, Western-blot, Immunohistochemistry and immunocytochemistry were performed.

**MATERIALS AND METHODS:** Fam9B was analyzed with blood and testicular biopsy samples from azoospermia patients by genome DNA sequencing analysis. These likely mutations were further screened in SCOS patients and in men proven to be fertile. And Fam9B was cloned, expressed and identified with testicular samples using RT-PCR, western blot, Immunohistochemistry and immunocytochemistry. The concentration of testosterone in azoospermia and SCOS patients were determined, and their relativity was studied by statistic methods.

**RESULTS:** Fam9B mRNAs and protein were detected in human testis, and Fam9B was expressed at different level in patients of azoospermia, SCOS and normal groups. Immunohistochemical staining showed that Fam9B was expressed in the nucleus of primary spermatocyte in fertile persons. Moreover, Fam9B was more similar to SYCP3 expression pattern and located on the SC during the leptotene and diplotene spermatocytes. Furthermore, genome DNA sequencing analysis revealed three fam9b deletion patients and five patients of point mutation in fam9b gene. Spermatogenesis of these three patients was arrested at spermatocytes and accompanied by germ cells lost. Interesting, testosterone concentrations levels of these three patients were decreased compared with controls (P < 0.01).

**CONCLUSIONS:** Fam9B may be a SC related protein participated in human normal spermatogenesis. And mutations of fam9b may be risk of spermatocytes arrest and male-specific sterility.


**SUPPORT:** This study was supported by Beijing Natural Science Foundation (NO.7172236) and National Natural Science Foundation of China (NO.81671513 and 81200466).

**P-671 Wednesday, October 16, 2019 6:30 AM**

**PSMA5 AND RARRES1, SEMINAL PLASMA PROTEIN MARKERS OF SPERM DNA FRAGMENTATION, ARE NOT ALTERED BY SMOKING.** Tamashiro. BSc.,* Paula Intasqui, PhD, a Ricardo P. Bertolla, DVM, PhD.b

**OBJECTIVE:** Sperm DNA fragmentation is associated with male infertility. The PSMA5 and RARRES1 genes encode seminal plasma proteins which may be involved in the DNA integrity. The objective of this study was to evaluate the relationship between sperm DNA fragmentation and the expression of PSMA5 and RARRES1 in men who smoke regularly.

**MATERIALS AND METHODS:** We evaluated 60 patients with smoking habit (smokers) and 60 control men (non-smokers). Sperm DNA fragmentation and expression of PSMA5 and RARRES1 were assessed by flow cytometry and RT-qPCR, respectively. The statistical analysis was performed using the Student t-test and the Pearson correlation coefficient.

**RESULTS:** The smoking group presented a higher percentage of sperm DNA fragmentation compared to the non-smoking group (p < 0.01). Moreover, the expression of PSMA5 and RARRES1 was lower in the smoking group (p < 0.05).

**CONCLUSIONS:** Smoking is associated with an increase in sperm DNA fragmentation and a decrease in the expression of PSMA5 and RARRES1. These findings highlight the importance of smoking cessation in the management of male infertility.
OBJECTIVE: Sperm DNA fragmentation is one of the major cellular mechanisms of male infertility and can be observed in 20% to 25% of infertile men. An earlier study has found that RARRES1 and PSMA5 proteins are altered in seminal plasma in men with high DNA fragmentation. Another study has shown that smokers present high sperm DNA fragmentation. Therefore, in this study, we wanted to evaluate whether these proteins are also altered in other causes of infertility, such as smoking.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: For this study, men aged between 20 and 50 years referred to our andrology laboratory were included. Controls, 29 normozoospermic, non-smoker men were included, and for the smoking group, 26 men who smoke only cigarettes were included. Samples were collected by masturbation, with an ejaculatory abstinence of 2 to 5 days. After liquefaction, an aliquot was used for semen analysis according to the 2010 World Health Organization manual and another was used for sperm DNA fragmentation analysis using an alkaline comet assay. The Comet Distributed Moment variable were recorded using software analysis. The remaining volume was centrifuged and seminal plasma was used for protein quantification. A volume corresponding to 50 μg protein was used for quantification of RARRES1 and PSMA5 proteins by Western blotting. Bands were then normalized by total protein by Ponceau-S. Protein contents were shown as normalized values as well as PSMA5/mL, and PSMA5/ejaculate and RARRES1/mL, and RARRES1/ejaculate. For statistical analysis, data normality of was assessed by a Kolmogorov-Smirnov test and groups were compared by an unpaired Student’s t test or Mann-Whitney test, with an alpha of 5%.

RESULTS: Control and smokers groups did not differ regarding DNA fragmentation (mean; standard deviation of 40.5; 17.45 and 47.3; 15.97 respectively). On the other hand, sperm concentration, count, and motility in smokers were lower than in the smoking group (p = 0.005, p = 0.002, p = 0.019), respectively. There was no difference between groups for PSMA5/mL (median; interquartile range of 0.23;0.18 and 0.17;0.21) and PSMA5/ejaculate (0.65;0.62 and 0.65;0.65). There was no difference between groups for RARRES1/mL (1.15;0.87 and 1.32;1.00) and RARRES1/ejaculate (4.02;3.64 and 4.57;4.79).

CONCLUSIONS: Seminal levels of PSMA5 and RARRES1 are not altered due to smoking. It is an important finding because it corroborates our hypothesis that these proteins are exclusively associated with sperm DNA fragmentation, but not with other infertility conditions, such as smoking.

P-673 Wednesday, October 16, 2019 6:30 AM

IMPACT OF INTERACTION BETWEEN OXIDATIVE STRESS ADDUCTS (OSA) LEVELS AND ACCESSORY CELLS ON SPERM DNA INTEGRITY AND COMPLEMENT REGULATORY PROTEIN. Denis Vaughan, MD, MRCP1, Denny Sakkas, PhD, Edna E. Tirado, PhD. Beth Israel Deaconess Medical Center, Boston, MA; Boston IVF, Waltham, MA; ReproSource-Quest Diagnostics, Woburn, MA.

OBJECTIVE: Factors present in the semen such as Zinc (Zn), white blood cells (WBC), Round (RC) and epithelial cells (EC) may increase the levels of oxidative stress (OS) and consequently, the formation of oxidative stress adducts (OSA) which may interact with sperm key biomolecules such as complement regulatory proteins required (CRP) for acrosome reaction and DNA producing sperm defective function. The aim of this study was to determine if OSA levels are associated with concentrations of Zn, WBC, RC, and EC and to consider if those OSA levels induce both the increase of DNA fragmentation and loss of expression of CRP.

DESIGN: Retrospective.

MATERIALS AND METHODS: Frozen semen samples from 186 men were evaluated for sperm, WBC, RC and EC concentrations by microscopy. Oxidative Stress (OSA) and Zinc (μM) were determined by spectrophotometry. The DFI (%), HDS (%), WBC (CD45) X 10⁹/mL and Expression of CD46 (CRP) were measured by flow cytometry. For the data analysis, the samples were classified into 3 OSA categories: Normal 3.8 ±(n=31), BL 3.8±1.4 (n=53) and Abnormal >4.4 (n=102). The statistical analysis was performed by ANOVA beta sigma (p<0.01).

RESULTS: The sperm DFI scores were increased both BL and Abnormal categories when were compared to Normal OSA (Normal 12.75 ± 3.39 BL 24.45 ±21 Abnormal 38.59 ± 8.16 <0.001). The concentrations of leukocytes were different for BL 0.8 ± 0.2 and Abnormal 6.8 ± 2.3 when were compared to Normal 0.4 ± 0.1 (p<0.01). The values of CRP measured as expression of CD46 indicated that BL 12.73 ± 3.07 and Abnormal 11.32 ± 4.07 are significant different when compared to Normal 15.48 ± 5.18 (p<0.05). Although no differences were found an increasing tendency are observed when the OSA levels are increasing for Zn (Normal 241.1 ± 17 μM, BL 256.4 ±19 μM and Abnormal 261.4 ± 18.4 μM), RC (Normal 3.06 ± 1.55, BL 4.55 ±3.67 and Abnormal 5.26 ± 5.74 x10⁹/mL), HDS (Normal 5.06 ± 2.12, BL 8.72 ± 3.27 and Abnormal 9.45 ± 3.60) and no differences were found among the 3 OSA groups for sperm and EC concentrations.

CONCLUSIONS: The levels of oxidative stress measured as (OSA) are associated with DNA fragmentation (DFI) and the loss of the expression of complement protein (CD46). These results also suggest a possible role for OSA in generating reactive oxygen species, and demonstrate the application of CD45 staining and flow cytometry to identify leukocytes.


5. Carver-Ward JA1, Hollanders JM, Jaroudi KA, Einspenner M, Al-Se diabetic ST, Sheht KV. Progesterone does not potentiate the acrosome reaction in human spermatozoa: flow cytometric analysis using CD46 antibody. Hum Reprod. 1996 Jan;11(1):121-
DOES THE gp130 ADENINE (A)/THYMINE (T) (rs1900173) GENE POLYMORPHISM AFFECT SEMEN QUALITY OR SPERM DNA DAMAGE? Joao Batista Oliveira, M.D., Ph.D.,a Claudia G. Petersen, Ph.D.,a Ana Lucia Mauri, B.Sc.,a Adriana Renzi, Ph.D.,a Laura D. Vagnini, B.Sc.,a Bruna Petersen, B.Sc.,a Mariana Mattila, B.Sc.,a Juliana Ricci, R.N.,a Felipe Dieamant, M.D.,a Ricardo L. R. Baruffi, M.D.,a Jose G. Franco Jr., M.D., Ph.D. Center for Human Reproduction Prof. Franco Jr, Ribeirao Preto, Brazil; aPaulista Center for Diagnosis, Research and Training, Ribeirao Preto, Brazil; bPaulista Center for Diagnosis, Research and Training, Ribeirao Preto, Brazil; cCenter for Human Reproduction Prof. Franco Jr, Ribeirao Preto, Brazil.

OBJECTIVE: To Investigate a possible correlation between the glycoprotein subunit 130 (gp130) gene adenine (A)>thymine (T) (rs1900173) polymorphism and semen quality or sperm DNA damage.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: A prospective cohort study enrolled 364 men seeking fertility care. DNA was extracted from peripheral blood, and the gp130 gene A>T (rs1900173) polymorphism was genotyped using real-time PCR with the Taqman Universal PCR Master Mix and Taqman SNP genotyping assays. Patients were genotyped for the gp130 polymorphism and were categorized as follow: A/A (n=286); A/T(n=75); or T/T(n=3). Semen analyses were compared between genotype groups.

A portion of each semen samples was used for analysis according to the WHO guidelines/morphological examination by motile sperm organelle morphology examination (MSOME). The remainder of the semen samples were tested for sperm DNA fragmentation using TUNEL assay; sperm chromatin packaging/protection was assessed using chromocycin A3(CMA3) staining; and sperm mitochondrial membrane potential(MMP) was analysed using MiToTracker Green. At least 200 spermatozoa were examined in each evaluation.

RESULTS: No correlation was observed between gp130 gene genotypes and semen quality or sperm DNA damage. Table 1 shows the data.

CONCLUSIONS: There appears to be no association between gp130 gene A>T single nucleotide polymorphism (SNP) and semen quality or sperm DNA damage. However, more studies stratified for different ethnic background should be performed in the future to clarify the possible roles of gp130 gene SNPs in the pathogenesis of male infertility.

SUPPORT: Merck Grant for Fertility Innovation (GFI-2014).

TABLE 1. gp130 gene A>T (rs1900173) genotypes vs. population and semen parameters

<table>
<thead>
<tr>
<th>Semen parameter</th>
<th>A/A</th>
<th>A/T</th>
<th>T/T</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>8.1±0.2</td>
<td>8.1±0.2</td>
<td>8.0±0.2</td>
<td>0.59</td>
</tr>
<tr>
<td>Volume (ml)</td>
<td>2.8±1.5</td>
<td>2.8±1.2</td>
<td>1.4±0.8</td>
<td>0.12</td>
</tr>
<tr>
<td>Concentration(mlx10^6)</td>
<td>62.4±50.4</td>
<td>64.2±56.4</td>
<td>90±78.6</td>
<td>0.82</td>
</tr>
<tr>
<td>Progressive motility(%)</td>
<td>53.0±16.5</td>
<td>53.6±16.0</td>
<td>68.3±8.1</td>
<td>0.16</td>
</tr>
<tr>
<td>Total motility (%)</td>
<td>60.1±16.4</td>
<td>60.9±16.0</td>
<td>74.7±8.5</td>
<td>0.17</td>
</tr>
<tr>
<td>Leukocytes (x10^6/ml)</td>
<td>0.4±0.8</td>
<td>0.3±0.3</td>
<td>0.2±0.2</td>
<td>0.19</td>
</tr>
<tr>
<td>Vitality (%)</td>
<td>61.6±15.9</td>
<td>64.3±14.4</td>
<td>73.0±7.1</td>
<td>0.26</td>
</tr>
<tr>
<td>Normal spermatozoa (%)</td>
<td>0.6±0.8</td>
<td>0.7±0.5</td>
<td>1.2±0.3</td>
<td>0.23</td>
</tr>
<tr>
<td>DNA fragmentation (%)</td>
<td>13.7±7.7</td>
<td>13.5±8.0</td>
<td>8.5±0.7</td>
<td>0.59</td>
</tr>
<tr>
<td>Apoptosis (%)</td>
<td>19.5±8.5</td>
<td>19.9±6.1</td>
<td>21.5±2.1</td>
<td>0.54</td>
</tr>
<tr>
<td>CMA3 positivity (%)</td>
<td>55.1±17.1</td>
<td>58.1±16.0</td>
<td>56±26.9</td>
<td>0.56</td>
</tr>
<tr>
<td>Abnormal MMP (%)</td>
<td>25.8±17.4</td>
<td>26.4±16.0</td>
<td>22.5±14.8</td>
<td>0.95</td>
</tr>
</tbody>
</table>
with higher precision. This application also highlights its ability to be used in other haploid samples such as second polar bodies or in vitro-generated gametes. In addition, our data supports the fact that aneuploidy rates in human sperm are low.

**P-676 Wednesday, October 16, 2019 6:30 AM**

**EFFECT OF OXIDATION-REDUCTION POTENTIAL ON MITOCHONDRIAL MEMBRANE POTENTIAL AND VITALITY OF PHYSIOLOGICALLY NORMAL HUMAN SPERMATOZOA.** Manesh Kumar Panner Selvam, PhD, Ashok Agarwal, PhD, Renata Finelli, PhD, Christopher M. Douglas, B.A., M.S., Ralf Henkel, PhD, Sajal Gupta, MD, Rakesh Sharma, PhD, American Center for Reproductive Medicine, Cleveland Clinic, Cleveland, OH; University of the Western Cape, Bellville, South Africa.

**OBJECTIVE:** Physiological levels of reactive oxygen species (ROS) are necessary for optimal sperm functions such as total and progressive motility. In our previous study, we have demonstrated that higher levels of seminal oxidation-reduction potential (ORP) negatively affects total and progressive motility. Furthermore, motility is directly related to sperm vitality and mitochondrial membrane integrity. The objective of the present study was to investigate the effect of ORP on vitality and mitochondrial membrane potential (MMP) of physiologically normal spermatozoa.

**DESIGN:** Physiologically normal sperm from donor semen samples (n=8) were exposed to different titrated levels of oxidative stress (ORP: 1.48 and 2.75 mV/10^6 sperm/mL) in sperm wash medium (SWM). MMP and sperm vitality were measured at different time intervals (0, 60 and 120 minutes). The sample size for this study was calculated with an 80% power and a significance of P<0.05.

**MATERIALS AND METHODS:** ORP of SWM was taken as base line (control) and the different ORP levels (1.48 and 2.75 mV/10^6 sperm/mL) were generated by titrating SMW with defined concentrations of the oxidative stress inducer, cumene hydroperoxide. Equal concentrations (>90%) were incubated in SMW with different ORP levels for up to 120 minutes. Eosin-nigrosin staining was performed to evaluate the vitality; whereas, JC-1 dye was used to stain the sperm cells (~1 x 10^6) to evaluate the depolarization of mitochondrial membrane. MMP was analyzed using flow cytometry after 60 and 120 minutes. Pairwise comparison analysis was carried out to determine the statistical significance.

**RESULTS:** MMP remained unchanged after sperm exposure for 60 minutes. MMP decreased to 2.5% (P=0.0014) and 61.1% (P<0.0001) at 120 minutes when sperm was exposed to ORP values of 1.48 mV/10^6 sperm/mL and 2.75 mV/10^6 sperm/mL, respectively. Vitality decreased to 21.2% (P=0.0001) at 60 minutes and 41.1% (P<0.0001) at 120 minutes when sperm were exposed to ORP values of 2.75 mV/10^6 sperm/mL.

**CONCLUSIONS:** The current findings demonstrate that spermatozoal MMP and vitality were affected at ORP levels of ≥1.48 mV/10^6 and ≥2.75 mV/10^6 sperm/mL, respectively. Hence, high seminal ORP may have a negative effect on sperm functionality and therefore on the fertilizing ability of spermatozoa.

Reference: None.

**SUPPORT:** None.

**P-677 Wednesday, October 16, 2019 6:30 AM**

**MAPPING EVOLUTION OF MAMMALIAN SPERMATOGENESIS VIA HIGH RESOLUTION TRANSCRIPTOMICS.** Adrienne N. Shami, B.S., a Sarah Munyoki, B.A., a Xianing Zheng, B.S., a Jun Z. Li, Ph.D., a Kyle E. Orwig, Ph.D., b Sue Hummoud, Ph.D., b University of Michigan, Ann Arbor, MI; University of Pittsburgh School of Medicine, Pittsburgh, PA.

**OBJECTIVE:** Sperm are unique, highly specialized cells that carry genetic information from father to offspring and provide a continuous link between the past, present, and future of a species. In all mammals, the foundational unit of fertility is the spermatogonial stem cell (SSC), which must balance self-renewal with differentiation to ensure continuous sperm production. This is reliant on coordinated intrinsic (germ-cell mediated) and extrinsic (soma mediated) regulation to guide differentiation, commitment to meiosis, and morphological maturation. While decades of research in mice have provided a critical foundation of data, studies in primates have been limited to targeted subtypes based on a priori knowledge applied from rodents. However, fundamental differences exist between lineages, limiting the utility of mouse models. As a result, these processes are not well understood in humans and efforts to restore impaired spermatogenic function have had limited success. Here, we aim to identify key differences among species in these processes by conducting unbiased global evolutionary comparisons of expression between rodents and primates in the germline and soma throughout the course of spermatogenesis.

**DESIGN:** Single cell RNA sequencing was performed on adult human and nonhuman primate testis, and datasets were analyzed both individually and also globally compared with our previously published mouse single cell atlas.

**MATERIALS AND METHODS:** Cryopreserved testes samples from 4 human and 5 macaque individuals were dissociated to single cell suspensions and isolated via microfluidics using the Drop-seq platform to conduct single-cell sequencing on multiple technical replicates.

**RESULTS:** The data revealed a continuous developmental progression from spermatogonia to spermatids in adult humans (n=4, ~14,000 cells) and rhesus macaques (n=5, ~22,000 cells), thus capturing the complete germ cell differentiation process and analogous somatic cell types across all three species. Comparing pseudotime alignments of germ cell trajectories across species identified areas of similarity and dis-synchrony of germ cell maturation program, including differences in starting and ending states and a variable “clock rate” within the trajectories. Targeted analysis of spermagonia computationally aligned discrete molecular states between species, revealing a unique undifferentiated population in primates, potentially containing SSCs. Characterization of underlying transcriptional programs and somatic cell inputs identified additional features of divergence.

**CONCLUSIONS:** Our datasets provide new insights into differences in the intrinsic germ cell program and extrinsic signals required to promote germ cell differentiation in human, nonhuman primate, and rodent testes.

**P-678 WITHDRAWN**

**P-679 Wednesday, October 16, 2019 6:30 AM**

**COMPARATIVE PROTEOMIC ANALYSIS REVEALS DIFFERENTIAL REGULATION OF REDOX HOMESTASIS AND PURPURBED OXIDATIVE PHOSPHORYLATION PATHWAY IN UNILATERAL COMPARED TO BILATERAL VARICOCELE CONDITION.** Manesh Kumar Panner Selvam, Thirumugam, PhD, Ashok Agarwal, PhD, Lunsa Samanta, PhD, American Center for Reproductive Medicine, Cleveland Clinic, Cleveland, OH; Redox Biology Laboratory, Department of Zoology, Ravenshaw University, Cuttack, India.

**OBJECTIVE:** Oxidative stress is pronounced in varicocele patients and differs between unilateral and bilateral conditions. At subcellular level, excess of oxidative stress induces damage to the cell organelles and plasma membrane. The main objective was to have a proteomic insight into seminal plasma for delineating the possible pathways involved in the etiology of sperm dysfunction in unilateral and bilateral varicocele condition.

**DESIGN:** Proteomic profiling of seminal plasma (unilateral varicocele, bilateral varicocele and fertile healthy men) was performed using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Bioinformatic analysis was conducted using ingenuity pathway analysis (IPA) software.

**MATERIALS AND METHODS:** Pooled seminal plasma samples from unilateral (n=5), bilateral (n=5) varicocele patients and fertile healthy men (n=5) were subjected to quantitative proteomic analysis. Proteins identified by LC-MS/MS in both varicocele groups were compared separately and also as combined varicocele group with the fertile group. Differentially expressed proteins (DEPs) obtained from three different analysis were subjected to comparison analysis using IPA software.
OBJECTIVE: Our recent study has shown that loss-of-function of QRICH2, a testic specific expressed gene, is associated with male infertility with multiple morphological abnormalities of the flagella (MMAF), the current study aim to determine whether QRICH2 mutations were associated with other more common forms of male infertility, such as oligo-astheno-teratozoospermia and asthenospermia

DESIGN: Experimental study recruited from male infertility clinic and human samples of case and control were collected.

MATERIALS AND METHODS: 84 cases of male infertility patients were recruited. WES was performed for all subjects. All identified variants were confirmed by Sanger sequencing. Immunostaining result was used to determine the specific localization of QRICH2 in human sperm. Western blot were used to detect the expression of QRICH2 in oligo-astheno-teratozoospermia. Co-Immunoprecipitation (Co-IP) with QRICH2 antibody in human testis and proteomics analysis were conducted to identify the binding partner. IVF/ICSI outcome were followed to determine whether the mutation of QRICH2 have effect on the normal development of offspring.

RESULTS: We identified five unrelated patients (3/84 5.9%) with homozygous and compound heterozygous mutations in the QRICH2 gene, which is specifically expressed in human and mouse testis. 5 of the samples harbor a recurrent deletion, (g.17:74288566-74288568del.e1.1742_1744del.p.581_582del) .None of these mutations were reported in control sequence databases. 4 of mutation is located in the SNC-N domain, while one mutation is located in the Glutamine rich domain. Co-IP result indicated that mitochondrial proteins, such as VDAC1 is associated with QRICH2. Western blot result shows that QRICH2 expression is down-regulated in patients. And IVF/ICSI outcome analysis indicates that normal offspring development could be observed in the patients.

CONCLUSIONS: Compared with other reported genes associated with male infertility, high frequency of QRICH2 mutations were detected with WES. QRICH2 is important for sperm motility. The mutation of QRICH2 gene, especially high frequency mutations of SMC_N domain are likely responsible for the phenotypes of both oligo-astheno-teratozoospermia and asthenospermia.
ASSOCIATION OF MENTAL HEALTH DIAGNOSES AND UTERINE ENDOMETRIAL THICKNESS IN WOMEN UNDERGOING IN-VITRO FERTILIZATION. Anna K. Knight, PhD, Heathcott S. Hipp, MD, a Laurie McKenzie, MD, b Jessica B. Spencer, MD, MSC, c Sabrina A. Gerkowitz, MD, a Emory University School of Medicine, Atlanta, GA; bEmory University School of Medicine, Department of Gynecology and Obstetrics, Atlanta, GA.

OBJECTIVE: To assess the association between mental health diagnoses and uterine receptivity, operationalized as endometrial thickness.

DESIGN: Due to the lack of data regarding the impact of mental health diagnoses on intermediate outcomes of in vitro fertilization (IVF), we performed an exploratory retrospective cohort study of women undergoing IVF at an academic medical center from 2018 to 2019.

MATERIALS AND METHODS: A total of 101 patients undergoing IVF were recruited and underwent controlled ovarian hyperstimulation with an antagonist protocol. Women on clomiphene or letrozole, those seeking fertility preservation and those with uterine factor were excluded. Mental health diagnoses and medications were abstracted from chart review. Endometrial thickness was assessed via transvaginal ultrasound on the final day of stimulation. We used linear regressions to assess the associations between 1) anxiety, 2) depression, 3) any psychiatric diagnosis, and 4) current treatment with antidepressant or anxiolytic medications.

RESULTS: Of the 101 women, 12 (11.9%) had previously been diagnosed with anxiety, 10 (9.9%) had been diagnosed with depression, of these women 15 (14.9%) were currently being treated with antidepressants or anxiolytic medications. Women had a mean of 35.1 ± 4.0 years of age, a mean BMI of 26.3 ± 5.6 kg/m², and a mean endometrial thickness of 10.3 ± 2.7 mm. Women self-reported as Caucasian (52.5%), Asian (24.8%), or African American (15.8%). A mental health diagnosis (p = 0.01) and use of antidepressants or anxiolytic medications (p = 0.002) were negatively associated with endometrial thickness. All associations remained significant after controlling for BMI. Endometrial thickness was not associated with cycle characteristics (peak estradiol level, total gonadotropin dose, or number of oocytes retrieved).

CONCLUSIONS: Mental health diagnoses and current antidepressant or anxiolytic treatment are associated with a thinner endometrial thickness, a marker of uterine receptivity. Prior studies have indicated women with a history of anxiety and depression may have lower live birth rates; this is perhaps due to the influence of stress on endometrial thickness and interaction with the reproductive hormonal axis. These findings are important given the strong association of mental health diagnoses and infertility, with anxiety and depression often exacerbated by the stress of fertility treatment. Future studies will examine biochemical markers of stress to further explore the mechanism behind this finding.
genetic testing options can raise moral, ethical, and personal issues that result in distress and uncertainty. We document initial reliability and validity of new instruments to measure these constructs in female patients who are considering PGT, either for single gene disorders or for chromosomal disorders. The novel Q’s can be used in research and clinical settings (e.g., genetic and reproductive psychology counseling). Educational materials can be developed to address information gaps, and counseling can ease psychological dilemmas. Data collection is ongoing for future analysis on whether decisional distress and uncertainty vary by patient demographics, PGT-M vs PGT-A, etc.

P-685 Wednesday, October 16, 2019 6:30 AM
IS A DIAGNOSIS OF UTERINE FIBROIDS WORSE THAN A DIAGNOSIS OF CONGESTIVE HEART FAILURE OR CHRONIC LUNG DISEASE? Bhuchitra Singh, M.D., MPH, MS,a Martha C. Thomas, M.D., b Holly Simns, RN, BSN, c James Segars, M.D. a Johns Hopkins School of Medicine, Baltimore, MD; b University of Mississippi Medical Center, Jackson, MS; c Johns Hopkins University, School of Medicine, Baltimore, MD.

OBJECTIVE: More than 80% of African American women and 70% of white women have detectable uterine fibroids by age 50. Despite the high prevalence of disease, the psychosocial impact of fibroid disease has not been quantitatively compared to other chronic conditions. Here we rigorously compared the impact of 5 conditions, including uterine fibroids, to chronic disease using quality of life indicators.


MATERIALS AND METHODS: Search phrases included: depression AND fibroids; stress AND fibroids; sexuality AND fibroids; psychological AND fibroids; and fear AND fibroids; in addition to: uterine fibroids compared to chronic diseases using quality of life indicators.

RESULTS: Of the 2,422 articles identified, 21 studies met inclusion/exclusion criteria, representing a total of 2,361 patients. Of note, the data showed that for 7 out 8 categories on the SF-36(Short Form (36) Health Survey) questionnaire, a diagnosis of uterine fibroids was accompanied by a disability score that exceeded (i.e., was a greater psychosocial stressor) than the diagnosis of congestive heart failure (CHF), diabetes mellitus (DM), or chronic lung disease (CLD). At baseline, quality of life scores were considerably lower in all instruments measuring these variables in women with uterine fibroids, indicating significantly impaired psychosocial functioning. Uterine fibroids were associated with significant patient-reported health disabilities related to bodily pain, emotional and mental health, social functioning, and satisfaction with sex life. Women with symptomatic fibroids regarded an improvement in quality of life as a major driver of decision making, more so than clinical indices, such as increase in hemoglobin levels or decrease in fibroid size.

CONCLUSIONS: The level of disability associated with uterine fibroids exceeded that of chronic diseases such as CHF, DM and CLD. Attention to the impact of uterine fibroids on the quality of life in women affected by fibroids will lead to increased patient satisfaction.

SUPPORT: This effort is supported in part by the Howard and Georgeanna Jones Research Endowment.

P-686 Wednesday, October 16, 2019 6:30 AM
A COMPREHENSIVE EXAMINATION OF INFERTILITY STIGMA AMONG FERTILE AND INFERTILE WOMEN IN THE UNITED STATES. Amber K. Worthington, PhD, a Erin E. Burke, PhD, a Carly Leathy, BA a Penn State University, University Park, PA; a Modern Fertility, San Francisco, CA.

OBJECTIVE: Infertility impacts 1 in 6 couples; however, having children is a social norm, potentially stigmatizing infertile individuals. This research expands previous qualitative and small-scale studies with a large-scale survey of both fertile and infertile women’s societal perceptions of female and male infertility stigma as well as infertile women’s internalized experiences of stigma.

DESIGN: A national, cross-sectional survey.

MATERIALS AND METHODS: 327 women were recruited through an email newsletter in March 2019; no incentive was provided. Eligible participants were ages 18 to 59, identified as women, and lived in the USA. After providing informed consent, participants completed an online survey to assess societal perceptions of female and male infertility stigma. The survey also assessed infertile women’s internalized experiences of stigma and emotions. The data were analyzed using one-sample and independent sample t-tests and bivariate correlations; the power for these analyses was excellent (98%)

RESULTS: Participants ranged in age from 18 to 59 (M = 34.11, SD = 6.64). The majority identified as heterosexual (95%) and had a partner (81%). Infertility was defined as a diagnosis of infertility or 12 months of unprotected sex without becoming pregnant; 33% of the participants were infertile.

An examination of societal perceptions of infertility stigma revealed that both fertile (M = 2.90, SD = 0.76) and infertile women (M = 2.76, SD = 0.81) felt that female infertility was stigmatized (the means were statistically higher than the midpoint of the 5-point scale; fertile women, t(217) = 4.89*; infertile women, t(108) = 5.48*). Fertile (M = 2.56, SD = 0.73) and infertile women (M = 2.49, SD = 0.71) did not believe male infertility was stigmatized (the means were not statistically higher than the midpoint; fertile women, t(217) = 0.15, ns; infertile women, t(108) = 0.95, ns). A comparison of societal perceptions of female and male infertility stigma revealed that both fertile (t(217) = 3.46*, p < .01) and infertile women (t(108) = 6.23*, p < .01) felt that female infertility stigma was significantly higher than male infertility stigma (fertile women: t(217) = 5.96*, p < .01; infertile women: t(108) = 8.20*, p < .01). Fertile women indicated feeling internalized stigma, as the mean (M = 4.18, SD = 0.84) was significantly higher than the midpoint of the 5-point scale, t(108) = 3.04*. Internalized stigma was associated with feeling afraid (r = .25*, p < .05), uncertainty (r = .22*, p < .05), anxious (r = .38*, p < .01), stressed (r = .45*, p < .01), and guilty (r = .52*, p < .01)

CONCLUSIONS: Despite the increased awareness of infertility and emergence of new technologies increasing treatment success, infertility stigma persists, particularly for women. The results suggest that women believe infertile women are stigmatized, and there is greater stigma for infertile women than men. Further, infertile women report feeling stigmatized, which is related to negative emotions. Infertility stigma puts strain on relationships, may lead individuals to hide their diagnoses from friends or family and delay or avoid treatment. In turn, this could lead to worse prognoses for these patients.

Note *p < .05; ns = not significant.

SUPPORT: This research was funded by Modern Health, Inc.

P-687 Wednesday, October 16, 2019 6:30 AM
THE PSYCHOLOGICAL IMPACT OF SURROGACY ON THE FAMILIES OF GESTATIONAL CARRIERS: IMPLICATIONS FOR CLINICAL PRACTICE. Mary P. Riddle, PhD, a Stephanie C. Michaud, B.S., a Quenell D. Redden, B.S., a Olivia R. Pozza, B.A., a Brendan L. Scanlan, B.S., a The Pennsylvania State University, University Park, PA.

OBJECTIVE: ASRM has issued ethics and practice committee guidelines for gestational carriers (GCs) that include recommendations for the psychological consideration of a GC’s own family. At present, there are no studies on the impact of surrogacy within GC family systems that can offer guidance to mental health professionals (MHPs) who counsel potential GCs. This study seeks to explore the psychological impact of surrogacy on families in order to guide MHPs in educating GCs on how this experience might affect their families.

DESIGN: IRB approved, cross-sectional survey study.

MATERIALS AND METHODS: Participants (n = 53) were recruited via an ad posted on surrogacy websites and forums. Research packets were mailed to GC families with designated questionnaires for each family member to fill out and return. All family members filled out a detailed questionnaire on the experience of surrogacy along with the Family Assessment Measure, Version III (FAM-III). Children were asked to fill out the Piers-Harris Children’s Self-Concept Scale, 2nd Edition (Piers-Harris 2). Data was entered and analyzed by SPSS software.

RESULTS: Children of GCs (n = 23) endorsed excitement, curiosity, surprise, and pride at the highest rate amongst emotions experienced from surrogacy. 74% of children reported the experience as having a positive impact on their life. Children scored within normal limits on all domain scales on the Piers Harris 2, including behavioral adjustment, freedom from anxiety.
popularity, and overall happiness. On the FAM-III, parents' overall rating scales were significantly more defensive than their children’s (p < .05). The overall ratings given by the children reflected more dysfunction, although scores were still within normal limits. Relative strengths reported by all family members were involvement (reflecting nurturing and supportive involvement between family members) and Values and Norms (reflecting a congruence of the family values system). Relative weaknesses endorsed included Role Performance (reflecting a lack of agreement regarding roles within the family system) and Task Accomplishment (reflecting problems with task identification and problem-solving strategies). Children’s advice to other kids whose mothers are considering surrogacy included: “Have fun... it’s a rollercoaster.” “Don’t be scared or angry... your parents will not get rid of you or your siblings;” “Be proud. Your mom is creating LIFE, People!”

CONCLUSIONS: Families in which the mother has been a GC appear to be functioning well across a number of psychosocial domains and feel that surrogacy has been a positive experience within their family system. These families appear to foster nurturing relationships and place importance on family values and consistency in interpersonal interactions within their families. Parents’ perceptions of the experience of surrogacy did not differ from their children’s endorsed emotions and children express pride in their mothers’ desire to help others. Research into the impact of surrogacy on the families of GCs is critical for MHPs who work with this unique population to ensure adequate psychological preparation.

P-688 Wednesday, October 16, 2019 6:30 AM
THE IMPACT OF THE FERTIFSTRONG APP ON ANXIETY AND DEPRESSION IN MEN. Alice D. Domar, PhD,a Paul J. Glovniak, MD,a Debra S. Stovall, PhD,a Laith J. Farre, M.A.,a Rachel Blair Danis, MD,a Semara A. Thomas, MD,a Richard J. Paulson, MD, MS,a Kristin Bendikson, M.D.,a Jacqueline Ho, MD MS,a Mary Katherine Samplaski, MD,a Rachel S. Mandelbaum, MD,a University of Southern California, Los Angeles, CA; Keck School of Medicine, University of Southern California, Los Angeles, CA.

OBJECTIVE: Motivating factors for pursuing fertility treatment may be difficult to ascertain, as there may be fear of a “wrong” answer. Given that infertility is a couples’ condition, it is important to understand the male’s perspective. We sought to assess the male motivations and quality of life (QoL) during fertility treatment.

DESIGN: Cross-sectional survey study.

MATERIALS AND METHODS: 2 anonymous paper surveys were given to 70 male partners after providing a semen sample for assisted reproductive technology at a fertility clinic. Men were alone during this time. 1st, a questionnaire assessed demographics, motivating factors, and fertility history. 2nd, the fertility quality of life (FertiQoL) survey assessed the impact of infertility on the life area of FertiQoL. Men who QoL contained 2 QoL domains: Core (with Mind-Body, Emotional, Relational, and Social subdomains) and Treatment (with Tolerability and Environment subdomains). Responses were scaled 0-100. A higher score indicated higher QoL. Eligible respondents included men receiving treatment as part of an infertile couple. Responses were analyzed via descriptive statistics, chi-square analysis, and multivariable regression analysis.

RESULTS: Out of 70 anonymous surveys, 61 (87.1%) and 52 (74.3%) completed the 1st and 2nd surveys respectively. 62 (88.6%) men were married, 51 (75.0%) did not have prior children, and 19 (27.9%) reported prior in vitro fertilizations. Particularly, in a patient population with poor health literacy and mostly non-English speaking, it is essential to explore crucial questions like how patients perceive, understand and decide for these options. In countries where the number of embryos transferred is still unregulated and left for clinician’s discretion, there is a need to reduce couples desire for multiple embryo transfer. Particularly, in a patient population with poor health literacy and mostly

FERTILITY & STERILITY®
taking self-funded treatment, understanding how patient balances the risks and benefits of single embryo transfer is vital. The purpose of this study is to assess the patients’ and spouses’ knowledge, attitude, and concerns regarding single embryo transfer.

**DESIGN:** Prospective questionnaire study at a tertiary-care, university-affiliated teaching hospital.

**MATERIALS AND METHODS:** 240 couples participated in this 25 item questionnaire survey at their routine counselling visit before embryo transfer. The common practice in the centre during the study period was double embryo transfer (DET). The treatment cycles were self-funded and the patients received no reimbursements. All couples received a psychological counselling session, written information as brochure and consultation with ART clinician, explaining DET, SET and Multiple pregnancy, before responding to questionnaire. Descriptive statistics were computed, chi square tests were performed to compare the frequencies according to population demographics and response characteristics.

**RESULTS:** 240 women and 232 men answered the questionnaire for analysis. 62% preferred singleton conception in their next embryo transfer cycle. Yet, 92% of men and 93% of women indicated that they would happily accept if conception resulted in twins in the current IVF attempt. Cancelled cycle (82%) was perceived as unacceptable risk followed by failed cycle (67%) and multiple pregnancy (45%). Twin conception risks are perceived as important by the couples but still prefer two embryo transfer stating ‘Have a positive attitude and wouldn’t happen to all’ (76%), 87% of men and 89% of women would prefer SET if results unchanged and compared to DET.

The top concerning factor for choosing DET over SET was ‘understand the benefits but feel it will prolong the time to conceive’ (69% men and 74% women). Compared to women, men were more likely to choose SET over the factor ‘less risks to mother’ in singleton conception (63% Vs 35%, P=0.04). About 74% choose DET over SET in the next cycle even after feeling well informed and understood benefits.

**CONCLUSIONS:** Twin conception risks were perceived as important by the couples but still prefer double embryo transfer. Couples believe accepting SET would prolong the time to conceive. These results could help in counselling patients addressing their concerns and specific information provision about risks. Couples would prefer SET programs if it may provide comparable success rates and time to conception which would require careful patient selection. Thus, strategies to maintain existing rates of successful conception per oocyte recovery may reduce couples desire to choose multiple embryo transfer.

---

**P-691 Wednesday, October 16, 2019 6:30 AM**

**LIFESTYLE RELATED FACTORS ASSOCIATED WITH PREGNANCY OUTCOME AFTER IN VITRO FERTILISATION-EMBRYO TRANSFER CYCLES.** Hema Vaithianathan, MD MRCOG, a P. M. Gopinath, MD, DGO, FMMC, FICS, FICOG, MBA(HSM), a S. S. Gayathri Devi MD, MOG, FRM, a Postdoctoral Fellow, Chennai, India; 3Director & Senior Consultant, Chennai, India; 4Consultant - Reproductive Medicine, Chennai, India.

**OBJECTIVE:** Lifestyle factors have a dramatic impact on the reproductive performance of infertile population undergoing Assisted Reproductive Technology. The present study focussed on IVF population and explored association between lifestyle factors primarily during the implantation window and implantation success. This study aims at determining the independent contribution of female lifestyle related factors following embryo transfer leading to ART success. Also, the secondary aim is to compare the differences between pregnant and non-pregnant cycles and to draw strategies to improve ART outcomes.

**DESIGN:** Cross sectional questionnaire based study.

**MATERIALS AND METHODS:** This study was undertaken in our university affiliated and tertiary referral private hospital. We recruited 130 women who underwent frozen/fresh embryo transfer (IVF/ICSI cycles) over a period of 12 months. We categorized lifestyle factors into diet and nutrition related, physical activity related and emotional support related behaviours. A structured questionnaire with 13 questions was framed. The survey was conducted using the computer assisted telephone interviewing system. The women completed the questionnaire based on their lifestyle factors from the time of embryo transfer to serum pregnancy testing. The primary outcomes were the result of Serum beta hCG (>25mIU/mL considered to be positive) on day 14 after embryo transfer.

**RESULTS:** Among the 130 women receiving ET, 50/130(38%) resulted in implantation. The mean age of the study population was 31.23±3.21 years with a mean BMI of 25.2± 3.2kg/m2. Age, duration of infertility, previous IVF attempts all showed a correlation with negative outcome. A BMI consistent with being overweight (BMI 25-29 kg/m2) and obese (BMI >30 kg/ m2) was associated with a lower pregnancy rate compared with women of a BMI of 19 - 24.9(Implantation rate- 23%). A comparison of the physical activity variables among the pregnant and non-pregnant groups yielded no significant differences among them in logistic regression analysis. There was a significant association between plant based diet and inclusion of fresh fruits to successful outcome (P = 0.043). All women responded that they had received adequate emotional/psychological support and there was no statistical differences between two groups (P = 0.521).

**CONCLUSIONS:** Women had a tendency to limit physical activity levels post embryo transfer and bed rest has no correlation with ART success and there is a clinical need to emphasize that prolonged bed rest following ET is not necessary. Women maintained a plant based diet showed an association to positive pregnancy outcome. A structured counselling to facilitate lifestyle changes may optimise reproductive performance and improve their chance of success.

---

**P-692 Wednesday, October 16, 2019 6:30 AM**

**FAMILY-BUILDING AFTER CANCER: UNDERSTANDING PATIENT SUPPORT NEEDS, PREFERENCES FOR SUPPORT, AND RECOMMENDATIONS FOR CARE.** Catherine Benedict, PhD,a Alexandria Louise Hahn, MSc,b Alyssa McCready, LMSW,b Michael A. Diefenbach, PhD,b Jennifer S. Ford, PhD,a 3Stanford University School of Medicine, Palo Alto, CA; 4Weinstein Institute for Medical Research, Manhasset, NY,b 5Hunter College and The Graduate Center, City University of New York (CUNY), New York, NY.

**OBJECTIVE:** Fertility is one of the most distressing issues for adolescent and young adult female (AYA-F) cancer survivors. Family-building often requires reproductive medicine, with associated challenges (e.g., high cost). This study examined AYA-F survivors’ fertility experiences and perceptions of care related to family-building after cancer treatment.

**DESIGN:** Semi-structured interviews (45-60 minutes) were conducted with AYA-F cancer survivors (N=25) exploring themes related to fertility and family-building.

**MATERIALS AND METHODS:** Cycles were derived based on the Ottawa Decision Support Framework and augmented by grounded theory. The coding team (n=3) completed an iterative process of coding and re-view, resulting in adequate inter-rater reliability (alpha>.7).

**RESULTS:** Participants averaged 29 years old (SD=6.2; range, 15-39) and were primarily White and well educated: 32% had undergone fertility preservation. Three main themes were identified: Unmet Needs, Preferences for Support Delivery, and Recommendations for Providing Support. Multiple support needs were identified, including lack of information about fertility and family-building options (36%), psychological support (16%), and logistical help navigating access to care and resources (32%). AYA-Fs believed the best way to learn about resources was through online platforms (72%) or doctor-initiated discussions during clinic visits (40%). Their preferred format for receiving in-depth information and counseling was through face-to-face interactions (80%). Thus, a combined approach was preferred such that information (via web-based communication) should be provided first, with follow-up in-person visits and referral to fertility specialists available when needed. AYA-Fs wanted providers to communicate with more empathy, spend more time discussing fertility and family-building, and initiate honest, open dialogues that could continue throughout care (40%). They also wanted to be referred to trusted resources tailored to their age group for informational and emotional support (36%). Specific recommendations to address family-building costs and financial planning were identified (16%).

**CONCLUSIONS:** Informational and psychological support services are needed to better educate patients about gonadotoxic effects and options to have children after cancer and address the emotional burden. Future work should evaluate how multidisciplinary care between cancer and reproductive medicine may inform the development of interactive web-based patient resources, coupled with in-person supportive interventions, and referrals.

**SUPPORT:** This research was supported by a grant from the National Cancer Institute (NCI, R03CA121924-02, PI: Benedict).
INSIGHTS FROM WOMEN WITH FERTILITY CONCERNS ABOUT THEIR CHOICES WHEN attempting to IMPROVE THEIR ABILITY TO CONCEIVE. Alice D. Domar, Ph.D.,* Elizabeth A. Grill, PsyD,† Mary Christ, MD, MBA,‡ Evgenii Malikov, MBA§ Boston IVF, Waltham, MA; †Weill Cornell Medical Center, Rye Brook, NY; §Nestle Health Science, Bridgewater, NJ.

OBJECTIVE: The goal of this survey-based research was to gather additional information from women who have been actively trying to conceive, on barriers to access of fertility-related treatment and perception of value of such services.

DESIGN: Three online surveys of women who were trying to conceive and voluntarily responded to a request for participation.

MATERIALS AND METHODS: 330 women ages 18-44 completed the first questionnaire on their overall feelings towards fertility. 132 unique women completed the second questionnaire on emotional state. 93 unique respondents answered questions regarding their interest in various fertility related services and sources of information.

RESULTS: 65% (214/330) had been trying less than seven months, 17% (55/330) 7-12 months, and 18% (61/330) more than a year. 54% (127/236) had not yet seen a physician in relation to fertility concerns. The two most common reasons for not seeing a physician were ‘feeling they could get pregnant on their own’ (42%; 96/230) and ‘wanting to try a more natural approach’ (23%; 53/230). 80% (180/224) believed that their emotions could have an impact on their fertility. When asked about most helpful fertility-related services, which could be made available to them, access to certified reproductive experts (39%; 36/92) was followed by nutrition-related services (22%; 21/93).

CONCLUSIONS: Most of the research available to fertility specialists is conducted on women already seeking consultation. A significant number of women not yet under fertility treatment prefer to seek out natural means of conception and believe in the importance of their emotional state in improving their chances of conception. Educating women about real options to increase chances of conception should be a priority.

SUPPORT: This research was sponsored by Nestle Healthcare Nutrition.

ASSOCIATIONS BETWEEN PSYCHOLOGICAL STATUS AND SEMEN QUALITY PARAMETERS AMONG MALE PARTNERS OF COUPLES ATTEMPTING FERTILITY. Jiahui Qiu, PhD,§ Jichun Tan, PhD,∥ Shengjing hospital of China medical university, Shenyang, China; §Key Laboratory of Reproductive Dysfunction Diseases and Fertility Remodelling of Liaoning Province, Shenyang, China.

OBJECTIVE: To study associations of semen quality parameters with psychological status including depression, stress and anxiety.

DESIGN: A cross-sectional single-center study.

MATERIALS AND METHODS: A total of 412 men attending fertility center from 2017 to 2018 were investigated. Participants completed a questionnaire on lifestyle factors, self-rating depression scale, self-rating anxiety scale and perceived stress scale. Semen samples were collected to test semen volume, sperm concentration, progressive motility rate, vitality, normal forms rate.

RESULTS: Men with depression symptoms were detected to have lower sperm vitality (p=0.026) and progressive motility rate (p=0.01). Higher anxiety scores were accompanied with decreased sperm vitality (p=0.03). While no significant associations between self-reported stress and semen parameters were found.

CONCLUSIONS: Depression and anxiety are associated with lower levels of semen quality, which may lead to infertility of men.

EFFECT OF PHYSICIANS’ PERSONAL REPRODUCTIVE EXPERIENCES ON COUNSELING INFERTILITY PATIENTS. Jenna M. Turocy, MD,*, Leslie V. Farland, Sc.D,*, Elizabeth S. Ginsburg, MD,*/ Paula C. Brady, MD,§ Columbia University Medical Center, New York, NY; *University of Arizona, Tucson, AZ; †Brigham & Women’s Hospital, Boston, MA.

OBJECTIVE: Physicians’ personal medical experiences have been shown to affect patient counseling and management. Our objective was to assess whether reproductive endocrinologists’ personal experience with infertility and multiple gestation correlates with clinical counseling and treatment recommendations.

DESIGN: A web-based cross-sectional survey.

MATERIALS AND METHODS: An anonymous survey was emailed to Society for Reproductive Endocrinology and Infertility members, regarding personal and close contacts’ experience with infertility and multiple gestation, and factors influencing embryo transfer (ET) number and twin risk counseling. Responses were compared using Fisher exact and Mann-Whitney U tests as appropriate, with significance at p<0.05.

RESULTS: Responses were provided by 109 physicians, who were 51% female, 85% white and 56% age 50 years or older. Most (91%) reported being parents, and 28% had a personal history of infertility. Among respondents, 12% reported they or their partners had conceived multiples (83% using assisted reproduction), and half had family or close friends with multiples. Physicians with a history of infertility regularly shared their experiences with multiples more often than those without infertility (50% vs. 16%; p=0.01). Twins were considered an adverse outcome by 86%, regardless of their reproductive experiences. When counseling about multiples, physicians rated their concern for preterm birth and neonatal morbidity highest (mean 4.9 on a scale of 1 [not at all] to 5 [to a large extent]); familial stress and maternal mental health were rated lowest (3.6). Incidence of preterm birth in twins was underestimated by 34% of physicians, and 44% underestimated twin infant mortality, irrespective of personal or close contacts’ multiple gestations (including preterm deliveries). Most (79%) “encourage SET whenever possible.” In deciding ET number, avoidance of multiples and patients’ obstetrical history were rated highest (mean 4.4) while self-pay status (2.5) and body mass index (BMI, 2.3) were rated lowest. These ratings did not vary by reproductive history, though physicians reporting strong influence of patient BMI on ET number had significantly lower BMI than those reporting little to no effect (22.8 vs. 25.0 kg/m², p=0.05).

CONCLUSIONS: There is a high incidence of infertility diagnoses (28%) and multiple gestation (12%) among reproductive endocrinologists. Physicians reported strongly advocating for SET to reduce risk of multiples, which were widely considered an adverse outcome, independent of personal experience with infertility or multiple gestation. This is despite at least one-third of respondents underestimating twin morbidity or mortality.
CONCLUSIONS: The depression level of infertile women was higher, and was negatively correlated with marital adjustment test and self-esteem. The mediating role of self-esteem may provide a potential mechanism for exploring the relationship between marital adjustment test and depression. These results suggested that medical staff should pay attention to the patients’ depression, especially to the infertile women with marital disorders and low level of self-esteem. And then, humanistic care which helps the patients to vent their inner depression in a variety of ways could be implemented during treatment. In addition, we should actively carry out health education for infertile women and their families, so that they could have an enhanced understanding of reproductive knowledge, and gradually improved psychosociality and coping ability to deal with various problems arising in the course of treatment.

DOES DURATION OF INFERTILITY AFFECT THE MALE’S FERTILITY QUALITY OF LIFE?

Rachel Blair Danis, MD, Semara A. Thomas, MD, Rachel S. Mandelbaum, MD, Richard J. Paulson, MD, MS, Kristin Bendikson, MD, Jacqueline Ho, MD, MS, Mary Katherine Sunplaski, MD; University of Southern California, Los Angeles, CA; USC Keck School of Medicine, Los Angeles, CA; Keck School of Medicine, University of Southern California, Los Angeles, CA.

OBJECTIVE: An infertility diagnosis can confer a significant amount of personal stress and strain on a couple. There is limited data on how infertility affects quality of Life (QoL) and the male’s perspective on his relationship with his partner. The purpose of this study was to determine if duration of infertility affects males’ QoL and partner intimacy.

METHODS AND MATERIALS: 2 anonymous paper surveys were given to 70 male partners after providing a semen sample for assisted reproductive technology at a fertility clinic. Men were alone during this time, a questionnaire assessed demographics, motivating factors, and fertility history. 2nd, the fertility quality of life (FertiQoL) survey assessed the impact of infertility in diverse life areas. The FertiQoL contained 2 QoL domains: Core and Treatment. The Core consisted of 4 subscales, each focusing on psychosocial QoL factors. Treatment consisted of 2 subscales: environment and tolerability (of treatment). Results were scaled 0-100; a higher score indicated higher QoL. Eligible respondents included men receiving treatment as part of an infertile couple. Responses were analyzed via descriptive statistics, chi-square analysis, and multivariable regression analysis.

RESULTS: Out of 70 anonymous surveys, 61 (87.1%) and 52 (74.3%) completed the 1st and 2nd surveys in their entirety. 62 (88.6%) men were married, 51 (75.0%) did not have prior children, and 19 (27.9%) reported prior infertility diagnosis. 20 (29.4%) for < 12 months, 24 (34.3%) for 12-24 months, and 25 (36.8%) for > 24 months. Mean FertiQoL scores for all men were: Overall 78.9 +/- 9.9, Core 79.0 +/- 9.9, Treatment 78.5 +/- 14.5. For infertility duration < 12 months, scores were 81.8 +/- 6.5, 83.1 +/- 6.4, and 78.7 +/- 13.9, respectively. For fertility duration 12-24 months, scores were 79.7 +/- 11.0, 79.6 +/- 10.8, and 79.5 +/- 15.4, respectively. For infertility duration > 24 months, scores were 76.1 +/- 10.8, 75.5 +/- 9.9, and 77.4 +/- 14.9, respectively. There were no significant differences between overall or domain scores and the duration of infertility groups (p>0.05). However, there was a downward trend in scores the longer the couple was trying to conceive, and duration of infertility >24 months was significantly related to one’s Relational score (subscale of the Core domain, p=0.019).

CONCLUSIONS: For most FertiQoL domains, duration of infertility did not affect scores. This is reassuring that longer durations of infertility do not seem to impact male QoL. Infertility for at least a 2-year period did affect scores. This is reassuring that longer durations of infertility do not affect scores. The question of duration of infertility still remains a pertinent issue for a couple’s intimate relationship. Awareness of how infertility affects the male partner’s quality of life and relationship with his partner provides an opportunity to enhance our care of the infertile couple.

PREVALENCE OF INFERTILITY TREATMENT IN PATIENTS WITH VULVODYNIA

Jenny S. George, MD, Ashley Hesson, MD, PhD, Natalie A. Saunders, MD, Hope K. Haefner, MD; University of Michigan, Ann Arbor, MI; University of Michigan, Obstetrics and Gynecology, Ann Arbor, MI.

OBJECTIVE: There is a paucity of data on the fertility desires of patients with vulvodynia, and if pain associated with vaginal intercourse limits these patients’ reproductive goals. Thus, the objective of this study was to determine the prevalence of infertility treatment in patients with vulvodynia. We hypothesized that patients with vulvodynia would have higher rates of infertility treatment compared to the general public and that, of those seeking infertility treatment, uptake of intrauterine insemination (IUI) would be higher compared to uptake of oral or gonadotropin cycles requiring vaginal intercourse, given the potential barrier of painful intercourse.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: Self-administered questionnaires detailing symptom history, vulvar pain characteristics, pregnancy desires, and history of infertility treatment, were completed by patients seeking evaluation at an ambulatory vulvar disorders clinic from 1996 to 2018. Patients with diagnoses other than vulvodynia were excluded. Primary outcome was prevalence of infertility treatment, defined as use of oral induction agents, gonadotropins, IUI, in-vitro fertilization (IVF), or surgical procedures for tubal factor infertility. Secondary outcomes included desire for pregnancy and frequency of vaginal intercourse. Descriptive statistics were used to characterize these distributions. Approval of this study was granted by the Institutional Review Board.

RESULTS: 379 patients diagnosed with generalized or localized vulvodynia were included in this study. Mean age of patients was 40.3 years (SD 14.9), 30.3% (N=115) patients reported desiring pregnancy, and 81.7% (N=94) of their partners were in agreement with this desire. 7.65% (N=29) patients had sought or were seeking infertility treatment, compared to 12.5% reported in population prevalence studies. 35.6% (N=135) patients reported having vaginal intercourse at least once weekly, while 0.53% (N=20) patients reported never having vaginal intercourse. Of the patients who sought infertility treatment, 10 (32.0%) received oral induction agents, 3 (9.6%) utilized gonadotropins, 5 (16.0%) employed IUI, 4 (12.9%) underwent surgical procedures for tubal factor infertility (9.6%) received IVF, and 6 (19.3%) were unaware of treatment modality.

CONCLUSIONS: Prevalence of infertility treatment in patients with vulvodynia is similar to that of the general public. A large proportion of patients with vulvodynia desire pregnancy; these patients do not refrain from vaginal intercourse and do not have higher rates of IUI uptake compared to other treatment modalities.

SPousal CONCORDANCE IN ASSISTED CONCEPTION: PROSPECTIVE COHORT STUDY OF COUPLES UNDERGOING THEIR FIRST IVF CYCLE

Karera Alrashid, MD, Scott M. Nelson, MD, PhD; University of Glasgow, Glasgow, United Kingdom.

OBJECTIVE: Assortative mating and cohabitation concordance cause married/cohabiting couples to share similar traits, with spousal concordance known to contribute to cardiovascular disease and be associated with worse treatment outcomes in other medical specialities. Maternal and paternal characteristics/behaviors are known to affect both natural fertility and success of treatment outcomes in other medical specialities. Maternal and paternal characteristics/behaviors are known to affect both natural fertility and success of IVF treatment but the contribution of concordance is unknown. This study was designed to examine the extent to which heterosexual couples undergoing IVF are concordant with respect to baseline characteristics/behaviors and whether this impacts upon outcome?

DESIGN: Prospective cohort study of consecutive couples undertaking their first IVF cycle.

MATERIALS AND METHODS: Couples were assessed prior to undertaking NHS Scotland funded IVF treatment, with assessment of demographic, anthropometric, lifestyle and medical factors. Spousal concordance was assessed by spearman correlation for continuous variables, whilst kappa analysis was employed for categorical variables, with regression modelling for their association with outcomes.

RESULTS: There were 306 couples with complete baseline data, of which 264 underwent fresh embryo transfer, with 125 ongoing pregnancies (47.3%). Couples were strongly concordant for age (r=0.59 p<0.000), alcohol consumption (k=0.661), educational attainment (k=0.655) and smoking status (k=0.45) but not BMI (r=0.11, p=0.44). Only exercise concordance was significantly associated with outcome, with exercise concordance a predictor of biochemical pregnancy (OR: 1.86; 95% CI 1.8-2.92 p=0.008). Furthermore, females in discordant couples were significantly less physically active than females in concordant couples (mean difference = 0.4527 times/week, p=0.003).
CONCLUSIONS: Couples undertaking assisted conception are concordant for many baseline characteristics, with couples with discordant exercise habits having increased rates of biochemical pregnancy. Shared education and public health initiatives to attain spousal concordance of lifestyle factors may be beneficial for overall health outcomes if they converge towards healthy behaviors, but concordance per se had limited impact on clinical ART outcomes.

P-700 Wednesday, October 16, 2019 6:30 AM

ATTITUDES TOWARDS PREGNANCY IN PATIENTS WITH VULVODYNIA. Jenny S. George, MD,a,b Sydney K. Willis, M.P.H., a Lauren A. Wise, Sc.D., a Hope K. Haefner, MD, a University of Michigan, Obstetrics and Gynecology, Ann Arbor, MI, University of Michigan, Obstetrics and Gynecology, Ann Arbor, MI.

OBJECTIVE: Qualitative studies indicate that vulvodynia affects women’s reproductive desires and timing [1]. However, little is known about the prevalence of these attitudes amongst patients with vulvodynia, or the relationship between pain severity and reproductive planning. We aimed to further characterize the effects of vulvodynia on women’s reproductive wishes, hypothesizing that desire for pregnancy would decrease with increasing pain score and fear of pregnancy would increase with worsening pain score.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: We retrospectively analyzed patient intake questionnaires completed prior to evaluation at an ambulatory vulvar disorders clinic from 1996 to 2018. Questions addressed symptom history, vulvar pain characteristics, and pregnancy desires. Only those diagnosed with vulvodynia in their subsequent clinic visit were included in our sample. Patients with incomplete questionnaires were excluded. Our primary outcomes were pain severity and unpleasantness scores (0-100) compared between women reporting presence versus absence of desire for pregnancy, as well as between those noting fear of pregnancy or lack thereof. Descriptive statistics and Student’s t-tests were used as appropriate. This study was approved by the University of Michigan Institutional Review Board.

RESULTS: 424 patients diagnosed with vulvodynia (generalized or localized) were eligible for analysis. Their mean age was 40.2 years (SD 15.1); 13.2% (N=56) of them had never had a pregnancy. Nearly one third of the sample (27.8%; N=118) reported a desire for pregnancy. Of those desiring pregnancy, 63.6% (N=75/118) were having at least weekly vaginal intercourse. Mean pain intensity score among those desiring pregnancy was not different between those having and not having at least weekly intercourse (67.1 vs 71.1, p=0.38). Similarly, mean pain unpleasantness was comparable between these groups (78.1 vs 79.0, p=0.81). Of the total 424 patients, 15.1% (N=64) fear pregnancy. This fear was not associated with increased pain intensity (p=0.09) or unpleasantness scores (p=0.28).

CONCLUSIONS: Although vulvodynia has far-reaching effects on women’s quality of life, our study suggests that women with more intense or unpleasant pain do not avoid or fear pregnancy more than those with less pain.


SUPPORT: None.

NUTRITION

P-701 Wednesday, October 16, 2019 6:30 AM

GLYCEMIC LOAD, DIETARY FIBER, AND ADDED SUGAR AND SPONTANEOUS ABORTION. Sydney K. Wills, M.P.H.,a Lauren A. Wise, Sc.D.,a Amelia K. Wesselin, Ph.D.,a Kenneth J. Rothman, Dr.P.H.,b Katherine L. Tucker, Ph.D.,c Ellen M. Mikkelsen, RN, MPH, Ph.D,d Elizabeth E. Hatch, Ph.D.,a “Boston University School of Public Health, Boston, MA; “Boston, MA; “University of Massachusetts Lowell, Lowell, MA; “Aarhus University, Department of Clinical Epidemiology, Aarhus, Denmark.

OBJECTIVE: To prospectively evaluate the association between preconception dietary factors including glycemic load (GL), dietary fiber (DF), and added sugar, and spontaneous abortion (SAB). To the authors’ knowledge, there have been no studies of the association between GL and SAB.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Pregnancy Study Online is a web-based preconception cohort study of pregnancy planners in North America. At baseline, female participants completed a questionnaire providing data on demographic, lifestyle, medical, and reproductive histories. Ten days after enrollment, participants completed the National Cancer Institute’s Dietary History Questionnaire II, a validated food frequency questionnaire. Participants were followed with bi-monthly questionnaires for up to 12 months or until a reported conception. Data on SAB, first positive pregnancy test date, due date, and gestational weeks at loss were ascertained from follow-up questionnaires, an early pregnancy (<12 weeks’ gestation) and a late pregnancy (>32 weeks’ gestation) questionnaire. We calculated GL (glycemic index times portion size); DF, soluble fiber, insoluble fiber (grams/g/day; and added sugar (teaspoons (tsp)/day), based on reported frequencies of individual foods, standard recipes for mixed foods, and average serving size. We used Cox proportional hazards regression to estimate hazard ratios (HR) and 95% confidence intervals (CI), using gestational weeks as the time scale. We adjusted for age, body mass index (BMI), healthy eating index score (HEI-2010), energy intake, and lifestyle and demographic factors.

RESULTS: Of the 3,565 female participants included in this analysis, 756 (21%) had a SAB over the course of follow-up. The median gestational week at loss was 6 weeks (interquartile range: 5-9 weeks). Compared with an average daily GL ≤100, HRs for GL of 101-114, 115-125, 126-140, and ≥141 were 0.95 (CI: 0.77-1.18), 0.80 (CI: 0.64-1.01), 0.89 (CI: 0.71-1.12), and 1.07 (CI: 0.84-1.35), respectively. Compared with daily total DF ≥16 g/day, HRs for 17-20, 21-24, and ≥25 g/day were 1.08 (CI: 0.85-1.30), 1.13 (CI: 0.90-1.43), 0.83 (CI: 0.64-1.07), respectively. Relative to soluble fiber intake of ≤4 g/day, HRs for 5-6, 7-8, and ≥9 g/day were 1.04 (CI: 0.85-1.27), 1.02 (CI: 0.81-1.27), and 0.86 (CI: 0.68-1.08), respectively. Relative to insoluble fiber intake of ≤10, HRs for 11-14, 15-17, and ≥18 g/day were 1.19 (CI: 0.96-1.48), 1.03 (CI: 0.80-1.33), and 1.02 (CI: 0.77-1.33), respectively. Compared with added sugar intake of ≤5 tsps/day, HRs for 7-9, 10-13, 14-17, and ≥18 tsps/day were 0.98 (CI: 0.77-1.24), 0.96 (CI: 0.75-1.22), 1.00 (CI: 0.78-1.28), and 1.04 (CI: 0.80-1.36), respectively. Results were similar for early (<8 weeks’ gestation) and late (≥8 weeks’ gestation) SAB.

CONCLUSIONS: GL, total DF, insoluble fiber, and added sugar intakes were not appreciably associated with SAB. A slight inverse association was seen for higher intake of soluble fiber and SAB risk. Chance remains a plausible explanation of these associations.

SUPPORT: This research was supported by NIH/NICHD grants R01HD086742 and R21HD072326.
P-703 Wednesday, October 16, 2019 6:30 AM

MATERNAL SERUM VITAMIN D LEVELS CORRELATE NEGATIVELY WITH THE LENGTH OF INTERBIRTH INTERVALS IN RHESUS MACAQUES. Jing Xu, Ph.D., a Allison L. Heagerty, Ph.D., b Rebecca Wales, B.S., a Daniel H. Gottlieb, Ph.D., a Byung S. Park, Ph.D., a Kristine Coleman, Ph.D., a Oregon National Primate Research Center, Oregon Health & Science University, Beaverton, OR; aOHSU-PSU School of Public Health, Oregon Health & Science University, Portland, OR.

OBJECTIVE: This study was to investigate the association between maternal vitamin D status and outcomes of spontaneous pregnancies in a nonhuman primate model.

DESIGN: Healthy rhesus macaques (Macaca mulatta) in the breeding groups, which had never participated in other research projects, were studied. MATERIALS AND METHODS: Adult female macaques (n = 53; 5-13 years old; relative to 18-35 year old women) were housed in outdoor shelters at a national research facility. Diet consists of monkey chow containing 6.6 kcal/g, 6.4% protein, 18.5% carbohydrate, 46.6% fat. Animals were not pregnant or lactating at the time of the study.

RESULTS: Two distinct cohorts of animals were identified based on their IBI. One group had IBIs less than 14 months (IBI < 14 months) and the other had IBIs greater than 14 months (IBI ≥ 14 months). Serum 25-hydroxyvitamin D3 (25(OH)D3) concentrations were not significantly different between the two groups. However, serum 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) concentrations were significantly higher in animals with shorter IBIs (p < 0.05).

CONCLUSIONS: The results of this study suggest that serum 1,25(OH)2D3 concentrations may be a useful indicator of maternal vitamin D status and may be associated with shorter IBI. Further studies are needed to confirm these findings.

SUPPORT: This study was supported by NIH OD 5150101092.

P-704 Wednesday, October 16, 2019 6:30 AM

HIGH-AGE DIET CAUSES ESTROUS CYCLE IRREGULARITIES AND OVARIAN FUNCTION CHANGES IN MICE. Zaher Merhi, MD, HCLD,a Kimberley A. Thornton, M.D., b Maureen Charron, Ph.D., c Erkan Buyuk, MD, D Albert Einstein College of Medicine & New Hope Fertility Center, New York, NY; bReproductive Medicine Associates of New York, New York, NY; cAlbert Einstein College of Medicine, Bronx, NY; dEinstein/Montefiore, Bronx, NY.

OBJECTIVE: Advanced glycation end products (AGEs) are highly reactive pro-inflammatory molecules that are formed following the heating process of several diets. Following their ingestion, these AGEs get absorbed and could cause several organs’ dysfunction, including the female reproductive system. Using human granulosa cell model, it was previously shown that AGEs in vitro induce changes in genes important in steroidogenesis and follicular development, potentially leading to ovarian dysfunction. This study aimed at studying the effects of dietary AGEs in vivo on female reproductive function.

DESIGN: In vivo experiments using mouse model.

MATERIALS AND METHODS: 6-week-old C57Bl/6 female mice were fed for 9-10 weeks either Low-AGE (AIN-93-G, 3.84 kcal/g, 64.6% carbohydrate, 18.8% protein, 16.6% fat) or High-AGE diet (n = 5) or High-AGE diet (n = 5). The High-AGE diet was prepared by heating up the Low-AGE diet at 120°C for 30 min. Mice were weighed weekly and vaginal smears were performed for 2 weeks after 8 weeks of feeding (at approximately 14 weeks of age). Mice were then superovulated with exogenous gonadotropins and were sacrificed 16 h after hCG, then oviducts were harvested, and oocytes that were deposited into the oviducts were quantified. The oocytes present within the oviducts were counted by an individual blinded to diet status. The oocytes were harvested and subjected to RT-PCR for genes important in steroidogenesis and folliculogenesis. Data are presented as mean ± SEM. Mann-Whitney U test was performed for comparison. To confirm that the conditions used to prepare the High-AGE diet indeed increased the AGE content (in particular CML [N-carboxymethyl-histidine]), an ELISA kit for CML was used on the diet itself before and after heating.

RESULTS: CML levels in the High-AGE diet were 10 times higher compared to levels in Low-AGE diet (60.5 ug/mL vs. 6.2 ug/mL, respectively) indicating that the heating process increased AGEs’ levels. Although there was no difference in weight or the number of oocytes deposited between both groups (19.2 ± 5.4 vs. 24.0 ± 5.1, respectively; p = 0.5), mice on High-AGE diet spent significantly more time in the diestrus phase compared to mice on Low-AGE diet (4.3 ± 0.3 vs. 3.2 ± 0.4, respectively; p = 0.04). RT-PCR data on ovarian tissue showed that fshr mRNA expression level was 100% higher (p = 0.049) and gdf9 mRNA expression level was 40% higher (p = 0.046) in the High-AGE diet group compared to the Low-AGE diet group.

CONCLUSIONS: These results indicate that feeding diet at high temperatures increases AGEs’ content in the food and could alter both estrous cyclicity and ovarian folliculogenesis/steroidogenesis. Future studies should adjust for macro- and micro-nutrients that could change due to the heating process of diet, and which represent a confounding variable for studies using High-AGE diet in female reproduction.


SUPPORT: 1) Grant from American Society for Reproductive Medicine (ASRM).

OVARIAN RESERVE

P-705 Wednesday, October 16, 2019 6:30 AM

PREGNANCY OUTCOMES FOLLOWING INTRAVENOUS INSEMINATION (IVI) IN YOUNG WOMEN WITH DECREASED OVARIAN RESERVE. Ashley W. Tieg, MD,a Shelby A. Neal, MD,a Emily K. Osman, MD,a Julia G. Kim, MD, MPH,a Brent M. Hanson, MD,a Jason M. Fransasi, MD,a Richard Thomas Scott Jr, MD,a

SUPPORT: The study was supported by NIH OD 5150101092.

ASRM Abstracts Vol. 11, No. 3, Supplement, September 2019
OBJECTIVE: To evaluate pregnancy outcomes following IUI in young women with low ovarian reserve compared to age-matched controls.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Patients aged <35 years undergoing their first IUI cycle with a documented anti-mullerian hormone (AMH) level at a single large IVF center between 1999 and 2018 were included. All patients had evidence of patent fallopian tubes and severe male factor infertility (total motile sperm count < 10 million on IUI) was excluded. Patients with AMH <1.0 ng/mL were compared to those with levels >1.0 ng/mL. The primary outcome was positive pregnancy test. Secondary outcomes included live birth, biochemical loss, clinical miscarriage (loss after visualized gestational sac) and ectopic pregnancy. Student’s t-tests and chi square testing were used where appropriate.

RESULTS: There were 3438 patients included: 428 with AMH <1.0 ng/mL, and 3010 with AMH >1.0 ng/mL. Mean AMH values were 0.63 ± 0.20 vs 5.7 ± 5.6 ng/mL, respectively. Mean antral follicle count was 10.6 ± 5.2 vs 22.9 ± 12.7. There were no differences in age (31.6 ± 2.4 vs 30.6 ± 2.7 years), body mass index (26.0 ± 6.4 vs 26.3 ± 6.5 kg/m²) or infertility diagnosis (54% vs 51% with unexplained or ovulatory dysfunction excluding polycystic ovarian syndrome) between patients with decreased ovarian reserve compared to those without. Reproductive outcomes are depicted in Table 1.

CONCLUSIONS: Young patients (<35 years) with decreased ovarian reserve conceived less often after IUI as compared with age-matched controls. However, once pregnant, such patients had fewer biochemical losses and similar live birth and clinical miscarriage rates as compared to controls. These data imply a quantitative, not qualitative, distinction between groups. Future prospective studies carefully controlling for infertility diagnosis are required to confirm these relationships.

SUPPORT: None.

P-706 Wednesday, October 16, 2019 6:30 AM

THE RATE OF ANTRAL FOLLICLE COUNT DECREASE DECREASES WITH OLDER AGE AND LOWER ANTRAL FOLLICLE COUNT. Xiaojie P. Zhou, M.D.,1 Charles E. McCulloch, Ph.D.,1 Mitchell P. Rosen, MD, HCLD,1 Marcelle I. Cedars, MD.1 1University of California - San Francisco, San Francisco, CA; 2UCSF, San Francisco, CA; 3University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: There is a paucity of longitudinal data examining the rate of antral follicle count (AFC) decline. We aimed to assess the correlation between baseline age and baseline AFC, and the rate of AFC loss over repeated measures in healthy, reproductive-aged women.

DESIGN: Prospective Cohort Study

MATERIALS AND METHODS: 265 women aged 25 to 45 with regular menstrual cycles lasting between 25-35 days enrolled in the Ovarian Aging (OVA) study between 2006 and 2010 were included. A baseline AFC was obtained during the initial study period and a follow-up AFC was obtained an average of 3.9 years later for each individual. Given the multilevel longitudinal data, mixed models with random intercepts and random slopes were used in order to account for the varying baseline ages and AFCs, and differing AFC decline rates between individuals. The models were adjusted for smoking status, oral contraceptive use and baseline age where appropriate.

RESULTS: The mean baseline AFC for the age groups 25-29, 30-34, 35-39 and 40-45 was 21.8 (SD 9.7), 17.8 (SD 9.5), 8.4 (SD 5.4) and 3.9 (SD 3.5), respectively. The rate of AFC decline was found to gradually accelerate with increasing baseline age until age 40 with the highest rate of AFC loss seen in the 35-39 age group. After age 40, there was a deceleration in the AFC loss rate compared to the 35-39 age group (-1.3 vs. -1.7 follicles per year, p<0.001). The rate of AFC decline was also found to gradually decelerate in women with lower baseline AFC, with the lowest AFC group of 0-9 follicles experiencing the slowest rate of loss of ~0.7 follicles per year compared to all other AFC groups including the 10-19 follicle group with a rate of loss of ~1.4 follicles per year (p<0.001) (Table).

CONCLUSIONS: In healthy, non-infertile women with regular menstrual cycles, our longitudinal data suggest that older women start with fewer follicles at baseline and experience follicle loss at a slower rate after the age of 40. In addition, women with lower baseline follicle counts, irrespective of age, experience slower declines than women with higher baseline follicle counts. These findings perhaps indicate a compensatory mechanism to preserve ovarian function in women of older age, or lower ovarian reserve, toward the end of their reproductive lifespan.

SUPPORT: Grant Support: A R01 HD044876; 1R01AG053332-01A1.

P-707 Wednesday, October 16, 2019 6:30 AM

EXOME SEQUENCING REVEALED SIGNIFICANT DELETORIOUS DNA VARIANTS ASSOCIATED WITH PREMATURE DIMINISHED OVARIAN RESERVE. Blair R. McCallie, BS, Mary E. Haywood, PhD, Rachel Makloski, RN, William B. Schoolcraft, MD, Mandy G. Katz-Jaffe, Ph.D. Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Diminished ovarian reserve (DOR) is a condition where the number or quality of oocytes is compromised, significantly impacting a woman’s reproductive potential. While this is common as women age, about 10% of younger women will be impacted by premature DOR, resulting in poor fertility outcomes. With the causes of early-onset DOR being largely unknown, the objective of this study was to utilize exome sequencing to investigate the underlying molecular mechanisms associated with DOR in young women (<31 years).

DESIGN: Research study.

MATERIALS AND METHODS: Whole peripheral blood was collected from IRB consented female patients and donated to research: young, fertile, oocyte donor controls (CONT ≤ 31 years; n=11), and age-matched young women presenting with diminished ovarian reserve (DOR ≤ 31 years; n=11). DNA was isolated using the QIAamp DNA Mini kit (Qiagen). Exome sequencing libraries were prepared using SureSelectXT (Agilent) and sequenced on the Illumina NovaSEQ 6000. Sequences were processed using the GATK4 Best Practices exome analysis pipeline. Functional and rare variants found exclusively in DOR samples were evaluated for pathogenicity and corresponding genes were tested for pathway enrichment using Ingenuity Pathway Analysis (Qiagen). Sequencing validation was performed using qPCR with Taqman SNP Genotyping Assays (Applied Biosystems).

RESULTS: Exome sequencing revealed 730 significant DNA variants across the genome that were observed exclusively in the young DOR sample set (P<0.001). Bioinformatic analysis revealed the top significantly enriched signaling pathways associated with young DOR: Glucocorticoid receptor (GR) and Notch (P<0.001). The GR signaling pathway had 32 deleterious DNA variants within 16 different genes, all of which would significantly affect protein function (P<0.001).
Each young DOR patient had an average of 2.9 different deleterious DNA variants impacting the GR signaling pathway. Glucocorticoid receptors are crucial for the establishment and maintenance of reproductive function and stress response, influencing oocyte maturation and developmental potential. The Noch pathway had 5 missense DNA variants observed in young DOR patients (P < 0.01), which could be responsible for abnormal folliculogenesis and affect meiotic spindle assembly. To date, DNA variant validation has been performed on 5 genes in the GR signaling pathway, including AGT which has been implicated in reduced ovulatory capacity, and KRT19, involved in proliferation of the surface epithelium during ovarian development.

CONCLUSIONS: A study of young DOR patients revealed significant deleterious DNA variants in genes crucial to ovarian function, folliculogenesis and oocyte maturation. The combination of these adverse hits across key signaling pathways would impact the reproductive stress response, growth and maturation of ovarian follicles, as well as downstream oocyte quality. Identifying the underlying molecular mechanisms responsible for premature DOR could lead to preventative treatments that slow the process of early ovarian aging.

SUPPORT: None.

P-708 Wednesday, October 16, 2019 6:30 AM

INTEREST OF THE USE AUTO-TRANSPLANTATION OF THE OVARIAN CORTEX AFTER DORMANT FOLLICLES IN VITRO ACTIVATION (IVA) IN PATIENTS WITH PREMATURE OVARIAN INSUFFICIENCY (POI). Khaled Mahmoud, Dr, Hanen Elloumi, Dr, Mohamed Khrouf, Dr, MED Habib Ben Aribia, Dr, Khaled Tarell, Dr, Sonia Mnallah, Dr, Mariem ben Khelifa, PhD, Fathi Ziaou, Dr, clinique La Rose, Centre FERTILLIA, jardins du lac 2, Tunisia; clinique la rose, Tunis, Tunisia; clinique la rose, centre FERTILLIA, Tunis, Tunisia.

OBJECTIVE: In women with POI, spontaneous conception and response to ovarian stimulation are considerably limited; oocyte donation is therefore the only effective treatment. But in some social cultures, like ours, egg donation is forbidden. The aim of this study is to evaluate the efficacy of autotransplantation of the ovarian cortex after in vitro activation of dormant follicles in these patients in order to have their own genetic children.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: From September 2018 to February 2019, 19 patients with POI according to the Bologna criteria agreed to participate in this study on IVA treatment. The main characteristics of women are: age (35.4 ±2.9 years), duration of amenorrhea: (2.6 ±1.9 years), FSH (51.5±20.3 IU/L), E2 (13.0±3.6 pg/ml) and AMH: (0.04±0.03 ng/ml). all women received pretreatment with an oral estrogen/progesterone (OEPP). on days 20 to 22 of this pretreatment, a first laparoscopy is performed to remove an entire ovary which will immediately be transferred to the IVF laboratory. The biologist separates the ovarian cortex from the medulla and cuts it into small cubes (0.5-1 cm x 1-2 mm thickness). 10 to 20% of this ovarian cortex is used to hisp-separates the ovarian cortex from the medulla and cuts it into small cubes pretreatment with an oral estrogen/progesterone (OEPP). on days 20 to 22 of these patients in order to have their own genetic children. But in some social cultures, like ours, egg donation is forbidden. The aim of this study is to evaluate the efficacy of autotransplantation of the ovarian cortex after in vitro activation of dormant follicles in these patients in order to have their own genetic children.

SUPPORT: None.

P-709 Wednesday, October 16, 2019 6:30 AM

DECLINING TREND OF AMH LEVELS IN INDIAN WOMEN OF REPRODUCTIVE AGE GROUP: THE JAS-LOK EXPERIENCE. Jyotshna Palgamkar, DGO, DNB, Sapna Agarwal, MD, Nilesh J. Shah, PhD, MDDeepak Rampikil Sanghavi pathology, Sr., Flavia D. Almeida, MBA JSBC, Dr Trupti Mehta, DNB, Dhananjay Kulkarni, Ph.D, Arundhati Athalye, PhD, Firuza Rajesh Parikh, MD DNB PhD Jaslok Hospital and Research Centre, MUMBAI, India; Metroplitis Healthcare Ltd, MUMBAI, India; Metropolis Healthcare Ltd, mumbai, India; Jaslok Hospital and Research Centre, Mumbai, India.

OBJECTIVE: To study the declining trend of AMH levels in young Indian women visiting our Fertility Center.

DESIGN: Retrospective case control study of AMH levels in Indian women visiting our Fertility Center.

MATERIALS AND METHODS: AMH (n=800) of these women was measured (ng/ml) using Electro-chemiluminescence Immuno Assay (Roche machine e601 ECLIA). Their age and AMH values were compared.

RESULTS: Of the 800 women (Table 1), 31 % of women in < 30 yrs of age group and 51 % of women in the 31 to 35 age group had AMH levels < 2.0 ng/ml as compared to 18 % and 35 % in the fertile control groups respectively (p < 0.05). It is interesting to note that 13.9 % of women in < 30 years age group and 26 % of women in 31-35 year age group had AMH of < 1 ng/ml as compared to 2.6 % and 13.4 % respectively in the control group. This study indicates the troubling trends of low AMH in Indian women in the reproductive age group.

CONCLUSIONS: Young Indian women in their late 20’s and early 30’s visiting our center for infertility treatment showed a worrisome declining trend of AMH. Speculation can point towards the ubiquitous role of plastics and Endocrine Disrupting Chemicals (EDCs) that entered the Indian environment 30-35 years ago.

| TABLE 1 |
|------------|-------------|
| Age (yrs) | AMH (ng/ml) |<0.55 | 0.56-1.0 | Total (<1) | 1.01-1.55 | 1.56-2.0 | Total (1-2) | Total (<2) | 2.01-2.55 | 2.56 - 3.0 | Total (2-3) | 3.01-4.0 | Total (4-)<4 |
| < 30 (n=215) | 6.0% | 7.9% | 13.9% | 10.7% | 6.5% | 17.2% | 31.1% | 9.8% | 10.2% | 20.0% | 16.7 | 36.7 | 32.10% |
| (n=39) | (0%) | (2.6%) | (2.6%) | (10.3%) | (5.1%) | (15.4%) | (18.0%) | (17.9%) | (10.2%) | (28.1%) | (17.9%) | (46.0%) | (35.90%) |
| 31-35 (n=327) | 12.5% | 13.5% | 26.0% | 14.1% | 10.7% | 24.8% | 50.8% | 11.3% | 7% | 18.3% | 11.9% | 30.2% | 19% |
| (n=52) | (1.9%) | (11.5%) | (13.4%) | (15.4%) | (5.8%) | (21.2%) | (34.6%) | (21.2%) | (19.2%) | (40.4%) | (13.5%) | (53.9%) | (11.50%) |
| 36-40 (n=202) | 17.3% | 18.3% | 35.6% | 18.3% | 12.4% | 30.7% | 66.3% | 8.4% | 5.9% | 14.3% | 8.4% | 22.7% | 10.9% |
| (n=9) | (0%) | (22.2%) | (22.2%) | (66.7%) | (5%) | (66.7%) | (88.9%) | (0%) | (0%) | (0%) | (0%) | (0%) | (11.10%) |
| > 40 (n=56) | 44.6% | 17.9% | 62.5% | 14.3% | 12.5% | 26.8% | 89.3% | 3.6% | 1.8% | 5.4% | 1.8% | 7.2% | 3.60% |
| Total n=800 | (0%) | (0%) | (0%) | (0%) | (0%) | (0%) | (0%) | (0%) | (0%) | (0%) | (0%) | (0%) | (0%) |

(Within parenthesis is the value from fertile control group) *p value (<0.05) from respective fertile control group e386 ASRM Abstracts Vol. 112, No. 3, Supplement, September 2019
THE EFFECT OF THE RELATIVE DEGREE OF HOW LOW IS THE SERUM ANTI-MULLERIAN HORMONE (AMH) LEVEL IN WOMEN AGED <39 ON OUTCOME FOLLOWING IN VITRO FERTILIZATION-EMBRYO TRANSFER (IVF-ET). Jerome H. Check, M.D., Ph.D.; Rachael Cohen, D.O.; Eric Chang, D.O.; Jung Choe, M.D.; Carrie K. Wilson, B.A.; Cooper Medical School of Rowan University, Camden, NJ; Cooper Institute for Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ.

OBJECTIVE: To determine the relative adverse effect of decreasing levels of AMH on IVF-ET in women aged ≤39 with diminished oocyte reserve.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: Women with diminished oocyte reserve, as evidenced by a serum AMH <1 ng/mL, who were undergoing IVF-ET during a finite time period, were divided into 4 subcategories: grp 1 – AMH ≤0.39, grp 2 – AMH 0.40 to 0.59, grp 3 – AMH 0.60 to 0.79, and grp 4 – AMH 0.80 to 0.99 ng/mL. Only mild gonadotropin stimulation was used. All transfers were on day 3. A couple was included only one time. Power analysis suggested a study group size of 75 patients having oocyte retrieval with marked DOR (AMH <0.39) and 75 with AMH 0.4 to 0.99 considering that the very low AMH group would be less likely to have oocyte retrieval result in embryo transfer.

RESULTS: Pregnancy rates following IVF-ET (day 3 transfers) according to serum AMH levels in women aged ≤39 with diminished oocyte reserve are seen in the table below.

<table>
<thead>
<tr>
<th>Group</th>
<th>AMH Levels (ng/mL)</th>
<th># Retrievals</th>
<th># Transfers</th>
<th>Average age</th>
<th>% Clinical/pregnancies/transfer</th>
<th>% Delivered</th>
<th>Avg. no. embryos transferred</th>
<th>Implantation rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;0.39</td>
<td>73</td>
<td>36</td>
<td>36.0</td>
<td>11% 27% 17% 16.7%</td>
<td>5.6%</td>
<td>1.47</td>
<td>6.7%</td>
</tr>
<tr>
<td>2</td>
<td>0.40-0.59</td>
<td>27</td>
<td>18</td>
<td>38.4</td>
<td>11.2% 27% 17% 16.7%</td>
<td>5.6%</td>
<td>1.7</td>
<td>22.6%</td>
</tr>
<tr>
<td>3</td>
<td>0.60-0.79</td>
<td>24</td>
<td>17</td>
<td>35.9</td>
<td>11.2% 27% 17% 16.7%</td>
<td>5.6%</td>
<td>1.9</td>
<td>26.3%</td>
</tr>
<tr>
<td>4</td>
<td>0.80-0.99</td>
<td>20</td>
<td>14</td>
<td>35.9</td>
<td>11.2% 27% 17% 16.7%</td>
<td>5.6%</td>
<td>1.6</td>
<td>26.1%</td>
</tr>
</tbody>
</table>

Live deliveries are possible even in women aged ≤39 with the lowest serum AMH levels (≤0.39 ng/mL). Overall, the live delivered pregnancy rate following day 3 embryo transfer was 13%/transfer (11/85) in women with diminished oocyte reserve as evidenced by serum AMH <1 ng/mL. Overall, oocyte retrieval led to an embryo transfer 53% of the time. Even grp 1 (AMH < .39) had an embryo transfer 50% of the time and had 1.7 embryos transferred. Excluding grp 1, the live delivered pregnancy rates for groups 2-4 was 18.3% (9/49).

CONCLUSIONS: Knowledge of the likelihood of success based on the degree of oocyte deficiency can help a couple aged ≤39 with diminished oocyte reserve to decide to try IVF with their own oocytes or choose donor oocytes. Comparing a 5.6% live delivered pregnancy rate in grp 1 vs. 18.3% for groups 2-4, with the same average number of embryos transferred, it would seem that oocyte quality is markedly reduced with serum AMH extremely low, but otherwise oocyte quality is only mildly to moderately compromised with serum AMH levels of 0.4 to 0.99 ng/mL.

PCOS/ANDROGEN EXCESS

BROWN ADIPOSE TISSUE IN WOMEN WITH POLYCYSTIC OVARY SYNDROME: RELATIONSHIP WITH BODY MEASURES, PLASMA IRISIN LEVELS AND THE USE OF METFORMIN. Flavia R. Oliveira, MD, PhD; Marcelo Mamede, MD, DMSc; Mariana F. Bizzi, M.Sc.; Ana Luiza L Rocha, MD, PhD; Claudia N. Ferreira, PhD; Karina B. Gomes, PhD; Ana L. Candido, MD, PhD; Fernando M. Reis, MD, PhD; “Universidade Federal de Minas Gerais, Belo Horizonte, Brazil; aAffiliation not provided; UFMG, Belo Horizonte, Brazil.

OBJECTIVE: Brown adipose tissue (BAT) has been recently identified in adult humans through positron emission tomography-computed tomography (PET-CT). Irisin is a myokine that can induce BAT formation. Polycystic ovary syndrome (PCOS) is a chronic dysfunction associated with obesity and metabolic disorders. The aim of this study was to evaluate whether BAT activity in women with PCOS differs from controls, correlates with plasma irisin levels and can be rescued by metformin.

DESIGN: Prospective cross-sectional study and randomized controlled trial.

MATERIALS AND METHODS: In the cross-sectional study, we included women aged 18-45 years with PCOS (n=45) and a healthy control group (n=25) matched by age and body mass index (BMI). The 45 participants of the PCOS group were subsequently randomized into a metformin subgroup (1500 mg/day during 60 days, n=21) and a placebo subgroup
pending on the level heterogeneity, determined by the
by using a specialized diet. IR measures (HOMA1-IR), pre- and post-inter-
with PCOS possibly due to increased central adiposity. In PCOS women, BAT activity did not correlate with plasma insulin levels and did not change after a brief treatment with metformin.

SUPPORT: Research supported by Fundación de Amaparo a la Pesquisa do Estado de Minas Gerais (FAPEMIG, grant # APQ-203796-16) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPG) through the National Institute of Hormones and Women’s Health (grant # 465482/2014-7) and the National Institute of Molecular Medicine. K.B.G and F.M.R. receive research grants from CNPq.

P-713 Wednesday, October 16, 2019 6:30 AM

WOMEN WITH POLYCYSTIC OVARY SYNDROME AND ELEVATED LEVELS OF INSULIN RESISTANCE ARE MORE PRONE TO BENEFIT FROM DIETS TO IMPROVE INSULIN SENSITIVITY: A META-ANALYSIS.

Esther López-Bayghen, PhD, Samantha García-Hernández, MD, M. Elba González-Mejía, MD, PhD, Leonardo M. Porchia, PhD. Centro de Investigación y Estudios Avanzados IPN, México, EM, Mexico.

OBJECTIVE: Women with polycystic ovary syndrome (PCOS) are associated with increased levels of insulin resistance (IR). Most likely, IR is exacerbated by obesity, which is common, but not exclusive, with these women. Other than treatment with insulin-sensitizing drugs, specialized diets have been also implemented concurrently with drug treatments, as to reduce the patient’s weight. However, the capacity of certain diets, with respect to the level of IR, to reduce IR has not fully been explored. Therefore, we conducted a meta-analysis to determine in subjects with higher IR, if hypocaloric diets improve insulin sensitivity.

DESIGN: Systematic review with a meta-analysis.

MATERIALS AND METHODS: PubMed, SCOPUS, EBSCO, and LILACS databases and retrieved studies’ bibliographies were searched for prospective studies that investigated the association between diet and IR in PCOS until October 2018. Diet was defined as a modification of the patients’ nutrition intake according to caloric restriction, change in protein intake, or filled the inclusion criteria. Due to the heterogeneity of the diets, the random effects model was used. In 52% of studies, the diets led to a decrease of IR, whereas 30% had no effect. In 3 studies, the diet increased IR. Overall, the diets decreased IR (-0.53 ± 0.21, p < 0.001). Subjects with high IR (HOMA1-IR > 9) had a marked improvement (-1.28 ± 0.44, p < 0.001). This was also determined with elevated IR (HOMA1-IR: 3.0-9.0: -0.68 ± 0.19, p < 0.01). However, subjects with low IR (HOMA1-IR<3.0), diets did not improve IR (-0.13 ± 0.32, p = 0.68).

CONCLUSIONS: Here, we demonstrate that in subjects with higher IR, diets are more likely to improve IR in women with PCOS. Therefore, it is crucial to determine a subjects IR status before considering any intervention containing a diet.

SUPPORT: Conacyt 231793.

P-714 Wednesday, October 16, 2019 6:30 AM

PREVALENCE AND PREDICTORS OF ADEQUATE PHYSICAL ACTIVITY IN A MULTIETHNIC POLYCYSTIC OVARY SYNDROME PATIENT POPULATION.

David Huang, MD,1 Eleni A. Greenwood, MD, MSc,1 Chia-Ning Kao, MS,2 Molly Quinn, MD,2 Marcelle I. Cedars, MD,* Heather G. Huddleston, MD,* University of California San Francisco, San Francisco, CA; University of California Los Angeles, Los Angeles, CA.

OBJECTIVE: To i) identify correlates of adequate physical activity and 2) describe exercise behaviors in a multiethnic polycystic ovary syndrome (PCOS) patient population, in order to identify high-risk group(s) that could benefit from targeted intervention.

DESIGN: Cross sectional cohort study.

MATERIALS AND METHODS: Participants were recruited from 2006-2019 from a PCOS multidisciplinary clinic at a single academic center. Exercise data were ascertained by the International Physical Activity Questionnaire, from which we calculated metabolic equivalents (METs) as the unit of energy expenditure. Adequate physical activity was defined by the US Department of Health and Human Services (DHHS) guidelines, either as 150 minutes/week of moderate-intensity, or 75 minutes/week of vigorous-intensity, or an equivalent combination of moderate- and vigorous-intensity aerobic exercise. Exercise data were analyzed by self-reported ethnicity (White, Hispanic, East/Southeast Asian, South Asian, and African American), income level, education, parity, and place of birth (US-born vs. foreign-born). Primary outcome was adequate physical activity, coded as a binary variable. Logistic regression analysis was used to identify correlates of adequate physical activity after controlling for age (SAS v9.4). Further, we used the Kuskal-Wallis test to compare the distribution of METs from moderate-intensity, vigorous-intensity, and total (moderate- plus vigorous-intensity) exercise between ethnic groups.

RESULTS: Of the 466 women evaluated, 62% (n = 287) were White, 15% (n = 71) were Hispanic, 11% (n = 52) were East/Southeast Asian, 7% (n = 32) were South Asian (SA), and 5% (n = 23) were African American (AA). The cohort was notable for AA patients being older (p = 0.02), and Hispanic and AA patients having higher BMI (p < 0.01) and waist circumference (p < 0.01) compared to other remaining ethnic groups. Overall prevalence of adequate physical activity was 66% in our cohort. Logistic regression analysis, controlling for age, demonstrated ethnicity as a predictor for adequate physical activity (p = 0.01), with SA patients having the lowest frequency of meeting DHHS guidelines (47%, compared to 71% in White patients). Parous status and education level (specifically, not having a college degree) were also identified as predictors of lower frequency of adequate physical activity (p < 0.02, and p < 0.01, respectively). Lastly, we noted significant differences in distribution of METs from vigorous exercise (METvig) and total exercise (METtotal) between ethnic groups (p = 0.01 and 0.01 respectively), with South Asian patients having the lowest mean rank METvig and METtotal.

CONCLUSIONS: We observed significant differences in frequency of adequate physical activity by ethnicity, parity, and education level in our cohort. Providers of PCOS patients should consider focusing on South Asian patients and women who are parous and/or with lower educational attainment with targeted interventions to promote healthy exercise behaviors.

P-715 Wednesday, October 16, 2019 6:30 AM

DECREASED LIFETIME FECUNDITY IN WOMEN WITH PCOS: FINDINGS FROM A HIGH FECUNDITY POPULATION.

Erica Johnstone, MD, Meredith Humphreys, MD, C Matthew Peterson, MD, Lisa Cannon-Albright, Ph.D., Kristina Allen-Brady, Ph.D., MSPH University of Utah, Salt Lake City, UT.

OBJECTIVE: European studies have shown that women with polycystic ovary syndrome have similar numbers of children to women without this diagnosis [1]. However, these studies have generally been conducted in populations in which the mean number of children born to a woman is less than 2. In Utah, the mean number of children per woman has ranged between 2.33 and 2.65 between 1990 and 2014 [2]. We sought to determine whether women with PCOS in a high fecundity population have similar numbers of children compared to women without PCOS, and whether there are differences in ages at first and last birth.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The Utah Population Database (UPDB), which contains demographic and detailed genealogy data, as well as medical records from the University of Utah healthcare system from 1994 through 2014, was queried for this study. PCOS cases were identified by ICD-9 codes. PCOS cases were diagnosed between the ages of 10 and 54, had least 3 generations of genealogical data in the UPDB (to increase the likelihood of having birth certificate data available for their children), and had given birth to at least one child. Controls were
matched for sex, birth place (Utah or elsewhere), and 5-year birth cohort. In addition, controls were required to have had at least one child. Children born to PCOS cases and controls, and maternal age at each birth, were determined using birth certificate data. We report mean values, standard deviation (SD) and range using conventional methods. As the data were not normally distributed, the Mann-Whitney U test was used to compare age and number of children between the PCOS cases and matched controls.

RESULTS: A total of 1,022 PCOS cases who had given birth to at least one child and 1,022 matched population controls were used in this analysis.

### Table 1. Fecundity patterns in women with and without PCOS

<table>
<thead>
<tr>
<th></th>
<th>PCOS cases: mean (SD), range</th>
<th>Controls: mean (SD), range</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at censoring (yrs)</td>
<td>38.96 (7.27), range: 23-70</td>
<td>39.02 (7.46), range: 23-73</td>
<td>0.891</td>
</tr>
<tr>
<td>Number of children born</td>
<td>2.20 (1.19), range: 1-10</td>
<td>2.60 (1.36), range: 1-11</td>
<td>6.75e-13</td>
</tr>
<tr>
<td>Age at first birth (yrs)</td>
<td>26.66 (4.97), range: 15-44</td>
<td>23.97 (3.94), range: 14-41</td>
<td>2.2e-16</td>
</tr>
<tr>
<td>Age at last birth (yrs)</td>
<td>30.37 (5.17), range: 17-44</td>
<td>28.82 (4.59), range: 16-44</td>
<td>4.04e-12</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The mean number of births for both PCOS cases and matched controls in this high fecundity population was greater than 2 for both groups. PCOS cases had significantly lower parity on average than matched controls. PCOS cases were an average of 2.7 years older at the birth of their first child and 1.5 years older at the birth of their last child. As only women with at least one live birth were included, the detrimental impact of PCOS on lifetime fecundity may be greater than estimated here.

### Table 1. Insulin and glucose levels during OGTT

<table>
<thead>
<tr>
<th></th>
<th>H/O H/NO CONTROLS p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>236 261 303</td>
</tr>
<tr>
<td>Age (SD) years</td>
<td>29.1 (6.6) 29.1 (7.0) 30.9 (7.1) 0.45</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>117 130 158 0.09</td>
</tr>
<tr>
<td>Hispanic</td>
<td>59 63 52</td>
</tr>
<tr>
<td>Black</td>
<td>35 35 40</td>
</tr>
<tr>
<td>Asian/Other</td>
<td>23 32 52</td>
</tr>
<tr>
<td>BMI (SD) kg/m2</td>
<td>31.5 (8.3) 30.9 (7.8) 28.6 (8.0) 0.0001a</td>
</tr>
<tr>
<td>OGTT time 0 (SD) mg/dL</td>
<td>87.3 (11.7) 86.4 (13.4) 87.6 (25.9) 0.44</td>
</tr>
<tr>
<td>OGTT 2-hr (SD) mg/dL</td>
<td>119.2 (78.3) 105.7 (40.3) 102.2 (30.1) 0.06</td>
</tr>
<tr>
<td>Insulin time 0 (SD) uIU/mL</td>
<td>21.8 (65.5) 15.0 (16.4) 11.9 (13.6) 0.01a</td>
</tr>
<tr>
<td>Insulin 1-hr (SD) uIU/mL</td>
<td>120.3 (122.2) 117.2 (107.3) 81.7 (77.8) 0.003a</td>
</tr>
<tr>
<td>Insulin 2-hr (SD) uIU/mL</td>
<td>86.7(83.6) 91.3 (103.9) 59.9 (58.4) 0.01a</td>
</tr>
</tbody>
</table>

Pairwise comparisons: H/O vs CONTROL and H/NO vs CONTROL p<0.05.

**P-716 Wednesday, October 16, 2019 6:30 AM**

**IS HIRSUTISM A MARKER OF METABOLIC DYSFUNCTION?**

Sahar a Werther, MD, MD; Jessica L. Chan, MD, MSCE; Ricardo Azziz, MD, MPH; Margaretta D. Pisarska, MD, M.D.

OBJECTIVE: To determine if hirsutism alone is a marker of metabolic dysfunction.

DESIGN: Prospective community-based cohort study.

MATERIALS AND METHODS: Women (age > 14) with a modified Ferriman-Gallwey (mFG) score and markers of metabolic dysfunction were included. Hirsutism was defined by an mFG score of ≥4 and oligome-norrhea as <8 cycles/year. Markers of metabolic dysfunction included body mass index (BMI), waist to hip ratio (WHR), high-density and low-density lipoprotein (HDL, LDL), insulin and glucose levels during a 2-hr oral glucose tolerance test (OGTT). Categorical variables were compared using χ² tests and continuous variables were compared using Kruskal-Wallis or ANOVA, as appropriate. Linear regression models were used to determine correlation of degree of hirsutism with severity of metabolic dysfunction.

RESULTS: 497 hirsute patients were identified, of which 236 were oligo-menorrheic (H/O) and 261 were eumenorrheic (H/NO); 303 non-hirsute controls (CONTROLS) were included. The groups were similar in race and age, WHR, LDL and HDL. Hirsute groups had higher BMI values (Table 1). Fast-ing, 1- and 2-hr insulin values were significantly higher for hirsute groups vs controls. In H/O women, mFG scores negatively correlated with HDL (β=-0.94% CI -1.82 - 0.06) and positively correlated with 1- and 2-hr insulin levels (1-hr:β=6.1 95% CI 1.1-11.0; and 2-hr: β= 4.3 95% CI 0.97-7.62). These relationships were not significant after adjusting for BMI. In H/NO women, mFG scores positively correlated with 1- and 2-hr insulin values (1-hr: β=5.38, 95% CI 1.7-9.1; and 2-hr: β 4.27 95% CI 0.67-7.88), even after adjusting for BMI.

### Table 1. Insulin and glucose levels during OGTT

<table>
<thead>
<tr>
<th></th>
<th>H/O H/NO CONTROLS p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>236 261 303</td>
</tr>
<tr>
<td>Age (SD) years</td>
<td>29.1 (6.6) 29.1 (7.0) 30.9 (7.1) 0.45</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>117 130 158 0.09</td>
</tr>
<tr>
<td>Hispanic</td>
<td>59 63 52</td>
</tr>
<tr>
<td>Black</td>
<td>35 35 40</td>
</tr>
<tr>
<td>Asian/Other</td>
<td>23 32 52</td>
</tr>
<tr>
<td>BMI (SD) kg/m2</td>
<td>31.5 (8.3) 30.9 (7.8) 28.6 (8.0) 0.0001a</td>
</tr>
<tr>
<td>OGTT time 0 (SD) mg/dL</td>
<td>87.3 (11.7) 86.4 (13.4) 87.6 (25.9) 0.44</td>
</tr>
<tr>
<td>OGTT 2-hr (SD) mg/dL</td>
<td>119.2 (78.3) 105.7 (40.3) 102.2 (30.1) 0.06</td>
</tr>
<tr>
<td>Insulin time 0 (SD) uIU/mL</td>
<td>21.8 (65.5) 15.0 (16.4) 11.9 (13.6) 0.01a</td>
</tr>
<tr>
<td>Insulin 1-hr (SD) uIU/mL</td>
<td>120.3 (122.2) 117.2 (107.3) 81.7 (77.8) 0.003a</td>
</tr>
<tr>
<td>Insulin 2-hr (SD) uIU/mL</td>
<td>86.7(83.6) 91.3 (103.9) 59.9 (58.4) 0.01a</td>
</tr>
</tbody>
</table>

Pairwise comparisons: H/O vs CONTROL and H/NO vs CONTROL p<0.05.

**H/

**P-717 Wednesday, October 16, 2019 6:30 AM**

**BONE MORPHOGENETIC PROTEIN SUPPRESSES THE ANDROGEN PRODUCTION IN PCOS THECA IN-VITRO CELL MODEL.**

Rishi Man Chugh, PhD,a Hang-Soo Park, PhD, a Amro Elsharoud, MD, b Mara Ulin, MD, c Hajra Takala, MD., MPH., a Ayman Al-Hendy, MD PhD.b aThe University of Illinois College of Medicine, Chicago, IL; bUniversity of Illinois College of Medicine, Chicago, IL; cCedars-Sinai Medical Center, Los Angeles, CA; dUniversity at Albany, SUNY, Albany, NY.

OBJECTIVE: Polycystic Ovarian Syndrome (PCOS) is a metabolic disorder characterized by inflammation, infertility and excess ovarian androgen production by theca cells in the ovary. Though its etiology is not fully understood. Women with PCOS exhibit the increased expression of steroidogenic pathway genes (CYP17A1, and CYP11A1) involved in androgen production. Most available therapies aim to decrease ovarian androgen production to enhance fertility. The Bone morphogenetic proteins (BMPs) which are members of the transforming growth factor β (TGFβ) family plays a significant role in controlling the enzymes of the steroidogenic pathway which suppresses the androgen production. Our previous study showed the effect of mesenchymal stem cells (MSCs) secretome on steroidogenic pathway genes. It is reported in the literature that MSCs also secrete BMPs in its secretome. In this study, we evaluated the utility of BMPs on Human H295R adrenocarcinoma cell line, an in-vitro model for the investigation of the steroidogenic pathway. The H295R cell line expresses genes that encode for the key enzymes for the steroidogenesis.

DESIGN: We hypothesize that bone morphogenetic proteins are able to inhibit the androgen biosynthesis in PCOS in-vitro cell model by affecting the steroidogenic pathway genes expression.

MATERIALS AND METHODS: Human adrenocarcinoma cell line (H295R), purchased from ATCC and cultured as per the protocol. Cells were seeded on six-well plates at a density of 1.8 x10³ cells per well and cultured for 60 hours. Cells were treated with BMP 6 and 7 with different concentrations 25, 50, 100 ng per mL with respective control (without BMP) for 48 hours. After 48 hours the media was removed and cells were washed with PBS and serum free media were added for further 24 hours. After 24 hours incubation, cells and media were collected for analysis. The
expression of mRNA for CYP17A1, CYP11A1, and DENND1A genes was quantified by real-time PCR while testosterone level in media estimated by radioimmunoassay (RIA). Student t-test was used for statistical analysis.

RESULTS: Human H295R cells treated with BMP 6 and 7 with concentrations of 25, 50 and 100ng/ml for 48h showed significantly lower level of testosterone in a dose-dependent manner (25ng/ml: BMP-6, 35.80 ± 0.70 ng/dl, BMP-7, 43.45 ± 0.91 ng/dl), (50ng/ml: BMP-6, 25.40 ± 0.00 ng/dl, BMP-7, 26.30 ± 0.00 ng/dl), (100ng/ml: BMP-6, 16.75 ± 0.21 ng/dl, BMP-7, 22.70 ± 2.54 ng/dl) with compared to their respective control (without BMP treatment) (Control: BMP-6, 80.65 ± 0.35 ng/dl, BMP-7, 58.00 ± 2.96 ng/dl) respectively. The expression of CYP17A1 and DENND1A gene was decreased significantly (P < 0.05) in a dose-dependent manner only in the case of BMP-6 in all the tested concentrations while the changes in CYP11A1 expression was not relevant.

CONCLUSIONS: The Bone morphogenetic protein (BMP-6) showed a significant change in steroidogenic pathway genes and decrease androgen production in H295R cells compared to the control. This result may offer a promising lead and explanation of MSCs secretome effect and offer a rational for its use in treatment of infertility associated with PCOS.

SUPPORT: This study was supported by grant MOST 105-2628B-002-043-MY4 from the Ministry of Science and Technology of Taiwan.

P-719 Wednesday, October 16, 2019 6:30 AM

ANDROGEN ALTERS SENP3 EXPRESSION AND INDUCES AUTOPHAGY IN GRANULOSA CELLS: A NOVEL MECHANISM INVOLVED IN POLYCYSTIC OVARY SYNDROME. Dongmei Sun master, Wei Ran Chai Doctor, Shanghai Ninth People’s Hospital, Shanghai Jiao Tong University School Of Medicine, Shanghai, China.

OBJECTIVE: Polycystic ovary syndrome (PCOS) is a common endocrine disorder in reproductive-aged women, which is mainly associated with androgen excess[1]. Autophagy is responsive to energy stress and is activated in the ovarian tissue of PCOS [2]. The role of autophagy in PCOS related metabolic disorders is increasingly recognized [3−4]. Small ubiquitin-like modifier (SUMO) modification is an important post-translational protein modification in various cell types and is associated with autophagy activation[5]. SENP3, one of Sentrin/SUMO-specific proteases (SEPNs) family members, can remove SUMO2/3 from proteins and SENP3 expression is closely related to oxidative stress [6]. Therefore, this study was designed to research the relationship between testosterone, SENP3 and autophagy in PCOS granulosa cells.

DESIGN: We collected granulosa cells of patients treated by in vitro fertilization with the same controlled ovarian stimulation protocol and were divided into two groups between January 2017 to January 2018. Group A included PCOS patients and group B included 75 tubal-factor infertile patients. Cultured human ovarian granulosa-like tumor cell line (KGN cells) were treated or not with testosterone.

MATERIALS AND METHODS: Granulosa cells were isolated by gradient centrifugation from the follicle fluid aspirated during oocyte retrieval. Western blotting, quantitative PCR analysis were used to detect the SENP3, LC3 and p62 levels in human granulosa cells and KGN cells.

RESULTS: In group A, LC3II/I expression (1.00 ± 0.05 vs 1.0 ± 0.05, P < 0.01) was significantly higher than group B, whereas p62 (0.69 ± 0.03 vs 1.0 ± 0.03, P < 0.01) expression was significantly decreased. After granulosa cells were treated by testosterone for 24 hours, the LC3II/I expression (1.5 ± 0.08 vs 1.0 ± 0.05, P = 0.02) was significantly higher than control group, whereas the expression of P62 levels (1.35 ± 0.08 vs 1.0 ± 0.05, P = 0.02) were obviously lower, which showed that ovarian granulosa cell of polycystic ovary syndrome and autophagy is activated and androgen excess is involved in the autophagy activation of granulosa cells in polycystic ovary syndrome patients. In KGN cells, SENP3 expression declined as the dose of androgen increased (0.61 ± 0.01 vs 0.93 ± 0.04, P < 0.01); whereas LC3II/I expression significantly increased (2.62 ± 0.04 vs 1.5 ± 0.06, P < 0.01), LC3II/I expression and mRNA levels were decreased after SENP3 overexpression and were elevated after the transfection of siRNA (P < 0.05). It suggested that SENP3 is involved in the process of hyperandrogenism induce autophagy in KGN, granular cell of two groups cultured and treated with 10 μM testosterone, SENP3 expression (1.13 ± 0.10 vs 1.54 ± 0.03, P = 0.02) was lower in PCOS group treated with testosterone, which suggested that SENP3 plays an important role in the autophagy activation of granulosa cells in patients with hyperandrogenism polycystic ovary syndrome.


SUPPORT: Scientific research program of Shanghai science and technology commission (15411964500).

P-720 Wednesday, October 16, 2019 6:30 AM

ESTABLISHING AN ANTI-MULLERIAN HORMONE (AMH) CUT-OFF TO DETERMINE POLYCYSTIC OVARIAN MORPHOLOGY (PCOM) SUPPORTING DIAGNOSIS OF POLYCYSTIC OVARIAN SYNDROME (PCOS): THE APHRODITE STUDY. Alexandra Dietz de Loos, PhD, a Martin Hund, PhD, a Katharina Buck, PhD, a Cindy Meun, MD, a Johanna Silliman, PhD, b Joop S. E. Laven, MD, PhD. a Erasmus University Medical Center, Rotterdam, Netherlands; b Roche Diagnostics International Ltd., Rotkreuz, Switzerland; c Roche Diagnostics GmbH, Penzberg, Germany.

OBJECTIVE: To derive and validate a cut-off for AMH to discriminate PCOM using the Elecsys® AMH Plus immunoassay.

DESIGN: APHRODITE is a case-control study of PCOS-positive (cases) and PCOS-negative (controls) women aged 25–45 years. Cases were defined using Rotterdam criteria, showing the full phenotype A (irregular cycles/ovulatory dysfunction, clinical or biochemical hyperandrogenism and hyperinsulinemia) with an AUC of 94.0% (95% CI 92.6–95.5). In women aged <35 years, the AMH cut-off of 3.5 ng/mL showed 84.2% (95% CI 81.3–86.9) sensitivity and 89.8% (95% CI 86.8–92.3) specificity. In the validation cohort, this cut-off achieved 82.4% (95% confidence interval CI) 78.6–85.8) sensitivity and 89.8% (95% CI 86.8–92.3) specificity. An AMH cut-off was optimised in the discovery cohort based on concordance analysis. Performance (sensitivity, specificity and area under the curve [AUC]) of the defined cut-off was evaluated in the validation cohort. Exploratory analyses in different sub-cohorts (including age groups) were also performed.

RESULTS: Compared with controls, PCOS cases were younger (median age 29.0 vs 34.0 years), with a higher body mass index (median 29.2 vs 23.8 kg/m²) and higher AMH level (median 6.23 vs 2.13 ng/mL). Good correlation was observed between AMH and AFC in the discovery and validation cohorts, with Spearman correlation coefficients of 0.83 and 0.84, respectively; A serum AMH cut-off of 3.5 ng/mL (25 pmol/L) was determined in the discovery cohort, which achieved 85.9% sensitivity and specificity. In the validation cohort, this cut-off achieved 82.4% (95% confidence interval CI) 78.6–85.8) sensitivity and 89.8% (95% CI 86.8–92.3) specificity, with an AUC of 94.0% (95% CI 92.6–95.5). In women aged <35 years, the AMH cut-off of 3.5 ng/mL showed 84.2% (95% CI 81.3–86.9) sensitivity and 83.5% (95% CI 80.8–86.6) specificity; in women aged ≥35 years, specificity remained high (91.8% [95% CI 89.2–93.9]) but sensitivity was lower (77.4% [95% CI 63.8–87.7]).

CONCLUSIONS: The Elecsys® AMH Plus immunoassay provides a robust method for identifying PCOM as part of PCOS diagnosis with a cut-off of 3.5 ng/mL (25 pmol/L).

SUPPORT: These analyses were sponsored by Roche Diagnostics International Ltd.

P-721 Wednesday, October 16, 2019 6:30 AM

PROBIOTICS AND SYNBIONTS FOR POLYCYSTIC OVARIAN SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS. Mauro Cozzolino, M.D, a b University of Padua, Padua, Italy.

OBJECTIVE: To evaluate the effectiveness of probiotics and synbiotics on metabolic, hormonal and inflammatory parameters of PCOS, to identify the effect on potential fertility mediators. Probiotics and synbiotics seems to have an effect on metabolic, hormonal and inflammatory aspect of PCOS.

CONCLUSIONS: There is a clear need to structure a robust and well driven RCT that analyses pregnancy-related outcomes in PCOS' women being treated with these substances to check their fertility-related effects, since previously available evidences points to recommend use of probiotic/synbiotic in the clinical practice.

SUPPORT: no financial support.
percentile, 20ng/ml), the predicted response to treatment was 0.96 (95%CI: 0.90-1.00) in models adjusting for age and BMI.

CONCLUSIONS: Among PCOS patients, higher serum AMH levels are associated with significantly lower probability of response to either CC or ITZ but not to FSH, even after adjusting for age and BMI.

Our findings suggest that such select groups of women might benefit from stimulation with gonadotropins.

SUPPORT: None.

P-723 Wednesday, October 16, 2019 6:30 AM
ELEVATED ANTIMULLERIAN HORMONE IS DUE TO INCREASED FOLLICLE NUMBER IN POLYCYSTIC OVARY SYNDROME COMPARED TO CONTROLS. Viji Sundaram, MD,1 Chia-Ning Kao, MS,2 Heather G. Huddleston, MD,3 Marcelle I. Cedars, MD.4 1University of California, San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA; 2University of California San Francisco, San Francisco, CA; 3University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA; 4University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: Although it is known that antinullerian hormone (AMH) levels are higher in polycystic ovary syndrome (PCOS), it is unclear if the elevated AMH is related to increased follicle number, over-production of AMH per follicle, or both. Thus, we sought to compare the AMH to AFC ratio in a population of PCOS and community-based controls.

DESIGN: Cross-sectional cohort study

MATERIALS AND METHODS: Study participants were recruited at the multidisciplinary PCOS clinic following a diagnosis of PCOS by Rotterdam criteria between July 2012 and September 2015. Controls included healthy, normo-ovulatory women from a community-based cohort (Ovarian Aging Study) between November 1997 to November 2010. Clinical and laboratory data were collected for all patients. Serum AMH was assessed for both cohorts at a central laboratory. T-tests were used to assess for significance between demographics variables. AMH, AFC, and AMH:AFC were compared between the PCOS and control cohorts using analysis of covariance (ANCOVA), while controlling for age, body mass index (BMI), smoking status, and race. Pairwise comparisons were adjusted using the Bonferroni method when necessary.

RESULTS: 160 patients with a diagnosis of PCOS and 310 community-based controls were included for analysis. The PCOS patients were younger on average by 7 years (p<0.001), had a higher BMI (p=0.038), as well as significantly higher total cholesterol, fasting insulin, AMH, total AFC, and AMH:AFC compared to controls. In ANCOVAs controlling for age, BMI, smoking, and race, a diagnosis of PCOS was an independent predictor of AMH and AFC but not of AMH:AFC. Age and BMI have a negative effect on AMH and AMH:AFC. African-Americans and Asians have a significantly lower AFC while Asians have a significant increase in their AMH:AFC compared to Caucasians.

CONCLUSIONS: PCOS is an independent predictor of AMH and AFC but not of AMH:AFC ratio when compared with community-based controls. Age and BMI are significant independent negative predictors of the AMH:AFC ratio. Interesting racial comparisons can be made while holding other factors stable: AFC is lower in African-Americans and Asians and AMH:AFC is higher in Asians compared to Caucasians.

TABLE 2. Predictors of Primary Outcome in Analysis of Covariance Multivariate Models

<table>
<thead>
<tr>
<th>Factor</th>
<th>Coefficient</th>
<th>95% Confidence Interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMH:AFC</td>
<td>0.001</td>
<td>0.000</td>
<td>0.98</td>
</tr>
</tbody>
</table>

| Have PCOS Diagnosis     | 0.04        | -0.01, 0.08              | 0.16    |

| Age (years)             | -0.005      | -0.008, -0.002           | 0.002   |
| BMI (kg/m2)             | -0.004      | -0.007, -0.001           | 0.005   |
| Ever Smoked             | -0.03       | -0.08, 0.02              | 0.254   |
| Race                    |             | <0.001                  |         |
| Caucasian               |             | -                     |         |
| African-American        | -0.03       | -0.10, 0.04              | 1.000   |
| Asian                   | 0.14        | 0.07, 0.21               | <0.001  |
| Hispanic                | -0.005      | -0.08, 0.07              | 1.000   |

P-724 Wednesday, October 16, 2019 6:30 AM
POLYCYSTIC OVARY SYNDROME IS ASSOCIATED WITH A SLOWER DECLINE IN ANTIMULLERIAN HORMONE PER ANTRAL FOLLICLE WITH INCREASING AGE. Viji Sundaram, MD,4 Chia-Ning Kao, MS,2 Heather G. Huddleston, MD,3 Marcelle I. Cedars, MD.4 1University of California, San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA; 2University of California San Francisco, San Francisco, CA; 3University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: It is well-known that antinullerian hormone (AMH) and antral follicle count (AFC) are higher in women with polycystic ovary syndrome (PCOS) and that age generally has an inverse relationship to AMH and AFC, however it is not understood if a relationship exists in the AMH produced per follicle between aging patients with PCOS and controls. Hence, we sought to compare the AMH to AFC ratio in a population of PCOS and community-based controls with respect to increasing age.

DESIGN: Cross-sectional cohort study.

MATERIALS AND METHODS: Study participants were recruited at the multidisciplinary PCOS clinic following a diagnosis of PCOS by Rotterdam criteria between July 2010 and September 2015. Controls included healthy, normo-ovulatory women from a community-based cohort (Ovarian Aging Study) between November 2006 to November 2010. Clinical and laboratory data were collected for all patients. Serum AMH was assayed for both cohorts at a central laboratory. T-tests were used to assess for significance between demographics variables. AMH, AFC, and AMH:AFC were compared between the PCOS and control cohorts using analysis of covariance (ANCOVA), while controlling for age, body mass index (BMI), smoking status, and race.

RESULTS: 160 patients with a diagnosis of PCOS and 310 community-based controls were identified for inclusion. The PCOS patients were younger on average by 7 years (p<0.001), had a higher BMI (p=0.038), as well as significantly higher total cholesterol, fasting insulin, AMH, total AFC, and AMH:AFC compared to controls. In ANCOVAs controlling for BMI, smoking, and race, increasing age in the control cohort shows an appropriately significant decline in AMH, AFC, and AMH:AFC ratio. However in the PCOS cohort, only AFC shows an apparent decline with increasing age while changes in AMH and AMH:AFC are not significantly altered.

CONCLUSIONS: Increasing age is associated with a significantly lower AMH:AFC ratio in controls, which is not seen in patients with PCOS. Aging controls have a larger drop in AMH per antral follicle, while those with PCOS are able to maintain a lower decline in AMH per antral follicle despite the decline in AFC with ovarian aging. PCOS may serve as a model for delayed aging with respect to ovarian markers as evidenced by the absence of decline in AMH and AMH:AFC ratio with age.

Predictors of Primary Outcomes in Analysis of Covariance Multivariate Models with Respect to Increasing Age

<table>
<thead>
<tr>
<th>Factor</th>
<th>PCOS</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMH</td>
<td>-0.038</td>
<td>0.794</td>
</tr>
<tr>
<td>AFC</td>
<td>-0.806</td>
<td>0.034</td>
</tr>
<tr>
<td>AMH:AFC</td>
<td>+0.00013</td>
<td>0.972</td>
</tr>
</tbody>
</table>

P-725 Wednesday, October 16, 2019 6:30 AM
DIVERGENT INFLAMMATORY PATHWAYS MODULATE KEY ANDROGENIC GENE EXPRESSION IN OVARian THECA-INTERSTITIAL CELLS. Chelsea Webb Fox, M.D.,1 Zhang Lingzhi, Ph.D.,2 Benjamin C. Moeller, Ph.D,.3 Antoni Duleba, M.D.4 1University of California San Diego, La Jolla, CA; 2University of California Davis, Davis, CA.

OBJECTIVE: Polycystic ovary syndrome is characterized by low-grade systemic inflammation and excessive androgen production by ovarian theca cells. This study evaluated the molecular mechanism through which inflammatory stimuli increase androgenic gene expression in theca-interstitial cells (TIC).

Vol. 112, No. 3, Supplement, September 2019
DESIGN: In vitro study exploring the mechanism of action of pro-inflammatory lipopolysaccharide (LPS) on androgenic gene expression in TIC.

MATERIALS AND METHODS: Isolated rat TICs were cultured in chemically defined media for 48 hours with or without LPS (100ng/mL) and/or TAK-242 (1uM; an inhibitor of TLR4), MCC950 (1uM; an inhibitor of the NLRP3 inflammasome) or ibuprofen (10^{-7} M), a non-selective inhibitor of cyclooxygenase (COX) enzymes. RNA was isolated and qPCR was performed to evaluate mRNA expression of Cyp17a1, Cyp11a, Hsd3b, Ptg2, Cebpd and Hprt (reference gene).

RESULTS: Compared to control cultures LPS increased Cyp17a1, Cyp11a, Hsd3b, Ptg2, and Cebpd by 4.7 fold (p<0.001), 7.1 fold (p<0.0001), 2.7 fold (p<0.0001), 5.6 fold (p<0.0001) and 3.2 fold (p<0.0001), respectively. These effects on androgenic gene expression were abrogated by ibuprofen (p<0.001) and TAK-242 (p<0.0001) treatment. The effect of LPS on Cyp17a1 expression was also abrogated by MCC-950 (p<0.0005); in contrast, effects of LPS on Cyp11a1, Hsd3b, ptg2, and cebpd were not significantly altered by MCC-950.

CONCLUSIONS: Collectively, our data demonstrate inflammatory stimuli affect androgen-synthesis and that the upregulation of key enzymes involved in androgen synthesis is mediated via activation of TLR4, and downstream effects mediated in part by NLRP3 inflammasome (MCC-950-sensitive pathway) and in part by other, NLRP3 independent pathway(s) including upregulation of Cebpd (transcription factor involved in regulation of Ptg2) and Ptg2(COX-2). This data provides a mechanism through which inflammatory stimuli modulates androgen production in theca-interstitial cells.

SUPPORT: T32 HD007203 Training in Reproductive Sciences Grant.

P-726 Wednesday, October 16, 2019 6:30 AM

SERUM OF POLYCYSTIC OVARY SYNDROME PATIENTS FROM THE PPCOSII TRIAL HAS HIGHER GONADOTROPIN RELEASING HORMONE RECEPTOR AUTOANTIBODY ACTIVITY THAN UNEXPLAINED INFERTILE PATIENTS FROM THE AMIGOS TRIAL. Elizabeth A. Weedin, DO,a Heather R. Burks, MD,a Xi Chen, Yu, MD,b Hong Lian Li, MD, PhD,b Christopher E. Aston, PhD,b David C. Kem, MD,b LaTasha B. Craig, MD,b* University of Oklahoma Health Sciences Center, Department of Obstetrics and Gynecology, Oklahoma City, OK; bUniversity of Oklahoma Health Sciences Center, Department of Internal Medicine, Oklahoma City, OK; bUniversity of Oklahoma Health Sciences Center, Department of Pediatrics, Oklahoma City, OK.

OBJECTIVE: Polycystic Ovary Syndrome (PCOS) is a complex disease of unknown etiology. We previously identified activating autoantibodies (AAbs) to the second extracellular loop of the gonadotropin-releasing hormone receptor (GnRHR) in people with the serum of infertility patients. This AAb may provide a screening/diagnostic test for PCOS. We aimed to (1) confirm the increased GnRHR AAb activity in PCOS patients from a large, well-defined cohort, and (2) demonstrate the effectiveness of GnRH antagonist in suppressing GnRHR AAb activity.

DESIGN: Cross-sectional, matched case-control study.

MATERIALS AND METHODS: Sera from 200 PCOS patients from the Pregnancy in Polycystic Ovary Syndrome II (PPCOS II) trial and from 200 race, parity, age, and body mass index (BMI) matched ovulatory, unexplained infertile control patients from the Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation (AMIGOS) trial were obtained. All serum samples were tested with and without cetrotrex, a GnRH antagonist, for GnRHR AAb activity using the GeneBLAzer cell-based fluorescence resonance energy transfer (FRET) assay. AAb activity values are expressed as fold increase over buffer baseline to normalize the individual values. Statistical analyses in R included paired T-tests and linear regression.

RESULTS: There were no statistically significant differences between groups for race (91% white) or parity (65% nulliparous), however, significant differences within pairs remained, including Anti-Mullerian hormone (AMH), despite matching for age and BMI, Table 1. GnRHR AAb activity levels in the PCOS group were significantly higher than in the control group, p<0.0001. With cetrotrex, GnRHR AAb activity was largely suppressed in the PCOS group (p<0.0001) but not in controls (p=0.93). These differences remained significant after adjusting for within pair differences in age, BMI, and AMH.

CONCLUSIONS: We have confirmed higher GnRHR AAb activity levels in the serum of an independent cohort of PCOS patients compared to unexplained infertile controls. Addition of cetrotrex resulted in significant suppression of AAb activity levels in PCOS patients but controls were unaffected. The GnRHR AAbs we have identified may provide a future screening/diagnostic test for PCOS or a target for treatment.

SUPPORT: College of Medicine Alumni Association (COMAA) Grant, University of Oklahoma Health College Medicine.

P-727 Wednesday, October 16, 2019 6:30 AM

PREGNANCY OUTCOMES WITHIN A PROSPECTIVE COHORT OF WOMEN WITH POLYCYSTIC OVARY SYNDROME (PCOS). Avanthi S. Ajjarapu, BA,a Karen M. Summers, MPH CHES,a Bradley J. Van Voorhis, MD,b Rachel Mejia, D.O.b* University of Iowa, Iowa City, IA; aUniversity of Iowa, Iowa City, OR.

OBJECTIVE: To assess treatment course, treatment outcomes and time to pregnancy following participation in the “Combined Letrozole and Clomid in Women with infertility and PCOS Randomized Control Trial” (NCT02802865) among women who were not pregnant following the study treatment cycle.

DESIGN: Prospective Cohort Study.

MATERIALS AND METHODS: 63 participants in the NCT02802865 who did not conceive, had a biochemical pregnancy, or miscarriage at the end of the active study period were followed for 9 months after first menses following the treatment cycle. Chart abstraction was completed to follow fertility treatment, type and number of treatment cycles, ongoing clinical pregnancy, as well as time to pregnancy for those participants that had positive results. SPSS was used for statistical analysis.

RESULTS: The cohort consisted of women with a mean age of 30±4.1 with a mean BMI of 34 ±7.3. Within the cohort, the treatments received and the per cycle clinical pregnancy rate of those treatments are presented in Table 1. For oral ovulation induction, many of the participants used letrozole monotherapy 44/63 (70%). During the follow up window 37/63 (59%) of the participants conceived one or more pregnancies. Of these 6 (16%) resulted in miscarriage, 2 (6%) had biochemical pregnancies, 1 (3%) ectopic pregnancy. The clinical pregnancy rate per participant was 31/63 (49%).

<table>
<thead>
<tr>
<th>Treatments Received</th>
<th>Frequency (%)</th>
<th>Clinical Pregnancy Rate/Per cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Ovulation Induction medication (w/ or w/o IUI)</td>
<td>53/63 (84%)</td>
<td>13/128 (10%)</td>
</tr>
<tr>
<td>Gonadotropins (w/ or w/o IUI)</td>
<td>15/63 (24%)</td>
<td>7/18 (39%)</td>
</tr>
<tr>
<td>IVF</td>
<td>7/63 (11%)</td>
<td>4/10 (40%)</td>
</tr>
<tr>
<td>Stopped seeking treatment</td>
<td>3/63 (5%)</td>
<td>–</td>
</tr>
</tbody>
</table>

Six participants conceived spontaneously with no treatment. The mean time to clinical pregnancy was 3 ± 2.5 months.

CONCLUSIONS: This prospective cohort provides valuable information for patient counseling with women with PCOS. About half of the women
conceived within a 9-month period with mean time to clinical pregnancy of 3 months. This demonstrates an overall good prognosis for patients with PCOS and continued efforts with low intervention treatments such as oral ovulation induction can still be effective and worth pursuing.

P-728 Wednesday, October 16, 2019 6:30 AM

INFLUENCE OF OBESITY ON CLINICAL OUTCOME IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME
Run-Xin Gan, M.S., Fei Gong, PhD.* "Reproductive and Genetic Hospital of CITIC-Xiangya, Changsha, China; *Reproductive and Genetic Hospital of CITIC-Xiangya, Changsha, Hunan, China.

OBJECTIVE: To determine the effect of obesity in patients with Polycystic Ovary Syndrome (PCOS).

DESIGN: Analysis of clinical outcome, immune status of serum and endometrium between obesity and normal weight patients with PCOS.

MATERIALS AND METHODS: A total of 1738 normal weight patients with PCOS and obesity patients with PCOS who received routine IVF or intracytoplasmic sperm injection (ICSI) in the first cycle from August 2015 to March 2017 at Reproductive and Genetic Hospital of CITIC-XIANGYA were included in the study. The clinical outcome was analyzed between obesity and normal weight patients with PCOS. Meantime, There were 67 patients to examine C-reactive protein, Interleukin-18, and white blood cell index from the blood samples. Interleukin-18 and percentage of endometrial Natural Killer cells were also examined from the endometrial sample. Two independent samples were compared using the r test. If the normal distribution is not followed (interquartile range is used), and the two independent samples were compared using the Wilcoxon rank-sum test. Count data were used to describe the rate, comparatively by chi-square test. A correlation between the indicators was drawn using linear correlation analysis.

RESULTS: There were no differences in first-trimester rate (6.91% vs. 5.63%, p = 0.443); ectopic rate (1.1% vs. 0.47%, p = 0.304) and live birth rate (65.4% vs. 65.3%, p = 0.954) between normal body weight group and obesity group. However, The clinical pregnancy rate in the PCOS normal body weight group was higher (78.2% vs. 72.2%, p = 0.017) in the PCOS normal body weight group. Serum levels of C-reactive protein and White blood cell in the early follicular and secretory phases were significantly higher in the PCOS obesity group (n=24) compared with the PCOS normal body weight group (n=43). However, there was no significant difference in serum and endometrial Interleukin-18 between the two groups in the early follicular phase and the luteal phase. uNK cells in the PCOS obesity group were significantly lower than those observed in the PCOS normal body weight group (P<0.05). No correlation was found between serum and endometrium of inflammatory status.

CONCLUSIONS: Clinical pregnancy rate decreased in obese patients with PCOS, whose serum inflammatory response and endometrial immune status may be disrupted by obesity.

Reference: N/A.

SUPPORT: This study was funded by the National Science Foundation of China (81501328).

P-729 Wednesday, October 16, 2019 6:30 AM

ASSESSMENT OF PSYCHOLOGICAL DISTRESS IN POLYCYSTIC OVARIAN SYNDROME INFERTILE PATIENTS AT A TERTIARY LEVEL INFERTILITY CARE CENTRE IN INDIA.
Kanad Dev Nayar, M.D., DOO., FI. COC., P. Shyam Nayar, Ph.D., MRCOG, Minal Singh, DGO, DNB, Monica Gupta, MD, FRM, Rahul Gahlot, M.D., Dip Clinical Embryology, Kapil Dev Nayar, MBBS Akanksha IVF Centre, Delhi, India.

OBJECTIVE: Polycystic ovarian syndrome (PCOS) is the commonest endocrine disease affecting young women. Thirty percent of infertile women are diagnosed with PCOS as a cause of infertility. Apart from infertility, PCOS has huge long term metabolic consequences that affects patient’s quality of life (QOL). Co-existing psychological distress have also been shown to impact patient’s QOL. However it is difficult to say if they are particularly attributable to some clinic-biochemical features of PCOS per se. The present study was undertaken to assess the prevalence of psychological distress among PCOS infertile patients and its association with clinical-biochemical features of the syndrome.

DESIGN: A single centre cross sectional study was carried out at a tertiary care infertility centre in India from 1st January 2018 through 31st March 2018. Three hundred infertile patients consented to participate in the study.

One hundred and fifty PCOS infertile patients were matched to one hundred and fifty infertile controls.

MATERIALS AND METHODS: Hamilton’s Rating Scales (HAM-A and HAM-D) were used for assessing levels of anxiety and depression. Fertility and Quality of Life Questionnaire (Ferti QoL) was used to index the quality of life. Body Image distress was measured by Feel Ideal Discrepancy (FID) Score using Stunkard Figure rating Scale. Hirsutism score (calculated using Modified Ferriman Gallyway score) and body mass index (BMI) were determined. Primary outcome measured was the prevalence of psychological disorders in PCOS infertile patients and their comparison with non PCOS infertile controls. Secondary outcome was association between psychological distress with BMI and hyperandrogenism.

RESULTS: The baseline prevalence of anxiety in PCOS infertile patients was 40.32% and in non PCOS infertile controls was 28.86% (p=0.039); baseline prevalence of depression in PCOS patients was 38.2% and in controls was 24.82% (p=0.018), both were statistically significant. The HAM-A scores in PCOS and non-PCOS infertile controls (14.58±7.46 vs. 11.95±7.45; p=0.002) and HAM-D scores (14.18±7.16 vs. 11.39±6.95; p<0.001) in PCOS and non-PCOS infertile controls; the difference was clinically significant. There was no difference in FertiQoL scores for both the groups. Both groups showed comparable reduced quality of life and increased overall life stress. FID scores were higher in PCOS patients (1.2 ± 1.4) compared to non PCOS infertile controls (0.5 ± 1.4, p<0.001). BMI and Hirsutism score were associated with depression in these patients(p<0.001).

CONCLUSIONS: PCOS is a complex disorder associated with alarming levels of psychological distress which is much greater when compared to infertile controls. Clinicians should routinely evaluate all infertile patients, especially PCOS from a mental health perspective otherwise their hidden psychological stress would remain undiagnosed. Psychotherapy in addition to pharmacotherapy would help improve quality of life thus helping patients cope up with financial and emotional burden of their treatment.


SUPPORT: NIL.

P-730 Wednesday, October 16, 2019 6:30 AM

HOMOZYGOUS ANTIMULLERIAN HORMONE (AMH) GENE MUTATION rs10417628 IN A POLYCYSTIC OVARY SYNDROME (PCOS) WOMAN WITH EXAGGERATED HYPERANDROGENISM.
Luis R. Hoyos, M.D.*, Jenny A. Visser, Ph.D., Anke McLuskey, B.A.S., Gregorio Chazenbalk, Ph.D.*, Tristan R. Grogan, M.S., Daniel A. Dumesic, M.D.* "UCLA, Los Angeles, CA; *Affiliation not provided.

OBJECTIVE: Gene mutations of anti-Müllerian hormone (AMH) have been reported in approximately 3% of women with polycystic ovary syndrome (PCOS), in whom impaired AMH inhibition of CYP17 transcription could occur, leading to enhanced androgen production (1, 2). We report an AMH gene mutation in a normal-weight PCOS woman with undetectable serum AMH levels. The purpose of this study was to determine whether the AMH mutation in this PCOS woman was associated with hyperandrogenemia in excess of that from a cohort of normal-weight PCOS women and, if so, whether it was accompanied by exaggerated LH hyperscercration.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Twelve normal-weight PCOS women (by 1990 NIH criteria), ages 18-35 years, and 19 age- and body mass index (18.5-24) compared with the PCOS normal body weight group(n=43). However, there was no significant difference in serum and endometrial Interleukin-18 between the two groups in the early follicular phase and the luteal phase. uNK cells in the PCOS obesity group were significantly lower than those observed in the PCOS normal body weight group (P<0.05). No correlation was found between serum and endometrium of inflammatory status.

CONCLUSIONS: Clinical pregnancy rate decreased in obese patients with PCOS, whose serum inflammatory response and endometrial immune status may be disrupted by obesity.

Reference: N/A.

SUPPORT: This study was funded by the National Science Foundation of China (81501328).

P-731 Wednesday, October 16, 2019 6:30 AM

GERATED HYPERANDROGENISM.
Luis R. Hoyos, M.D.*, Jenny A. Visser, Ph.D., Anke McLuskey, B.A.S., Gregorio Chazenbalk, Ph.D.*, Tristan R. Grogan, M.S., Daniel A. Dumesic, M.D.* "UCLA, Los Angeles, CA; *Affiliation not provided.

OBJECTIVE: Gene mutations of anti-Müllerian hormone (AMH) have been reported in approximately 3% of women with polycystic ovary syndrome (PCOS), in whom impaired AMH inhibition of CYP17 transcription could occur, leading to enhanced androgen production (1, 2). We report an AMH gene mutation in a normal-weight PCOS woman with undetectable serum AMH levels. The purpose of this study was to determine whether the AMH mutation in this PCOS woman was associated with hyperandrogenemia in excess of that from a cohort of normal-weight PCOS women and, if so, whether it was accompanied by exaggerated LH hyperscercration.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Twelve normal-weight PCOS women (by 1990 NIH criteria), ages 18-35 years, and 19 age- and body mass index (18.5-25 kg/m²) matched controls underwent serum hormone and metabolic measurements as part of a NIH-funded study. Serum AMH levels were measured by ELISA (Ansh Labs, Webster, TX) in all subjects and were undetectable in the PCOS woman with a homozygous missense gene variant in exon 5 (T/C [Aa]515Val); rs10417628). Serum androgen and LH levels were measured by LC/MS/MS (Quest Diagnostics, San Juan Capistrano, CA) and chemiluminescence, respectively. Outcome variables between the cohorts of PCOS and control women were compared by the Wilcoxon rank-sum test. The same outcome variables of the PCOS woman with the AMH gene mutation were ranked in order of magnitude relative to those of the cohort of PCOS women.

RESULTS: Undetectable serum levels of AMH immunoreactivity occurred in this PCOS woman with homozygous AMH gene mutation

CONCLUSIONS: Undetectable serum levels of AMH immunoreactivity occurred in this PCOS woman with homozygous AMH gene mutation
rs10417628 and could reduce its bioactivity to exaggarate the PCOS phenotype through impaired AMH inhibition of CYP17 transcription, promoting androgen induced loss of steroid negative feedback on LH.

References: Å

SUPPORT: NIH P50 HD071836; NIH P51 OD011092; U1LTR001881; Santa Monica Bay Woman’s Club.

P.731 Wednesday, October 16, 2019 6:30 AM

EXPRESSION PROFILES OF miRNA -369-5P AND miRNA-671-3P IN THE PLASMA OF PREGNANT WOMEN WITH POLYCYSTIC OVARY SYNDROME VERSUS NORMAL PREGNANCIES. Meryem Hocaoglu, M.D. a,b Selin Demirer, Specialist, b Eser Kaynak, Student, c Erkut Altar, M.D. a,b Sibel Bulgurcuoglu Kuran, Ph.D. a,b Ayse Altun, specialist, a,b Abdulkadir Turgut, M.D. a,b Ervim Komurcu Bayrak, Ph.D. b "Obstetrics and Gynecology, Goztepe Training and Research Hospital, Istanbul Medeniyet University, Istanbul, Turkey; Obstetrics and Gynecology, Reproductive Endocrinology and Infertility, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkey; Genetics, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkey.

OBJECTIVE: Women with polycystic ovary syndrome (PCOS) exhibit increased risk of pregnancy complications (1). MicroRNA-369-5p (miRNA) and miR-671-3p were associated with adipogenic differentiation of mesenchymal stromal cells (2), diabetes (3) and insulin secretion (4, 5). The aim was to determine if there are differences in expression levels of miR-369-5p and miR-671-3p in the cell free plasma samples between pregnant women with PCOS and healthy controls.

TABLE 1. Patient demographics, clinical and biochemical characteristics

<table>
<thead>
<tr>
<th>Index Characteristics</th>
<th>PCOS (n=14)</th>
<th>Control Group (n=12)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
</tr>
<tr>
<td>29.6 ± 4.34</td>
<td>26.6 ± 4.9</td>
<td>0.561</td>
<td></td>
</tr>
<tr>
<td>Gestational age at sampling (weeks)</td>
<td>29.1 ± 5.1</td>
<td>28.9 ± 0.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pre-Pregnancy</td>
<td>28.3 ± 6.1</td>
<td>23.6 ± 2.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>31.2 ± 5.7</td>
<td>26.4 ± 2.9</td>
<td>0.004</td>
</tr>
<tr>
<td>Systolic blood pressure at sampling (mmHg)</td>
<td>106.4 ± 10.1</td>
<td>101.7 ± 5.8</td>
<td>0.028</td>
</tr>
<tr>
<td>Diastolic blood pressure at sampling (mmHg)</td>
<td>62.8 ± 7.3</td>
<td>60.0 ± 6.0</td>
<td>0.106</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.3 ± 0.2</td>
<td>5.1 ± 0.3</td>
<td>0.844</td>
</tr>
<tr>
<td>Fasting glucose (mg/dl) at sampling</td>
<td>76.0 ± 9.1</td>
<td>75.9 ± 8.7</td>
<td>0.670</td>
</tr>
<tr>
<td>1-h glucose (mg/dl) at sampling following a 75-g OGTT</td>
<td>139.7 ± 27.5</td>
<td>122.7 ± 28.9</td>
<td>0.952</td>
</tr>
<tr>
<td>2-h glucose (mg/dl) at sampling following a 75-g OGTT</td>
<td>108.0 ± 24.4</td>
<td>97.5 ± 19.0</td>
<td>0.386</td>
</tr>
</tbody>
</table>

PCOS, polycystic ovary syndrome; SD, standard deviation; BMI, body mass index; GA, gestational age; OGTT, oral glucose tolerance test Data presented as mean ± SD and compared using unpaired t-test *p < 0.05.
THE IMPACT OF A BRIEF INTERVENTION ON RETENTION RATES WITH PATIENTS WHO DID NOT RETURN TO CARE AFTER AN INITIAL PHYSICIAN VISIT.

Alice D. Domar, Ph.D., Kristin L. Rooney, BA, Dan W. Duvall, Jr., BA, Denny Sakkas, PhD. Boston IVF, Waltham, MA.

OBJECTIVE: The goal of this study was to determine a) if a follow-up email to selected patients who had an initial consult with an infertility specialist, but did not return for a second visit, would change return to care behavior and b) why patients had not returned.

DESIGN: Controlled prospective trial.

MATERIALS AND METHODS: From July 2017 to March 2018 all patients who had attended an initial visit with an infertility specialist at the clinic, but had not returned for at least three months were selected to receive a follow-up email. Those selected for an email excluded patients who we knew had achieved a pregnancy, already had a plan for treatment, had visited for an egg freeze and all LGTQ patients. The email asked if the patient had any questions about that visit, offered support to the patient and included contact information for the patient liaison sending the email. The email also asked each participant to indicate why they had not returned and were provided 4 options and an opportunity to write in a response. From April 2018 to December 2018 no emails were sent to patients. No other changes of patient contact practice was initiated during the trial period. All patients were then followed for 11 months after their initial visit to observe return to care behavior.

RESULTS: A total of 647 patients were selected to be sent 301 emails (Group 1) and 657 did not receive an email (Group 2). Forty-one percent of the patients in Group 1 returned to care, compared to 32% who did not receive an email (Group 2) (P=0.014). Of the Group 1 patients 116 replied (38.9%). For those who gave a reason why they hadn’t returned, 32% of the respondents conceived on their own, 3% transferred care to another infertility center, 31% were taking a break/holding off from treatment, and 3% were unhappy with their care at the first visit. A total of 31% made a follow-up appointment.

CONCLUSIONS: A simple follow-up email sent to patients who had an initial visit with an infertility specialist but did not return to the clinic within three months was associated with a significant increase in return to care when compared to patients who did not receive an email.

P-734 Wednesday, October 16, 2019 6:30 AM

INFERTILITY PATIENT CLINICAL JOURNEY OUTCOME DEPENDS ON INITIAL TREATMENT, STARTING WITH OVULATION INDUCTION (OI) VS IN VITRO FERTILIZATION (IVF); RESULTS FROM A LARGE REAL-WORLD DATABASE.

Mary Mahony, PhD,a Gilbert L. Mottla, MD,b Kevin S. Richter, PhD,c G. David Ball, PhD,d Soudhe Ansari, PhD.e Brooke Hayward, SM, MBA.f “US Medical Affairs, EMD Serono, Inc., Rockland, MA; Shady Grove Fertility Center, Annapolis, MD; Fertility Science Consulting, Silver Spring, MD; Seattle Reproductive Medicine Center, Seattle, WA; Prometrika LLC, Cambridge, MA; EMD Serono, Inc., Rockland, MA.

OBJECTIVE: In January 2018, Connecticut became the first state to mandate coverage for fertility preservation in patients diagnosed with cancer and facing medically necessary but potentially gonadotoxic therapies. We assessed the impact of this legislation on conversion rate to fertility preservation (FP) treatment for patients seen at our clinic.

MATERIALS AND METHODS: A chart review was conducted on all patients seen in the oncologic fertility clinic in two-time periods: from April 2016 to December 2018 (pre-legislation) and from January 2018 to January 2019 (post-legislation). Patients currently receiving, or planning to initiate, potentially gonadotoxic therapies were included in the study. Data was analyzed using the unpaired t-test and chi square test. A p-value of less than 0.05 was considered to be statistically significant.

RESULTS: A total of 98 male and female patients were included in the study (59 seen pre-legislation and 39 post-legislation). The two groups did not differ in mean age or gender composition (mean age 30.2 years). The overall pre-legislation conversion rate from initial consultation to initiation of FP was 28.8%; post-legislation conversion rate was 46.2%, a change which approached but did not achieve statistical significance (p = 0.079). The rate of sperm cryopreservation significantly increased, from 14.3% to 71.4% (p = 0.031). The rates of oocyte and/or embryo cryopreservation were not statistically different, 26.9% vs 28.1% (p = 0.905). There were no differences in the number of patients who chose to self-pay for FP (23.5% vs 22.2%, p = 0.927) or who indicated that they did not pursue treatment specifically due to financial constraints (11.9% vs 14.3%, p = 0.789).

CONCLUSIONS: Mandated insurance coverage for FP was associated with an increase in sperm cryopreservation rates. However, this may be more reflective of differences in cancer types between the groups as there were more aggressive malignancies in the pre-legislation male patients. Overall, there was a nonsignificant but clinically relevant increase in patients pursuing FP after initial consultation, suggesting increased access and utilization as a result of this legislation in Connecticut. Further efforts are needed to reduce the time to get approval from insurances and to expand coverage to include patients with self-funded health plans or state insurance.

P-734 Wednesday, October 16, 2019 6:30 AM

INFERTILITY PATIENT CLINICAL JOURNEY OUTCOME DEPENDS ON INITIAL TREATMENT, STARTING WITH OVULATION INDUCTION (OI) VS IN VITRO FERTILIZATION (IVF); RESULTS FROM A LARGE REAL-WORLD DATABASE.

Mary Mahony, PhD,a Gilbert L. Mottla, MD,b Kevin S. Richter, PhD,c G. David Ball, PhD,d Soudhe Ansari, PhD.e Brooke Hayward, SM, MBA.f “US Medical Affairs, EMD Serono, Inc., Rockland, MA; Shady Grove Fertility Center, Annapolis, MD; Fertility Science Consulting, Silver Spring, MD; Seattle Reproductive Medicine Center, Seattle, WA; Prometrika LLC, Cambridge, MA; EMD Serono, Inc., Rockland, MA.

OBJECTIVE: In January 2018, Connecticut became the first state to mandate coverage for fertility preservation in patients diagnosed with cancer and facing medically necessary but potentially gonadotoxic therapies. We assessed the impact of this legislation on conversion rate to fertility preservation (FP) treatment for patients seen at our clinic.

MATERIALS AND METHODS: A chart review was conducted on all patients seen in the oncologic fertility clinic in two-time periods: from April 2016 to December 2018 (pre-legislation) and from January 2018 to January 2019 (post-legislation). Patients currently receiving, or planning to initiate, potentially gonadotoxic therapies were included in the study. Data was analyzed using the unpaired t-test and chi square test. A p-value of less than 0.05 was considered to be statistically significant.

RESULTS: A total of 98 male and female patients were included in the study (59 seen pre-legislation and 39 post-legislation). The two groups did not differ in mean age or gender composition (mean age 30.2 years). The overall pre-legislation conversion rate from initial consultation to initiation of FP was 28.8%; post-legislation conversion rate was 46.2%, a change which approached but did not achieve statistical significance (p = 0.079). The rate of sperm cryopreservation significantly increased, from 14.3% to 71.4% (p = 0.031). The rates of oocyte and/or embryo cryopreservation were not statistically different, 26.9% vs 28.1% (p = 0.905). There were no differences in the number of patients who chose to self-pay for FP (23.5% vs 22.2%, p = 0.927) or who indicated that they did not pursue treatment specifically due to financial constraints (11.9% vs 14.3%, p = 0.789).

CONCLUSIONS: Mandated insurance coverage for FP was associated with an increase in sperm cryopreservation rates. However, this may be more reflective of differences in cancer types between the groups as there were more aggressive malignancies in the pre-legislation male patients. Overall, there was a nonsignificant but clinically relevant increase in patients pursuing FP after initial consultation, suggesting increased access and utilization as a result of this legislation in Connecticut. Further efforts are needed to reduce the time to get approval from insurances and to expand coverage to include patients with self-funded health plans or state insurance.
OBJECTIVE: To provide cumulative clinical pregnancy rates, time to pregnancy, and treatment discontinuation rates depending on initial fertility treatment and prognosis.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Electronic medical records data from 78958 treatment-naive infertile patients whose initial treatments were OI (with or without intrauterine insemination) with oral medication (clomiphene or letrozole), OI with gonadotropins (Gn), or IVF (fresh or cryopreserved embryo transfer) between Jul 2009–Sep 2015 were analyzed. The overall population and prognosis subgroups were studied and stratified by initial treatment type.

RESULTS: Patients with a good prognosis were more likely to begin treatment with OI orals, while patients with a poor progression were more likely to start with IVF. Regardless of prognosis, the proportion of patients who achieved a pregnancy was highest among those who initiated treatment with IVF rather than OI. Patients who started treatment with OI required more cycles to achieve pregnancy than those who started with IVF (mean 3.5 vs 1.8 cycles). A large percentage (26–48%) of pregnancies among patients who started with OI resulted from IVF after OI failed. Treatment discontinuation without a pregnancy was most common among patients who started with OI oral.

CONCLUSIONS: Beginning clinical treatment with IVF rather than OI resulted in higher cumulative pregnancy rates, fewer total treatment cycles, and lower rates of treatment discontinuation without a pregnancy. The advantage of IVF was greater among patients with a poorer prognosis (eg, diminished ovarian reserve ≥35 years). These results favor initiating treatment with IVF unless a patient has a strong personal preference for less invasive approaches.

SUPPORT: Study sponsored by EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany), Rockland, MA, USA.

P-735 Wednesday, October 16, 2019 6:30 AM


OBJECTIVE: To ascertain how often US IVF patients change clinics, what their underlying motivations are and how they perceive how much time and expense their initial choice of clinic may have cost.

DESIGN: 28,000 US IVF patients were surveyed on the number of clinics they received IVF treatment from. A sub-segment (1,000) of those who were treated at multiple clinics were re-surveyed on their reasons for switching and their perception of how being treated at multiple clinics impacted their financial and emotional well-being.

MATERIALS AND METHODS: Patients were surveyed at www.FertilityIQ.com and thereafter followed-up by email, whereby additional questions were posed using the the Qualtrics survey tool.

RESULTS: 48% percent of surveyed fertility patients are treated at one clinic, 27% at two clinics and 25% at three-or-more clinics. Of those who were treated at more than one clinic, 32% left their first clinic due to inadequate attention or service, 30% due to inadequate clinical results, 18% due to personality conflicts with the doctor or staff, 6% due to cost considerations ("Other" comprised the remaining responses). Patients who were treated at multiple clinics believe they needlessly suffered a 6.3 month in delay in treatment and needlessly spent over $12,725 in care. 84% of patients who went to multiple clinics believe having been dissatisfied with their primary choice of clinic negatively impacted their emotional well-being and 58% believe it impacted their ability to work.

CONCLUSIONS: "Clinic switching" is a meaningful phenomenon amongst US fertility patients, non-medical and non-cost factors may drive the preponderance of such choices and patients perceive the medical, financial and emotional consequences associated with such moves to be meaningful.

P-736 Wednesday, October 16, 2019 6:30 AM

RECONSIDERING THE WEEKEND FREE IN-VITRO FERTILIZATION TREATMENT. ARE RESULTS COMPROMISED BY A FIVE-DAY WORKWEEK? Amir Weiss, MD,a Shira Baram, MD,b Simon Nothman, MD,c Yoel Geslevich, MD,c "Rappaport School of Medi- cine, Technion Israel, Haifa, Israel; cCREAte Fertility Centre, Toronto, ON, Canada; "Emek Medical Center, Afula, Israel.

OBJECTIVE: To determine if treatment results differ as a function of the weekday of the first day of menstruation when implementing a five-day workweek.

DESIGN: A retrospective study covering 676 antagonist cycles from November 2010 to April 2017 in a public in-vitro fertilization unit serving the general public and operating five days a week.

MATERIALS AND METHODS: Included were women and couples with infertility requiring in-vitro fertilization at a public unit serving the general local population. Cycle data was recorded on an excel spread sheet prospectively and analyzed retrospectively following local ethics committee approval. Patient, treatment and outcome parameters were compared as a function of the day of the week menstruation began. Only antagonist cycles were included, each patient was included only once (the first treatment) and freeze all cycles were excluded.

SAS 9.4 software was used for statistical analysis. Categorical data was analyzed with the chi-squared test while continuous data were compared between groups with the Kruskall-Wallis test. P<0.05 was considered significant.

RESULTS: Included were 676 cycles. The live birth rate for each weekday menstruation began is as follows: weekday 1 – 14.56%, weekday 2 – 14.56%, weekday 3 – 22.02%, weekday 4 – 26.09%, weekday 5 – 27.78%, weekday 6 – 15.38%, weekday 7 – 12.90% (P=0.0407). The treatment groups did not differ for age, infertility duration, BMI, FSH, parity, cause of infertility. The groups differed significantly for number of days of gonadotropin stimulation (P=0.0066), though they did not differ for the amount of gonadotropins administered, the numbers of oocytes aspirated, or the fertilization rate (P=0.0742). They differed significantly for pregnancy rate (P=0.0143) and clinical pregnancy rate (0.0292) as well.

In a subgroup of 363 ICSI cycles, the percent of M2 oocytes differed significantly among treatment groups (P=0.0383) but the live birth rate did not.

CONCLUSIONS: The study is limited by its retrospective nature. We are unaware of prospective randomized trials which compare a five-day work week to a six- or seven-day work week. Since the day menstruation begins is a rather random occurrence, the finding that there are differential results suggests that the lack of flexibility in scheduling the OPU after an ideal stimulation duration, may be compromising results.

Adding weekend OPU to the workschedule may improve outcomes but at considerable cost to the public sector. Alternatively, cycle scheduling using hormonal therapy may be considered. More research should be invested in exploring how work schedules may impact results.

P-737 Wednesday, October 16, 2019 6:30 AM

INSIGHTS INTO INFERTILITY PATIENT DISCONTINUATION OF CARE: RESULTS OF A NATIONAL SURVEY. Barbara Collura, MA,a Brooke Hayward, SM, MBA,b Krysten Modrzejewski, PharmD,c Gilbert L. Mottila, MD,d Kevin S. Richter, PhD,a Allison B. Catherino, PhD,a RESOLVE: The National Infertility Association, McLean, VA; bEMD Serono, Inc., Rockland, MA; cShady Grove Fertility Center, Annapolis, MD; dFertility Science Consulting, Silver Spring, MD.

OBJECTIVE: To illustrate perspectives of patients on the infertility treatment journey, and their motivations for treatment discontinuation and return to care.

DESIGN: Online, cross-sectional, quantitative–qualitative patient survey.

MATERIALS AND METHODS: Participants were recruited from the infertility patient community and invited to complete the survey, administered in March–April 2019. Descriptive statistics were calculated for all survey items.

RESULTS: Among 359 respondents from 40 US states, 99% were female. Forty-one percent had earned a graduate degree (master’s or doctoral), and an additional 41% had a bachelor’s degree. Most (69%) were 31–40 years of age, 18% being 30 or younger, and 13% being older than 40 years. The majority (51%) reported an annual household income of $100k or greater, while 7% reported an income below $50k. Of 180 patients who reported that they were done with treatment, 62% (n=111) completed treatment with a live birth and 38% (n=69) ended treatment without a live birth.
birth. Of the 200 respondents who considered discontinuation of care, 30% (n=60) continued without ever stopping, 36% (n=71) stopped for a period of time and then restarted, and 35% (n=69) stopped with no plan to restart. Commonly cited reasons (patients could choose multiple reasons) for treatment discontinuation were financial (62%), psychological burden/treatment fatigue (58%), poor prognosis (26%), and natural conception (6%); the reasons most often cited for staying in treatment were patient’s desire for a family (47%), hope (21%), and partner’s desire for a family (13%). The expected vs actual time to pregnancy was vastly different. Of patients who thought it would take <1 year to become pregnant, 42% (78/185) reported it took >2 years before pregnancy while 45% (83/185) reported still being on their treatment journey.

CONCLUSIONS: Fertility patients predominantly cite psychological burden/treatment fatigue and cost as reasons for discontinuation, and hope and desire for family as reasons for staying in treatment. Fostering more realistic patient expectations by fertility providers regarding the time it often takes to achieve pregnancy may play a role in reducing treatment discontinuation and dropout.

SUPPORT: Study sponsored by EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany), Rockland, MA, USA.

P-738 Wednesday, October 16, 2019 6:30 AM

DETERMINING THE REASONS WHY INSURED WOMEN DROP OUT OF IVF TREATMENT AFTER ONE UNSUCCESSFUL CYCLE. Alice D. Domar, Ph.D. a, Kristin L. Rooney, BA a, Laura E. Dodge, ScD, MPH b. aBoston IVF, Waltham, MA; bHarvard Medical School, Boston, MA.

OBJECTIVE: To determine reasons why insured patients discontinue in vitro fertilization (IVF) treatment after a single unsuccessful cycle.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: Women whose first autologous IVF cycle began June 2014–October 2018, who did not have a live birth, and who did not return for treatment for at least four months were eligible. Women completed a survey regarding treatment termination either online or via phone. Results were compared to those from a prior study of 237 insured patients who discontinued treatment after more than one unsuccessful cycle, the last of which began January 2010–May 2014, and who did not return to care for a one-year period.

RESULTS: Of 262 eligible women, 93 (36%) completed surveys. Of these, 25 (27%) did not have insurance coverage for IVF treatment and were excluded. Of the remaining 68 participants, 14 (21%) sought care elsewhere after their single unsuccessful cycle, which was significantly fewer than participants who completed more than one unsuccessful cycle (37%; P=0.002). Those who sought care elsewhere after a single unsuccessful cycle reported doing so because they were unhappy with their care (50%), they had moved away (29%), they wanted a second opinion (21%), or they had heard good things about another center (21%); these reasons were similar to those who did multiple unsuccessful cycles, with the exception that those doing multiple cycles were more likely to want a second opinion (60%; P=0.01). Of the 54 participants who had not sought additional care after one unsuccessful cycle, over half (52%) reported that they were taking a break from treatment, and nearly one-quarter reported that they could not afford the out-of-pocket costs (24%). Other reasons included losing insurance coverage (22%) and conceiving spontaneously (22%). Participants not seeking care after multiple unsuccessful cycles were more likely to be pursuing or have adopted a child (23% vs. 4%; P=0.002), to report that further treatment was too stressful (45% vs. 20%; P=0.001), and to report that they had been advised to stop treatment (15% vs. 4%; P=0.03).

CONCLUSIONS: Half of participants who did not return to care within four months of a single unsuccessful IVF cycle reported that they were taking a break from treatment, and despite having partial or full insurance coverage, nearly one-quarter reported not returning due to financial difficulties. Treatment stress was less of an issue for participants who had undergone a single unsuccessful cycle compared to those who had undergone multiple unsuccessful cycles.

P-739 Wednesday, October 16, 2019 6:30 AM

DOES IN VITRO FERTILIZATION (IVF) INSURANCE COVERAGE CHANGE PRACTICE PATTERNS? Jenny S. George, MD, a, Micaela J. Stevenson, BS, b Samantha B. Schon, MD, MTR, a Michael Lanham, MD, a Jim M. Dupree, IV, MD, MPH, b Molly B. Moravek, MD, MPH c. aUniversity of Michigan, Ann Arbor, MI; bUniversity of Michigan Medical School, Ann Arbor, MI; cMichigan Medicine, Ann Arbor, MI.

OBJECTIVE: On January 1, 2015, a single, large academic institution implemented self-directed IVF insurance coverage for employees and students with an infertility diagnosis; however intrauterine insemination (IUI) remained an uncovered benefit. The insurance benefit mandated single embryo transfer ≤35 years, single or double embryo transfer >35 years, and imposed a lifetime limit on gonadotropin prescription coverage, regardless of whether the gonadotropins were used for IVF. The objective of this study was to examine practice patterns within the context of this insurance change. We hypothesized that patients with IVF coverage would undergo fewer injectable (gonadotropin or hybrid) cycles prior to IVF, fewer IUI cycles prior to IVF, and have less embryos transferred overall, compared to patients without IVF coverage.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: We used ICD-9/10 and CPT codes to identify patients who underwent IVF from 1/1/15 through 4/28/18 (n = 568). Exclusion criteria included initial evaluation prior to 1/1/15, history of IVF treatment at an outside facility, IVF for fertility preservation, severe male factor or tubal factor infertility necessitating IVF treatment, and use of preimplantation genetic testing for aneuploidy (PGT-A). Primary outcome was number of embryos transferred. Secondary outcomes included number of injectable cycles prior to IVF and number of IUI cycles prior to IVF. Descriptive statistics and Student’s t-test were used to characterize these distributions.

RESULTS: 321 patients met inclusion criteria (142 without insurance coverage and 179 with insurance coverage). Mean age in both the uncovered and covered groups was 33.3 years (SD = 4.26, NS). Mean number of embryos transferred was similar between uncovered and covered patients (1.42 vs 1.47, NS). Number of injectable cycles prior to IVF was similar between groups (3.82 vs 2.33, NS), as was the number IUIs prior to IVF (2.68 vs 2.64, NS). In patients with unexplained infertility, number of IUI cycles prior to IVF was similar between groups (3.31 vs 3.13, NS). In patients with a diagnosis of unexplained infertility, diminished ovarian reserve (DOR), or endometriosis, there were no significant differences in number of IUI cycles prior to IVF between groups (2.83 vs 2.6, NS).

CONCLUSIONS: Number of embryos transferred, number of IUI cycles prior to IVF, and number of injectable cycles prior to IVF was similar between patients with and without insurance coverage for IVF. These data provide reassurance that coverage status is unlikely to alter infertility provider practice and treatment strategy. Despite IUI being an uncovered benefit, providers still followed standard guidelines for treatment of conditions such as unexplained infertility and endometriosis.
DECREASING THE BURDEN OF PROGRAMMED FET CYCLES. Kathleen M. Doody, MD,a Martin Langley, MS,b Kevin J. Doody, M.D.a,4CARE Fertility, Bedford, TX; Center for Assisted Reproduction, Bedford, TX.

OBJECTIVE: Current management of FET cycles in programmed cycles generally entails monitoring with sonography and/or hormonal measurements. Endometrial thickness has shown correlation with implantation rate, prompting many clinicians to attempt to detect and correct poor endometrial response. To date, however, no studies have demonstrated that monitoring and active management of endometrial response is beneficial. This is important because the monitoring requirements associated with FET cycles add to the complexity and decrease the predictability of the day of embryo transfer. In an effort to increase access to care, our clinic has recently implemented a programmed cycle protocol performed without monitoring for patients undergoing FET following intravaginal culture (IVC). We examined the pregnancy outcomes of these cycles compared to contemporaneous programmed cycles with conventional monitoring.

DESIGN: FET cycles between April 2017 and March 2019 were retrospectively analyzed. 74 patients underwent a FET cycle with no monitoring and 145 underwent an FET cycle with monitoring. Non-monitored cycles: Patients began 6 mg of oral estradiol on cycle day 1 and were instructed to call the IVF coordinator to schedule their FET. IM progesterone (PIO) was begun after 12 or more days of estradiol. No ultrasounds or hormonal testing was performed during the cycle. Monitored cycles: The cycle was timed with oral contraceptives. A sonogram was performed prior to starting leuprolide SQ daily. OCPs were discontinued after 5 days of leuprolide overlap. A second sonogram was performed after 7 to 9 days of leuprolide to assess endometrial thickness and ovarian suppression. Additionally, serum was obtained for an estradiol level. Oral estradiol 6 mg/d was begun daily if the serum E2 was < 85 pg/ml and endometrial thickness < 5 mm. A third sonogram was performed after 12 to 14 days of estradiol supplementation. If the endometrium was < 8 mm in thickness and trilaminar in appearance, PIO was begun. If not, a fourth sonogram was performed 7 days later. All FETs were performed on the 6th day of PIO.

RESULTS: 72 women completed the survey, with 33% reporting a multifetal gestation of twins or greater as the ideal treatment outcome and 67% preferring a singleton gestation. There were no significant differences in mean age, partner age, marital status, education or religious affiliation between groups (Table). The ideal family size was significantly higher in women desiring a multifetal gestation, 2.5 children vs 2.2, p=0.03. Women who preferred multifetal gestation were less likely to have an income < $100,000 per year, 63% vs 85%, p=0.04. Women with insurance coverage for infertility who were aware of their benefits (n=48) were more likely to prefer a singleton gestation, with 22% desiring a multifetal gestation and 78% desiring a singleton.

CONCLUSIONS: Streamlined IVF processes offer the possibility to increase patient access to care through fewer visits and lower patient cost. FET cycles with no monitoring have comparable outcomes to FET cycles with conventional monitoring.

P-740 Wednesday, October 16, 2019 6:30 AM

IMPACT OF INSURANCE COVERAGE FOR FERTILITY TREATMENT ON PATIENT PREFERENCE FOR SINGLETON GESTATION. Seth J. Barishansky, MS,a Anne Hutchinson, M.D.a Dana B. McQueen, MD, MAS,b Rafael Confino, BS,b Angela K. Lawton, Ph.D.a Mary Ellen Pavone, MD, MSc. aNorthwestern University, Chicago, IL; bNorthwestern University Feinberg School of Medicine.

OBJECTIVE: To evaluate predictors for patient preference regarding multifetal or singleton gestation among women presenting for infertility care.

DESIGN: Cross-Sectional Study.

MATERIALS AND METHODS: IRB approval was obtained. Couples undergoing treatment at a university-based infertility clinic between February 2019 and April 2019 participated in a 40-question previously validated digital survey (Ryan et al, 2004). All patients received treatment in a location with state mandated infertility insurance coverage. The desire for singleton versus multifetal gestation was recorded. Baseline characteristics and demographic data compared between groups.

RESULTS: 72 women completed the survey, with 33% reporting a multifetal gestation of twins or greater as the ideal treatment outcome and 67% preferring a singleton gestation. There were no significant differences in mean age, partner age, marital status, education or religious affiliation between groups (Table). The ideal family size was significantly higher in women desiring a multifetal gestation, 2.5 children vs 2.2, p=0.03. Women who preferred multifetal gestation were less likely to have an income < $100,000 per year, 63% vs 85%, p=0.04. Women with insurance coverage for infertility who were aware of their benefits (n=48) were more likely to prefer a singleton gestation, with 22% desiring a multifetal gestation and 78% desiring a singleton.

CONCLUSIONS: Multifetal gestations have a significantly increased risk of maternal and neonatal morbidity and mortality. Despite this, one third of women presenting for infertility care reported multifetal gestation as the ideal treatment outcome. Interestingly, patients with a higher income and insurance coverage for fertility care are more likely to desire singleton gestation, with 22% desiring a multifetal gestation and 78% desiring a singleton.

CONCLUSIONS: Streamlined IVF processes offer the possibility to increase patient access to care through fewer visits and lower patient cost. FET cycles with no monitoring have comparable outcomes to FET cycles with conventional monitoring.

Impact of Insurance Coverage for Fertility Treatment on Patient Preference for Singleton Gestation. Seth J. Barishansky, MS, Anne Hutchinson, M.D., Dana B. McQueen, MD, MAS, Rafael Confino, BS, Angela K. Lawton, Ph.D., Mary Ellen Pavone, MD, MSc. Northwestern University, Chicago, IL; Northwestern University Feinberg School of Medicine.

OBJECTIVE: To evaluate predictors for patient preference regarding multifetal or singleton gestation among women presenting for infertility care.

DESIGN: Cross-Sectional Study.

MATERIALS AND METHODS: IRB approval was obtained. Couples undergoing treatment at a university-based infertility clinic between February 2019 and April 2019 participated in a 40-question previously validated digital survey (Ryan et al, 2004). All patients received treatment in a location with state mandated infertility insurance coverage. The desire for singleton versus multifetal gestation was recorded. Baseline characteristics and demographic data compared between groups.

RESULTS: 72 women completed the survey, with 33% reporting a multifetal gestation of twins or greater as the ideal treatment outcome and 67% preferring a singleton gestation. There were no significant differences in mean age, partner age, marital status, education or religious affiliation between groups (Table). The ideal family size was significantly higher in women desiring a multifetal gestation, 2.5 children vs 2.2, p=0.03. Women who preferred multifetal gestation were less likely to have an income < $100,000 per year, 63% vs 85%, p=0.04. Women with insurance coverage for infertility who were aware of their benefits (n=48) were more likely to prefer a singleton gestation, with 22% desiring a multifetal gestation and 78% desiring a singleton.

CONCLUSIONS: Multifetal gestations have a significantly increased risk of maternal and neonatal morbidity and mortality. Despite this, one third of women presenting for infertility care reported multifetal gestation as the ideal treatment outcome. Interestingly, patients with a higher income and insurance coverage for fertility care are more likely to desire singleton gestation. This data suggests that patients perceive multifetal gestation as a cost-effective treatment strategy. Future research should evaluate if improved access to insurance coverage decreases multiple pregnancy rates.
OBJECTIVE: Injectable follicle stimulating hormone (FSH) provides ovarian stimulation (OS) in women undergoing both in vitro fertilization (IVF) and oocyte cryopreservation (OCP). Brand FSH (B-FSH) is prohibitively expensive and can be a major roadblock to couples pursuing fertility treatment. Introduced in late 2017, compounded FSH (C-FSH) offers a cost-effective alternative to B-FSH with promising early clinical results. Here we provide the first analysis of the clinical efficacy and cost-effectiveness of C-FSH in women pursuing OCP and IVF.

DESIGN: Retrospective chart review identified all females receiving C-FSH for IVF or OCP from late 2017 to present.

MATERIALS AND METHODS: Clinical outcomes including oocyte retrieval rates, fertilizations rates, blast/embryo yield, pregnancies and live births were evaluated. All C-FSH prescriptions were obtained through the same specialty compounding pharmacy in Houston, TX. The average cost of B-FSH was derived from the top 9 commercial pharmacies listed on www.GoodRx.com and compared to C-FSH to determine the estimated cost of a typical course of therapy.

RESULTS: 34 female patients (mean age 35.3) initiated IVF or OCP. 29 women showed good response resulting in a mean retrieval of 12.75 (4-36) mature oocytes. Of the 21 women pursuing IVF, we observed a 74% fertilization rate and a mean yield of 4.3 (0-13) mature blastocysts per cycle. 8 total embryo transfers were performed. 6 of these were frozen transfers with single cryopreserved day 6 blastocysts. 1 transfer consisted of 3 fresh day 3 embryos and another consisted of 2 fresh day 5 embryos. These have resulted in 5 singleton pregnancies with 3 ongoing and 1 live birth. Cost analysis demonstrated significantly lower cost for C-FSH ($0.32) compared to B-FSH ($2.20).

CONCLUSIONS: In this novel analysis, C-FSH therapy showed excellent OS of women undergoing IVF and yielded several pregnancies, validating the clinical effectiveness of C-FSH. Compared to B-FSH, C-FSH provides unprecedented cost savings to patients undergoing IVF therapy and may allow some couples to achieve parenthood who otherwise would be prohibited by cost.

P-743 Wednesday, October 16, 2019 6:30 AM

FACTORS ASSOCIATED WITH A PATIENT’S DECISION TO DISCONTINUE FERTILITY TREATMENT BEFORE ACHIEVING PREGNANCY. Barbara Collura, MA;^1 Brooke Hayward, SM, MBA;^2 Krysten Modrzejewski, PharmD;^3 Gilbert L. Mottla, MD;^2 Kevin S. Richter, PhD;^3 Allison B. Catherino, PhD;^2 ‘RESOLVE: The National Infertility Association, McLean, VA; ^3EMD Serono, Inc., Rockland, MA; ‘Shady Grove Fertility Center, Annapolis, MD; ‘Fertility Science Consulting, Silver Spring, MD.

OBJECTIVE: To identify factors correlated with fertility patients’ likelihood of stopping, or considering stopping, treatment before achieving pregnancy.

DESIGN: Online, quantitative–qualitative survey of patients’ experience with infertility treatment.

MATERIALS AND METHODS: Patients with a history of infertility treatment (ovulation induction with or without intrauterine insemination [OI/IUI], or in vitro fertilization [IVF]) were invited to take the survey. In addition to questions about considering or discontinuing treatment before achieving pregnancy, the survey addressed demographic factors suspected of affecting this decision. Associations between demographic factors and treatment discontinuation (or consideration) were evaluated by chi-square or logistic regression with independent variable ordinally coded, as appropriate.

RESULTS: Among 291 completed surveys, 91 (31%) patients never considered discontinuing treatment, 69 (24%) patients discontinued fertility treatment without pregnancy, and 131 (45%) considered quitting but did not or resumed treatment after a break of <1 year. Compared with patients treated with OI/IUI only, patients who underwent ≥1 IVF cycle were less likely to consider quitting (64% vs 77%; p=0.014) or to quit treatment unsuccessfully (40% vs 58%; p=0.004). Higher education level was associated with a decline in the probability of considering treatment discontinuation (91%, high school only vs 58%, doctoral degree; p=0.014) but was unrelated to actual discontinuation (p=0.97). Patients with annual household income ≤$50,000 were somewhat more likely to consider discontinuing treatment (80% vs 68%; p=0.25) or to actually do so (54% vs 39%; p=0.32). A diagnosis of diminished ovarian reserve was not associated with considering quitting or doing so, despite a poorer prognosis than other patients of comparable age. There were also no trends associated with age, extent of insurance coverage (for IVF, for OI/IUI only, or for none), starting treatment with Ob/Gyn or at IVF center, or number of OI/IUI or IVF cycles completed. Most patients discontinuing treatment (76%) did so for financial reasons (58%), psychological reasons, including treatment fatigue, and 46% indicated both psychological and financial reasons.

CONCLUSIONS: IVF patients are less likely to discontinue treatment before achieving pregnancy than patients who undergo OI/IUI only, with most discontinuations due to financial and/or psychological reasons.

SUPPORT: Study sponsored by EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany), Rockland, MA, USA.
PROTEOMIC SIGNATURES OF EPIGENETIC AND TRANSCRIPTION REGULATORS ARE PIVOTAL IN CONTROLLING PATERNAL FACTORS IN RECURRENT PREGNANCY LOSS. Gayatri Mohanty, PhD, Sunilaya Ranjan Jena, M.Phil, Jasmine Mehta, M.Phil, Sujata Kar, MBBS, MD, DNBR, Luna Samanta, PhD, Redox Biology Laboratory, Department of Zoology, Center of Excellence in Environment and Public Health, Ravenshaw University, Cuttack, Odisha, India; *A-32, Unit-4, Kharvel Nagar, Bhubaneswar, India.

OBJECTIVE: Recurrent pregnancy loss (RPL) is a problem often experienced with embryo loss within first trimester of gestation while in fifty percent of cases the cause remains unknown [1]. The epigenetic machinery of the spermatozoa is tailored in a way to meet the demands of the highly specialised sperm cell while the integrity of the sperm epigenome is essential for initiation and maintenance of a successful pregnancy. Increased oxidative stress has been a cause for damaged chromatin, proteins and lipids [2]. The objective is to investigate and identify altered proteomic signatures that control paternal factors post-fertilisation in RPL patients.

RESULTS: The findings of the study indicate six proteins to be differentially expressed based on 2D-DIGE analysis that includes (HSPA2, GPX4, ZNF492, NAPRT1, UNCG, KRT10). These proteins were validated by western blotting. Key proteins after pathway analysis was considered statistically significant.

CONCLUSIONS: Although low sample size may be considered as a limitation of our study, data suggests that altered proteins identified play a pivotal role in epigenetic programming and transcriptional regulation of paternal factors both during spermatogenesis and early development. In addition, although we cannot confirm these signature differences at proteomic level as independent cause for unexplained RPL, the findings of the study are interesting and impose a better understanding of their biological implications.

Department of Science and Technology, Govt. of India.
Council for Scientific and Industrial Research.


SUPPORT: University Grants Commission, Govt. of India.

P-745 Wednesday, October 16, 2019 6:30 AM
PREIMPLANTATION GENETIC TESTING FOR ANEUPOLOIDY (PGT-A) REDUCES MISCARRIAGE AND IMPROVES LIVE BIRTH RATES IN RECURRENT PREGNANCY LOSS PATIENTS. Julia G. Kim, MD, MPH, Gayathree Murugappan, MD, Ruth B. Lathi, MD, Jonathan D. Kort, MD, Brent M. Hanson, MD, Ashley W. Tieg, MD, Emily K. Osman, MD, Shelby A. Neal, MD, Richard Thomas Scott Jr., MD, TIVI-RMA New Jersey, Basking Ridge, NJ; Stanford University Medical Center, Sunnyvale, CA; Stanford Fertility and Reproductive Medicine Center, Sunnyvale, CA; TIVI/Reproductive Medicine Associates of Northern California, San Francisco, CA; *Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA.

OBJECTIVE: Recurrent pregnancy loss (RPL) is a diverse syndrome with many causes, the most common being embryo aneuploidy. PGT-A should thus improve outcomes in RPL patients, but studies conflict as to whether PGT-A reduces clinical losses or improves live birth. This study seeks to determine if PGT-A improves outcomes in RPL patients.

RESULTS: 3975 infertile and 660 RPL patients had euploid SETs. An additional 101 RPL patients underwent frozen SET without PGT-A. Clinical pregnancy rates were higher in RPL patients using PGT-A (73%) than those not (61%) demonstrating a positive impact of selection. In fact, they normalized to that of infertile controls (72%). Most importantly, PGT-A reduced clinical loss risk amongst RPL patients. The risk remained higher than infertile controls (15% vs 12%) indicating that aneuploidy is not the lone source of RPL. Ultimately the higher initial pregnancy rate and lower loss risk increased live birth rates in the RPL PGT-A group to 62% compared to those not using PGT-A (41%).

CONCLUSIONS: PGT-A use in RPL patients significantly raises clinical pregnancy rates while reducing loss rates and provides a 50% relative increase in delivery rates (62% vs 41%). While clinical loss rates are reduced, they remain 3% higher than in infertile controls. These findings reflect that much of RPL may be attributed to aneuploidy, but that other factors also lead to RPL. PGT-A is a useful adjunct in the care of patients with RPL. While our large sample size provides powerful insight into this question, definitive resolution awaits class I data.

SUPPORT: University Grants Commission, Govt. of India.
aneuploidy by gestational age, maternal age, and positive findings on RPL investigations. A polynomial regression model was constructed based on the relationships of these variables.

RESULTS: A total of 604 miscarriages were included in the study. There was a significant relationship between the odds of aneuploidy and both maternal age and gestational age. There was a linear relationship between aneuploidy and maternal age, with a nearly 2-fold increase in the odds of aneuploidy with every 5-year increase in maternal age (OR 1.83, 95% CI 1.40-1.83). In contrast, the association between aneuploidy and gestational age was curvilinear, with a peak probability of aneuploidy with pregnancy losses at approximately 8 weeks gestation (p<0.02). While women with positive findings on RPL investigations had a slightly lower odds of aneuploidy as compared to those with a normal work-up, this difference was minimal and did not reach statistical significance (p=0.18).

CONCLUSIONS: There is an overall high rate of aneuploidy among the RPL population, even in women with positive findings on traditional RPL investigations. Across all maternal ages, the odds of aneuploidy significantly drop in pregnancy losses over 12 weeks gestation. These findings suggest that genetic testing on POC should be offered at the time of second and subsequent pregnancy losses <12 weeks gestation to all RPL patients.

P-747 Wednesday, October 16, 2019 6:30 AM

PREGNANCY LOSS AFTER FROZEN EMBRYO TRANSFER OF BLASTOCYSTS, EUPLOID BY NEXT GENERATION SEQUENCING (NGS): IS IT THE STIMULATION FOR RETRIEVAL, THE UTERINE PREPARATION FOR FET, THE EMBRYO TRANSFER OR THE EMBRYO?

Objective: The use of PGT-A and vitrification to select euploid embryos for transfer has led to improved live birth success in IVF; however, some euploid embryos fail to progress following implantation. Our objective was to compare parameters from 1) the retrieval cycle (IVF) in which blastocysts were biopsied and vitrified, 2) the frozen embryo cycle (FETu) during which euploid embryos fail to progress following implantation. Our objective was for transfer has led to improved live birth success in IVF; however, some euploid embryos fail to progress following implantation. Our objective was to compare parameters from 1) the retrieval cycle (IVF) in which blastocysts were biopsied and vitrified, 2) the frozen embryo cycle (FETu) during which the uterus is prepared for transfer, 3) the embryo transfer (FETt), and 4) the generation sequencing (NGS): Is it the stimulation for retrieval, the uterine preparation for the embryo transfer or the embryo?

James A. Grifo, MD, PhD., Caroline McCaffrey, Ph.D., NYU Langone Health, New York, NY; New York Langone Health, NYU Fertility Center, New York, NY.

MATERIALS AND METHODS: Data were collected from our electronic records for patients with transfers of thawed single euploid embryos diagnosed as euploid by NGS during the IVF cycle. Parameters from IVF (17), FETu (5), FETt (4), and Lab (19) were considered. All cases of STEET using euploid embryos tested with Next Generation Sequencing (908) were considered for analysis. Transfers without +hCG (204) and clinical pregnancies without positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); positive hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the tro
IS ANTIMULLERIAN HORMONE PREDICTIVE OF OUTCOMES AFTER PGT-A IN PATIENTS WITH RECURRENT PREGNANCY LOSS? Gayathree Murugappan, MD,a Lora K. Shahine, MD,a Ruth B. Lathi, MD,a 2Stanford University Medical Center, Sunnyvale, CA;3Pacific Northwest Fertility and IVF Specialists, Seattle, WA;4Stanford University Medical Center, SUNNYVALE, CA.

OBJECTIVE: Serum biomarkers of ovarian reserve have been utilized in non-RPL cohorts to stratify patients who may benefit from PGT-A. The goal of this study was to determine if AMH levels are predictive of outcomes in RPL patients pursuing PGT-A.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Unexplained RPL patients undergoing PGT-A at two fertility centers from 2009-2018 were included. All patients with the intent to perform PGT-A (propheticderm biopsy and 24 chromosome screening) were included regardless of final cycle outcome. Pregnancy loss was defined as loss of pregnancy from conception (bHCG level >5mIU/mL) through twenty weeks gestation.

RESULTS: 157 patients underwent 191 retrievals (RET), 146 of which completed PGT-A. Patient demographics and outcomes stratified by AMH <1 ng/mL and AMH ≥ 1 ng/mL are shown in Table 1. Patients with AMH < 1 ng/mL were significantly older with similar BMI and number of prior losses compared to patients with AMH ≥1 ng/mL. Patients with AMH <1 ng/mL had fewer oocytes (p<0.01) and a higher average aneuploidy rate (p=0.02) compared to patients with AMH ≥ 1 ng/mL. In a regression model adjusting for age, AMH is not a significant predictor of having at least one euploid blastocyst (p=0.10, CI 0.97-1.43), reaching ET (p=0.97, CI 0.84-1.18), achieving pregnancy (p =0.42, CI 0.82-1.09), achieving live birth (p=0.12, CI 0.86-1.02) or undergoing pregnancy loss (p=0.42, CI 0.90-28).

CONCLUSIONS: Although ovarian reserve is associated with IVF success rates, we report that RPL patients with diminished ovarian reserve (DOR) have similar likelihood of achieving pregnancy and live birth with PGT-A compared to RPL patients with AMH > 1 ng/mL. Future studies should incorporate total cycle potential in evaluation of clinical outcomes and consider lowering AMH cutoff for evaluating DOR.

Reference: None.

SUPPORT: None.

<table>
<thead>
<tr>
<th>AMH &lt;1 ng/mL n=42 RET</th>
<th>AMH ≥ 1 ng/mL n=149 RET</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs (mean ± SD, range)</td>
<td>37.6±4.2 (28-44)</td>
<td>36.2±3.6 (29-43)</td>
</tr>
<tr>
<td>No. of prior losses (mean ± SD, range)</td>
<td>3.1±1.2 (2-6)</td>
<td>3.1±1.0 (2-7)</td>
</tr>
<tr>
<td>BMI, kg/m² (mean ± SD, range)</td>
<td>24.1±3.6 (18-31)</td>
<td>23.2±3.5 (17-39)</td>
</tr>
<tr>
<td>No. of oocytes (mean ± SD, range)</td>
<td>11.1±9.2 (4-41)</td>
<td>18.8±8.5 (4-43)</td>
</tr>
<tr>
<td>% of cycles reaching euploid ET (% , n)</td>
<td>48% (n=20/42)</td>
<td>59% (n=88/149)</td>
</tr>
<tr>
<td>% of cycles transferring untested embryos (% , n)</td>
<td>21% (n=9/42)</td>
<td>13% (n=20/149)</td>
</tr>
<tr>
<td>% of cycles not reaching ET (% , n)</td>
<td>31% (n=13/42)</td>
<td>28% (n=41/149)</td>
</tr>
<tr>
<td>PR per RET (% , n)</td>
<td>40% (n=17/42)</td>
<td>49% (n=73/149)</td>
</tr>
<tr>
<td>Avg. aneuploidy rate (mean ± SD)</td>
<td>69% ± 84%</td>
<td>53% ± 28%</td>
</tr>
<tr>
<td>PR per PGT-A cycle (% , n)</td>
<td>52% (n=14/27)</td>
<td>50% (n=60/119)</td>
</tr>
<tr>
<td>PR per euploid ET (% , n)</td>
<td>70% (n=14/20)</td>
<td>68% (n=60/88)</td>
</tr>
<tr>
<td>Pregnancy loss rate per pregnancy (% , n)</td>
<td>35% (n=6/17)</td>
<td>30% (n=22/73)</td>
</tr>
<tr>
<td>LBR per RET (% , n)</td>
<td>26% (n=11/42)</td>
<td>34% (n=51/149)</td>
</tr>
</tbody>
</table>

1Student’s T Test, 2-tailed, unpaired.
2Chi-squared analysis.

MANAGEMENT OF EARLY PREGNANCY LOSS WITH MIFEPRISTONE AND MISOPROSTOL: CLINICAL PREDICTORS OF SUCCESS FROM A RANDOMIZED TRIAL. Sarita Sonalkar, MD MPH, Nathanael C. Koelper, MPH,a Mitchell D. Creinin, MD,b Jessica M. Atrio, MD, MSc,c Mary D. Sammel, ScD, Courtney A. Schreiner, MD, MPH,a 5University of Pennsylvania, Philadelphia, PA; 6University of California - Davis, Sacramento, CA; 7Montefiore Hospital & Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: To evaluate characteristics associated with treatment success in women receiving medical management for early pregnancy loss (EPL).

DESIGN; We performed a secondary analysis of a randomized trial of 300 participants comparing mifepristone-misoprostol to misoprostol alone for EPL treatment.

MATERIALS AND METHODS: We tested the ability of characteristics associated with misoprostol success in a previous study, vaginal bleeding and parity of 0 or 1, to discriminate successful from failed treatment in each arm of our study population and in the combined cohort using receiver-operator characteristic curves. We calculated the area under the curve (AUC) to quantify the ability of the score to discriminate between treatment success or failure in each arm as well as in the entire cohort. Using multivariable logistic regression, we then assessed our study population for other predictors of treatment success in both treatment groups, with and without mifepristone.

RESULTS: The clinical characteristics of vaginal bleeding and parity of 0 or 1 did not predict success above chance alone in the misoprostrol-alone arm (AUC=0.55, 95% CI 0.44-0.65), the mifepristone pretreatment arm (AUC=0.59, 95% CI 0.45-0.72) or the combined cohort (AUC=0.56, 95% CI 0.48-0.64). No other baseline clinical factors predicted treatment success in the misoprostrol-alone or mifepristone pretreatment arms individually. In the full cohort, randomization to pretreatment with mifepristone was a positive predictor of treatment success (aOR 2.51, 95% CI 1.43-4.43), while smoking was a negative predictor (aOR 0.47, 95% CI 0.23-0.97).

CONCLUSIONS: Pretreatment with mifepristone is a more useful intervention than applying baseline clinical factors to maximize treatment success in women undergoing medical management of EPL with misoprostol.

4. Supported by the National Institute of Child Health and Human Development of the National Institutes of Health (Eunice Kennedy Shriver award number R01-HD071920 [to Dr. Schreiber] and Women’s Reproductive Health Research award number K12-HD001265-18 [to Dr. Sonalkar]), and a Society of Family Planning Research Fund Midcareer Mentor Award (Schreiber).

P-751 Wednesday, October 16, 2019 6:30 AM

THE CELLULAR ROLES OF RPL-PROTEASE A IN THE RECURRENT PREGNANCY LOSS. Chang-Zhu Pei, MD,a Jun-Hyeok Park, MS,a Bum Chae Choi, MD, PHD,b In Kyung Oh, MD,a Hyo Young Park, PHD,b Kwang-Hyun Baek, PHD,^ aCHA University, Seongnam-Si Gyeyonggi-Do, Korea, Republic of (South);^ Creation and Love Women’s Hospital, Gwangju, Korea, Republic of (South).

OBJECTIVE: To investigate cellular functions of RPL-serine protease A on cell apoptosis, invasion, and proliferation that lead to recurrent pregnancy loss (RPL).
DESIGN: RPL-serine protease A was investigated to identify its putative substrates using proteomics and bioinformatics tools. XIAP was identified to interact with the RPL-serine protease A. XIAP was differentially expressed in a dose-dependent manner of RPL-serine protease A. To check the effect of RPL-serine protease A on cell proliferation and cell invasion, RPL-serine protease A and its mutant form were transfected into BeWo cells, and knock-out BeWo cell line was established.

MATERIALS AND METHODS: Immunoprecipitation: Flag-RPL-serine protease A and myc-XIAP were transfected into 293T cells for performing immunoprecipitation. GST pull-down assay: Recombinant GST and GST-RPL-serine protease A proteins were incubated in cell lysates overexpressed with Myc-xIAP. The bound proteins were analyzed with an anti-Myc antibody.

Cell Counting Kit (CCK-8): CCK-8 assay was performed to investigate effect of RPL-serine protease A on cell proliferation. Invasion assay: Overexpression RPL-serine protease A and its mutant form, and knock-out of RPL-serine protease A BeWo cells were divided into trans-well with the same numbers of cells to check the effect of RPL-serine protease A on cell invasion. To study the functions of RPL-serine protease A, CRISP-Cas9 system was applied for making the knock-out of RPL-serine protease A in reproductive cell lines.

RESULTS: In a previous study, we identified that an RPL-serine protease A gene is more expressed in chorionic villi from normal controls than in those from RPL patients. In this study, XIAP selected from candidate proteins identified from proteomics and bioinformatics tools, interacted with the RPL-serine protease A. Immunoprecipitation assay revealed that putative substrates such as XIAP and CPBP interacted with the RPL-serine protease A. Antibody investigation with GST pull-down assay indicates that RPL-serine protease A directly binds to XIAP. Exogenous and endogenous expression levels of XIAP were decreased by the RPL-serine protease A in a dose-dependent manner. It is of interest that RPL-serine protease A suppresses cell proliferation in vitro, and the proliferation rate of RPL-serine protease A knock-out cells was significantly higher than that of wild type cells. Over-expressed RPL-serine protease A stimulates BeWo cell invasion.

CONCLUSIONS: RPL-serine protease A interacts with XIAP, and expression of XIAP was decreased by RPL-serine protease A. Through these mechanisms, trophoblast apoptosis and proliferation may be regulated in placenta. The molecular functions of RPL-serine protease A in promoting cell proliferation needs to be investigated.

SUPPORT: This study was supported by the Ministry of Health & Welfare of the Republic of Korea (grant numbers, H16C0378) through the Korea Health Industry Development Institute.

P-752 Wednesday, October 16, 2019 6:30 AM

ANTIO-MULLERIAN HORMONE (AMH) AND SPONTANEOUS ABORTION (SAB): IS AMH AN INDEPENDENT RISK FACTOR FOR SAB IN GONADOTROPIN-IUI CYCLES? Jennifer Y. Hsu, MD, Kaitlyn E. James, PhD, Irene Dimitriadis, MD, Georgios Christou, MD, Stylianos Vagios, MD, Charles L. Bornmann, PhD, Irene Souter, MD, Massachusetts General Hospital, Harvard Medical School, Boston, MA; Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: Emerging studies suggest that in infertile women undergoing IVF, AMH levels are associated with adverse obstetric outcomes, though the data remain inconclusive [1, 2]. Our objective was to evaluate if AMH is independently associated with risk of SAB among women undergoing gonadotropin-intrauterine insemination (Gn-IUI) cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Intervention: 1861 Gn-IUI cycles from 821 women were analyzed (11/2007 to 3/2019). Cycles were stratified by the following AMH (ng/ml) serum concentration cutoffs, based previously published literature [3]: LOW (<0.7), NORMAL (0.7-8.4), and HIGH (≥8.5).

Outcome measures: Rate of SAB, defined as pregnancy loss following sonographic confirmation of clinical pregnancy, within each AMH group.

Statistics: Fisher’s exact or x² tests were used as appropriate. Multilevel mixed-effects Poisson regression models, adjusted for age, were used to determine the incidence risk ratios (IRR) for SAB within each AMH group. P-value <0.05 was considered significant.

RESULTS: The mean (SD) age of the study population was 35.4 (4.0) years with mean body mass index (BMI): 25.1 (5.2) kg/m². The median (IQR) AMH value was 1.9 ng/ml (0.7, 4.7) with 24%, 64%, and 12% of the women categorized into the LOW, NORMAL, and HIGH AMH groups, respectively. Clinical pregnancy rates were: 8.2% 12.4%, and 19.0% for LOW, NORMAL, and HIGH AMH groups, respectively (p<0.001). The overall SAB rate was 18.1%. Women in the NORMAL and HIGH AMH groups had lower incidence of SAB (15.6% and 16.3%, respectively) compared to those in the LOW AMH group (29.7%). However, after adjusting for age, the risk difference was no longer statistically significant.

Table 1 summarizes the adjusted and unadjusted IRR for SAB utilizing the NORMAL group as a reference. After adjusting for age, AMH was not associated with risk of SAB. There was also a trend toward higher SAB risk in women with AMH below the 10th percentile (AMH ≤0.4), a finding that lost its significance in the adjusted models.

CONCLUSIONS: In women pursuing Gn-IUI treatment, lower AMH does not appear to be an independent risk factor for SAB. Therefore, younger women with lower ovarian reserve should not be counseled that they are at risk of worse early pregnancy outcomes compared to their age-matched counterparts with normal or high ovarian reserve.


SUPPORT: None.

P-753 Wednesday, October 16, 2019 6:30 AM

CHARACTERISTICS OF FIRST TRimestER MISCARRIAGES ASSESSED BY CHROMOSOMAL ANALYSIS OF PRODUCTS OF CONCEPTION WITH NEXT GENERATION SEQUENCING. Takumi Takeuchi, MD, PhD, Masakazu Doshida, MD, Yukiko Takaya, MD, Kohei Yamaguchi, MD, Hidetiko Matsubayashi, MD, Kotaro Kitaya, MD, Yasuhisa Araki, PhD, Tomomoto Ishikawa, MD, Reproduction Clinic Tokyo, Tokyo, Japan; Reproduction Clinic Osaka, Osaka, Japan; Nippon Reprogenetics Inc, Maebashi, Japan.

OBJECTIVE: Chromosomal abnormalities are the major cause of early pregnancy loss. Chromosome testing of products of conception (POC) provides valuable information for counseling and clinical managing of patients. We previously showed that next generation sequencing (NGS) can be utilized as a technique demanding lesser specimen with a lower failure rate, higher resolution, and shorter turnaround time than conventional karyotyping which is requiring labor-intensive and time-consuming cell culture with possible maternal cell contamination. We aimed to assess the efficacy of NGS method for chromosomal analysis of POC. In addition, we attempted to identify any associations between the incidence of chromosomal abnormalities and the profile of patients as well as fetal development in an assisted reproductive technology (ART) program.

DESIGN: Retrospective study with a single reference genetic laboratory.

MATERIALS AND METHODS: Total of 131 consenting patients with first trimester miscarriages after vitrified-warmed embryo transfer were involved. POC samples were obtained bbylation and curettage between 7 to 10 gestational weeks. Chorionic villi were isolated under a dissecting microscope, subsequently processed for NGS chromosomal analysis. Incidence of each chromosomal abnormality was reported and evaluated according to the patient profile, such as maternal age, previous history of miscarriage and fetal development. Finally, frequency of mosaics was also assessed.

<table>
<thead>
<tr>
<th>AMH GROUP</th>
<th>UNADJUSTED IRR (95%CI)</th>
<th>ADJUSTED IRR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>1.9 (1.0, 3.6)*</td>
<td>1.6 (0.8, 3.1)</td>
</tr>
<tr>
<td>Normal</td>
<td>1.0 (0.5, 2.2)</td>
<td>1.3 (0.6, 2.8)</td>
</tr>
<tr>
<td>High</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMH PERCENTILE ≤10th (AMH ≤0.4)</td>
<td>2.1 (1.1, 3.9)*</td>
<td>1.7 (0.9, 3.4)</td>
</tr>
<tr>
<td>≤25th (AMH ≤1.1)</td>
<td>1.5 (0.9, 2.7)</td>
<td>1.2 (0.7, 2.2)</td>
</tr>
<tr>
<td>≥75th (AMH ≥6.0)</td>
<td>0.7 (0.4, 1.4)</td>
<td>0.9 (0.4, 1.9)</td>
</tr>
<tr>
<td>≥90th (AMH ≥13.0)</td>
<td>0.9 (0.4, 2.2)</td>
<td>1.2 (0.5, 2.8)</td>
</tr>
</tbody>
</table>

*P<0.05.
RESULTS: After NGS analysis, 28 cases (21.4%) were found to be normal, and the remaining 103 (78.6%) were abnormal, including 10 (7.6%) mosaics. Among normal karyotypes, ratio of female to male was 1.15 (15/13). Trisomies were the most common abnormalities except for the chromosome X monosomy (10.7%). Aneuploidy of chromosome 22 (20/113, 17.7%), 15 (16/113, 14.2%), 16 (16/113, 14.2%), X (13/113, 11.5%) and 21 (11/113, 9.7%) including overlaps, were most frequently involved. Mean maternal age of chromosomally abnormal cases was significantly higher than that of normal karyotypes (39.0 ± 18.5 vs. 36.9 ± 16.5 years, P < 0.05). Patients with more than equal 3 previous miscarriages showed a significantly lower rate of abnormalities than those with <3 miscarriages (28.6% vs. 81.5%, P < 0.01). Rate of abnormalities with positive fetal cardiac activity was not different from that of anembryonic pregnancies (80.0% vs. 76.1%), although fetal cardiac activity was detected in all the 45,XO cases. Interestingly, however, mosaic abnormalities were significantly more often detected in anembryonic pregnancies (80.0% vs. 76.1%), although fetal cardiac activity was not different from that of normal karyotypes (15.2% vs. 3.5%, P < 0.05).

CONCLUSIONS: With more conclusive and accurate results and higher reputation by NGS, we were able to characterize early pregnancy loss after ART, demonstrating relatively high rate of abnormalities with gender ratio being close to 1. Patients with repeated pregnancy loss showed lower chromosomal abnormalities indicating other causes for miscarriages in this group of patients. A higher incidence of mosaics detected in anembryonic pregnancies warrants further investigation.

SUPPORT: None.

P-754 Wednesday, October 16, 2019 6:30 AM

VITAMIN D INSUFFICIENCY IS THE RISK FACTOR FOR HYPERHOMOCYSTEINEMIA DERIVED FROM MTHFR C677T GENE POLYMORPHISM IN WOMEN WITH RECURRENT PREGNANCY LOSSES.

Keiichi Ota, M.D., a Yoshifumi Takahashi, M.D., a Joanne Kwak-Kim, MD, MPH, b Fukushima Medical University, Fukushima, Japan; cChicago Medical School, Rosalind Franklin University of Medicine and Science, North Chicago, IL, Vernon Hills, IL.

OBJECTIVE: Vitamin D insufficiency, methylene tetrahydrofolate reductase (MTHFR) C677T gene polymorphism, and hyperhomocysteinemia have been reported as risk factors for recurrent pregnancy losses (RPL). However, the relationship among vitamin D, homocysteine, and MTHFR C677T gene polymorphism in women with RPL remain unknown. In the current study, we aim to investigate whether the MTHFR gene polymorphism affects the levels of homocysteine and vitamin D in women with RPL.

DESIGN: This study was a cross-sectional study of 837 women with RPL at a university hospital.

MATERIALS AND METHODS: Total 837 women with unexplained RPL were registered, and MTHFR C677T genotypes (homozygous (TT), heterozygous (CT) and wild (CC)) were investigated by PCR. Biochemical tests were used to determine plasma homocysteine and serum 25 (OH) vitamin D levels, and neutrophil and lymphocyte counts were analyzed by the flow cytometry. Data were analyzed by MTHFR C677T genotypes.

RESULTS: The level of 25 (OH) vitamin D in the TT group was significantly lower compared to CT and CC groups (p < 0.05), while the level of homocysteine in the TT group was significantly higher than the CT and CC groups (p < 0.01). NK cytotoxicity of TT group was significantly higher than those of CC but not CT group (p < 0.01). There was a significant negative correlation between the levels of 25 (OH) vitamin D and homocysteine in the TT group (r = -0.357). In multivariate analysis, 25 (OH) vitamin D insufficiency (<30 ng/ml) was an independent risk factor for hyperhomocysteinemia (adjusted odds ratio 1.89, 95% CI 1.41–2.52).

CONCLUSIONS: Both MTHFR C677T gene polymorphism and vitamin D insufficiency may involve in the pathogenesis of unexplained RPL via hyperhomocysteinemia. It is speculated that lowering the homocysteine level may improve the reproductive outcome in women with RPL.

PROFESSIONAL DEVELOPMENT

P-755 Wednesday, October 16, 2019 6:30 AM

SURGICAL SIMULATION SUPPLEMENTS REI FELLOWSHIP TRAINING.

Tess E. Chase, MD, a Stephanie J. Estes, MD, a Divya Kelath Shah, MD, MME, a Preston Parry, MD, a Balasubramanian Bhagavath, M.B.B.S., a Steven R. Lindheim, M.D., a John C. Petrozza, M.D., a, Samantha Pfeifer, M.D., b Penn State Milton S Hershey Medical Center, Hershey, PA; cPenn State Milton S. Hershey Medical Center, Hershey, PA; dUniversity of Pennsylvania, Philadelphia, PA; eParryscope Fertility, Madison, MS, MS; fUniversity of Rochester Medical Center, Rochester, NY; gWright State University, Dayton, OH; hMassachusetts General Hospital Fertility Center, Boston, MA; iWeill Medical College of Cornell University, New York, NY.

OBJECTIVE: To characterize interest and skill in minimally invasive reproductive surgery among Reproductive Endocrinology and Infertility (REI) fellows and the utility of an intensive “boot camp” in improving performance of select surgical tasks.

DESIGN: Prospective evaluation of 40 REI fellows during the 2-day 2019 SRS-SREI boot camp.

MATERIALS AND METHODS: Surveys collected data on fellow demographics, prior surgical and IVF experience, and perceived competency with reproductive surgery. Surveys were administered before, immediately after, and 1 month after the boot camp. Simulations focused on laparoscopic suturing, knot tying using both box trainers and cadavers, robotic suturing, and operative hysteroscopy. Wilcoxon signed-rank tests and rank-sum tests were used to compare suturing times for a given fellow over time and changes in suturing time across fellows by year of training, respectively. Spearman correlation coefficients assessed associations between prior clinical experience and surgical skill.

RESULTS: Forty fellows (25 first, 11 second, and 4 third year) provided data, representing 72% of REI fellowship programs in the USA. Fellows reported an average of 15 hours of prior simulation experience for conventional laparoscopy, 8 hours for robotics and 5 hours for hysteroscopy. Prior to the boot camp, most fellows felt prepared to perform hysteroscopy (100%) and conventional laparoscopy (82%), but only a minority felt prepared to perform robotic surgery (46%) or tubal anastomosis (15%). Significant improvement was seen across all levels of training in laparoscopic suturing (both trainers): by 44 seconds (sec) for running suture, 82 sec for intercorporal knots, and 71 sec for extracorporal knots (p < 0.001 for all comparisons). The magnitude of improvement was significantly higher for first year fellows as compared to their second and third year peers (60 sec vs 28 sec running suture improvement, p = 0.04). There were no strong associations observed between fellowship IVF case volume and the surgical skill of the fellow (all Spearman correlation coefficients < 0.34). Interest in incorporating reproductive surgery into subsequent clinical practice was high when assessed immediately after the boot camp using a 5-point Likert scale and did not change when reassessed one month later (all p > 0.36).

CONCLUSIONS: Given the heterogenous training in reproductive surgery among REI fellowship programs, a surgical boot camp may be useful in enhancing surgical skill among REI fellows. Improvements in laparoscopic suturing were most significant for first year fellows. Increasing IVF volume was not associated with less surgical skill.

P-756 Wednesday, October 16, 2019 6:30 AM

CLINICAL EXPOSURE IN OB/GYN RESIDENT TRAINING PROGRAMS IN THE UNITED STATES TO INFERTILITY CARE FOR LOW RESOURCE AND UNDERSERVED COMMUNITIES.

Holly Mehr, MD, MS Ed, a Tia Jackson-Bey, MD MPH, b Jacqueline Ho, MD MS, c Lusine Aghajanian, MD PhD, d Holly M. Quinn, MD, d Jacqueline Rose Hoffman, BA, e Christopher N. Herndon, MD, c University of California, Los Angeles, Los Angeles, CA; eUniversity of Illinois at Chicago, College of Medicine, Chicago, IL; fUniversity of Southern California, Los Angeles, CA; gStanford University School of Medicine, Stanford, CA; hUniversity of Arizona College of Medicine - Tucson, Tucson, AZ; iUniversity of Washington, Seattle, WA.

OBJECTIVE: Assess exposure of US OB/GYN residents to the provision of clinical infertility care for low resource and underserved communities. DESIGN: Cross-sectional survey.

MATERIALS AND METHODS: An anonymous, self-administered 28 question survey was emailed to REI division directors or REI resident rotation directors affiliated with ACCME accredited OB/GYN residency programs. Respondents answered questions regarding REI practice and residency demographics, the presence of clinical programs designed to improve access to care, resident involvement in such programs, and perceived barriers to expanding access to care. Responses were analyzed descriptively and through logistic regression analysis using STATA software, with significance defined as p < 0.05.

RESULTS: The response rate for the survey was 30% (80/270). Of respondents, average OB/GYN residency size was 6.1 graduating residents per year.
Residents spent an average of 7.2 weeks rotating through REI during a 4-year residency. 38% (n=30) of practices had an affiliated REI fellowship. Less than half of OB/GYN residency programs (39%, n=31) responded have an associated REI clinic in which OB/GYN residents provide direct infertility care to patients. Laparoscopy for tubal disease and 19% (n=6) offered tubal reversal surgery. Size of residency program, REI practice setting (academic/hybrid/private), size of practice, geographic region, location in an IVF insurance mandated state, or presence of a REI fellowship was not significantly predictive of the presence of a trainee clinic. Regarding barriers encountered in the provision of fertility services to patients who are medically underserved or unable to afford infertility care, the majority of respondents cited prohibitive cost of treatment (97%), lack of insurance or public health coverage (97%), difficulty for patients with low income to qualify for loans or other financing plans (61%), patient language (61%) and health literacy (58%) as barriers to expanding access to care. An additional percentage cited low level of interest or support from hospital administration (29%), clinicians in practice (6.5%) and limited availability of trainees (6.5%).

CONCLUSIONS: In addition to understanding the limited infertility care available to low resource populations in the United States, the findings indicate significant educational gaps among OB/GYN residency programs in exposure to infertility and its clinical management in low resource and underserved communities.

P-757 Wednesday, October 16, 2019 6:30 AM
CURRENT ONCOLOGY TRAINING PROGRAMS LACK ADEQUATE EDUCATION IN FERTILITY PRESERVATION COUNSELING. Elizabeth Brackett, MD,1 Vicky Moy, MD,1 Abhinav Hasija, BS, MS,2 Michael A. Thomas, MD,3 Julie Sroga Rios, MD,4 Suruchi Thakore, MD,4 1University of Cincinnati Medical Center, Cincinnati, OH; 2University of Cincinnati Medical Center, West Chester, OH; 3The Ohio State University-Fisher College of Business, Columbus, OH; 4University of Cincinnati, Cincinnati, OH; 5University of Cincinnati and Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

OBJECTIVE: Given that oncologic treatments can cause damage to reproductive organs leading to infertility, multiple national organizations recommend that all health care providers counsel patients on risk of infertility and fertility preservation options. Studies demonstrate a lack of counseling and referral to reproductive services in this population. Our aim was to develop an original survey for resident and fellow physicians in oncology subspecialties to assess their attitudes, awareness and knowledge on fertility preservation and identify barriers in training.

DESIGN: Questionnaire-based observational study.

MATERIALS AND METHODS: An IRB-approved survey study was electronically distributed to all ACGME-accredited programs in gynecologic oncology (GO), radiation oncology (RO), surgical oncology (SO), hematology oncology (HO) and pediatric oncology (PO) in the United States. The survey was distributed between January and April 2019. The questionnaire assessed attitudes and knowledge about fertility counseling and preservation for the newly diagnosed oncology patient. Comparisons between groups were evaluated with chi-squared tests and pairwise comparisons with significance defined as p < 0.05.

RESULTS: Two hundred and sixty-eight surveys were completed (GO: n=25; HO: n=93; PO: n=128; RO: n=60; SO: n=6). All respondents agreed that it is their responsibility to discuss the impact of treatment effects on fertility; however, only 51% (n=119) responded that they often or always personally counsel patients on the impact of treatment on fertility. GO was more likely to refer patients >50% of the time to fertility preservation counseling compared to HO (p=0.017) or RO (p=0.022). RO was also significantly more likely than HO (p=0.009) or PO (p=0.007) to consider a patient’s future fertility when planning treatment. Among all respondents, the primary reason given for not discussing fertility risk was not discussed was poor prognosis (41.6%). Furthermore, 61% of all respondents reported that there is no specific person in their office setting responsible for these discussions. Most trainees did not feel their program prepared them for counseling on fertility preservation (55.5%, n=122). When asked what materials would be helpful to increase learning, lectures (48%, n=105) and practice bulletins (43%, n=95) were the most common answers.

CONCLUSIONS: Our study demonstrates that while all residents and fellows in oncology training programs believe that oncology counseling is important, they lack the adequate education and resources to do so. There is also a significant difference between subspecialties in the level of comfort in completing these discussions. Curriculum for residents and fellows should address these disparities and focus on improving patient counseling.

P-758 Wednesday, October 16, 2019 6:30 AM
FERTILITY AWARENESS AND ATTITUDES AMONG RESIDENT PHYSICIANS ACROSS DIFFERENT SPECIALTIES. Shelan Tsai, MD,1 Tracy Truong, MS,2 Carl F. Pieper, DrPH,3 Jennifer L. Eaton, MD, MSCE,4 Division of Reproductive Endocrinology and Infertility, Duke University Medical Center, Durham, NC; 5Department of Biostatistics & Bioinformatics, Duke University Medical Center, Durham, NC.

OBJECTIVE: Among the general population, knowledge about natural fertility decline and the opportunity to cryopreserve oocytes is limited.4,5 This limitation contributes to age-related infertility, particularly among women who choose to postpone childbearing. Although resident physicians often delay family building, little is known about their fertility knowledge or attitudes. The primary objective of this study was to compare knowledge of age-related fertility decline and oocyte cryopreservation among resident physicians in different specialties. Our secondary objective was to examine their attitudes toward family building.

DESIGN: National online survey.

MATERIALS AND METHODS: A hyperlink to an online survey was sent to program directors of ACGME-accredited residency programs in the United States for Obstetrics and Gynecology (Ob/Gyn), Internal Medicine, Emergency Medicine, Family Medicine, General Surgery, Pediatrics, and Psychiatry. They were asked to forward the survey link to their respective residents. The survey consisted of three sections: 1) fertility knowledge, 2) oocyte cryopreservation knowledge, and 3) attitudes toward family building and fertility preservation.2 Outcomes were compared between Ob/Gyn residents and all other specialties, both combined and separately. Wilcoxon rank sum test or Chi-square test was used to compare variables, as appropriate. Multivariable logistic regression models were used to investigate the association between the number of correct answers and specialties with and without adjustment for age, gender, race/ethnicity, PGY year, marital status, preexisting children, and history of infertility.

RESULTS: Of the 2,828 completed surveys, 450 (15.9%) were by Ob/Gyn residents and 2,378 (84.1%) were by residents of other specialties. The median number of correct answers was 2 out of 5 on the fertility knowledge section and 1 out of 3 on the oocyte cryopreservation knowledge section among all survey participants. The adjusted and unadjusted models showed that specialties were not significantly associated with answering these questions correctly in either section. The majority of residents who had a child during residency or planned to have a child during residency was similar between Ob/Gyn and all other specialties, 33.9% vs. 35.5%, respectively, P=0.50. Ob/Gyn residents were significantly more likely than residents of other specialties to feel “somewhat supported” or “very supported” by their program to pursue family building goals (83.5% vs. 75.8%, P=0.0005).

CONCLUSIONS: Resident physicians have limited knowledge of natural fertility decline and the opportunity to cryopreserve oocytes. Knowledge of these topics is similar between Ob/Gyn residents and residents of other specialties. These data suggest a need for improved fertility education, particularly within Ob/Gyn residency programs. The majority of residents do feel supported to build their families during training, particularly Ob/Gyn residents.

P-759 Wednesday, October 16, 2019 6:30 AM

THE EFFECT OF RESIDENT PHYSICIAN INVOLVEMENT ON SURGICAL OUTCOMES AND COMPLICATIONS OF FERTILITY SURGICAL. 1 Wesley Yip, MD; 2 Sarah C. Vilj, MD; 3 Jianbo Li, PhD; 4 Lauren Beeder, BS; 5 Mary Katherine Sampalski, MD; 6 University of Southern California, Los Angeles, CA; 7 Cleveland Clinic Foundation, Cleveland, OH; 8 Keck School of Medicine, University of Southern California, Los Angeles, CA.

OBJECTIVE: To determine the effect of resident physician involvement in fertility surgical procedures on patient surgical outcomes and complications.

DESIGN: A review of fertility-specific surgical procedures in the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database was performed, followed by statistical analyses.

MATERIALS AND METHODS: The NSQIP database was reviewed for fertility surgical procedures from 2006 to 2012. The procedures included: epididymectomy, spermatocelectomy, varicocelectomy +/- hernia repair, ejaculatory duct resection, vasovasostomy, vasoepididymostomy, and unlisted procedure male genital system (to capture sperm retrieval procedures).

Patient factors analyzed were: patient age, race, body mass index (BMI), morbidity probability, mortality probability, American Society of Anesthesiologists physical status classification (ASA), smoker status, alcohol usage status, history of diabetes, chronic obstructive pulmonary disease, congestive heart failure, peripheral vascular disease, cerebrovascular accident, and/or steroid usage. Outcomes examined included operative time, length of hospital stay, superficial infection, deep wound infection, wound dehiscence, urinary tract infection (UTI), and reoperation rate. Resident and non-resident groups were compared by Wilcoxon rank sum tests, followed by logistic regression, univariate, and multivariate analyses.

RESULTS: 924 cases were included: 309 with residents, and 615 without residents. The median post-graduate resident year was 3 (range: 0-10). There was no difference in baseline demographics between groups. On univariate analysis, mean operative time was longer with resident involvement, even after controlling for other covariates (76.2 vs 49.5 minutes, p=0.00). Length of hospital stay was also longer in cases with resident involvement (0.41 vs 0.35 days, p<0.02). There was no difference in superficial infections (p=0.57) or UTIs (p=1.00) with or without resident involvement.

CONCLUSIONS: While resident physician involvement in fertility surgical procedures may lengthen operative time, there were no significant differences in length of hospital stay, superficial infections, deep wound infections, wound dehiscence, UTIs, and reoperation rates. This data is reassuring for attending physicians operating with residents.

P-760 Wednesday, October 16, 2019 6:30 AM

INFERTILITY, FERTILITY PRESERVATION, AND ACCESS TO CARE DURING TRAINING: A NATIONAL WIDE MULTI-SPECIALTY SURVEY OF UNITED STATES RESIDENTS AND FELLOWS. Ange Wang, MD; Christopher N. Herndon, MD; Evelyn Mok-Lin, MD; Lusine Aghajanova, MD PhD; Stanford University School of Medicine, Stanford, CA; University of Washington, Seattle, WA; REI UCSF, Center for Reproductive Health, San Francisco, CA.

OBJECTIVE: To investigate the prevalence of and experience related to infertility and utilization of fertility preservation during training for United States (US) medical residents and fellows.

DESIGN: Cross-sectional survey study.

MATERIALS AND METHODS: An online-based survey distributed to US postgraduate residents and fellows across medical specialties, via program directors and graduate medical office of residency/fellowship programs.

RESULTS: Respondents included 732 residents and fellows, with the highest percentage in Obstetrics & Gynecology (26.0%), Pediatrics (14.1%), and Internal Medicine (13.9%). 75.5% of respondents were residents and 73.2% were PGY1-4. Respondents were 75.4% female and 18.4% male, with the most common ethnicities Caucasian (61.2%) and Asian/Pacific Islander (10.4%). 75.8% of respondents reported being married or partnered. In total, over half of respondents (56.6%) reported delaying childbearing plans due to medical training. 51 respondents (7.0%) reported infertility, while 11 (1.5%) reported recurrent pregnancy loss (RPL). For the infertility/RPL group, 19 respondents reported undergoing IUI, 11 reported undergoing IVF, and 14 reported using oral medications for fertility purposes. For the fertility preservation group, 18 respondents reported undergoing IVF for embryo or oocyte cryopreservation. Additionally, 208 respondents (28.4%) reported that they had considered oocyte or embryo cryopreservation, though only 46 respondents underwent a fertility consultation for this purpose. Of those seeking treatment, respondents most commonly reported their own insurance or partner’s insurance as the source of financial support, in addition to salary and parents/friends. Only 13.1% reported living in a state where fertility coverage is mandated by insurance. Respondents reported lack of time/flexibility (35.4%) and financial concerns (29.4%) as the top reasons for being unable to pursue fertility consultation or treatment. The majority of respondents (65.5%) experiencing infertility/RPL or desire for fertility preservation reported that colleagues and program administration were unaware of treatments or challenges. However, of those whose challenges were known, the majority felt some degree of support by their program administrators (80.1%) and colleagues (84.4%).

CONCLUSIONS: The majority of residents and fellows delay childbearing due to medical training. The reported infertility rate in postgraduate medical trainees is comparable to general population, though may be underestimated as individuals may further delay childbearing until established in practice. Time/flexibility and financial concerns were identified by residents and fellows as the greatest barriers to seeking and pursuing medical assistance with infertility during training. Most trainees facing fertility-related challenges do not share their concerns with program administrators or colleagues, but most who did felt supported. Specific measures and awareness are needed in order to increase access to fertility services for US medical trainees.

P-761 Wednesday, October 16, 2019 6:30 AM

UTILIZING A NOVEL RESIDENT EDUCATION INITIATIVE TO PROVIDE REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY CARE FOR UNDERINSURED WOMEN. Elizabeth S. Rubin, MD; Ana Chereminski, MD; Samantha Butts, MD; Catherine R. Salva, MD; University of Pennsylvania, Philadelphia, PA.

OBJECTIVE: Few reports exist in the literature describing infertility evaluations or care in patients covered by Medicaid, but disparities in access are well documented. The objective of this study was to describe the health care received by a cohort of underinsured women with infertility after implementation of a novel quality improvement project designed to increase access to reproductive endocrinology and infertility (REI) specialists.

DESIGN: Retrospective observational study.

MATERIALS AND METHODS: We created a system for provision of infertility consultations from the REI division at an academic tertiary care institution. The Obstetrics and Gynecology (Ob/Gyn) resident clinic at our institution provides care for primarily African American and Latinx underinsured women. Patients are screened in by Ob/Gyn residents staffing routine gyn clinic when a patient presents with infertility. As part of their REI curriculum, Ob/Gyn residents reviewed patient charts in virtual visits under supervision of REI specialists.

RESULTS: Twenty-eight consultations were performed for underinsured patients in the first year of service. Of these patients, 22 patients (78%) had Medicaid insurance. Two patients (7%) were seen in the REI office after initial consultation. Nine (22%) completed bloodwork and 10 patients (35%) underwent pelvic ultrasounds. Six evaluations of fallopian tube patency were completed via either imaging (hysterosalpingogram) or surgery (chromotubation). Eight patients (28%) initiated ovulation induction. Five patients (17%) achieved pregnancy. Pelvic ultrasounds and blood work were fully covered by all insurance.

CONCLUSIONS: Though our resident clinic remains unable to provide standard infertility treatments like IUI and IVF to our Medicaid patients, patients were still able to benefit from the robust REI division at our institution. Academic institutions may be able to connect uninsured and underinsured patients to care.
P-762 Wednesday, October 16, 2019 6:30 AM

DOES LONGER EDUCATION MEAN POSTPONED PREGNANCY? Ecem Esencan, M.D.,1 Burcin Simsek, Ph.D.,2 Emre Seli, M.D.3 Yale School of Medicine, New Haven, CT;4University of Pittsburgh, Pittsburgh, PA.

OBJECTIVE: To delineate the continually increasing participation of women in education at bachelor’s, master’s, and doctoral degree levels and how it correlates with changes in age of marriage, pregnancy rate after age 35, and rates of diminished ovarian reserve (DOR) diagnosis and use of donor eggs, over time in the United States (US).

DESIGN: Population-based epidemiologic study.

MATERIALS AND METHODS: Education data (between 1970-2018) were collected from records and projections reported by National Center for Education Statistics, Institute of Education Sciences, and US Department of Education. Results on percent married and age at first marriage were gathered from Current Population Survey of U.S Census Bureau. Data on mean age of mother, mean age of mother at first birth, pregnancy and birth rates were gathered from annual National Vital Statistics Reports of Center for Disease Control and Prevention (CDC). Information on rates of DOR diagnosis and donor oocyte use among assisted reproduction technology (ART) cycles were collected from annual National Summary Reports on ART of CDC.

RESULTS: In 2018, proportion women earning bachelor’s degrees (per 10,000 female citizens) almost doubled compared to 1970 (50.8 vs 61.9%; p<.001). In the same time period, percentage of bachelor’s degrees awarded to females in a given year, increased significantly (57.5 vs 43.1%; p<.001), surpassing males. Moreover, percentage of total US female population who completed four years of college raised significantly between 1970 to 2018 (8.2 to 35). This trend was followed in postgraduate education, with significant increase in proportion of women earning master’s (27.3 to 10,000 vs 7.9/10,000; p<.001) and doctoral degrees (5.7/10,000 vs 0.54/10,000; p<.001) in 2018 compared to 1970. The percentages of master’s (from 38.8 to 61.0%; p<.001) and doctoral degrees (from 9.6 to 52.7%; p<.001) awarded to females also increased in the study period, both surpassing males. In the same time period the percentage of married women and median age at first marriage demonstrated an opposite trend. Less women were married (50.8% vs 61.9%) and marriages occurred at a more advanced age (27.8 vs 20.8). In parallel with this finding, an increase in mean age at first birth from 21.4 to 26.8 was observed between 1970 and 2017. Similarly, pregnancy rates of women in ages 35-39 and 40-44 more than doubled between 1980 and 2010 (0.036 to 0.077 and 0.009 to 0.019/1,000 respectively). The rise in birth rates of 1st child in those age brackets was even more dramatic (0.002 to 0.01 and 0.0003 to 0.002/1,000 respectively). In parallel, rate of DOR diagnosis in women undergoing ART raised significantly from 12% to 31% in 2005 to 2016, and number of ART cycles using donor eggs increased from 16,161 to 24,300 in the same time period.

CONCLUSIONS: Since 1970, participation of women in education in the US has risen significantly. This trend is paralleled by decreased rates and later occurrence of marriage as well as increasing age for childbearing, which in turn are reflected in the dramatic increase in DOR diagnosis and utilization of donor eggs in ART.

P-763 Wednesday, October 16, 2019 6:30 AM

MEDICAL STUDENTS’ KNOWLEDGE ABOUT THIRD-PARTY REPRODUCTION. Kajal Khodamoradi, phd student;1 Fardin Amidi, phd,2 Zahra Khorasvazadeh, phd student,1 Ali Talebi, phd,3 Zahra Rashidi, phd student,1 Mohammad Hossein Ayati, MD, PhD,2 Parva Namiranian, MD,4 School of Medicine, Tehran University of Medical Sciences, Tehran, Iran, miami, FL;5School of Medicine, Tehran University of Medical Sciences, Tehran, Iran, Tehran, FL, Iran (Islamic Republic of);6School of Medicine, Tehran University of Medical Sciences, Tehran, Iran, Tehran, FL, Iran, (Islamic Republic of);7School of Medicine, Tehran University of Medical Sciences, Tehran, Iran, Tehran, FL, Iran, (Islamic Republic of);8School of Medicine, Shahroud University of Medical Sciences, Shahroud, Iran, Shahroud, FL, Iran (Islamic Republic of);9School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran, Tehran, Iran (Islamic Republic of);10Department of Persisitve Medicine, School of Persian Medicine, Tehran University of Medical Sciences, Tehran, Iran., tehran, Iran (Islamic Republic of).

OBJECTIVE: To investigate obesity associated inflammatory factors in follicular fluid that may affect gene expression in cumulus cells of women undergoing IVF-ICSI.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Follicular fluid and cumulus cells were collected during oocyte retrieval in women undergoing IVF-ICSI, and group ed based on body mass index (BMI). Cytokine levels were measured from the follicular fluid using enzyme-linked immunosorbent assay (ELISA). Expression of 4 genes (GREM1, IL-1β, CTGF, MRPS6) were positively correlated with oocyte maturity and/or pregnancy outcome in cumulus cells, was determined by quantitative reverse transcription polymerase chain reaction (RT-qPCR). Mann Whitney tests were utilized to compare cohorts by BMI and reported as medians with interquartile ranges. Cumulus cells of normal BMI (21.1 kg/m² to 23.6 kg/m²) women were cultured with IL-1β to investigate its impact on gene expression. Change in gene

IL-1β IS ASSOCIATED WITH DECREASED EXPRESSION OF GREM1 IN OBESE WOMEN UNDERGOING IN VITRO FERTILIZATION WITH INTRACYTOPLASMIC SPERM INJECTION (IVF-ICSI). Tana Kim, MD,a Yulian Zhuo, PhD,1 Elizabeth Ann Enninga, PhD1 Division of Reproductive Endocrinology and Infertility, Rochester, MN;2Department of Obstetrics and Gynecology, Mayo Clinic, Rochester, MN.

OBJECTIVE: To investigate obesity associated inflammatory factors in follicular fluid that may affect gene expression in cumulus cells of women undergoing IVF-ICSI.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Follicular fluid and cumulus cells were collected during oocyte retrieval in women undergoing IVF-ICSI, and grouped based on body mass index (BMI). Cytokine levels were measured from the follicular fluid using enzyme-linked immunosorbent assay (ELISA). Expression of 4 genes (GREM1, IL-1β, CTGF, MRPS6) were positively correlated with oocyte maturity and/or pregnancy outcome in cumulus cells, was determined by quantitative reverse transcription polymerase chain reaction (RT-qPCR). Mann Whitney tests were utilized to compare cohorts by BMI and reported as medians with interquartile ranges. Cumulus cells of normal BMI (21.1 kg/m² to 23.6 kg/m²) women were cultured with IL-1β to investigate its impact on gene expression. Change in gene
expression following IL-1β was analyzed by paired t test. P values <0.05 were considered significant.

RESULTS: A total of 68 women were included in the ELISA analysis. Women were grouped based on BMI with 57 women having BMI <35 kg/m² and 11 women with BMI ≥35 kg/m². Women with BMI ≥35 kg/m² had increased levels of IL-1β in the follicular fluid as compared to women with lower BMI (5.18 pg/mL vs 1.92 pg/mL, p = 0.02).

Gene expression from cumulus cells was measured from a representative cohort based on BMI, with 6 in the normal group (BMI 21.1 kg/m² to 23.6 kg/m²) and 6 in the obese group (35.6 kg/m² to 42.0 kg/m²). The obese group had a significantly lower relative expression of GREM1 compared to the normal group (0.51 [0.38, 0.74] vs 1.01 [0.66, 1.40], p = 0.03). No differences were seen with HAS2 (0.73 [0.49, 1.17] vs 1.06 [0.65, 1.78], p = 0.39), PTGS2 (1.54 [1.09, 3.11] vs 0.58 [0.47, 4.19], p=0.22), or VCAN (0.88 [0.61, 1.56] vs 0.93 [0.63, 1.56], p = 0.82).

Given increased levels of IL-1β in follicular fluid of obese women, cumulus cells from women with normal BMI were cultured with IL-1β to investigate the impact on GREM1 expression. Following IL-1β incubation, GREM1 levels significantly decreased in cumulus cells of normal BMI women (p = 0.02) similar to the obese cohort.

CONCLUSIONS: Compared to women with normal BMI, obese women had higher levels of pro-inflammatory IL-1β in the follicular fluid and had lower cumulus cell expression of GREM1. Decreased expression of GREM1 in cumulus cells of normal BMI women following culture with IL-1β suggests that this pro-inflammatory cytokine may play a role in suppressing GREM1 levels in obese women. These molecular discrepancies may give insight into physiologic differences in oocyte development and cycle outcomes in obese women undergoing IVF-ICSI. Further studies are required to correlate these molecular findings to clinical outcomes.

P-766 Wednesday, October 16, 2019 6:30 AM
DECREASED EXPRESSION OF PDI IN PERIPHERAL BLOOD TH17 CELLS IN WOMEN WITH UNEXPLAINED RECURRENT PREGNANCY LOSS.
Wenjuan Wang, MD, PhD; Maria Dinorah Salazar Garcia, MD; Xinxiu Yang, PhD, MD; Qiaoqiao He, PhD, MD; Giovanni Jubiz, MD, PhD; Svetlana Dambaeva, Ph.D.; Alice Gilman-Sachs, Ph.D.; Kenneth Beaman, Ph.D.; Joanne Kwak-Kim, MD, MPH.
Reproductive Medicine and Immunology, Chicago Medical School, Rosalind Franklin University of Medicine and Science, Vernon Hills, IL; Mount Sinai Hospital, Chicago, IL; Clinical Immunology Lab, Department of Microbiology and Immunology, Chicago Medical School, Rosalind Franklin University of Medicine and Science, North Chicago, IL; Rosalind Franklin University of Medicine and Science, North Chicago, IL.

OBJECTIVE: Programmed Death-1 (PDI) and PD-ligand (PDL)-1 have been reported to participate in the regulation of T cells homeostasis and peripheral tolerance and have an important role in fetomaternal tolerance during pregnancy. PDI blockade leads to CD4+ T (especially Th1, Th17 cells) activation and proliferation, which in turn increases embryo resorption and reduces litter size in a mouse model. The goal of this study was to investigate the expression of PDI/PDL1 on CD4+ T cells of peripheral blood in women with recurrent pregnancy loss (RPL).

DESIGN: A prospective cohort study.

MATERIALS AND METHODS: Forty-five women with RPL and 12 fertile women who had at least one or more live-born infants were enrolled in this pilot study. The expression of PDI/PDL1 on CD4+ T cells in the peripheral blood, including Th1, Th17, and Treg cells were analyzed by flow cytometry. The expression of PDI/PDL1 was tested using monoclonal antibodies (mAB) to CD279 (PD1) and CD274 (PDL1). The expression of Tregs was tested using mAbs to CD45, CD3, CD4, CD25, and CD127. The expression of Th1 cells was tested using mAB to CD45, CD3, CD8, IFN-g or TNF-α. The expression of Th17 cells was tested using mAB to CD45, CD3, CD8, and IL-17.

RESULTS: The proportions of PDI+ Th17 cells (CD4+IL17+CD279+ cells out of total CD4+T cells) were significantly lower in the RPL group than controls (P<0.05). However, there are no differences in PDI+ Th1 (CD4+TNF-α+CD279+ and CD4+IFN-g+CD279+) and Treg (CD4+CD25+CD127+CD279+) cells between the RPL group and controls. The proportions of PDL1+ Th1 (CD4+IFN-g+CD274+ and CD4+TNF-a+CD274+), Th17 (CD4+IL17+CD274+), and Treg (CD4+CD25+CD127+CD279+) cells are not different between the RPL group and controls (P>0.05, respectively).

In Th1 and Th17 cells, the proportions of PDL1+ (CD274+) cells were significantly higher than those of PD1+ (CD279+) cells in both the RPL group and controls (P<0.01 respectively). However, there were no differences in PDL1+ and PDI+ Treg cells in both groups.

CONCLUSIONS: Decreased expression of PDI on Th17 cells may lead to enhanced Th17 immunity and result in the imbalance between Treg and Th17 cells in women with RPL.

SUPPORT: This work was partially supported by grants from the National Natural Science Foundation of China (grant numbers 81741027, 81300533, 81601276), Chinese Medical Association Clinical Medicine Research Special Fund-2017, Reproductive Medicine Young Physicians Research and Development project (17020160685, 16020220638), and Yantai Key Development project (2017YD6000941).

P-767 Wednesday, October 16, 2019 6:30 AM
DOES SERUM ANTI-NUCLEAR ANTIBODY PREDICT OUTCOMES OF PREGNANCY AMONG WOMEN WITH A HISTORY OF RECURRENT PREGNANCY LOSS, WITHOUT COEXISTING ANTI-PHOSPHO-LIPID ANTIBODY SYNDROME? A SYSTEMATIC REVIEW AND META-ANALYSIS.
Trenton Place, DO, PhD; Karen M. Summers, MPH CHES.
Matt Regan, MA MLIS; Patrick Ten Eyck, MS PhD; Yunshu Zhou, MS; Brittany Bettendorf, MD; Abey Eapen, MBBS
OBJECTIVE: The concept of immune-mediated Recurrent Pregnancy Loss (im-RPL) is gradually being accepted as a true clinical entity. However, there is no universally accepted screening test or a diagnostic test for this condition. Anti-nuclear antibody (ANA) screening is widely used for screening auto-immune diseases in clinical medicine. The objective of this study was to determine whether serum ANA would be a reliable marker to predict outcomes in women diagnosed with Recurrent Pregnancy Loss (RPL) without co-existing anti-phospholipid antibody syndrome (APS).

DESIGN: Systematic review and meta-analysis.

MATERIALS AND METHODS: This systematic review and meta-analysis was registered with PROSPERO. The search strategy was applied to Medline, EMBASE and Cochrane Central Register of Controlled Trials (from database inception to Oct 2018). Studies retrieved by the search and the reference lists of relevant studies were included in the review if; the study population was described as having a diagnosis of RPL; had serum ANA testing done; if there was a control group and if the outcomes of miscarriage (or live birth) were reported. Studies in women who had co-existing APS were excluded. There were no other restrictions, including ANA titer or co-interventions. The primary outcome was the miscarriage rate.

RESULTS: Thirty-two studies involving 4,375 women fulfilled the inclusion criteria and were subjected to quantitative and qualitative analysis. All studies included pregnant women in their analysis. There was a statistically significant increase in risk of miscarriages in women with positive ANA (Odds Ratio [OR] 2.99; 95% CI [2.22 – 4.04]; I² = 67%; P < 0.01). Subgroup analysis also confirmed a statistically significant association of an increase in the risk of miscarriage. In women with three or more previous miscarriages, analysis confirmed OR 2.47; 95% CI [1.66 – 3.65]; I² = 41%; P < 0.01. In women who had two or more previous miscarriages, analysis confirmed OR 3.47; 95% CI [2.24 – 5.39]; I² = 79%; P < 0.01. The total heterogeneity was high with I² = 67%; I² = 0.4, p < 0.01.

CONCLUSIONS: This systematic review postulates that positive ANA in women with RPL increases the risk of further miscarriage by three-fold. This finding underscores the importance of the immune system in RPL and suggests that ANA could be useful in outcome prediction for APS negative women with RPL. This study also opens a new direction for future research in women with RPL. The addition of serum ANA titer levels, women who had two or more previous miscarriages, analysis confirmed OR 3.47; 95% CI [2.24 – 5.39]; I² = 79%; P < 0.01), and those with co-morbidities (RR 2.06, 95% CI: 1.98, 2.15, older patients (RR 1.07, 95% CI: 1.04, 1.10, p<0.01), and those with co-morbidities (RR 2.06, 95% CI: 1.98, 2.15, p<0.01). The total heterogeneity was high with I² = 67%; I² = 0.4, p < 0.01.

CONCLUSIONS: Increase in CD45+CD3+CD56+ NK cells was observed in women with detected hCG. Pregnancy status and pregnancy serum have a significant impact on the cytokytic potential of peripheral blood NK cells. In this regard, hCG, not VEGF-A or VEGF-C, may impart a non-cytotoxic phenotype on peripheral blood NK cells.
p<0.01) were more likely to be admitted to the hospital. Of patients admitted, those on the weekend (RR 96.95% CI: .95, .97 < p<0.01), black patients (RR .97 95% CI: .95, .98 < p<0.01), younger patients (RR .92 95% CI: .89, .94 < p<0.01), and those with co-morbidities (RR .86 95% CI: .84, .88 < p<0.01) were less likely to undergo same-day surgery for ectopic pregnancy. Similari-ly, patients admitted on the weekend (RR .97 95% CI: .95, .97 < p<0.01) and those with co-morbidities (RR .88 95% CI: .86, .89 < p<0.01) were also less likely to receive surgery within one day. Furthermore, patients on the weekend (RR 1.49, 95% CI: 1.46, 1.53 < p<0.01) and those with co-morbidities (RR 3.90, 95% CI: 3.73, 4.09, < p<0.01) were more likely to have a blood transfusion during admission.

CONCLUSIONS: Ectopic pregnancies evaluated in the ED during the weekend are more likely to be admitted to the hospital, but less likely to un-dergo same day or surgery within one day of admission. Weekend admissions were independently at significantly higher risk for blood transusions even after adjustment for timing of surgical management. Further studies are needed to understand factors such as provider staffing which may contribute to this weekend effect, and to work to mitigate this impact.

P-770 Wednesday, October 16, 2019 6:30 AM

NORMAL SALINE SOLUTION IS AS EFFECTIVE AS POVIDONE IODINE IN PREOPERATIVE VAGINAL CLEANSING BEFORE SHORT DURATION GYNECOLOGICAL LAPAROSCOPY. Ahmed M. Abbas, MD, Mohammed Khairy Ali, MD, Ahmed M. Abdelmagied, MD, Osama S. Abdalmageed, MD, Esraa Badran, MD Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: Laparoscopy is a minimally invasive method used for diagnostic and therapeutic purposes. Our objective was to compare the postoperative vaginal irritation symptoms and infection rates after using povidone-iodine (PI) and normal saline (NS) solution in vaginal cleansing before short duration gynecological laparoscopy.

DESIGN: Randomized, single arm clinical trial.

MATERIALS AND METHODS: All eligible participants who scheduled for short duration gynecologic laparoscopic procedures included diagnostic laparoscopy, bilateral ovarian drilling, and tubal sterilization were invited to participate in the study. Eligible participants were randomly allocated in 1:1 ratio to two groups. Group I “PI group” where they subjected to PI for vaginal cleansing before laparoscopy and group II “NS group” where they subjected to the standard saline solution for vaginal cleansing. Two sponges of the same size and type were used for cleansing by both preparations. The primary outcome of the study was the difference in the rate of self-reported postoperative vaginal irritation symptoms after using PI and NS for vaginal cleansing. The secondary outcomes included the rate of postoperative fever ≥ 38°C during the first 24 hours, persistent vaginal irritation symptoms, urinary tract infection, candidal vaginitis and bacterial vaginosis and endometritis at one-week post-procedure. The outcome variables were calculated using an unpaired t-test and chi-square test.

RESULTS: Two-hundred forty-four women were analyzed in both groups (121 women in the arm). Both groups were similar regarding the mean age, residency, woman’s education, parity, BMI and operative time. Diagnostic laparoscopy was the most common laparoscopic procedure performed during the study period (84.29%), tubal sterilization (7.85%) then bilateral ovarian drilling (7.4%). The mean overall vaginal irritation symptoms in PI group were significantly more than that observed in the NS group (p=0.0001). The overall infection rates in the PI group were 15.9%, while in the NS group was 10.16 % without a statistically significant difference in both groups (p=0.567). Both groups were quite similar in the rate of postoperative fever (p=0.505), urinary tract infection (p=0.654), vaginal candidiasis (p=0.254), bacterial vaginosis (p=0.366) and postoperative endometritis (p=0.749).

CONCLUSIONS: Being less irritant, normal saline can substitute iodide solution as a vaginal cleansing tool before short duration gynecologic laparoscopy without increasing the risk of postoperative infection.

SUPPORT: None.

FLUID DEFICIT CALCULATION AT HYSTEROSCOPY IN PATIENTS WITH AND WITHOUT TUBAL OCCLUSION: COULD CONSIDERATION OF TUBAL PASSAGE CHANGE SAFETY LIMITS? Irene Peregriín-Alvarez, MD, Robert Roman, MD, Mary Emily Christiansen, MD, Joshua Morris, MD, Laura Detti, MD. University of Tennessee Health Science Center, Memphis, TN.

OBJECTIVE: Hysteroscopy (HSC) fluid management guidelines (1) are not well-defined regarding the contribution on the fallopian tube patency to the fluid deficit (FD) during HSC and most surgeons attribute the entire FD to intravasation (2). Women with patent tubes undergoing HSC have accumulation of distention media in the pelvis which can be seen during laparoscopy (LSC) and could be in part due to transtubal passage (3). We explored whether FD could be in part due to transtubal passage.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: We studied 164 patients aged 20-45 years, who underwent HSC using normal saline as distension media between January 2014 and August 2017. Tubal patency was previously assessed at sonohystrogram. FD and, in LSC cases, the amount of fluid found in the pelvis, were prospectively recorded. Whitney U test was used to compare distributions with a p value <0.05 defining statistical significance (SPSS v25 for Windows; Chicago, Illinois).

RESULTS: 164 patients were included in the study. 77 underwent HSC prior to LSC and 87 patients underwent HSC only. In the LSC group, 69 had at least one patent tube with an average FD of 438.96 ml and a calculated FD due to extravasation of 175.61 ml; 8 patients had bilateral tubal occlusion and all were found to have 0 ml of peritoneal fluid with an average FD of 141. In the HSC only group, 83 had at least one patent tube with an average FD of 307.48 ml; 4 patients had bilateral tubal occlusion with an average FD of 375.75 ml. There was no correlation between intraperitoneal fluid pressure and the amount of FD, or the presence of peritoneal fluid.

CONCLUSIONS: Most women with patent tubes undergoing HSC have accumulation of distention media in the pelvis and transtubal passage was not correlated with the intraperitoneal fluid pressure. FD in patients with tubal occlusion appears to be entirely attributed to intravasation. These findings add new insight to our understanding of fluid dynamics during operative hysteroscopy that can help develop more accurate and patient-centered safety protocols.


FERTILITY & STERILITY®

P-771 Wednesday, October 16, 2019 6:30 AM

SEVERE HAEMATOPERITONEUM AFTER TRANSVA- GINAL OOCYTE RETRIEVAL RELATED OVARIAN BLEEDING COULD BE MOSTLY MANAGED BY CONSERVATIVE TREATMENT: 832 CASES OF ONE CLINICIAN’S EXPERIENCE IN 5 YEARS. Melih Aygun, M.D.,* Carolina Pirkci, Cetinkaya, PhD,† Murat Cetinkaya, M.D., PhD,‡ Semra Kahraman, Prof.*, ‡Infertility specialist, ISTANBUL, Turkey; †Istanb ul Memorial Hospital, Istanbul, Turkey.

OBJECTIVE: TVOR is the most common surgical procedure during in vitro fertilization (IVF) cycles. One of the most serious complications of the
procedure is intra-abdominal bleeding. Hospitalization is reported to be needed with an incidence between 0.06% and 0.35%. According to the literature, the rate of cases requiring abdominal surgery with severe haematoperitoneum (SHP) is very different, between 40% to 70% in large series. The aim of this study was to compare single clinician’s complication rate for SHP caused by ovarian bleeding after TVOR with literature and to compare the outcome of treatment strategies.

DESIGN: This retrospective cohort study included all of 8332 consecutive TVOR procedures performed by a single clinician (65.2%) among a total of 12776 TVORs, between June 2014 and March 2019 and in one IVF center. All the suspected SHP cases who were hospitalized were enrolled in the study group. This “complication” group was categorized according to the need for a conservative or surgical treatment. General SHP rates and the treatment approaches were compared with the literature.

MATERIALS AND METHODS: The complications of SHP included in the study were grouped into two: Group I included patients in whom conservative treatment with or without red blood cell (RBC) transfusion was performed; Group II consisted of patients who were indicated for surgical treatment. Patients with non-ovarian bleedings were excluded. Number of RBC units for transfusion, duration of hospitalization of SHP patients, general body mass index (BMI) and women ages in TVOR were considered.

RESULTS: A total number of 79097 oocytes (8832 TVOR) were retrieved by the same clinician between June 2014 and March 2019. The mean female age was 35.04±5.67, the mean body mass index was 24.92±4.49, the mean number of retrieved oocytes and metaphase II oocytes was 9.50±8.35 and 7.92±6.97 respectively. The number of SHP related ovarian bleeding complications during TVOR was 17 out of 8332 (0.2%). The mean duration of hospitalization was 1.76 days/patient. The mean RBC units administered was 1.65 U/patient. Whereas 15 patients (88.23%) needed only conservative treatment, only two (11.77%) needed a laparoscopic intervention. None of the patients (17) had severe infections such as pelvic abscess or sepsis after the treatment.

CONCLUSIONS: The real complication rates of SHP after TVOR and heterotopic interstitial pregnancy can achieve a good IUP outcome.

OBJECTIVE: To investigate the intrauterine pregnancy (IUP) outcomes of heterotopic fallopian tubal pregnancy after in vitro fertilization - embryo transfer.

ANALYSIS OF THE PREGNANCY OUTCOMES OF HETEROTOPIC FALLOPIAN TUBAL PREGNANCY AND HETEROTOPIC INTERSTITIAL PREGNANCY AFTER IN VITRO FERTILIZATION - EMBRYO TRANSFER. Mingxiang Zheng, Bachelor’s degree,a Xihong Li, MD, Ph.D. b Yan Youyang, MD, Ph.D. c Yuyao Mao, Master, d Jingzi Xiao, Master. e Qingqing Wu, Bachelor’s degree. f Reproductive and Genetic hospital of CITIC-Xiangya, Changsha, China; g Reproductive and Genetic hospital of CITIC-Xiangya, Changsha, China.

OBJECTIVE: To investigate the intrauterine pregnancy (IUP) outcomes of heterotopic interstitial pregnancy and heterotopic fallopian tubal pregnancy after in vitro fertilization - embryo transfer (IVF-ET).

TABLE A. Comparison of the IUP between the heterotopic fallopian tubal pregnancy and heterotopic interstitial pregnancy

<table>
<thead>
<tr>
<th>Pregnancy outcomes</th>
<th>Heterotopic fallopian tubal pregnancy (n=347)</th>
<th>Heterotopic interstitial pregnancy (n=160)</th>
<th>P-value</th>
<th>OR (95%-CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early pregnancy loss rate, % (n)</td>
<td>28.5% (99/347)</td>
<td>26.9% (43/160)</td>
<td>0.7</td>
<td>1.086 (0.714-1.653)</td>
</tr>
<tr>
<td>Late miscarriage rate, % (n)</td>
<td>0.6% (2/347)</td>
<td>0</td>
<td>1</td>
<td>1.464 (1.379-1.553)</td>
</tr>
<tr>
<td>Preterm delivery rate, % (n)</td>
<td>7.5% (26/347)</td>
<td>6.3% (10/160)</td>
<td>0.613</td>
<td>1.215 (0.571-2.584)</td>
</tr>
<tr>
<td>Term delivery rate, % (n)</td>
<td>62.8% (218/347)</td>
<td>66.9% (107/160)</td>
<td>0.377</td>
<td>0.837 (0.564-1.242)</td>
</tr>
<tr>
<td>Labor induction rate, % (n)</td>
<td>0.6% (2/347)</td>
<td>0</td>
<td>1</td>
<td>1.464 (1.379-1.553)</td>
</tr>
<tr>
<td>Babies born</td>
<td>255</td>
<td>119</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perinatal mortality rate, % (n)</td>
<td>1.6% (4/255)</td>
<td>0.8% (1/119)</td>
<td>1</td>
<td>1.880 (0.208-17.009)</td>
</tr>
<tr>
<td>Live birth rate, % (n)</td>
<td>69.2% (220/347)</td>
<td>72.5% (116/160)</td>
<td>0.345</td>
<td>0.851 (0.562-1.289)</td>
</tr>
<tr>
<td>Caesarean section rate, % (n)</td>
<td>77.1% (188/244)</td>
<td>86.3% (101/117)</td>
<td>0</td>
<td>0.334 (0.180-0.618)</td>
</tr>
<tr>
<td>Gestational age at delivery</td>
<td>38.345 ± 2.322</td>
<td>38.406 ± 2.271</td>
<td>0.818</td>
<td></td>
</tr>
<tr>
<td>Live birth weight (kg)</td>
<td>3.2 ± 0.6</td>
<td>3.2 ± 0.5</td>
<td>0.747</td>
<td></td>
</tr>
</tbody>
</table>
RESULTS: Of the 141 men who were included, 20 were in the TA group and 121 were in the NTA group. There was no statistically significant difference in age between the 2 groups, 34.3 (6.5) in TA group and 34.1 (5.8) in the NTA group. The grades of varicoceles were similar in both groups; TA group had 10% grade 1, 55% grade 2, 35% grade 3; while the NTA group had 6.7% grade 1, 58.7% grade 2, and 34.7% grade 3. There was no statistically significant difference in preoperative semen parameters between the two groups including semen volume, sperm concentration, motility, forward progressive motility (FP), and total motile count (TMC). The NTA group had a higher preoperative DFI than the TA group; 35.3% vs 29.7% respectively. Although both groups showed an improvement in semen parameters postoperatively, the TA group only showed a statistically significant improvement in DFI from 29.7% (5) to 22% (0), whereas the NTA group showed statistically significant improvements in concentration, motility, FP, TMC, and DFI. The mean change in preoperative to postoperative parameters when comparing groups only revealed a significant difference in TMC and DFI with a larger mean improvement in the NTA group than the TA group.

CONCLUSIONS: Men with ipsilateral testicular atrophy secondary to varicoceles have improved overall semen parameters and DFI after varicocele repair, but do not get as significant of an improvement as men without testicular atrophy. However, only TMC and DFI have a significantly greater mean change in preoperative to postoperative response in the NTA group compared to the TA group.

SUPPORT: None.

P-775 Wednesday, October 16, 2019 6:30 AM

Efficacy and Safety of Oral Versus Vaginal Misoprostol in Cervical Priming Before Hysteroscopy: A Systematic Review and Meta-analysis of Randomized Controlled Trials, Ahmed M. Abdelhamik, MBChB, Al-Hussein Gadallah, MBChB, Ahmed M. Abbas, MD, Ksar Al-Ainy Faculty of Medicine, Cairo University, Cairo, Egypt; Faculty of Medicine, Assiut University, Assiut, Egypt; Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: Hysteroscopy is common to be used in the diagnosis and management of many problems related to gynecology. Most of the complications of hysteroscopy occur throughout the cervical entry including cervical lacerations, false tract and uterine rupture. Cervical priming can be used to decrease the incidence of these problems and hazards before performing hysteroscopy. Our objective is to evaluate the evidence from published randomized clinical trials (RCTs) about the efficacy and safety of oral versus vaginal misoprostol in cervical priming before hysteroscopy.

DESIGN: Systematic review and meta-analysis.

MATERIALS AND METHODS: We searched in different electronic data-bases including PubMed, Cochrane Library, Scopus, ClinicalTrials.gov and Web of Science using the relevant keywords ((misoprostol OR Cytotec) AND (cervical dilatation OR cervical priming OR hysteroscopy)). All RCTs assessing the effect of oral versus vaginal misoprostol before hysteroscopy were considered. The extracted outcomes were: width of the cervical canal, ease of dilatation, the time needed for cervical dilatation; adverse effects and any complications during the procedure. For continuous data, efficacy outcomes were pooled as weighted mean difference (MD) or standardized mean difference (SMD). For dichotomous data of safety outcomes, we used pooled risks ratios (RR) using the Mantel-Hansel method. All statistical analyses in this study were completed by the RevMan software package.

RESULTS: Our search found 110 studies from the electronic databases out of which, 35 were duplicates. Out of the remaining 75 studies, 65 studies were excluded based on the title, and abstract screening and ten studies were excluded during the full-text screening. About eight studies met our inclusion criteria. The quality of the included RCTs was from moderate to high, according to the Cochrane risk of bias assessment tool. Both groups did not differ significantly in terms of cervical width diameter (MD = 0.25 mm, 95% CI [-0.92, 0.42], p = 0.47). However, the vaginal route significantly superior to the oral route of misoprostol in reducing the time needed for cervical dilatation (SMD = 0.17, 95%CI [0.02, 0.32], P = 0.03). We found no significant difference in any of the two routes regarding ease of dilatation (MD = 0.00, 95%CI [-0.15, 0.15], P = 0.96). Regarding safety profile, no significant difference between oral and vaginal misoprostol groups except for diarrhea, which favored vaginal more than oral misoprostol (RR = 2.48, 95% CI [1.17, 5.26], p = 0.02). No significant difference was found in both oral and vaginal route of administration for increasing the risk of any other complications (RR = 1.7, 95% CI [0.74, 3.92], P = 0.21).

CONCLUSIONS: Oral and vaginal misoprostol administration are similar regarding efficacy and safety in cervical priming before hysteroscopy, except that the vaginal route is associated with a lower incidence of diarrhea.

SUPPORT: None.

P-776 Wednesday, October 16, 2019 6:30 AM

Outcome of Laparoscopic Repair of Cesarean Scar Defect, Hesham A. Salem, FA, M.D., M.D., Moustafa Z. Moustafa, M.D., Diaa M. Aglan, M.D., Emam A. Abdelnaby, M.D., Adel E. Elgergawy, M.D., Ayman Shehata Dawood, M.D., Amro D. Aghlan, MBBCCH, Mohamed H. A. Salem, MBCHBC. Professor at Faculty of Medicine, Tanta University, Tanta, Egypt; Consultant at Faculty of Medicine Tanta University Hospitals, Tanta, Egypt; Assistant Professor at Faculty of Medicine, Tanta University, Tanta, Egypt; Lecturer at Faculty of Medicine, Tanta University, Tanta, Egypt; House Officer at Tanta University Hospitals, Tanta, Egypt; Medical Student at Faculty of Medicine, Tanta University, Tanta, Egypt.

OBJECTIVE: To evaluate the gynecologic and obstetric outcomes of laparoscopic repair of symptomatic cesarean scar defect.

DESIGN: Prospective clinical study.

SETTING: University hospital and private gynecologic endoscopy center.

MATERIALS AND METHODS: Patients: A total of 52 women (age between 25 – 35 years) with symptomatic cesarean scar defect, who wish to conceive, and the remaining myometrial thickness at the site of defect is less than 3 mm. according to vaginal US examination and/or MRI.

Intervention: Laparoscopic excision and repair of the defective cesarean scar.

Main Outcome measures: Relief of relevant symptoms, restored myometrial thickness at the site of repair, achievement of pregnancy in infertile patients, obstetric outcome in those who become pregnant, and incidence of operative complications.

RESULTS: The mean thickness of the myometrium increased significantly from 1.62 ± 0.8 before surgery to 9.0 ± 2.1 mm after surgery. Among the 47 patients presented with menstrual abnormalities and/or pelvic pains, 34 patients (72.3%) demonstrated complete relief of symptoms, 8 patients (17.02%) demonstrated partial improvement, and 5 patients (10.64%) stated no improvement.

Among the 25 patients who tried pregnancy 17 patients (68%) became pregnant. 12 patients demonstrated healthy pregnancy courses and delivered healthy babies by cesarean section at term (48%). There were no relevant major obstetric complications like scar deshiscence, placenta accreta, or cesarean scar ectopic pregnancy. The were no operative complications.

CONCLUSIONS: In women with symptomatic cesarean scar defect who wish to conceive, the laparoscopic approach for excision and repair of the defective scar is safe and efficient technique, ensures satisfactory symptoms relief, adequate restoration of sufficient myometrial thickness and strength, and results in good reproductive outcome.

P-777 Wednesday, October 16, 2019 6:30 AM

Predictive Value of Hormones in Sperm Retrieval Surgery, Kent Russell Edwards, Jr, MD, Nicholas Ross Major, BS, Kit N. Simpson, DrPh, Marc J. Rogers, MD Medical University of South Carolina, Charleston, SC.

OBJECTIVE: Non-obstructive azoospermia (NOA) causes male factor infertility in about 10% of cases. Multiple techniques have been described to obtain sperm from the testicle for use with assisted reproductive technologies. Conventional testicular sperm extraction (cTESE) is the most common but some argue that microdissection testicular sperm extraction (mTESE) is preferred for its superior sperm retrieval rates (SRR) and decreased microvascular damage to the testicle. However, mTESE is generally more expensive, time consuming, and requires more equipment. Previous work has attempted to identify variables that predict positive SRR with mTESE versus cTESE. The objective of this review was to create a model comparing the commonly evaluated variables; follicle stimulation hormone (FSH), testicular volume (TV), and testosterone (T), to better predict SRR.

DESIGN: The authors included 29 studies in the data analysis, with 9 studies including data on cTESE for a total of 1227 patients and 20 studies including data on mTESE for a total of 4760 patients. Not all studies included data for each variable.
MATERIALS AND METHODS: While not all studies included data for each variable, the authors were however able to create a weighted-means values of SRR, FSH, testosterone, and volume for the 29 studies. The authors then used weighted linear regression to describe associations between SRR, type of procedure, FSH, T, and volume.

RESULTS: Weighted-means values of SRR, FSH, testosterone, and volume were calculated and demonstrated mTESE to be superior to cTESE with a SRR of 51.9% versus 40.1% when there were no significant differences in FSH, T, or TV. Multiple weighted linear regressions were created to describe associations between SRR, procedure type, FSH, T, and TV. Model A demonstrated that one may expect an 11.8% increase in SRR when utilizing mTESE compared to cTESE. Model B showed that for every 1.19 IU/mL increase in FSH there will be a significant decrease in SRR by 1%. FSH values were then divided into low, medium, and high categories (FSH < 10, 10-19, and > 20 IU/mL respectively). The model demonstrated that for an index patient undergoing cTESE retrieval rates would be 57%, 44%, and 31% for values low, medium, and high respectively.

CONCLUSIONS: Based upon pooled available data, mTESE is more successful than cTESE for sperm retrievals in NOA patients. The models generated in this study demonstrated an ability for FSH to predict SRR using mTESE and cTESE however the models were not suggestive for a correlation regarding SRR and T and TV. FSH alone can be predictive of retrieval success and used to counsel patients. More standardized data collection and publication will be useful for future modeling to allow improved outcomes and counseling for patients.

SUPPORT: None.

P-778 Wednesday, October 16, 2019 6:30 AM

PREGNANCY RATES AFTER LAPAROSCOPIC OVARIAN DRILLING IN POLYCYSTIC OVARY SYNDROME PATIENTS FOLLOWING UNSUCCESSFUL OVULATION INDUCTION. Shrutl Agarwal, DO.a Mark P. Trolince, MD.b 1UCF College of Medicine/HCA Consortium of Greater Orlando, Kissimmee, FL. Fertility CARE: The IVF Center; University of Central Florida College of Medicine – Associate Professor, Winter Park, FL.

OBJECTIVE: Polycystic ovary syndrome (PCOS) is one of the most common endocrine pathologies and is a frequent cause of anovulatory infertility affecting 5-20% of reproductive age women1. Medical induction of ovulation is considered the first-line treatment option for infertile PCOS women. Laparoscopic ovarian drilling (LOD) is currently accepted as a successful second-line treatment in drug-resistant PCOS2. Many authors have reported high pregnancy (~80%) and pregnancy (~60%) rates following LOD3. The aim of this study was to evaluate the efficacy of laparoscopic ovarian drilling (LOD) on the reproductive outcome of anovulatory PCOS women. The results of our study were compared to historical controls from literature.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Women unable to achieve pregnancy with ovulation drugs who underwent LOD from 2013-2018 were included. One physician followed a standard technique for LOD and performed all surgeries. Age, BMI, years of infertility, tobacco or alcohol use, pre and post surgery ovulation rates, pre and post surgery pregnancy rate, time until ovulation and pregnancy after surgery were documented.

RESULTS: 136 patients who underwent LOD were included in this study. Demographics were divided as follows: mean age 28.9; mean BMI 22.2 kg/m², and mean duration of infertility 2.9 years. Race was divided as follows: 58.8% Caucasian, 22.8% Hispanic, 14% African American, 3.7% Asian, 0.7% other. Tobacco use was reported by 4.4% and social alcohol use was reported by 37.5%. 39.0% reported successful ovulation with drugs prior to surgery but were unable to achieve a pregnancy. Ovulation after LOD was reported by 77.2% with a live birth rate of 47.1% and mean time until ovulation of 70.9 days. Statistical analysis showed a woman was 2.27% (95% CI 1.83 - 2.82) more likely to ovulate following LOD. This was considered significant on a Chi Square test (X² = 69.8, P<0.05). Furthermore, a patient was 1.95% (95% CI 1.48 - 2.58) more likely to achieve a live birth following LOD with a mean time of 241.1 days until pregnancy. This was also considered significant on a Chi Square test (X² = 22.9, P<0.05). (Table 1).

CONCLUSION: Our study demonstrates slightly improved ovulation and pregnancy rates in drug resistant PCOS women after LOD. Although the rates are lower than those reported in previous published studies, this may be attributed to 37 out of 136 patients (27.2%) being lost to follow up. Some patients also did not achieve desirable results after the surgery due to other factors like male infertility, marital issues and diagnosis of cancer.


SUPPORT: NONE.

P-779 Wednesday, October 16, 2019 6:30 AM

IMPACT OF SAFETY PROTOCOL IN AN AMBULATORY SURGICAL SETTING VS A HOSPITAL SETTING FOR LAPAROSCOPIC-ASSISTED MYOMECTOMY (LAM). Mamta Mamik, MD, Vanesa Sarfoh, MD MPH, Nilofar Kazi, BS, Faraj Touchan, MD, Leah Haworth, BS, Louise Van Der Does, PhD, Natalya Danilyants, MD, Paul Mackoul, MD "Center for Modern Surgery, Montclair, NJ; "Center for Innovative Gyn Care, Rockville, MD; "The Center for Innovative GYN Care, Rockville, MD; "Center for Innovative GYN Care, Rockville, MD.

OBJECTIVE: Ambulatory surgery center (ASC) for major gynecological surgery improves efficiency and decreases cost compared to a hospital setting. Protocols to ensure safety when performing major gynecologic surgeries are critical in the ASC setting. The objective of this study is to assess whether protocols do ensure safety when performing major gynecological surgeries such as laparoscopic-assisted myomectomy (LAM) in a high-volume ASC and compare it with protocols and outcomes in a hospital setting.

DESIGN: This is a descriptive / retrospective study.

MATERIALS AND METHODS: This paper descriptively outlines the similarities and differences of a surgical safety protocol in an ambulatory surgery center compared to a hospital setting. Furthermore there is retrospective analysis of LAM outcomes that are commonly considered as safety standards in both settings including intraoperative and postoperative complications.

RESULTS: The protocols were similar with regards to preoperative patient selection and checklist, surgical precautions including prevention of retained surgical items, DVT prophylaxis, infection control, surgical wound classification, vaginal and genital antisepsis for the surgical patient, postoperative care in PACU and discharge criteria for surgical management.

The major preoperative differences from hospital protocol were transfusion criteria preoperatively. In the ASC, a cut-off of 9.0 g/dl was used, and a cut-off of < 7.5 g/dl was used in the hospital setting. LAM cases are only scheduled as morning cases. 23 hour observation is available at ASC. Additionally myomectomy patients at the ASC have STAT (blood analysis system to check Hemoglobin/Hematocrit) prior to procedure and at 1 and 2 hours after the procedure in the PACU to detect any signs of bleeding. Any patients that did require blood transfusion postoperatively were transferred to the local hospital from the ASC.

There were 588 patients that underwent LAM at the ASC compared to 228 patients at the hospital. There was no significant difference in case complexity factors between settings including BMI, number of previous abdominal and pelvic surgeries or other comorbidities. Intraoperative complication rate was 3.4% (95% CI 1.8-5.0) at the ASC compared to 4.9% (95% CI 1.7-8.1) , p = 0.4430. There were no significant differences in postoperative complications between the ASC and the hospital setting including infections and thromboembolic events. Blood transfusion was required in 1.7% of the cases at ASC compared to 8.8% at the hospital setting. The estimated blood loss and average fibrinogen weight were not statistically different between the two groups.
CONCLUSIONS: The LAM safety protocol at a free-standing ASC allows for patient complication outcomes that are comparable to an in-hospital setting without apparent limitations in patient complexity.

P-780 Wednesday, October 16, 2019 6:30 AM

OVARIAN CYSTS REQUIRING SURGERY AND INFERTILITY. Lisa M. Shandley, MD, MSc, Jessica B. Spencer, MD, MSc, Lauren M. Kipling, MPH, Banna Hussain, MPH, Ann C. Mertens, PhD, Penelope P. Howards, PhD, Emory University School of Medicine, Atlanta, GA; Emory University Rollins School of Public Health, Atlanta, GA; Aflac Cancer Center, Atlanta, GA.

OBJECTIVE: Benign ovarian cysts are a common condition in reproductive-aged women. The long-term effect of surgery for ovarian cysts on fertility remains unknown.

DESIGN: Women aged 22-45 years were interviewed about their reproductive histories (n=2,219), including whether they ever had infertility (defined as 12 months of unprotected sex without getting pregnant) or surgery for ovarian cysts. Women who reported a hysterectomy prior to ovarian cyst surgery were excluded. A subset of women (n=717) was invited to attend a clinic visit where markers of ovarian reserve (anti-Müllerian hormone [AMH], antral follicle count [AFC]) were measured. Women who reported surgery for benign ovarian cysts were compared with those who did not report ovarian cyst surgery.

MATERIALS AND METHODS: To account for age at surgery, each woman with a history of ovarian cyst surgery was randomly matched to a woman without surgery who was the same age, race, and parity. The artificial age at surgery equal to that of her match. This matching was repeated 1000 times. For each matching iteration, adjusted Cox models were fit examining time to infertility after surgery; the median hazard ratio (HR) and 95% simulation intervals (SI) are reported. Log-transformed and negative log binomial models were fit for AMH and AFC, respectively, to examine the relationship between ovarian reserve and history of ovarian cyst surgery; AMH and AFC were predicted for a woman at the median age at clinical visit.

RESULTS: Approximately 6.6% of women reported ovarian cyst surgery. The median age at surgery was 26 years. Women with and without ovarian cysts requiring surgery were similar with regards to race, level of education, relationship status at the interview, income, health insurance status, and body mass index. Infertility after age at surgery was more common for women reporting ovarian cyst surgery than those without surgery after adjusting for age, history of cancer, race, body mass index, parity before surgery age, and history of infertility before surgery age (median HR 1.74, 95% SI 1.06-2.94). This difference remained after also adjusting for history of endometriosis (median HR 1.79, 95% SI 1.02-3.23). The difference was more marked amongst those who reported attempting pregnancy (median HR 2.49, 95% SI 1.16-6.40). The model-based predicted mean level of AMH and AFC were predicted for a woman at the median age at clinic visit.

OBJECTIVE: To test the feasibility of rete tests ultrasound guided puncture in humans for either sperm retrieval or spermatogenic stem cell injection and colonization.

DESIGN: Tests ultrasound exploration first in rhesus monkeys, and later in humans undergoing vasectomy reversal or micro-surgical tests sperm retrieval (TESE).

MATERIALS AND METHODS: 7 Rhesus monkeys were anesthetized and subjected to ultrasound guided exploration of each testis. In one animal with large testis, it was difficult to visualize the rete. But in all animals, a 25 gauge needle was used to puncture the rete under ultrasound guidance. Then the same technique was applied to humans undergoing conventional micro-TESE or microsurgical vasectomy reversal.

RESULTS: Germ cells were successfully retrieved from all 6 Rhesus monkeys in which the rete could be visualized. Visualization depended on the proper settings (Musculo-Skeletal) not the factory settings. In smaller testes, the rete was easier to see. The rete was easiest to visualize in the smaller testes. The anatomy of the human and Rhesus rete was different from what is depicted in most textbooks, which base their description and drawings on rodent testes. Actually the rete of the human and Rhesus is a linear collecting system from top to bottom in the center of the testis, similar to an apple core.

CONCLUSIONS: The rete tests is the perfect collecting point for TESE in non-obstructive azoospermia, because it will contain sperm from every single seminiferous tubule, and it is easy to visualize with the proper ultrasound settings, which makes it accessible to simple needle puncture.

P-782 Wednesday, October 16, 2019 6:30 AM

VISUALIZATION AND INJECTION OF RETE TESTIS FOR GER M CELL TRANSPLANTATION AND SPERM RETRIEVALS IN RHE SUS MONKEYS AND HUMANS. Sherman Silber, MD, Yuting Fan, MD, Sierra Goldsmith, B.S., Infertility Center of St. Louis, Chesterfield, MO; University of Michigan, Ann Arbor, MI.

OBJECTIVE: To test the feasibility of rete tests ultrasound guided puncture in humans for either sperm retrieval or spermatogenic stem cell injection and colonization.

DESIGN: Testis ultrasound exploration first in rhesus monkeys, and later in humans undergoing vasectomy reversal or micro-surgical tests sperm retrieval (TESE).

MATERIALS AND METHODS: 7 Rhesus monkeys were anesthetized and subjected to ultrasound guided exploration of each testis. In one animal with large testis, it was difficult to visualize the rete. But in all animals, a 25 gauge needle was used to puncture the rete under ultrasound guidance. Then the same technique was applied to humans undergoing conventional micro-TESE or microsurgical vasectomy reversal.

RESULTS: Germ cells were successfully retrieved from all 6 Rhesus monkeys in which the rete could be visualized. Visualization depended on the proper settings (Musculo-Skeletal) not the factory settings. In smaller testes, the rete was easier to see. The rete was easiest to visualize in the smaller testes. The anatomy of the human and Rhesus rete was different from what is depicted in most textbooks, which base their description and drawings on rodent testes. Actually the rete of the human and Rhesus is a linear collecting system from top to bottom in the center of the testis, similar to an apple core.

CONCLUSIONS: The rete tests is the perfect collecting point for TESE in non-obstructive azoospermia, because it will contain sperm from every single seminiferous tubule, and it is easy to visualize with the proper ultrasound settings, which makes it accessible to simple needle puncture.
BACKGROUND: Cesarean section scar defect is currently a more frequently detected problem due to increased rate of cesarean section deliveries worldwide. Cesarean scar defect may be manifested by: Post-menstrual uterine bleeding, chronic pelvic pain, dysmenorrhea and dyspareunia.

OBJECTIVE: Evaluation of efficacy and safety of hysteroscopic treatment of symptomatic cesarean scar defect.

DESIGN: Prospective clinical observational study.

MATERIALS AND METHODS: ● Setting: University hospital and private gynecologic endoscopy center.

● Patients: 40 patients with symptomatic cesarean scar defect who do not desire future pregnancy with myometrial thickness ≥ 3 mm at site of cesarean scar by transvaginal ultrasonography.

● Intervention: Hysteroscopic repair of cesarean scar defect.

● Main Outcome Measure: Relief of symptoms, occurrence of operative related complications and adequacy of repair of the defect evaluated by transvaginal ultrasonography.

RESULTS: Among 40 patients postmenstrual bleeding was completely resolved in 29 patients (72.5%) of patients and partially improved in 5 patients (12.5%). On the other hand, complete relief of chronic pelvic pain was reported in 23 patients (69.7%) out of 33 patients, while partial relief was recorded in 5 patients (15.2%). As regard dysmenorrhea, complete improvement was recognized in 15 patients (60.9%) out of 23 patients, and partial improvement in 4 patients (17.4%).

CONCLUSIONS: Hysteroscopic repair of symptomatic cesarean scar defect is an efficient minimally invasive safe procedure suggested for management of this lesion.

P-784 Wednesday, October 16, 2019 6:30 AM

POST-CESAREAN SECTION VENTRAL UTERINE ADHESIONS, CLINICAL AND LAPAROSCOPIC CHARACTERISTICS OF 167 CASES. A PRELIMINARY REPORT OF UTEROLYSIS, Mahmoud A. Abdel-Aleem, MD, Ahmed M. Abbas, MD. ● Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut university, Assiut, Egypt; Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: Rising cesarean section (CS) rate increase the possibility of pelvic adhesions. A recognized type is ventral adhesions between the anterior wall of the uterus and anterior abdominal wall. The current study aims to estimate the link between post CS ventral uterine adhesions and female fertility.

DESIGN: A case control study included patients undergoing laparoscopy for secondary infertility after previous CS.

MATERIALS AND METHODS: Patients were described as "cases" if there were abnormal adhesions between the uterus and anterior abdominal wall, while "control" patients had no such adhesions. Lysis of pelvic adhesions was done up to the maximum restoration of anatomical relationship between different pelvic organs. Patients were followed for 6 months after the procedure waiting for pregnancy to occur. Quantitative variables were presented in terms of mean and standard deviation. They were compared using a Student’s t test. Qualitative variables were presented as frequency and percentage. Chi-square test was used for comparison between groups. For analysis, p <0.05 was considered to be significant.

RESULTS: The study included 167 cases (study group) and 40 patients in the control group. Adhesion between the uterus and anterior abdominal wall were mainly grade 2. Satisfactory uterolysis was achieved in 56% of cases. Pregnancy occurred in 71% of cases. Among a total of 134 patients who got pregnant over the 6 months follow up period, 88.1% were cases and only 12 % were control (P=0.000). The extent of uterine adhesions had a definite effect on the occurrence of pregnancy; most cases had either grade 1 or 2. Associated severe adnexal adhesions were commoner in patients who didn’t get pregnancy than pregnant ones (19 % vs. 0.2%).

CONCLUSIONS: Ventral adhesions between the uterus and anterior abdominal wall secondary to CS seem to have a significant impact on fertility and can be successfully treated by laparoscopic uterolysis.
transplantation of spermatogonial stem cells under conditions of testicular tissue culture. DESIGN: Testicular tissue samples from azoospermic patients were obtained and then these were freeze-thawed. Spermatogonial stem cells were isolated by digestion steps and the identification of these cells was confirmed by detecting the PLZF protein. These cells, after being labeled with DiI, were transplanted in azoospermia adult mice model. The host testes were placed on agarose gel as tissue culture system. After 8 weeks, histomorphometric, immunohistochemical and molecular studies were performed.

MATERIALS AND METHODS: For each experimental group, 3 to 5 NMRI mice were used at the age of 4 weeks. These mice are treated with Busulfan 40 mg/kg and after 4 weeks, the Azoospermia model is developed. This study is based on 5 biopsy samples taken from different obstructive azoospermic patients. SSCs were isolated by Mirzapour et al. (2012) protocol under two steps of enzymatic digestion. SSCs were transplanted into the host testes below the stereo microscope then they were cut into small pieces and placed under 3-D tissue culture conditions on the agarose support layer.

RESULTS: The results of histomorphometric studies showed that the mean number of spermatogonial cells, spermatocytes and spermatids in the experimental group was significantly more than the control group (without transplantation) (P<0.05) and most of the cells responded positively to the detection of DiI. Immunohistochemical studies in host testes fragments in the experimental group express the PLZF, SCP3 and ACRBP proteins in spermatogonial maturation, spermatocyte and spermatid, respectively, which confirmed the human nature of these cells. Also, in molecular studies of PLZF, SCP3 and ACRBP results indicated that the genes were positive in the test group, while not in the control group.

CONCLUSIONS: These results suggest that the slow freezing of SSCs can support the induction of spermatogenesis to produce haploid cells under the 3-Dimensional testicular tissue culture. References: Geens M, De Block G, Goossens E, Frederickx V, Van Steirteghem A, Tournaye H. Spermatogonial survival after grafting human testicular tissue to immunodeficient mice. Hum Reprod. 2006; 21: 390–396.

**P-787**

**Wednesday, October 16, 2019 6:30 AM**

**AUTOLOGOUS STEM CELL OVARIAN TRANSPLANTATION (ASCOT) REVITALIZED THE AGED BLOOD-BORNE SECRETOME IN POOR RESPONDER (PR) WOMEN.** Nuria Pellicer, MD, a Anna Buigues, B.Sc., b Francisco Dominguez, Ph.D., a,b Susana Martinez-Cuenca, M.D., a Antonio Pellicer, MD, c Sonia Herraza, Ph.D.d Hospital Universitario y Politécnico La Fe, Valencia, Spain; cIVI Foundation - ISSLaFe Biomedical Research Institute, Valencia, Spain; dIVI Foundation - ISSLaFe Biomedical Research Institute, Valencia, Spain; cIVI Foundation - ISSLaFe Biomedical Research Institute, Valencia, Italy; dIVI Foundation Innovation - Reproductive Medicine IIS La Fe, Valencia, Spain.

OBJECTIVE: Do the non-cellular components of ASCOT optimize impaired ovarian reserve and allowed spontaneous pregnancies in PR, by reestablishing the aged-associated plasma secretome profile?

DESIGN: Plasma samples were obtained from 17 PR women (35-40yr) recruited in the ASCOT prospective pilot study developed at La Fe University Hospital (NCT02240342). Three samples of peripheral blood were collected per patient, at recruitment (PRE), during aphaeresis for stem cell collection (APHAERESIS) and 3 months after ASCOT (POST). Plasma was obtained by centrifugation following standard procedures.

MATERIALS AND METHODS: PRE, APHAERESIS and POST paired plasma samples from same patient underwent protein relative quantitation by SWATH LCMS/MS analysis. The protein areas were calculated and normalized by the total sum of the areas of all quantified proteins. Then, statistical tests of reduction of the dimensionality, Principal component Analysis (PCA) and discriminant analysis (DA) (with Pareto scaling) were performed. Linear regression analysis was then applied to identify relevant proteins involved in differential proteomic profile between samples.
RESULTS: The dimensionality reduction tests PCA and DA showed a clear separation of PRE, ASCOT and POST samples (PC1:38.9%, PC2 16.8% and D1 50%, D2 50%). Proteomic analysis identified a total of 296 proteins in our plasma samples. Elution of proteins (3.7% PPI enrichment p = 1.56e-04) were found differentially expressed in aphaeresis when compared to previous samples, while increased to 70 (23.6%, PPI enrichment p < 0.0001). SUSD2 expression was also significantly decreased in 3D culture compared to previous samples, while we did not observe significant differences in the percentage and gene expression profile of eMSCs in vitro. Presence of higher TSP-1 aphaeresis levels were found in patients whom AMH increased (p=0.04).

CONCLUSIONS: Non-cellular components of aphaeresis could be crucial on the ovarian reserve optimization observed after ASCOT in PR. These results allowed us the identification of specific proteins related to tissue regeneration and raised the possibility of long-term systemic effects induced by stem cell, according to several spontaneous pregnancies reported up to 6 months after ASCOT treatment. Nevertheless, this is a descriptive analysis of the proteomic modifications induced by stem cell ovarian transplant that should be confirmed in a larger population of patients with advanced maternal age or diminished ovarian reserve.

P-788 Wednesday, October 16, 2019 6:30 AM
MAINTAINING ENDOMETRIAL STROMAL STEM CELLS IN A NON-SCAFFOLD BASED 3D CULTURE SYSTEM. Sule Yildiz, MD, Bahar D. Yilmaz, MD, Stacy A. Kujawa, BS, Serdar Bulun, MD. Northwestern University, Chicago, IL.

OBJECTIVE: Endometrial stem cells are crucial for the cyclical regeneration of endometrium under the orchestration of steroid hormones. Currently, there are no standardized in-vitro systems to maintain endometrial mesenchymal stem cells (eMSC) in culture. We hypothesize that culturing endometrial stromal cells in a 3-dimensional (3D) system would mimic physiologic environment more closely and overcome problems arising from contact inhibition in monolayer culture. The objective of this study is to identify a novel culturing method for endometrial stromal cells to maintain the percentage and gene expression profile of eMSCs in vitro.

DESIGN: Prospective experimental design.

MATERIALS AND METHODS: Endometrial tissues obtained from hysterectomies were enzymatically digested and cell suspension was filtered through 70 and 20 micron-sieves consecutively for isolating the stromal-enriched portion. Cells were cultured in conventional monolayer culture method till confluence and then were seeded to 96 well round-bottom ultra-low attachment plates for 3D culture and 6-well monolayer plates for 2-dimensional (2D) culture. Cell aggregates were grown in either regular culture media (DME/F12 with 10% FBS) or a mesenchymal stem cell media (MSC media). Spheroid formation was monitored every 24 hours for 3D plates via live-cell imaging. Samples were harvested at day 6 for RNA extraction, RNA expression profile was investigated by RT-qPCR.

RESULTS: Stromal cells in the 3D system formed spheroids consistently within the first 24 hours. While we did not observe significant differences in spheroid size between regular vs. MSC media, spheroids cultured in regular media had a darker center which suggests higher viability with MSC media. mRNA expression of steroid hormone receptors (ESR1, ESR2, PGR, preovulatory and progesterone endometrial stem cell markers ABCG2, SUSD2, and endometrial differentiation marker HOXA10) were analyzed. When compared to 2D, PGR expression was decreased significantly in 3D culture with both media (n=3, p<0.0001). SUSD2 expression was also significantly decreased in 3D cultures (n=3, p<0.0006). Besides, we saw a trend for HOXA10 showing decreased expression in 3D culture methods (n=3, p=0.06). Our results demonstrated that both the type of culturing plate (2D vs 3D) and the type of supplementing media are crucially important to provide optimal conditions and maintaining gene signature of endometrial stromal cell culture.

CONCLUSIONS: We suggest that a non-scaffold based 3D culture method with ultra-low attachment plates can be a promising method to maintain endometrial stem cells in culture. Decreased expression of mature endometrial stromal markers PGR and HOXA10 suggest a less differentiated stage. We, however, have not observed an increase in the expression of known stem cell markers in eMSCs cultured 3D. Our findings are the first steps in advancing consistent and accessible 3D culture system for altering the phenotype of eMSCs in-vitro and exploring their stemness potential.

SUPPORT: National Institutes of Health Grant R37-HD36891, USA.

P-789 Wednesday, October 16, 2019 6:30 AM
AUTOLOGOUS PRP FOR THE MANAGEMENT OF THIN ENDOMETRIUM IN FROZEN EMBRYO TRANSFER CYCLES: WOULD IT IMPROVE THE OUTCOME? Siddhartha Nagireddy, MCh(Reproductive medicine and Surgery),1 N. Sanjeeva Reddy, MD (Obstetrics and Gynaecology),2 DGO,3 Monna Pandurangi, MD (Ob & Gyn),4 Radha Vembu, DGO, DNB (Obstetrics and Gynaecology), MNAMS, FICS, FIGOG, PhD,5 Manjula Daniel G, PhD,6 Sindhuja Nambooriri Srinivasan, MBBS, M.Sc Clinical Embryology, PhD Research Scholar,7 Lahari Katneni, MS (Ob & Gyn),5 Assistant Professor, Sri Ramachandra Institute of Higher Education and Research, Chennai, India; Professor and Head, Department of Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, India; Associate Professor, Department of Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, India; Embryologist, Chennai, India; Bachelor of medicine, bachelor of surgery(MBBS), Msc Clinical Embryology, Chennai, India; Postgraduate in MCh Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, India.

OBJECTIVE: Autologous platelet rich plasma (PRP) has emerged as a newer modality of treatment to improve endometrial thickness (ET) in cases of thin endometrium. Platelet activation would release growth factors from the alpha granules such as VEGF, EGF, PDGF, TGF and other cytokines, which may facilitate endometrial development. The present study was aimed to study the effect of autologous PRP on endometrial development in cases of thin endometrium in frozen embryo transfer cycles.

DESIGN: Non-randomized single arm trial.

MATERIALS AND METHODS: All women aged 20 - 40 years, presenting with thin endometrium (<7mm) on day 11 of HRT (hormone replacement therapy) for FET (frozen embryo transfer) were included in the study. Patients with previous endometrial disease such as asherman syndrome, tubercular endometritis, mullerian anomalies, and premature ovarian failure were excluded. Endometrial preparation was performed by GnRHa down regulation and HRT by estradiol valerate at 6mg/day. PRP was prepared by two step centrifugation method, and administered intrauterine by IUI catheter. Reuse USG evaluation of endometrium was performed on Day 15 (4 days after PRP instillation). Statistical analysis was performed by Paired sample T test and Chi square test through SPSS version 17 software. P<0.05 was considered statistically significant.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>32 ± 3.79</td>
</tr>
<tr>
<td>Male factor</td>
<td>13 (46.4%)</td>
</tr>
<tr>
<td>PCOS</td>
<td>03 (10.7%)</td>
</tr>
<tr>
<td>Tubal factor</td>
<td>05 (17.9%)</td>
</tr>
<tr>
<td>Fibroid uterus</td>
<td>01 (3.6%)</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>01 (3.6%)</td>
</tr>
<tr>
<td>Decreased ovarian reserve</td>
<td>03 (10.7%)</td>
</tr>
<tr>
<td>Unexplained</td>
<td>02 (7.1%)</td>
</tr>
<tr>
<td>Endometrial thickness (ET) before PRP</td>
<td>6.3 ± 1.0</td>
</tr>
<tr>
<td>Endometrial thickness (ET) after PRP</td>
<td>7.0 ± 1.1</td>
</tr>
<tr>
<td>No. of patients with good endometrial vascularity (Grade II &amp; III) before PRP</td>
<td>11 (39.3%)</td>
</tr>
<tr>
<td>No. of patients with good endometrial vascularity after PRP</td>
<td>12 (42.8%)</td>
</tr>
<tr>
<td>No. of patients with improved ET (≥ 7 mm)</td>
<td>20 (71.4%)</td>
</tr>
<tr>
<td>No. of patients with cycle cancellation</td>
<td>08 (28.6%)</td>
</tr>
<tr>
<td>Pregnancy rate in transferred patients</td>
<td>35% (7/20)</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>14.2%</td>
</tr>
<tr>
<td>Miscarriage rate</td>
<td>14.2% (1/7)</td>
</tr>
<tr>
<td>Ongoing pregnancy</td>
<td>02 (10.0%)</td>
</tr>
<tr>
<td>Live birth rate</td>
<td>04 (20.0%)</td>
</tr>
</tbody>
</table>
RESULTS: Of the 28 women who presented with thin endometrium, 20 patients (71.4%) had increased ET to ≥ 7 mm, and underwent frozen embryo transfer. Eight patients (28.6%) had cycle cancellation due to persistent thin ET. There was a significant increase in the ET after PRP instillation: from 6.3 ± 1.0 to 7.0 ± 1.1 mm, P= 0.003. In transferred cycles, the pregnancy rate was 35% and implantation rate was 14.2%. The ongoing pregnancy and live birth rates were 14.2% and 20% respectively.

CONCLUSIONS: 1. Autologous PRP significantly improves endometrial thickness in cases of thin endometrium in FET cycles.

2. Intrauterine instillation of autologous PRP considerably reduces cycle cancellation in FET cycles.


CONCLUSIONS: We demonstrated that testicular cells and hESCs can be co-cultured for prolonged time in a 3D microenvironment.

SUPPORT: KY Cha Award in Stem Cell Technology.

P-791 Wednesday, October 16, 2019 6:30 AM
EXOSOMAL MIR-664-5p DERIVED FROM HUMAN BONE MARROW MESISCHYMAEL STEM CELLS IMPROVE OVARY FUNCTION OF PREMATURE OVARIAN FAILURE BY TARGETING p53 SIGNALING PATHWAY.

Bo Sun, M.D., Ph.D., Yinggu Sun, M.D., Ph.D., The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China.

OBJECTIVE: Although many reports show that various kinds of stem cells have the ability to recover the function of premature ovarian failure (POF), few studies are associated with the mechanism of stem cell treatment of POF. We designed this experimental study to investigate whether human bone marrow stem cell-derived exosomes(hMSC-Exos) retain the ability to restore ovarian function and how hMSC-Exos work in this process.

DESIGN: A POF mouse model was established and Cisplatin-damaged granulosa cells (GCs) were prepared to illuminate the mechanism of hMSCs in curing POF.

MATERIALS AND METHODS: The hematopoietic and eosin assay was employed to assess the number of follicles. Enzyme-linked immunosorbent assay (ELISA) was used to detect the serum levels of sex hormones. Cellular activity and apoptosis were measured by flow cytometry and CCK-8. Real-time PCR was used to determine protein expression levels of p53 and exosomal miRNA secreted by hMSCs. Real-time PCR was used to detect the expression of p53 mRNA and the expression of in ovarian and granulosa cells. Site-directed mutagenesis was used to establish p53 3'UTR mutant granulosa cells; miRNA mimics and miRNA inhibitor were used to target regulating the expression of hMSCs exosome-derived miR-664-5p. Western blot assays were used to test the protein expression levels of apoptosis genes (p53, Fas, FasL, caspase-3, and caspase-9).

RESULTS: After the hMSCs-Exos were transplanted into the POF mice model, they exerted better therapeutic activity on mouse ovarian function, improving follicle numbers during four stages. ELISA results showed that the level of estradiol was elevated to the normal level. After hMSCs-Exos were cocultured with POFGCs, our results showed that hMSCs-Exos significantly promoted the proliferation rate and inhibited the apoptosis rate. Besides, miRNA and protein assays demonstrated that hMSCs-Exos downregulated the expression of p53 in vivo and in vitro. A series of microRNAs targeting p53 were screened by bioinformatics, and the expression of miR-664-5p was significantly increased in MSC exosomes. Western blot assay demonstrated that hMSCs-Exos inhibited expression of the apoptosis genes in POFGCs.

CONCLUSIONS: These findings demonstrate for the first time the molecular cascade and related cell biology events involved in the mechanism by which exosomal miR-664-5p derived from hMSCs improved ovarian function of POF disease via regulation of the p53 signaling pathway.

References:
**P-792** Wednesday, October 16, 2019 6:30 AM

**IN VITRO STUDY FOR STIMULATION EFFECT OF HUMAN BONE MARROW MESENCHYMAL STEM CELL SECRETOME ON HUMAN GRANULOSA CELL.** Hang-Soo Park, PhD,4 Abdeljabar El Andaloussi, PhD,3 Rishi Man Chugh, PhD,3 Amro Elsharoud, MD,3 Mara Ulin, MD,4 Hajar Takala, MD, MPH,4 Ayman Al-Hendy, MD PhD.5 The University of Illinois College of Medicine, Chicago, IL;3The University of Illinois College of Medicine Department of Pathology, Chicago, IL.

OBJECTIVE: Primary ovarian insufficiency (POI) refers to ovarian loss of function under the age of 40 years and lead those patients to usually present by amenorrhea and infertility. One of the reasons of POI is chemotherapy for cancer patients. It is broadly believed that chemotherapy drugs may vastly eliminate granulosa cells which are essential for oocyte survival and follicular development. Our previous study shows that transplantation of human bone marrow derived mesenchymal stem cell (hBM-MSC) in chemotherapy induced POI mouse ovary can reverse POI through correction of serum hormonal level, promote follicular generation in ovary, increase in granulosa cell population, and achieving pregnancy. According to this research, BM-MSC is a promising cell source to treat POI patients, however, it is still not clear how hBM-MSC reverse POI. BM-MSC is already known that secreting various type of cytokines including growth factors and anti-inflammatory factors and some of those factors could be contribute on granulosa cell function or population in ovary. Understanding the mechanism of hBM-MSC secretome on granulosa cells will explain, how BM-MSC work to treat on chemotherapy induced POI ovary.

DESIGN: Secretome from hBM-MSC can increase the proliferation and function of human granulosa cell.

MATERIALS AND METHODS: In this study, we used hBM-MSC conditioned media (hBM-MSC CM) for secrerome treatment. HGrC1 human non-luteinized granulosa cell line (RRID:CVCL_KB28) were plated in culture flask and cultured 24 hours and treated with hBM-MSC CM. The hBM-MSC CM treated HGrC1 cells were compared with control CM treated HGc1 cells. We examined proliferation of HGrC1 cells by cell doubling time and Ki67 positive population. We also analyzed the expression of granulosa cell markers such Cyp19 and StAR at mRNA and protein level by real time RT-PCR, FACS analysis and western blot.

RESULTS: We found that hBM-MSC CM treated HGc1 cells shows higher cell number in cell counting and more Ki67 positive cells in FACS analysis. We also found that BM-MSC CM treated HGc1 cells shows higher expression of Cyp19, StAR, and FOXL2 gene quantified by real-time RT-PCR. The higher expression of Cyp19 and StAR also confirmed in protein level by FACS and Western blot.

CONCLUSIONS: Our data reveal that hMSC CM treated human granulosa cells shows higher proliferation and marker gene expression. It suggests that some factors in hBM-MSC secrerome can stimulate granulosa cell proliferation and function which can explain the therapeutic effect on chemotherapy induced POI animal model. Our study suggests that using BM-MSC secretome may present a novel treatment modality for POI patients.

SUPPORT: Startup fund of University of Illinois at Chicago.

**P-793** Wednesday, October 16, 2019 6:30 AM

**EMBRYONIC DEVELOPMENT KINETICS AFTER AUTOLOGOUS BONE MARROW MESENCHYMAL STEM CELL-DERIVED MITOCHONDRIA TRANSFER INTO COMPROMISED OCYTES: A PROSPECTIVE SELF-CONTROLLED STUDY.** Xiaolan Li, MD, Lei Jia, MD, SELF-CONTROLED STUDY. Xiaolan Li, MD, Lei Jia, MD.

OBJECTIVE: We aimed to explore whether autologous bone marrow mesenchymal stem cell(BMSC)-derived mitochondria transfer into compromised oocytes change their embryonic development kinetics and improve outcomes in women with multi-vitro fertilization (IVF)/Intracytoplasmic sperm injection (ICSI) failures due to low oocyte quality.

DESIGN: A prospective self-controlled study

MATERIALS AND METHODS: This prospective self-controlled study was conducted at the Department of Assisted Reproduction of the sixth affiliated hospital of Sun-Yat-sen University, Guangzhou, China.

CONCLUSIONS: Our data reveal that hMSC CM treated human granulosa cells shows higher proliferation and marker gene expression. It suggests that some factors in hBM-MSC secrerome can stimulate granulosa cell proliferation and function which can explain the therapeutic effect on chemotherapy induced POI animal model. Our study suggests that using BM-MSC secretome may present a novel treatment modality for POI patients.

SUPPORT: Startup fund of University of Illinois at Chicago.
embryo quality was understood as 1) no fertilized MIIIs; 2) deficient-quality embryos according to morphologic criteria; 3) arrested embryos. Patients with abnormal chromosome were excluded. BMSCs were isolated from 20ml bone marrow and cultured. Three days before oocyte retrieval, mitochondria were isolated by differential centrifugation from BMSCs. The mitochondria DNA were injected into each oocyte during intracytoplasmic sperm injection. In 710 accounts (347 TW, 363 IG) were included. Of which 537 (278 TW, 259 IG) were included. There were 4 academic/professional societies (82, 13, 14, 15), 57 (18), and 8 organizations (42, 5, 9) and 23 wellness accounts (18, 1, 10). We examined the motivations of two consecutive cleavage stages were the time from the division into a twoblastomere embryo until the time to the division into a three-blastomere embryo, and second synchrony (t2 = t4 – t3) is the time from this division into a four-blastomere embryo.

RESULTS: A total of 25 patients were included and we got 231 oocytes in total. Their average age was 33.00 years old. The average antimalerian hormone level and antral follicles was 3.86 ng/ml and 14.68 respectively. Most of patients was primary infertility (72.22%) and the major cause of infertility was tubar factor (64.0%). We observed that the timings of all embryo cleavage stages (from 2to 8) together with fragmentation values showed no significant differences between embryos deriving from oocytes with MT or without MT. It was noteworthy that t2 was shorter in MT group, although differences didn’t reach statistical significance (4.20 vs. 5.90). In addition, Ococytes of MT group had lower higher fertilization rate (89.06% vs. 88.35%; P=0.865).

CONCLUSIONS: This study demonstrated that BMSC-derived autologous mitochondria transfer didn’t alter embryonic development kinetics. It might help to improve embryo development synchrony and fertilization.

THE WEB

P-794 Wednesday, October 16, 2019 6:30 AM

HASHTAGS AND HATCHING: AN ANALYSIS OF INFORMATION AND INFLUENCE IN FERTILITY-RELATED SOCIAL MEDIA. Arielle H. Bayer, MD, a Jennifer K. Blakemore, MD, a Meghan B. Smith, MD, a James A. Grifo, MD, PhD, a NYU Langone School of Medicine, New York, NY. aNYU University of Southern California, Los Angeles, CA. aNYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: 79.9% of patients surveyed in a fertility clinic felt social media (SM), the use of electronic communication to share information, benefited the patient experience.1 Up to 40% of Americans doubt professionally when it conflicts with web-based findings.2 We examined fertility-related SM accounts and factors that contribute to influencer status (credibility to a large SM audience).

DESIGN: Cross-sectional analysis.

MATERIALS AND METHODS: The search function of Twitter (TW) and Instagram (IG) was used on 3/26/19 to generate a list of accounts with the terms: fertility, infertility, ttc, egg freezing, ivf, endometriosis and reproductive. Accounts not in English, private, no posts in > 1 year, or content unrelated to infertility were excluded. Between 3/31/19 - 4/7/19, accounts were assessed for: author type; REI board certification (REI-BC); influence (INF) status (>10K followers on IG); verified check mark on TW); age of account (mo); number (n) of followers; n of posts; hashtags and content in last 5 posts. Statistical analysis included unpaired t-tests and a classification and regression tree (CART) using n of posts per month (ppm) and most frequent posts. Statistical analysis included unpaired t-tests and a classification and regression tree (CART) using n of posts per month (ppm) and most frequent posts. Statistical analysis included unpaired t-tests and a classification and regression tree (CART) using n of posts per month (ppm) and most frequent posts. Statistical analysis included unpaired t-tests and a classification and regression tree (CART) using n of posts per month (ppm) and most frequent posts.

Table 1. Interest in Topics Posted by Physicians

<table>
<thead>
<tr>
<th>Topic</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical facts</td>
<td>91.2%</td>
</tr>
<tr>
<td>Behind the scenes as a physician</td>
<td>88.1%</td>
</tr>
<tr>
<td>News-worthy research</td>
<td>87.6%</td>
</tr>
<tr>
<td>Work-life balance</td>
<td>86.6%</td>
</tr>
<tr>
<td>Clinical cases</td>
<td>84.6%</td>
</tr>
<tr>
<td>Behind the scenes personal</td>
<td>78.3%</td>
</tr>
<tr>
<td>Motivational posts</td>
<td>77.4%</td>
</tr>
<tr>
<td>Medical pictures</td>
<td>73.8%</td>
</tr>
<tr>
<td>Educational videos</td>
<td>73.7%</td>
</tr>
<tr>
<td>Local activities</td>
<td>68.7%</td>
</tr>
<tr>
<td>Live Q&amp;A</td>
<td>62.7%</td>
</tr>
<tr>
<td>Path to becoming a physician</td>
<td>62.6%</td>
</tr>
<tr>
<td>Giveaways</td>
<td>50.4%</td>
</tr>
</tbody>
</table>

FERTILITY & STERILITY® e421
doctor does (55.6%), getting to know their doctor better (48.6%), understanding their health better (41.1%), and feeling like their doctor is up to date with technology (33.1%). Topics of highest interest included medical facts, behind the scenes, and news-worthy research (Table 1). Of the 24.7% of respondents who do not follow physicians, 44.2% reported they did not know physicians to follow and 23.3% felt like physicians were advertising.

CONCLUSIONS: As consumers have a high interest in utilizing social platforms for access to medical information, physicians have an opportunity to reach potential patients through utilization of popular platforms for education and patient recruitment. Given that Instagram is currently the platform with the highest usage and interest for medical information, physicians and medical practices should consider initiating or expanding use of this platform.

P-796 Wednesday, October 16, 2019 6:30 AM
NATIONAL INFERTILITY AWARENESS WEEK AND INTERNET SEARCH VOLUME: A GOOGLE TRENDS ANALYSIS
Mehul S. Patel, MD,a Joshua A. Halpern, MD, MS,a Anne L. Darves-Bornoz, MD,b Mary Kate Keeter, MPH,a Nelson E. Bennett Jr., MD,a Robert E. Brannigan, MD,a,b Northwestern University Feinberg School of Medicine, Chicago, IL; bVanderbilt University, Nashville, IL.

OBJECTIVE: National Infertility Awareness Week (NIAW) aims to raise awareness among the general public regarding infertility and “remove the stigmas and barriers that stand in the way of building families.” While the success of other health awareness campaigns, most notably breast cancer, have been well documented, the efficacy of infertility awareness campaigns is less well characterized. Using internet search volume as a surrogate for public interest, we sought to assess the efficacy of NIAW.

DESIGN: Retrospective, cross-sectional study examining internet search trends.

MATERIALS AND METHODS: Using Google Trends, the relative search volumes (RSV) were determined for each year from 2010 – 2018 for “infertility” and “breast cancer,” the latter serving as a comparison campaign with well-documented success. Baseline annual RSV was calculated by determining the median weekly RSV for each year. The RSV was then determined for NIAW and Breast Cancer Awareness Month (BCAM). Awareness campaign RSV was then compared with the yearly baseline RSV. Significant increase was defined as a two-fold rise from baseline.

RESULTS: Search volumes for “infertility” increased from a mean RSV of 77.5 at baseline to 97.98 during NIAW with a mean yearly search volume increase of 27.1% during the study period, not meeting the definition of significance. In contrast, BCAM led to a significant increase in mean RSV for “breast cancer” from 28.1 at baseline to 100 during the awareness month with a mean increase of 263.1%.

CONCLUSIONS: NIAW is associated with an increase in internet search volume for the term “infertility,” but this was substantially less than the increase for “breast cancer” seen during BCAM. Many parameters might influence this disparity, including duration of the campaign and resources expended for campaign promotion. While additional metrics are needed to evaluate the efficacy of public health campaigns, the current data suggest there is opportunity to further increase public awareness of infertility through the NIAW campaign.

SUPPORT: None.

TABLE 1. Percent rise in relative search volume (RSV) for the terms “breast cancer” and “infertility” during Breast Cancer Awareness Month and National Infertility Awareness Week from 2010 – 2018. *Denotes significant rise in RSV from baseline.

<table>
<thead>
<tr>
<th>Year</th>
<th>National Infertility Awareness Week (%)</th>
<th>Breast Cancer Awareness Month (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>23.5</td>
<td>284.6*</td>
</tr>
<tr>
<td>2011</td>
<td>1.8</td>
<td>257.1*</td>
</tr>
<tr>
<td>2012</td>
<td>37.0</td>
<td>334.8*</td>
</tr>
<tr>
<td>2013</td>
<td>12.8</td>
<td>308.2*</td>
</tr>
<tr>
<td>2014</td>
<td>19.0</td>
<td>316.7*</td>
</tr>
<tr>
<td>2015</td>
<td>37.9</td>
<td>257.1*</td>
</tr>
<tr>
<td>2016</td>
<td>34.2</td>
<td>194.1*</td>
</tr>
<tr>
<td>2017</td>
<td>44.9</td>
<td>203.0*</td>
</tr>
<tr>
<td>2018</td>
<td>32.5</td>
<td>212.5*</td>
</tr>
</tbody>
</table>

P-797 Wednesday, October 16, 2019 6:30 AM
CONTENT ANALYSIS OF AN ONLINE MALE INFERTILITY COMMUNITY ON THE SOCIAL MEDIA WEBSITE REDDIT.
Vadam Osadchy, BS,a Jesse Mills, MD, b Sriiram Eleswarapu, M.D., Ph.D. a,b Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, CA; Los Angeles, CA; bDavid Geffen School of Medicine at UCLA, Los Angeles, CA; University of California, Los Angeles, Los Angeles, CA.

OBJECTIVE: As social media plays an increasingly influential role in healthcare, we aimed to understand the concerns and experiences of discusants in an online male infertility community and to provide insight into their perceptions of interactions with healthcare professionals.

DESIGN: We performed a qualitative and quantitative content analysis of posts in an online male infertility community on the anonymous social media website Reddit, which represents the 3rd most visited website in the United States and 6th in the world.

MATERIALS AND METHODS: We extracted all posts from the “Male infertility” Reddit community from 11/2017 to 10/2018 and used an inducive approach to perform content analysis to identify major themes and subthemes. For semantic analysis, the Language Inquiry and Word Count 2015 program was used; Mann-Whitney U tests were employed to identify differences in the linguistic attributes of text authored by men versus their partners, when it was possible to identify author gender.

RESULTS: We analyzed 97 posts. Notable themes and subthemes emerged: 72% shared personal experiences/emotions, including feeling emasculated or alone, or describing a negative (29%), positive (13%), or neutral (58%) experience with a healthcare professional; 35% indicated searching shared experiences, such as with microdissection testicular sperm collection or use of a donor sperm; 19% posed questions about personal semen analysis (SA) results; and 14% shared resources or information. Men authored 53 posts (55%), women 21 (22%), and gender was not identifiable among 23 posts (24%). Based on semantic analysis, posts by men had higher authenticity scores (Z=3.44, p<0.001), suggesting more honest or personal text, but lower clout scores (Z=-4.57, p<0.001), suggesting a more tentative or anxious style of writing compared to posts by women.

CONCLUSIONS: To our knowledge, this study represents the first evaluation of a social media community focused on male infertility. Despite the prevalence of male factor infertility in the general population, many patients anonymously express feeling alone in their struggles with infertility, are searching for others who have gone through similar experiences, and may tie their self-worth to their ability to conceive a child. Perceived poor physician communication may compound these feelings, as nearly 20% of posts involve a question related to interpretation of SA results, even after a recent visit with a fertility specialist. These results suggest a potential role for physicians on social media to engage with patients and connect them to accurate resources. Moreover, the data also indicate opportunities to improve in-office patient education.

P-798 Wednesday, October 16, 2019 6:30 AM
MALE INFERTILITY WEBSITES: WHAT ARE OUR PATIENTS READING?
English Margaret, BS,a Wesley Yip, MD,a Manan Darshan Mehta, BS,a Mary Katherine Samplaski, MD,a Keck School of Medicine, University of Southern California, Los Angeles, CA; University of California, Los Angeles, CA; Keck USC School of Medicine, Los Angeles, CA; Keck School of Medicine, University of Southern California, Los Angeles, CA.

OBJECTIVE: People ages 20-45 years (reproductive age) have been shown to use the Internet as a source of health information more frequently than their older counterparts. We sought to evaluate the quality and readability of highly visible websites on male infertility.

DESIGN: Structured website review.

MATERIALS AND METHODS: Using Google, the first 60 relevant websites from the search “male infertility” were classified by source and analyzed. Content was evaluated by 4 blinded reviewers. We chose Google because it is the most widely used search engine, comprising 74.5% of Internet searches. Website quality of information was evaluated using the DISCERN score (assesses the quality of written information on treatment choices for a health problem), JAMA benchmark criteria (uses four core standards to evaluate web sites; authorship, attribution, disclosure, currency), and Health on the Net code (HONcode) accreditation status (assesses the reliability and credibility of online information). Readability was assessed using the Dale-Chall and Flesh Reading Ease indexes.
RESULTS: Websites were classified as: 43% hospital based, 12% fertility clinic based, 5% other clinic based, 33% society/association based, and 7% government based. The mean total DISCERN score was 44 ± 12 (maximum score 80). 75% (45/60) of websites had clear aims or achieved their aims (scores of 4 or 5 [good]), but only 15% (9/60) described areas of clinical uncertainty. 25% (15/60) described the benefits of treatments, but only 5% (3/60) described the risks of treatments. 72% (43/60) provided unbiased information. 68% (41/60) websites made it clear that there was more than one possible treatment choice. 27% (16/60) of websites encouraged shared decision making. Overall, 60% (36/60) of websites were “poor quality” (score 1-2.3) on the final question of the DISCERN instrument. Only 4/60 (6.7%) websites met all four JAMA benchmark criteria. The mean Dale-Chall score was 9.53 +/- 1.30, indicating a graduate degree level of readability. The mean Flesh Reading Ease index was 34.01 +/- 16.26, indicating a graduate degree level of readability. 20% (12/60) of websites were HONcode certified.

CONCLUSIONS: Websites on “male infertility” are of low quality, and only 6.7% met JAMA benchmark criteria. Minimal information on treatments was present, with only 25% of websites describing treatment benefits, but only 5% describing treatment risks. Only 15% of websites described areas of clinical uncertainty. Despite that these websites were written at a college to graduate degree level of reading, only 27% encouraged shared decision making. Reassuringly, most of these websites were hospital based, and 72% provided unbiased information. Patients should be cautioned that incomplete and potentially biased information on male infertility is prevalent online.

P-799 Wednesday, October 16, 2019 6:30 AM

ONLINE PATIENT EDUCATION INCREASES USE OF SINGLE EMBRYO TRANSFER. Deborah Anderson, JD FertilityIQ, San Francisco, CA.

OBJECTIVE: To ascertain to how online patient education impacts a US patient’s decision of whether to transfer one embryo per transfer (eSET).

DESIGN: 62 US patients were surveyed who met two strict criteria: #1 Would soon undergo a transfer whereby multiple embryos were available for transfer and B. Had completed a 10-minute online video course on the trade-offs of “Single or Multiple Embryo Transfer.”

MATERIALS AND METHODS: Surveys were sent to patients electronically following their date of expected embryo transfer. Results were compiled using Qualtrics Surveys & regression was run to account for patient age, embryo stage, PGT-A results and insurance coverage.

RESULTS: Of the 62 surveyed patients, 33 (79%) elected for a single-embryo transfer, of whom 72% believed the online course was “critically influential” in their decision of how many embryos to transfer. By contrast, less than 42% of patients described areas of clinical uncertainty. Despite that these websites were written at a college to graduate degree level of reading, only 27% encouraged shared decision making. Reassuringly, most of these websites were hospital based, and 72% provided unbiased information. Patients should be cautioned that incomplete and potentially biased information on male infertility is prevalent online.

CONCLUSIONS: Opportunities for personal branding and educating target populations via social media are likely underutilized by current physicians. Although the majority of physicians believe consumers enjoy medically related content on social media, there is a reluctance to posting medical content on a social platform. Efforts for personal branding and marketing could be improved by targeting popular platforms and topics preferred by the ideal audience.

P-813 Wednesday, October 16, 2019 6:30 AM

PATERNAL FACTORS AND EMBRYO ANEUPLOIDY: IS SOMETHING RELATED?; Thiago F. Nunes, MD, Andrea Belo, BSc, Nathaly M. Menezes, BSc, Thiago A. C. L. Lotfi, BSc, Nathalia Moreti, BSc, Bruna Lima, BSc, Isabela Mantelato, BSc, Caroline Fauth, BSc, Paulo Cesar Serafini, MD, Phd, Thais S. Domingues, MD, Phd, Aline R. Lorenzon, PhD, Jose Roberto Alegretti, MSc, Eduardo L. A. Motta, MD, PhD, Guilherme J. A. Wood, MD, PhD “Huntington Medicina Reprodutiva, Sao Paulo, Brazil; “Huntington Medicina Reprodutiva, Embryology Department, Sao Paulo, Brazil; “Scientific Coordinator, Huntington Medicina Reprodutiva, Sao Paulo, Brazil.

OBJECTIVE: The high incidence of aneuploidy observed in preimplantation embryos is one of the most significant factors affecting the clinical outcomes in assisted reproduction treatments. We investigate the correlation between paternal factors that could have impact on embryo aneuploidy in an oocyte donation program, including male age, sperm concentration, morphology and DNA sperm fragmentation.

DESIGN: Retrospective analysis of Preimplantation Genetic Testing for Aneuploidy (PGT-A) data of biopsied embryos from an oocyte donation program in a private clinic in Sao Paulo, Brazil.

MATERIALS AND METHODS: The present study analyzed cycles from an oocyte donation program, which minimized the impact of maternal factors arising from the female gamete. Between January 2017 and March 2019, a total of 229 biopsied embryos from 75 cycles have been analyzed by NGS (next generation sequencing) for numerical and structural abnormalities in chromosomes. Embryo biopsies were performed at blastocyst stage (day 5 or 6), and were allocated according to paternal age in two groups: <= 41 years (n = 26) and > 42 years (n = 49); sperm concentration in normozoospermic (n = 67) and oligozoospermic (n = 8); morphology according to ISCO strict criteria (n = 49, > 40%, n = 26) and < 4 (n = 58). DNA sperm fragmentation has been assessed in 29 cases.

RESULTS: The results show a median paternal age of 44.7 years, with an average number of fertilized embryos of 6.2 and 1.9 of blastocystcs at day 5 and 6. Of the 229 biopsied embryos, 143 were normal and 86 altered embryos
Achieving an optimal proportion of mature oocytes may enhance fertilization potential, and 37.5% in the minimal groups (P < 0.0001), whereas pregnancy loss rose inversely with oocyte maturity, from 22.6% in the optimal group to 29.1% in the minimal group (P < 0.0001).

CONCLUSIONS: The different ICSI outcomes seen with the use of MII oocytes can only be explained by differences in ooplasmic maturity. Achieving an optimal proportion of mature oocytes may enhance fertilization and consequent embryo development and implantation.

OBJECTIVE: To determine the incidence of euploidy and implantation and delivery of blastocysts derived from 0PN and 1PN compared with 2PN embryos.

DESIGN: Single center retrospective review of PGT-A cases over a 4 year period (2015-2018) where a biopsy and ploidy determination was performed on blastocysts (blasts) derived from zygotes where pronuclei (PNs) were either not evident (0 PN) or only 1 pronucleus (1 PN) was evident at the 18 hours post insemination or ICSI. The number of PNs in each egg is recorded and zygotes cultured individually. Cases where ≤50% of the mature eggs exhibit 2PN are routinely rechecked later on Day 1 and omitted from this study if additional PNs seen. In cases for PGT-A, all viable inseminated eggs excluding those with ≥3 PN remain in culture to Day 6/7. Good quality blastocysts with a distinct Inner cell mass and cohesive trophectoderm are considered for PGT-A regardless of

(37.55%), including 79 numerical and 7 structural abnormalities. Comparing the variables, the advanced paternal age was not related to an increase in the absolute number of embryo aneuploidy (P = 0.15). The sperm concentration showed no statistical difference between normo and oligospermic males (P = 0.70). According to strict morphology, Kruger < 4% had 36% of aneuploidy comparing with 42.5% in Kruger ≥ 4 (P = 0.38). Comparing sperm DNA fragmentation and aneuploidy, we did not observe difference between the groups using a cut-off of 15% in the fragmentation rate (P = 0.08).

CONCLUSIONS: Therefore, these results suggested that the paternal factors, including age, sperm count, strict morphology and DNA sperm fragmentation were not related to the aneuploidy rate in preimplantation embryos in an oocyte donation program.

**P-814 Wednesday, October 16, 2019 6:30 AM**

**THE NUCLEAR AND CYTOPLASMIC MATURITY OF RETRIEVED OOCYTES CONTRIBUTE TO ICSI OUTCOME.** Derek Keating, B.A., Alessandra Parrella, M.Sc., Mohamad Irani, MD, Zev Rosenwaks, M.D., Gianpietro D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To evaluate whether the proportion of mature oocytes retrieved affects clinical intracytoplasmic sperm injection (ICSI) outcome.

DESIGN: Consenting couples with a female partner ≤35 years of age treated by ICSI at our center between 1993 and 2017 were included in this study. Cycles were allocated to four groups based on the proportion of metaphase-II (MII) oocytes at the time of injection: optimal (100-76%), adequate (75-51%), partial (50-26%), and minimal (25-1%). Clinical outcome was compared among the four groups.

MATERIALS AND METHODS: Couple age, body mass index, smoking and drinking habits, and demographics were controlled for in our study. Oocyte retrieval and the ICSI procedure were performed in the standard fashion. Cycles without oocytes injected on the day of retrieval were excluded. Embryology and clinical outcome were recorded.

RESULTS: In total, there were 7,672 ICSI cycles included: 4,838 in the optimal group, 2,252 in the adequate group, 518 in the partial group, and 64 in the minimal group. There was no difference in the average number of oocytes retrieved per cycle.

Among the four groups, a decreasing proportion of MII oocytes lowered the fertilization rate from 78% to 71% (P < 0.0001) while raising the rate of 3PN embryos from 2% to 4% (P < 0.01). There was a concurrent reduced number of good-quality embryos (P < 0.0001) that resulted in a decreasing number of blastocysts cryopreserved (P < 0.0001).

The implantation rate fell from 33% in the optimal group to as low as 17% in the minimal group (P = 0.0001); thus, the clinical pregnancy rate dropped from 63.6% in the optimal group to 60.9% in the adequate, 52.1% in the partial, and 37.5% in the minimal groups (P < 0.0001). Consequently, the live birth rate decreased from 49.2% in the optimal group to 26.6% in the minimal group (P < 0.0001), whereas pregnancy loss rose inversely with oocyte maturity, from 22.6% in the optimal group to 29.1% in the minimal group (P = 0.0001).

CONCLUSIONS: The different ICSI outcomes seen with the use of MII oocytes can only be explained by differences in ooplasmic maturity. Achieving an optimal proportion of mature oocytes may enhance fertilization and consequent embryo development and implantation.

**P-815 Wednesday, October 16, 2019 6:30 AM**

**LONG-ANTAGONIST PROTOCOL: A NEW PROTOCOL WHERE A BOLUS LUTEAL DOSE OF LONG-ACTING GnRH-ANTAGONIST DEGARELIX CAN EFFICIENTLY DOWNREGULATE LH DURING OVARIAN STIMULATION FOR IVF ADDRESSING FLEXIBILITY IN AN ANTAGONIST PROTOCOL.** Evangelos Papanikolaou, MD, PhD, Evangelia Timotheou, MSc, Carlo Alivaggi, MD, PhD, Petroula Tatsi, MSc, Tatiana Charitmatosidou, MSc, Eirini Asouchidou, MD, PhD, Dimitrios Petriogianis, Sr. MD, PhD, Robert Najdecki, MD, PhD, Apostolos Athanasiadis, MD, PhD “Assisting Nature, Center of Assisted Reproduction and Genetics, Thessaloniki, Greece; “Fertility Unit, University of Naples Federico II, Naples, Italy; “Medical Department, Aristotle University of Thessaloniki, Thessaloniki, Greece; “PetriogianisKosimos, Deputy Director of IVF Unit Naval and Veterans Hospital of Athens, ATHENS, Greece; “3rd Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Thessaloniki, Greece.

OBJECTIVE: The purpose of that study was to evaluate whether a bolus luteal dose of a new long-acting GnRH-antagonist can be compared with the classical short with follicular multiple doses antagonist protocol.

DESIGN: In this randomized control trial, did participate 129 infertile women≤39 years of age prepared to undergo IVF treatment in Assisting Nature Centre. Trial registration number was NCT03684421 and performed between January 2017-January 2019. Two groups of patients were compared: Control-Group (Short Antagonist group) consisted of 69 women, who followed a classic fixed day-6 GnRH-antagonist protocol whereas, Study-Group (new Long Antagonist Group) involved 60 women undergoing the new long-antagonist protocol.

MATERIALS AND METHODS: The new protocol was as follows: in late luteal phase (day-24) a bolus injection of 0.5 ml Degarelix was administrated subcutaneously. After menses, initiation of ovarian stimulation was flexible, with gonadotropins (200-300IU) could be initiated from cycle-day-2 to cycle-day-10 and no other dose of antagonists was allowed. In the classical short antagonist-group gonadotropins 200-300IU started on day-2 or 3 of the cycle and the 0.25 mg of antagonist (ganiirelix) was administered daily from stimulation day-6 in a fixed way. Ovulation triggering was administered when 3 follicles of 18mm were present and recHCG was used (unless more than 14 follicles were present then agonist triggering was proffered). Oocyte pick and performed 36h later. Classical long agonist protocol, the security of the antagonist protocol, and eventually similar pregnancy efficacy as both of them used to. This new Long-Antagonist protocol addresses cycle programming that was missing with antagonist protocols and at the same time minimizes the risk for OHSS. It is for first time that a single dose of long-acting antagonist Degarelix, during luteal phase is described to efficiently down-regulate LH, produce mature eggs and implantable embryos. However, larger studies are required to confirm the success of this protocol.

**P-816 Wednesday, October 16, 2019 6:30 AM**

**EUPLOID EMBRYOS WHEREA ONLY 1PN OR NO PRONUCLEI (PN) WERE SEEN HAVE DELIVERY RATES COMPARABLE TO EUPLOID 2PN EMBRYOS.** Caroline McCaffrey, Ph.D., David H. McCulloh, Ph.D., Hsiao-Ling Lee, BS, Andria G. Besser, MS, Xinjian He, MS, Frederick L. Licciardi, M.D., James A. Grifo, MD, PhD “New York Langone Health, NYU Fertility Center, New York, NY; “NYU Langone Fertility Center, New York, NY; “NYU Langone Health, New York, NY.

OBJECTIVE: To determine the incidence of euploidy and implantation and delivery of Blastocysts derived from 0PN and 1PN compared with 2PN embryos.

DESIGN: Single center retrospective review of PGT-A cases over a 4 year period (2015-2018) where a biopsy and ploidy determination was performed on blastocysts (blasts) derived from zygotes where pronuclei (PNs) were either not evident (0 PN) or only 1 pronucleus (1 PN) was evident at the time of fertilization check.

MATERIALS AND METHODS: At our center fertilization checks are routinely conducted ~18 hours post insemination or ICSI. The number of PN in each egg is recorded and zygotes cultured individually. Cases where ≤50% of the mature eggs exhibit 2PN are routinely rechecked later on Day 1 and omitted from this study if additional PNs seen. In cases for PGT-A, all viable inseminated eggs excluding those with ≥3 PN remain in culture to Day 6/7. Good quality blastocysts with a distinct Inner cell mass and cohesive trophectoderm are considered for PGT-A regardless of
whether they were 0PN, 1PN or 2PN at fertilization check. PGT-A results are shown in Table 1 along with PGT-A sex of blasts derived from each group. RESULTS: CONCLUSIONS: Prior to utilization of PGT-A and/or time-lapse zygotes not exhibiting 2PN at fertilization check were routinely discarded. However, it is now obvious that a percentage of these, albeit small, are fertilized normally and are euploid. Though they account for only a small percentage, they may be the only euploid blast available. Implantation rates and LR rates following transfer of these blasts are similar to those for 2PN blastocysts. Of interest, ratios of XX:XY blasts derived from 1PN and 0PN zygotes were skewed towards female while those from 2PN zygotes were ~1:1. It should be noted that NGS cannot detect pure haploidy (23,X) or triploidy (69,XXX) thereby possibly misdiagnosing these as euploid although our IR and LR results indicate otherwise. SUPPORT: None References: None

P-817 Wednesday, October 16, 2019 6:30 AM

SPERM MOTILITY IS ASSOCIATED WITH THE NUMBER OF GOOD QUALITY EMBRYOS PRODUCED IN WOMEN WITH DIMINISHED OVARIAN RESERVE. Amanda Adeleye, MD, Liza Jalalian, BS, CLS,g Teresa Leung, B.S., Fleurdeliza Rabara, BS, CLS,c Marcelle I. Cedars, MD, Mitchell P. Rosen, MD, HCLD, UCSD REI fellow, San Francisco, CA; gUniversity of California San Francisco, San Francisco, CA; cUniversity of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA. BACKGROUND: Previous data suggests that semen parameters do not predict pregnancy rates after in vitro fertilization (IVF) in egg donation (OD) cycles. Less is known about the impact of semen parameters on IVF laboratory outcomes with good quality eggs and among women with diminished ovarian reserve (DOR) for who may be more sensitive to subtle differences in semen parameters. OBJECTIVE: To determine if semen parameters are associated with (1) IVF laboratory outcomes among egg donors with multiple cycles (2) IVF outcomes among women with DOR. DESIGN: Retrospective cohort study MATERIALS AND METHODS: Records of oocyte donation cycles performed at a single ART center from November 2011 through April 2019 were evaluated by linear regression analysis. RESULTS: A total of 91 oocyte donation cycles among 18 oocyte donors were analyzed. Number of normally fertilized eggs, number of good quality embryos (embryo(s) transferred + cryopreserved) and euploid rate were assessed in donor cycles and DOR with a mixed effects Poisson regression adjusting for age, eggs collected and repeated cycles. RESULTS: 465 egg donation cycles and 2,456 DOR cycles were reviewed. The number of normally fertilized eggs differed in egg donation cycles in a univariate and multivariate model but these were not explained by semen parameters or male or female age (p > 0.01 for both). There were no differences in the number of good quality embryos produced (p = 0.700). Among women with DOR, in a bivariate model adjusting for the number of eggs inseminated, sperm concentration was predictive of the number of normally fertilized embryos (p = 0.037). After adjusting for male and female age and the method of sperm procurement (ejaculation vs surgical), concentration was not predictive of the number of normally fertilized eggs (p = 0.082). In a bivariate model, adjusting for the number of normally fertilized eggs, motility was predictive of the number of good quality embryos (p = 0.042). Adjusting for male and female age and the method of sperm production, motility continued to be marginally predictive of the number of good quality embryos produced (p = 0.046). A 10% increase in motility was associated with a predicted 0.012 increase in the number of good quality embryos. CONCLUSIONS: When adjusting for within patient and between patient differences, semen parameters do not impact donor egg cycles but other male related predictors yet to be elucidated that impact fertilization. Among women with DOR, increased sperm motility is marginally associated with an increasing number of good quality embryos. Eggs from women with DOR may be less able to compensate for abnormal sperm function. SUPPORT: None

P-818 Wednesday, October 16, 2019 6:30 AM

EVIDENCE-BASED EVALUATION OF REPEATED CYCLES OF OOCYTE DONATION BY THE SAME WOMAN: TREATMENT OUTCOMES ARE NOT ADVERSELY AFFECTED BY MULTIPLE PRIOR DONATIONS. Carol Lynn Curcchio, PhD, TS (ABB), Ashley Geka, BS, Heather Coulter, B.S. M.A., Rebecca Gu, MS, V. Julie Collier, TS, Sara Berkshire, BA, Lindsay Gates, BS, L.Linda Anderson, BA, TS (ABB), Sigourney Anne Francisco, BS, Vanessa Julaton, PhD, TS (ABB), Jennifer Collins, MS, William Venier, MSc, ELD (ABB), Susanna Park, MD, Brooke Friedman, MD, Said Daneshmand, MD, Sandy Chuan, MD, L. Michael Kettel, MD San Diego Fertility Center, San Diego, CA. OBJECTIVE: To evaluate the quality of oocyte cohorts retrieved from healthy young women undergoing repeated cycles of oocyte donation. DESIGN: Retrospective cohort study MATERIALS AND METHODS: Records of oocyte donation cycles performed at a single ART center from November 2011 through April 2019 were reviewed. The associations between oocyte donation cycle number and pretreatment antral follicle count (AFC), total dosage of follicle-stimulating hormone (FSH) administered during ovarian stimulation, days of ovarian stimulation, follicles > 14 mm at trigger, retrieved oocyte number, mature (MII) oocyte number, the number of good quality blastocysts, and the percentage of euploid blastocysts among cycles undergoing PGT-A analysis by NGS were evaluated by linear regression analysis. RESULTS: A total of 91 oocyte donation cycles among 18 oocyte donors (3 to 6 cycles each) were available for analysis. The total dosage of FSH administered per cycle remained constant across treatment cycle numbers. However, a higher number of prior oocyte donation cycles was associated with significantly increasing numbers of antral follicles, mature follicles (>14mm) at trigger, and mature (MII) oocytes retrieved. CONCLUSIONS: Our investigative efforts focus on providing more couples the opportunity to have healthy children. One such group is egg donor recipients. There are limited available data on repeated ovulation stimulation cycles. It has been suggested that FSH stimulation may hasten ovarian aging by increasing recruitment of small growing follicles, thereby accelerating the depletion of follicle reserve. It has not been reported if repetitive oocyte donation affects average follicles recruited, oocyte maturity, blastocyst rate or ploidy status. Increasing numbers of prior oocyte donation cycles are associated with a better response to ovarian stimulation, rather than adversely affecting treatment outcomes. Egg donation cycles 3-6 are associated with higher AFC.

FERTILITY & STERILITY®

e425

TABLE 1.

<table>
<thead>
<tr>
<th>All Patient Ages</th>
<th>2PN</th>
<th>1PN</th>
<th>0PN</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conventional insemin</strong></td>
<td>Rate of Good Quality Blast form rate</td>
<td>11287/21819 (51.7%)</td>
<td>428 / 1538 (27.8%)</td>
<td>147 / 7657 (1.9%)</td>
</tr>
<tr>
<td>Number Eggs Bx'd</td>
<td>11287</td>
<td>428</td>
<td>147</td>
<td></td>
</tr>
<tr>
<td>Number Euploid Blastocysts (% Bx'd)</td>
<td>3864 (34%)</td>
<td>114 (27%)</td>
<td>35 (24%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ratio XX:XY</td>
<td>1820:2044</td>
<td>69:45</td>
<td>19:16</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td><strong>ICSI</strong></td>
<td>Rate of Good Quality Blast form rate</td>
<td>6553/12533 (52.2%)</td>
<td>76/490 (16%)</td>
<td>31/7657 (1.9%)</td>
</tr>
<tr>
<td>Number Eggs Bx'd</td>
<td>6553</td>
<td>76</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Number Euploid (% Bx'd)</td>
<td>2188 (33%)</td>
<td>29 (38%)</td>
<td>11 (35%)</td>
<td>NSD</td>
</tr>
<tr>
<td>Ratio XX:XY</td>
<td>1092:1096</td>
<td>25:4</td>
<td>7:4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Insemin-ICSI</strong></td>
<td>IR (sac/ ET) (%)</td>
<td>1235/1809 (68%)</td>
<td>24/40 (60%)</td>
<td>8/10 (80%)</td>
</tr>
<tr>
<td>Number Blasts Bx'd</td>
<td>756/1452 (52%)</td>
<td>16/36 (44%)</td>
<td>6/9 (67%)</td>
<td>NSD</td>
</tr>
<tr>
<td>LR Ratio XX:XY</td>
<td>362:394</td>
<td>11:5</td>
<td>4:2</td>
<td>NSD</td>
</tr>
</tbody>
</table>

---

In conventional insemination, the rate of good quality blast formation was 51.7%, compared to 52.2% in ICSI. There was a significant difference in the number of normally fertilized eggs (2PN) between the two groups (p < 0.001). The euploid rate was higher in ICSI (25.4%) compared to conventional insemination (25%). Insemin-ICSI had a higher IR (sac/ET) rate of 68% compared to 60% in ICSI. The number of good quality embryos transferred + cryopreserved was also higher in insemin-ICSI (44%) compared to ICSI (40%).
more follicles > 14 mm at trigger, and retrieval of approximately one third more mature (MII) oocytes, relative to cycle 1. A reevaluation of the ASRM guidelines regarding numbers of oocyte donation cycles per woman may be warranted.

References: Reproductive oocyte donation does not decrease serum anti-Mullerian hormone levels. Bukulmez, Orhan et al. Fertility and Sterility, Volume 94, Issue 3, 905 - 912


DESIGN: Prospective randomized controlled clinical trial comparing LH supplementation versus FSH only in poor ovarian responders during controlled ovarian stimulation(COS) for assisted reproductive technologies (ART).

OBJECTIVE: To compare the granulosa cells apoptosis rate with or without luteinizing hormone (LH) supplementation in poor ovarian responders during controlled ovarian stimulation(COS) for assisted reproductive technologies (ART).

MATERIALS AND METHODS: The protocol has been applied to all 40 women with poor ovarian response according to Bologna criteria enrolled. Patients were randomly separated into two clinical trial groups: 20 patients were in group A, in which ovarian stimulation included rFSH and LH, and group B, in which 20 patients received rFSH without further LH addition. After oocyte retrieval, the oocytes were extracted with hyaluronidase treatment for ART procedure by the embryologist. The rest of follicular fluid was transferred to the HLA Typing Laboratory within the same day. To eliminate the effect of hyaluronidase treatment on granulosa cell viability and apoptosis, the validation of the cytometry protocol has been performed initially.

RESULTS: Between 2015-2018, 12,583 blastocysts were vitrified in 2,139 cycles (94.2%; mean AFC ¼ 27.9). The rate of clinical pregnancy was %25 for group A whereas %20 for group B. No statistically significant differences were determined in the rate of clinical pregnancy rates were 3.0656 and 6.8267 for group A and B respectively, these differences did not reach statistical significance (p õ 0.04). Similarly, when clinical pregnancy rates were analyzed, no significant difference were observed; the rate of clinical pregnancy was <25% for group A and >20% for group B.

CONCLUSIONS: The results of this prospective and randomized trial show that the supplementation of LH in COS for ART decreases the late granulosa cell apoptosis rate in poor ovarian responder patients. Although LH supplementation seems necessary in poor responders to decrease the late granulosa apoptosis rates, this does not improve clinical pregnancy rates.

P-819 Wednesday, October 16, 2019 6:30 AM

DOES LH SUPPLEMENTATION IN POOR RESPONDERS AFFECT GRANULOSA CELL APOPTOSIS RATE IN ART?. Sebnem alanya Tosun, MD,a Enis Ozkaya, MD,b Basak Aru, PhD,c Guldenler Yanikka Demirer, MD, PhD,d Ebuc Cogenduz, Jr., MD,e Mehmet Sipahi, MDf Giresun University School of Medicine, Department of Obstetrics and Gynaecology, Giresun, Turkey;g Zeynep Kamil Women and Children Diseases Education and Research Hospital, Istanbul, Turkey; h Yeditepe University, School of Medicine, Istanbul, Turkey; i Yeditepe University, Faculty of Medicine, Istanbul, Turkey; j Zeynep Kamil Women and Children Education and Research Hospital, Istanbul, Turkey.

OBJECTIVE: To compare the granulosa cells apoptosis rate with or without luteinizing hormone (LH) supplementation in poor ovarian responders during controlled ovarian stimulation(COS) for assisted reproductive technologies (ART).

DESIGN: Prospective randomized controlled clinical trial comparing LH supplementation versus FSH only in poor ovarian response patients.

MATERIALS AND METHODS: A total of 40 women with poor ovarian response according to Bologna criteria enrolled. Patients were randomly separated into two clinical trial groups: 20 patients were in group A, in which ovarian stimulation included rFSH and LH, and group B, in which 20 patients received rFSH without further LH addition. After oocyte retrieval, the oocytes were extracted with hyaluronidase treatment for ART procedure by the embryologist. The rest of follicular fluid was transferred to the HLA Typing Laboratory within the same day. To eliminate the effect of hyaluronidase treatment on granulosa cell viability and apoptosis, the validation of the cytometry protocol has been performed initially.

The verified flow cytometry protocol analyzing with Annexin V-FITC/Propidium Iodide has been applied to all 40 women to determine the apoptosis rate of granulosa cells. A sufficient number of cells required for evaluation could not be obtained from 5 samples of study group, 4 samples of control group and were excluded from the study.

Primary outcome measure was granulosa cells apoptosis rate in terms of viability, early apoptosis, late apoptosis and necrosis. Secondary outcomes were total r-FSH dose, metaphase II oocytes retrieved, clinical pregnancy rate.

RESULTS: No statistically significant differences were determined in mean age, BMI, duration of infertility, FSH level, AMH level and AFC between the groups. Mean values of viability were 93.30 and 74.74 for groups A and B respectively (p<0.001). The granulosa cells apoptosis rates were compared as early apoptosis, late apoptosis and necrosis. Late apoptosis rates were significantly lower in group A (mean value = 4.2975) than group B (mean value = 17.3473)(p<0.001). Interestingly, although early apoptosis rates were 3.0656 and 6.8267 for group A and B respectively, these differences did not reach statistical significance (p=0.04). Similarly, when clinical pregnancy rates were analyzed, no significant difference were observed; the rate of clinical pregnancy was <25% for group A and >20% for group B.

CONCLUSIONS: Since 2014, our clinical practice has predominantly (>85%) applied blastocyst biopsy/PGT-A. A sufficient number of cells required for evaluation could not be obtained from 5 samples of study group, 4 samples of control group and were excluded from the study.

Primary outcome measure was granulosa cells apoptosis rate in terms of viability, early apoptosis, late apoptosis and necrosis. Secondary outcomes were total r-FSH dose, metaphase II oocytes retrieved, clinical pregnancy rate.

RESULTS: No statistically significant differences were determined in mean age, BMI, duration of infertility, FSH level, AMH level and AFC between the groups. Mean values of viability were 93.30 and 74.74 for groups A and B respectively (p<0.001). The granulosa cells apoptosis rates were compared as early apoptosis, late apoptosis and necrosis. Late apoptosis rates were significantly lower in group A (mean value = 4.2975) than group B (mean value = 17.3473)(p<0.001). Interestingly, although early apoptosis rates were 3.0656 and 6.8267 for group A and B respectively, these differences did not reach statistical significance (p=0.04). Similarly, when clinical pregnancy rates were analyzed, no significant difference were observed; the rate of clinical pregnancy was <25% for group A and >20% for group B.

CONCLUSIONS: Since 2014, our clinical practice has predominantly (>85%) applied blastocyst biopsy/PGT-A and >99% VTF-all cycles. Vitrified embryo transfer cycles have become our clinical norm. In turn, mu-S-VTF using non-DMSO, glycerol based solutions has been associated with some of the highest % healthy single term live birth rate as reported by the annual CDC/ART Surveillance survey (2014-2017). mu-S-VTF has continued to be safe, secure, simple and inexpensive technique.
OBJECTIVE: Thus far, predicting segregant outcomes has been done using a diagram of the presumed pachytene configuration of the quadrivalent to deduce which modes of segregation are likely to lead the formation of embryos in reciprocal translocation carriers. However, it is very difficult to predict segregation outcomes precisely. As the Stengel-Rutkovski method (S-R method) (1998) and HC-Forum web site (HC-F site) (Cohen et al. 2001) are well known to predict risks of having "a liveborn aneuploid child" due to imbalance from 3 modes (adjacent-1 segregation (ADJ-1), adjacent-2 segregation (ADJ-2), and 3:1 segregation (3:1)), these methods have not been utilized for predicting segregation outcomes of embryos of IVF by preimplantation genetic testing for structural rearrangement (PGT-SR). It is important to know if the most frequent imbalance segregation mode for reciprocal translocation carriers can be predicted by the S-R method or HC-F site in PGT-SR.

DESIGN: Chromosome segregations in embryos of 33 female and 20 male reciprocal translocation heterozygotes were studied by PGT-SR as reported in Table 5-3 in the 5th edition of Gardner and Southerland’s “Chromosome abnormalities and genetic counseling.” Although Table 5-3 indicates that, in 53 cases, alternate segregation, ADJ-1, ADJ-2, and 3:1, each carrier had different mode patterns of segregation due to their different breakpoints. We tried to predict most frequent imbalance mode in embryos.

MATERIALS AND METHODS: We predicted “the most frequent imbalance mode” instead of risks of having “a liveborn aneuploid child” in embryos of 53 reciprocal translocation carriers using the S-R method and HC-F site. Then, we compared the most frequent modes predicted by these 2 methods with the actual most frequent modes detected by PGT-SR. We also compared the results of the S-R method with the results from the HC-F site in PGT-SR.

RESULTS: There were multiple modes of segregation in embryos in 61% female, and in 55% male carriers. The S-R method predicted the risk of having a liveborn aneuploid child was 1.81±0.60% (mean±SE) and the HC-F site predicted 18.8±1.82% in female carriers. In male carriers the risks were 3.35±1.70, and 17.60±3.82 by 2 methods. Thus, these risk figures were quite different. However, the most frequent segregation mode determined by the 2 methods was the same in 82% of the subjects in female carriers and 90% in male carriers. The most frequent segregation modes predicted by the S-R method and by HC-F site were the same in 85% and 86%, respectively, as those of the actual most frequent mode determined by PGT-SR. On the contrary, those modes by S-R method and by HC-F site were the same in 55% and 60%, respectively, as those of the actual most frequent mode determined by PGT-SR. Unfortunately, the HC-F site has been closed since December 31, 2001.

CONCLUSIONS: In PGT-SR for reciprocal translocation carriers, prediction of the most frequent imbalance segregation mode is quite important for genetic counseling. In this study, it is proposed that the S-R method and HC-F site are both good tools to predict the most frequent segregation mode of embryos for reciprocal translocation female carriers, not for male carriers.

Support: no support

References: no references

P-821 Wednesday, October 16, 2019 6:30 AM

CAN THE MOST FREQUENT IMBALANCE SEGREGATION MODE FOR RECIPROCAL TRANSLOCATION CARRIERS BE PREDICTED BY THE STENGEL-RUTKOWSKI METHOD OR HC-FORUM WEB SITE IN PRE-IMPLANTATION GENETIC TESTING FOR STRUCTURAL REARRANGEMENT?: Toshiaki Endo, M.D., Tsuyoshi Baba, M.D., Takema Kato, Ph.D., Hiroki Kurahashi, M.D. 1Assistant Professor, Sapporo, Japan; 2Sapporo Medical University, Sapporo, Japan; 3Research assistant, Nagoya, Japan; 4Div. Molecular Genetics, ICMS, Fujita Health University, Nagoya, Japan.

References: no references

Support: no support

P-822 Wednesday, October 16, 2019 6:30 AM

THE MORPHOKINETIC EFFECTS OF CULTURE MEDIA WITH LOW LACTATE DURING EARLY EMBRYONIC DEVELOPMENT. Sule Dogan, PhD, Mike Urich, BSc, Fang Li, MD PhD, Ahmad Hammoud, MD, Hanh N. Cottrell, MD, Iqbal Khan, PhD, Nicholas Shamma, MD 1IVF Michigan Fertility Clinics, Bloomfield Hills, MI; 2IVF Michigan Fertility Centers, Bloomfield Hills, MI.

OBJECTIVE: To investigate the morphokinetic effects of culture media in early embryonic development.

DESIGN: Retrospective randomized study.

MATERIALS AND METHODS: Data used in this study were collected from our routine IVF-PGT patients who used either autologous and/or donor oocytes between February and December 2018. All cases whose embryos were incubated in conventional incubators were excluded. Embryoscope slides were prepared using two different media where well 1-6 contained one media vs. well 7-12 had the second media and equilibrated overnight. On the day of retrieval, patients with at least 10 MII oocytes were randomly selected for this study. After ICSI, MII oocytes (n=35 patients, n=404 MII oocytes) were divided into two groups, and cultured in the same embryoscope (Vitrolife) slides including two different media: Group #1 (Global total by Life global) vs Group #2 (Low lactate: 1mM, CSCM-NX by Irvine). The embryos were hatched on Day 3 and trophoderm cells were counted and cultured in the same embryoscope (Vitrolife) slides including two different media: Group #1 (Global total by Life global) vs Group #2 (High lactate: 1mM, CSCM-NX by Irvine). All differences were considered statistically significant once p-values are < 0.05.

RESULTS: According to our findings, all results were shown in Table 1. The differences were considered statistically significant once p-values are < 0.05.

CONCLUSIONS: In this study, we only demonstrated that the t2 and t3 divisions were earlier, and blastulation was later in Group #1 than Group #2. Although the epuloid rate was higher in media with low lactate (Group #2), this difference was not statistically significant. In conclusion, a larger sample size is needed to conclude the positive effects of culture media with low lactate.

Support: None


Annemieke Wilcox, MD, a INTELLIGENCE. CISM THROUGH ARTIFICIAL REDUCING THE FREQUENCY OF EMBRYO MOSAIC-824 Wednesday, October 16, 2019 6:30 AM diagnoses. For women with DOR plus endometriosis, better IVF outcomes as ion of DOR and IVF outcomes is confounded by other infertility plantation rates, and lower pregnancy rates after IVF. However the associa-

‘DOR Plus Tubal factors’ or ‘DOR Plus Male factor’ had similar outcomes compared to those with ‘DOR Only’. However, women with ‘DOR Plus Tubal factors’ or ‘DOR Plus Male factor’ had similar outcomes compared to those with ‘DOR Only’. CONCLUSIONS: DOR is associated with lower oocyte yield, lower implantation rates, and lower pregnancy rates after IVF. However the association of DOR and IVF outcomes is confounded by other infertility diagnoses. For women with DOR plus endometriosis, better IVF outcomes are demonstrated.

REPRODUCTIVE GENETICS

P-824 Wednesday, October 16, 2019 6:30 AM REDUCING THE FREQUENCY OF EMBRYO MOSAICISM THROUGH ARTIFICIAL INTELLIGENCE, Amemiek Wilcox, MD, Jeffrey Thorne, MD, John Nulsen, MD, Claudio Benadiva, MD, Daniel R. Grow, MD aCenter for Advanced Reproductive Services, University of Connecticut School of Medicine, Farmington, CT; bCenter for Advanced Reproductive Services, Farmington, CT; cUniversity of Connecticut Health Center, Center for Assisted Reproductive Services, Farmington, CT.

OBJECTIVE: With the advent of Next Generation Sequencing (NGS) used in Preimplantation genetic testing (PGT), identifying mosaicism within a sample biopsy of trophectoderm has become increasingly common. While reports show that transfer of these embryos can result in live births, the implantation of mosaic embryos remains controversial. With advancement in artificial intelligence (AI) algorithms, it may be possible to detect embryo mosaicism with higher efficiency and accuracy. This study seeks to determine the difference in identification of embryo mosaicism between subjective calling (SC) by trained technicians and the use of AI algorithms at a single academic center.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: PGT data of 1,090 blastocysts from 351 patients at our center was obtained through CooperGenomics. 522 embryos evaluated using PGT with SC (4/2018 to 11/2018) were compared to 568 embryos evaluated using PGT with AI (11/2018 to 4/2019). PGT results were reported as euploid, low level mosaic (20-40% mosaicism), high level mosaic (40-80% mosaicism) and abnormal or complex abnormal (containing 3 or more aneuploid or mosaic chromosomes). Embryos listed as other contained polyembryos and those with insufficient data. Embryo data was further stratified by age. Chi-square test was used to assess categorical variables. A p-value < 0.05 was considered statistically significant.

RESULTS: Overall, PGT using AI technology identified a significantly higher percentage of euploid embryos compared to SC (45.8% vs. 33.1%, p < 0.05) as well as a lower percentage of low level mosaic embryos (5.1% vs. 12.6%, p < 0.05). The overall percentage of high level mosaics and abnormal/complex abnormal embryos identified were similar (8% vs 6.7% and 42.2% vs 37.1%, respectively). These differences persisted after stratifying by age, except in the >35yo group in which AI identified fewer abnormal/complex abnormal embryos than SC (46.6% vs. 50.0%).

CONCLUSIONS: AI technology identified a higher number of euploid embryos and fewer low level mosaic embryos, leading to the identification of more embryos suitable for transfer. Further analysis of pregnancy outcomes is needed to determine if this translates into a clinically significant increase in livebirths.


V-1 Monday, October 14, 2019 4:30 PM
TECHNIQUES FOR SUCCESSFUL VAGINAL ANASTOMOSIS IN THE UTERINE TRANSPLANT PATIENT. Jenna M. Rehmer, MD, Elliott G. Richards, MD, Cecile A. Ferrando, MD, MPH, Rebecca Flyckt, MD. Cleveland Clinic Foundation, Cleveland, OH.

OBJECTIVE: To demonstrate our techniques for successful vaginal anastomosis in the uterine transplant patient.

METHODOLOGY: We report the case of a recent uterine transplant from a deceased multi-organ donor and highlight the vaginal anastomosis portion of this multi-step surgery. This video uses live action footage from surgery and detailed descriptions review our techniques for successful vaginal anastomosis in the uterine transplant patient.

CONCLUSIONS: Following uterine transplantation, access to the donor allograft cervix is important for many reasons. Vaginal strictures pose a unique problem in this surgical population. We believe strictures result from difficulty in approximating donor vaginal mucosa to recipient vaginal mucosa, and that this is paramount in reducing this untoward postop complication. Given the difficulty of surgery and tendency for the recipient vaginal mucosa to retract, our teams has employed techniques from vaginal reconstructive surgery to reduce the occurrence of postoperative vaginal strictures.

Reference: None.

SUPPORT: No financial support to disclose.

V-2 Monday, October 14, 2019 4:42 PM
SURGICAL MANAGEMENT OF DEEP INFILTRATING ENDOMETRIOSIS INVOLVING THE RECTOSIGMOID COLON. Natalia C. Llarena, MD, Anup B. Shah, MD, MS, Hermann Kessler, MD, PhD, Tommaso Falcone, M.D., Rebecca Flyckt, MD. 1Cleveland Clinic Foundation, Cleveland, OH; 1Cleveland Clinic, Cleveland, OH; 1cleveland Clinic, cleveland, OH.

OBJECTIVE: To discuss the surgical management of deep infiltrating endometriosis involving the rectosigmoid colon.

METHODOLOGY: Here we demonstrate a case of a 34-year-old female with chronic pelvic pain, infertility, and a 1-cm rectosigmoid endometriotic implant noted on preoperative MRI. She underwent segmental bowel resection of the involved rectosigmoid colon with colorectal reanastomosis.

CONCLUSIONS: There are several surgical approaches to managing endometriosis involving the rectosigmoid colon, including rectal shaving, disc resection, and segmental resection. Segmental resection allows for complete resection of endometriotic lesions and histologic analysis of the specimen.

Reference: None.

SUPPORT: No financial support to disclose.

V-3 Monday, October 14, 2019 4:53 PM
NO-SCALPEL VASECTOMY: PUNCTURE-FIRST WITH MULTI-OCCCLUSION TECHNIQUE. Khushabu Kasahwala, MD, Helen Levey Bernie, DO MPH, Soo Jeong Kim, MD, Vanessa L. Dudley, MSMS, Marc Goldstein, MD 1New York Presbyterian - Weill Cornell Medical Center, New York, NY; 1Memorial Sloan Kettering Cancer Center, New York, NY; 1Weill Cornell Medicine, New York, NY; 1Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY.

OBJECTIVE: Vasectomy is a widely used, permanent contraceptive method. Vasectomy failure may occur secondary to recanalization (1-10%) and is a major cause of malpractice suits and pregnancy. The no-scalpel vasectomy (NSV) is a minimally invasive technique where failure rates depend on occlusion techniques. We describe a puncture-first NSV with four occlusion techniques to optimize outcomes and minimize technical difficulty.

METHODOLOGY: Men who had a puncture-first NSV by a single surgeon (MG) over 25 years (1993 - 2018) were included in this study. The procedure begins administering local anesthesia to the skin overlying the vas. The vas, excluding vasal vessels and nerves, is then delivered through a single midline puncture hole. After securing both ends of the vas and hemi-transecting them, the first occlusive step, intraluminal cautery, is performed on the testicular end of the vas by rotating the cautery for 10 seconds to ensure a 360-degree burn. A hemoclip is lightly placed on the testicular end to prevent sperm leakage until cautery causes a permanent seal. The abdominal end of the vas is cauterized intraluminally, completed transected, and allowed to retract into the vasal sheath. The sheath is grasped and sealed over the abdominal end with a hemoclip, accomplishing fascial interposition. A 5mm vas segment is excised. The ends are dabbed with betadine before retraction into the scrotum. The contralateral vas is accessed through the same puncture hole and occluded identically. No antibiotics are administered before or after the procedure. Post-vasectomy semen analysis (PVASA) is performed 6-8 weeks or 15 ejaculations after the procedure. Complications were graded using the Clavien-Dindo classification scale.

Over 25 years, 819 vasectomies were performed. The mean age of the patient and partner was 41.6 years (+/- 5.8 years) and 38.6 years (+/- 3.8 years), respectively. At least one PVSA was performed in 484 (59%) of men, at a median of 53 days post-procedure. Nearly half of those, 222 men (45%) required a second PVSA to confirm vasal occlusion. No pregnancies were reported after vasectomy. Three complications occurred including one abscess requiring incision and drainage (Grade IIIa) and two hematomas managed conservatively (Grade I). No chronic pain or orchitis was reported.

CONCLUSIONS: Vasectomy failure and complications can be minimized by utilizing a combination of four occlusion techniques: 1) intraluminal cautery for 10 seconds; 2) testicular end occluding clip; 3) fascial interposition and 4) removal of 1/2 to 1 cm segment of vas. Additionally, the puncture-first technique eliminates the need to grasp the scrotal skin with the vas in the ring clamp, decreasing technical difficulty. This technique has minimal complications and a 100% success rate in our patient cohort.

SUPPORT: No financial support to disclose.

V-4 Monday, October 14, 2019 5:06 PM
DEVELOPMENT OF AN AUTOMATIC PRONUCLEAR DETECTION SYSTEM FOR HUMAN EMBRYOS USING DEEP LEARNING TECHNOLOGY. Hiroaki Watanabe, M.S., Yoritaka Fukunaga, Ph.D., Sho Sanami, Ph.D., Hiroya Kitasaka, Ph.D., Yuta Kida, M.S., Seiji Takeda, M.S., Yoshimasa Asada, M.D., Ph.D., Asada Ladies Clinic, Nagoya, Aichi, Japan; Research and Development Center, Dai Nippon Printing Co., Ltd., Kita-ku, Tokyo, Japan.

OBJECTIVE: Fertilization is generally evaluated by pronuclear number. Correct judgment may sometimes be difficult due to morphology and number of pronuclei of pronuclear embryos.

Correct evaluation of the pronuclear number is important in order to reduce the possibility of transferring abnormal embryo.

Therefore, in this study, we aimed to develop an automatic pronuclear detection system by deep learning technology using time lapse embryo images.

Deep Learning technology is an information processing system using Deep Learning Neural Networks (DLNN). DLNN is a multi-layered combination of neural networks that mimics a cranial nerve network. This technology has several important features such as a) high-precision learning is possible, b) currently it is the highest performance image recognition method, and c) it makes effective use of all time-lapse embryo images.

METHODOLOGY: 70-80 images before and after pronuclear formation of one embryo were extracted from the time-lapse incubator. Using these 70-80 images as one set, each 400 sets of 2PN, 1PN and 0PN images that were evaluated by an embryologist were prepared in order to construct the automatic pronuclei detection system.

The automatic pronuclear detection system used DLNN which outputs the number of pronuclei to the inputted embryo image.

Of the 400 sets of images, 300 sets of each were input to the DLNN with labels of 2 PN, 1 PN and 0 PN, and the DLNN learned from these images by DL Learning.

The remaining 100 sets of images that were not used for learning, were entered without labels to the DLNN which completed the learning, and the DLNN detected the number of pronuclei from these images.

CONCLUSIONS: In 2PN embryos, the rate of correctly detected 2PN was 97% and the rate of incorrectly detected 1PN, 0PN was 3%, 0% respectively, with respect to the input of 100 unlabeled time-lapse images. In 1PN embryos, the rate of correctly detected 1PN was 68%, and the rate of incorrectly detected 2PN, 0PN was 20%, 12% respectively, with respect to the input of 100 unlabeled time-lapse images.

In 0PN embryo, the rate of correctly detected 0PN was 78%, and the rate of incorrectly detected 2PN, 1PN was 4%, 18% respectively, with respect to the input of 100 unlabeled time-lapse images.

FERTILITY & STERILITY®
As a result of this study, we succeeded in constructing a system for automatic detection of pronuclear number from embryo images using Deep Learning technology.

The correct answer rate was 97% in 2PN embryos, but the rate was lower in 1PN and 0PN embryos compared to 2PN embryos. These results are very promising, but it is necessary to improve the detection system further and apply this technology to embryos with 3 or more PN number.

Reference: None.

SUPPORT: None.

V-5 Monday, October 14, 2019 5:18 PM

TRANSGENDER YOUTH: EXPLAINING HORMONAL AFFIRMATION TREATMENT VIA POWTOON FORMAT (MTF).

OBJECTIVE: To explain to transgender youth in an animated format containing auditory, visual and written explanations, the pros and cons of hormone use that may be prescribed to them in order to achieve their desired gender changes.

METHODOLOGY: Written materials on hormonal therapy used for affirmation of gender may not be comprehensively read by young individuals seeking this intervention. To address this issue, an animated presentation was developed that addresses the pros and cons of hormonal use for gender affirmation. The script was developed by clinicians who care for transgender individuals with the input of learner and community groups. The Powtoon format was utilized for creating the animated presentations.

CONCLUSIONS: The appropriate Powtoon is being shown to transgender individuals being cared for by a pediatric endocrinologist, who has over 200 transgender youth in his practice. Parents and guardians are also encouraged to watch them. Comments have been overall positive both from the individuals being managed with hormonal therapy and the parents/guardians.

Reference: None.

SUPPORT: None.

V-6 Tuesday, October 15, 2019 4:15 PM

CONTINUOUS MONITORING OF THE EMBRYO DEVELOPMENT: A LEAP TOWARDS AUTOMATED SYSTEMS.

OBJECTIVE: To illustrate the introduction of automated systems to assess the embryos in daily clinical practice in IVF laboratories.

METHODOLOGY: More than 80,000 embryos have been cultured in time-lapse incubators since 2009 at IVIRMA Valencia. Abnormal embryo development has been observed thanks to the high number of videos available. The best examples of zygotes with one or three pronuclei and embryos with irregular divisions that achieved good quality blastocysts were gathered. Blastocysts that changed their quality few hours before embryo selection were also selected for the project. Automated systems based on image analysis technology have been introduced in our laboratory to assess embryo development. A step by step video demonstration of the automatic annotations performed by EmbryoScope ® and Geri Connect and Assess 2.0 ® was conducted. Additionally, a table of the comparison between the manual annotations performed by an embryologist team and the automated annotations performed by the software software Geri Assess 2.0.a in 1360 embryos (10,880 development events) at IVIRMA Valencia is shown. The parameters included were: pronuclear fading (tPNF), division time to 2 cells (t2), division time to 3 cells (t3), division time to four cells (t4), division time to five cells (t5), division time to six cells (t6), appearance of morula (tM) and expanded blastocyst (tEB). High accordance was found between both, showing a struggle in the detection of late parameters by the embryologist team. Finally, a demonstration of a method to measure novel embryo parameters, impossible to assess with automated systems, were performed by embryologists through the drawing tools provided by the EmbryoViewer ®. The parameters included were: blastocyst expanded diameter, inner cell mass area and trophectoderm cell cycle length. Additionally, the impact of these parameters over the implantation rate was analyzed and illustrated through graphs.

CONCLUSIONS: Time-lapse technology allows monitoring of unusual patterns of embryo development and makes it possible to progress towards automated and objective systems to assess the embryos. The use of big data technology as a tool to detect embryo development events combined with embryologist skills are a promising approach towards the improvement of IVF treatments.

V-7 Tuesday, October 15, 2019 4:23 PM

COMPARISON OF SPERM RETRIEVAL TECHNIQUES FOR MEN WITH OBSTRUCTIVE AZOOSPERMIA.

OBJECTIVE: To compare the Percutaneous Epididymal Sperm Aspiration (PESA) and Microsurgical Epididymal Sperm Aspiration (MESA) techniques, requirements, and outcomes for men with obstructive azoospermia.

METHODOLOGY: Intra-operative video highlights the main steps for performing PESA and MESA, along with their complications and sperm retrieval outcomes. Intra-operative table microscope was used to visualize sperm from PESA and MESA.

CONCLUSIONS: PESA and MESA are both effective means for obtaining sperm for in-vitro fertilization with differences in technique, equipment required, complications, and sperm quality outcomes.

V-8 Tuesday, October 15, 2019 4:28 PM

POST-ABLATION RESIDUAL DISEASE: HISTOLOGICAL ASSESSMENT OF EXCISED PERITONEAL ENDOMETRIOSIS.

OBJECTIVE: The objective of this video is to present a case of post ablation residual peritoneal endometriosis while also highlighting surgical techniques of excision of endometriosis.

METHODOLOGY: This video presents a case of a 25 year old para 2 who had a history of a prior diagnostic laparoscopy with ablation of peritoneal endometriosis two months prior. The surgical case presented is her second laparoscopy, which was performed with the intention of excision of endometriosis per patient preference. Surgical findings were significant for remaining endometriosis in areas of previous ablation. The histological findings included residual endometriosis deep to prior superficial ablation.

CONCLUSIONS: Superficial ablation may not treat deeper forms of endometriosis. Ablation without appropriate dissection and mobilization risks injury to the bowel, ureters and bladder. For these reasons, excision of endometriosis may be a superior form of treatment for deep peritoneal endometriosis.

METHODOLOGY: 4 patients with massive adenomyosis in China who wished to get pregnant and have a baby were enlisted for the teaching the Chinese surgical team. Subsequently 20 more such patients were operated on in China by the surgical team we taught. For the first two teaching cases, we did the surgery, and the Chinese team assisted. For the next two cases, the Chinese team did the surgery, and we assisted. We described the quintuple flap reconstruction with no overlapping suture lines to prevent uterine rupture. Video documentation was performed.

CONCLUSIONS: Following this intense two day training in China, the Chinese team did 20 more cases on their own over the next six months, with a live birth rate of 55%, and uneventful pregnancies with no uterine rupture.

V-11 Tuesday, October 15, 2019 5:01 PM

OPTIMIZING FERTILITY PRESERVATION USING MULTIPLE MODALITIES IN A YOUNG PATIENT WITH CERVICAL CANCER. Natalia C. Llarena, MD, Bouran Kilany, MD, Mariam Alhilli, MD, Rebecca Flyckt, MD. Cleveland Clinic, Cleveland, OH.

OBJECTIVE: Oocyte cryopreservation is the mainstay of fertility preservation in patients with malignancy; however, live birth rates after oocyte cryopreservation are lower in cancer patients than in healthy patients. Multiple modalities of fertility preservation can be combined to optimize success rates.

METHODOLOGY: We demonstrate a case of a 24-year-old female who was diagnosed with cervical clear cell adenocarcinoma and was advised to undergo treatment with cisplatin and radiation therapy. She strongly desired fertility preservation and opted to proceed with oocyte cryopreservation, ovarian tissue cryopreservation, and ovarian transposition.

CONCLUSIONS: Ovarian transposition is a surgical approach to fertility preservation that preserves both fertility and gonadal function. Different modes of fertility preservation may be combined to optimize live birth rates in patients with malignancy.

SUPPORT: None.

V-12 Tuesday, October 15, 2019 5:09 PM

LEFT OVARIAN TRANSPOSITION OF UNDESCENDED OVARY WITH UNDESCENDED UTERUS. Kirsten Sasaki, M.D., a Charles E. Miller, M.D. b

“Advocate Lutheran General Hospital, Naperville, IL; bThe Advanced Gynecologic Surgery Institute/The Advanced IVF Institute, Charles E. Miller, MD & Associates, Naperville, IL.

OBJECTIVE: To review the presentation, symptoms, diagnosis and treatment of an undescended ovary, and to demonstrate a laparoscopic technique for ovarian transposition to facilitate trans-vaginal oocyte monitoring and retrieval.

METHODOLOGY: Left ovarian transposition and ovarian drilling.

CONCLUSIONS: Ovarian transposition in women with uterine anomalies is feasible, safe option to facilitate oocyte retrieval in cases of undescended ovaries.


SUPPORT: None.

V-13 Tuesday, October 15, 2019 5:15 PM

EXCISION OF A PELVIC SIDE-WALL FIBROID. Alexander Kotlyar, MD, a Pinar Kodaman, MD, PhD b

aYale University, New Haven, CT; bYale School of Medicine, New Haven, CT.

OBJECTIVE: To share our experience in excising a retroperitoneal pelvic fibroid.

FERTILITY & STERILITY® e431
VIDEO SESSION 3

V-14 Wednesday, October 16, 2019 3:45 PM

2. PORT MYOMECTOMY TECHNIQUE FOR UTERUS ADHERENT TO THE ANTERIOR ABDOMINAL WALL. Hadi Ramadan, M.D., Jerri A. Walter, M.D., Traci E. Ito, M.D., Joseph L. Hudgens, M.D., Eastern Virginia Medical School, Norfolk, VA.

OBJECTIVE: To describe a 2 port myomectomy technique in the setting of extensive adhesions aiming for fertility preservation.

METHODOLOGY: Our patient is a 40 year old female G3P2012 presenting with symptomatic fibroids with a history of prior C-section. Her MRI showed extensive adhesions requiring specific surgical techniques. Using a 2 port method and gel point mini, lysis of adhesions was performed. Enucleation of fibroids followed. This multistep process ensures hemostatic and efficient myomectomies without jeopardizing the integrity of the endometrium.

CONCLUSIONS: This case is an example of how reduced port technique can be utilized in complex fertility preserving techniques.

SUPPORT: None.

V-16 Wednesday, October 16, 2019 3:56 PM

LAPAROSCOPIC RESECTION OF FUNCTIONAL, NON-COMMUNICATING UTERINE HORN. Rachel M. Whynott, M.D., Rachel Mejia, D.O. University of Iowa Hospitals and Clinics, Iowa City, IA; University of Iowa, Iowa City, IA.

OBJECTIVE: To review a common presentation of unicornuate uterus with a functional, non-communicating rudimentary uterine horn and a laparoscopic method of management, highlighting laparoscopic surgical techniques.

METHODOLOGY: A 13-year-old G0 was referred to the clinic for severe, cyclic right lower quadrant pain during menses. A transvaginal ultrasound revealed a left unicornuate uterus with a right-sided, non-communicating rudimentary horn measuring 4.8 x 4.7 x 4.6 cm, containing blood consistent with hematometra. Kidneys were bilaterally present and normal by ultrasound. Due to the patient’s worsening pain and presence of hematometra, decision was made to proceed with diagnostic laparoscopy and removal of the rudimentary uterine horn. The entire procedure was performed laparoscopically, with an estimated total blood loss of 20 cc. She had no complications or readmissions. Her severe menstrual pain was resolved at her follow up appointments.

CONCLUSIONS: In patients with severe menstrual pain from outflow obstruction from a non-communicating rudimentary uterine horn with functional endometrium, laparoscopic resection can be a safe and effective method of treatment.

SUPPORT: None.

V-17 Wednesday, October 16, 2019 4:03 PM


OBJECTIVE: To assess the impact of routine meiotic spindle identification during intra-cytoplasmic sperm injection (SI-ICSI), on fertilization and blastocyst formation rates when compared against conventional intra-cytoplasmic sperm injection (ICSI).

METHODOLOGY: All ICSI cycles undertaken between February 2015 and December 2016 in two similarly run IVF centers were included. At February 2016, spindle identification was introduced into routine practice. ICSI was performed following standard protocols: polar body was positioned either at 6 or 12 o’clock and used as reference for sperm injection at 3 o’clock. SI-ICSI oocyte identification was performed just before ICSI under 40 times magnification and then rotated until polar body was positioned at 12 o’clock. At this point a polarizer filter (Olympus IX2), was inserted while light turned to maximum intensity. Oocytes were rotated until a birefringent spindle was identified. Spindle position and intensity was recorded by embryologist as 0/+//++/+ and 0+ being assigned to spindle absence and +++ to maximum spindle intensity when compared against the most birefringent area in zona pellucida. Sperm injection was performed at 3 o’clock. Fertilization and blastocyst formation rates were recorded blind to spindle characteristics. Comparison was performed using Fisher’s Exact test.
CONCLUSIONS: With an increased 5% normal fertilization rate and 7% higher blastocyst rate, this study suggests that visualizing the oocyte meiotic spindle using an inexpensive polarizing filter at the time of ICSI can avoid inadvertent damage and leads to improved normal fertilization and blastocyst formation. Other potential benefits could include better timing for injection in accordance with cytoplasmic maturation. Prospective studies would be needed to validate this later concept.

V-20 Wednesday, October 16, 2019 4:35 PM

SPECIALIZED PIEZO-ICSI FOR LOW QUALITY OOCYTES. Atsushi Tanaka, M.D., Ph.D., Motoi Nagayoshi, M.D., Izumi Tanaka, Ph.D., Takashi Yamaguchi, M.D., Ph.D., Motoharu Ohno, M.D., Saint Mother Hospital, Kitakyushu, Japan.

OBJECTIVE: In 1995, Kimura and Yanagimachi reported the usefulness of ICSI using Piezo-micro manipulator by applying a Piezo pulse which produced ultra-fast sub-micron forward momentum using uniquely shaped flat-tipped micropipettes with no bevel or spike (Piezo-ICSI).

Hirakoa et al reported that Piezo-ICSI has advantage of high fertilization rate, low damage rate of oocyte at ICSI and high clinical outcome in 2015. However, we have worried about one problem in Piezo-ICSI, that is the volume of injected medium at ICSI. So, we developed a newly specialized Piezo-ICSI with sperm with a shortened sperm tail after cutting the tails to lessen the damage to the cytoplasm of these low-quality oocytes. We then investigated the effect of the specialized Piezo-ICSI.

METHODOLOGY: Prospective study to improve clinical outcome of Specialized Piezo-ICSI for low quality oocytes.

The sperm tail was cut with injection pipette a little below the mid piece then aspirate it injection pipette head first. The zona pellucida was penetrated using a weak piezo pulse (speed 1.5, intensity 1) and the tip of injection pipette was introduced forward to stretch the cytoplasmic membrane. A weaker pulse (speed 1.0, intensity 1) was added to break it and the sperm injected simultaneously. Pushing the sperm forward and aspiration of the medium injected at ICSI were unnecessary.

CONCLUSIONS: Oocytes that received ICSI, Oocytes that survived after ICSI (%), Oocytes fertilized (%), ood quality day-3 embryos (%), Blastocysts (%). Clinical pregnancies (%) between conventional Piezo-ICSI and Specialized Piezo-ICSI were [512, 124] [435 (85),112 (90)] [409 (80),103 (83)] [266 (52),69 (56)] [230 (45),60 (48)] [27,31] respectively.

This newly developed Piezo-ICSI, using tail-cut shortened sperm through tail first was successful in making the injection easier. The reduction in injected volume of medium resulted in production of high-quality embryos.

V-21 Wednesday, October 16, 2019 4:42 PM

NOVEL UTERINE CLOSURE TECHNIQUE TO PREVENT INTRAUTERINE ADHESIONS. Clarissa J. Lam, MD. Anthony N. Imudia, MD. University of South Florida, Tampa, FL.

OBJECTIVE: The purpose of this video is to describe a novel uterine closure technique to prevent intrauterine adhesions after myomectomy. This is an important topic in the field as intrauterine adhesions can result in infertility, recurrent pregnancy loss, and future pregnancy complications, such as morbidity adherent placenta.

METHODOLOGY: In this video, we first discussed the epidemiology and the existing techniques that have been studied regarding the prevention of intrauterine adhesions. We then used an illustration to describe the suturing technique. We concluded with video clips demonstrating the technique from three of our myomectomy cases.

CONCLUSIONS: This novel intraoperative uterine closure technique is one method that can potentially reduce the risk of intrauterine adhesion formation.

TREATMENT OF SYMPTOMS OF UTERINE FIBROIDS WITH RELUGOLIX COMBINATION THERAPY: EFFICACY AND SAFETY RESULTS FROM THE PHASE 3 LIBERTY I CLINICAL TRIAL. Ayman Al-Hendy, MD PhD, Andrea S. Lukes, MD, Alfred Poindexter, III, MD, Roberta Venturina, III, MD, Claudia Visintin, MD, Yulan Li, PhD, Laura F. McKain, MD, Elizabeth A. Stewart, M.D., PhD.* University of Illinois College of Medicine, Chicago, IL;† Carolina Women’s Research and Wellness Center, Durham, NC; ‡Advances In Health, Houston, TX; §Magna Graecia University of Catanzaro, Department of Obstetrics, Catanzaro, Italy; ¶Institute for Mother and Child Research (IDIMI), Faculty of Medicine, University of Chile, Santiago, Chile; #Myovant Sciences, Inc., Brisbane, CA; $Mayo Clinic, Rochester, MN.

OBJECTIVE: To evaluate the efficacy and safety of relugolix, in combination with estradiol (E2) and norethindrone acetate (NETA) compared with placebo in women with uterine fibroid (UF)-associated heavy menstral bleeding (HMB).

DESIGN: Multinational phase 3 randomized, double-blind, placebo-controlled trial.

MATERIALS AND METHODS: Premenopausal women (18-50 years) with menstrual blood loss (MBL) volume ≥ 80 mL/cycle assessed by the alkaline hematim method and ultrasound-confirmed UF, were eligible to participate in the study. Women were randomized 1:1:1 to one of three arms: once daily treatment with relugolix 40 mg + E2 1 mg/NETA 0.5 mg for 24 weeks (Group A); relugolix 40 mg alone for 12 weeks followed by relugolix 40 mg + E2 1 mg/NETA 0.5 mg for 12 weeks (Group B), or placebo for 24 weeks (Group C). The primary efficacy endpoint was the proportion of women in Group A vs Group C who achieved an MBL of < 80 mL and ≥ 50% reduction from baseline MBL over the last 35 days of treatment. Secondary endpoints included mean % reduction in MBL, amenorrhea rate, improved anemia, and reduced UF-associated pain. Group B was included to explore the impact of E2/NETA on the anticipated hypoestrogenic effects of relugolix. Adverse events (AEs) and bone mineral density (BMD) changes by dual-energy X-ray absorptiometry were assessed.

RESULTS: In LIBERTY I, 388 women were randomized and 308 (79%) completed the study. In Group A 73.4% met the primary endpoint vs 18.9% in Group C (p = 0.0001). Mean % reduction in MBL from baseline at Week 24 was 84.3% for the Group A and 23.2% for Group C (p < 0.0001). The proportion of women who achieved amenorrhea was 52.3% vs 5.5% in Groups A vs C, respectively (p = 0.0001). In women with anemia (hemoglobin ≤ 10.5 g/ dL) at baseline who completed 24 weeks treatment, 50.0% experienced a 2 g/dL increase in Hb with relugolix in Group A vs 28.6% in Group C (p = 0.002). A greater proportion of women reported moderate/severe UF-associated pain (based on a maximum daily pain score of ≥ 4 at baseline where 0 = no pain, 10 = worst pain ever) 43.1% in Group A reported minimal/no pain (maximum pain score ≤ 1) in the last month of treatment vs 10.1% in Group C (p = 0.0001). Efficacy results in Group B were similar to those of Group A. Incidence of AEs was comparable between Groups A and C (62% vs 66%, respectively) and higher in Group B (73%), including the most common AE, hot flushes (11% and 8% in Groups A and C, respectively vs 36% in B). The mean % change from baseline to Week 24 in lumbar spine BMD was -0.36% -1.82%, and 0.05% in Groups A, B, and C, respectively. The distribution of the % change in BMD was similar between Groups A and C, including outliers.

CONCLUSIONS: In this Phase 3 pivotal study, relugolix combination significantly reduced MBL in women with UF-associated HMB and was generally well tolerated. Additional benefits were observed including a clinically meaningful reduction of UF-related pain, a high rate of amenorrhea, and improved anemia. Coadministration of E2/NETA maintained BMD and mitigated vasomotor symptoms. Relugolix combination with E2/NETA represents a potential long-term treatment option for women with UF.

SUPPORT: The Phase 3 LIBERTY clinical trial was funded by Myovant Sciences, Inc.
hypogonadal symptoms and 2 semen analyses (SA) with total motile sperm counts (TMSC) > 5 million. Eligible men began Natesto TID for 3 months. T, LH, FSH, and 2 semen analyses were collected at baseline and after 3 months of therapy. Symptoms were evaluated using the international index of erectile function (IIEF-6) and the short form 36 (SF-36) questionnaires. The primary endpoints were change in T, LH, FSH, spermatogenesis, sperm motility and TMSC. Secondary end points were change of symptoms and adverse events (AEs). Data are presented as means (SD), p-values were used to compare changes after 3 months, p<0.05 was considered significant. The study was adequately powered to detect a decline in 30% of gonadotropin levels at 80% with alpha set at 0.05.

RESULTS: In total, 55 men (age 19-55 years) were eligible and enrolled into the trial. Of the 55 who enrolled, 38 completed the trial and 17 dropped out (nasal irritation was a common cause of dropout). Among the men that completed the trial, mean T increased from 230.62 (605.278) ng/dL (p=0.005). LH and FSH decreased but remained within the normal range (2-5 IU/mL). Most importantly, semen parameters remained unchanged; sperm concentration 26.6(15.2) vs 26.0(21.2) million/cc (p=0.6), sperm motility 49.6(12.4) vs 48.9(12.5)%; p<0.01, how-ever this trend was not statistically significant in the adjusted model p(trend) = 0.46. (Table 1)

OBJECTIVE: To evaluate the effect of controlled ovarian stimulation length on first transfer live birth rates in fresh and freeze-all antagonist IVF cycles.

RESULTS: In fresh cycles, days of ovarian stimulation ranged from 4 to 40 days, with 24% of patients having 4-8 days, 62% 9-11 days, 8% 12 days, and 6% with 13 or more days. In fresh transfer cycles, live birth rates decreased significantly with each additional day of stimulation from ≤ 8 days to 12 days by univariate analysis ranging from 47.36% to 41.49%, p-value (trend) = <0.0001. These findings were validated in a multivariable model controlling for age, gravidity, BMI, Max FSH, and etiology of infertility with a p-value (trend) = 0.005. In freeze-all cycles, a decline in the live birth rate with increasing days of stimulation was observed with p(trend)=0.01, however this trend was not statistically significant in the adjusted model p(trend) = 0.46. (Table 1)

CONCLUSIONS: Increasing length of ovarian stimulation negatively affects live birth rates in fresh but not freeze-all antagonist IVF cycles. In fresh transfer cycles, live birth rate is highest with stimulation of ≤ 8 days (47.4%), and was observed to decline with increasing days of stimulation (4.15%) with 13 or more stimulation days. This points to an endometrial cause for the adverse impact on live birth rates with longer stimulation in fresh transfer cycles that may not be relevant in freeze-all cycles.

---

TABLE 1. Association between Days of Stimulation and Live Birth Rate Stratified by Type of Transfer

<table>
<thead>
<tr>
<th>Days of Stimulation</th>
<th>Fresh (n=14,866)</th>
<th>Frozen (n=2,964)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-8</td>
<td>1716</td>
<td>308</td>
</tr>
<tr>
<td>9</td>
<td>1756</td>
<td>349</td>
</tr>
<tr>
<td>10</td>
<td>1413</td>
<td>304</td>
</tr>
<tr>
<td>11</td>
<td>193</td>
<td>129</td>
</tr>
<tr>
<td>12</td>
<td>489</td>
<td>112</td>
</tr>
<tr>
<td>&gt;12</td>
<td>395</td>
<td>115</td>
</tr>
</tbody>
</table>

O-268

IN VITRO MATURATION (IVM) VERSUS IN VITRO FERTILIZATION (IVF) IN WOMEN WITH HIGH ANTRAL FOLLICLE COUNT (AFC): A RANDOMIZED CONTROLLED TRIAL (NCT03405701).

OBJECTIVE: IVM has been proposed as an alternative to IVF for women at increased risk of ovarian hyperstimulation syndrome (OHSS) due to a high antral follicle count (AFC) and/or polycystic ovary syndrome (PCOS). Here, we compare the effectiveness and safety of one IVM and one IVF cycle in women with infertility and high AFC.

RESULTS: Patients entered the study from October 2015 to March 2016. Of the 578 eligible women, 286 were randomized to IVM and 292 to IVF. A total of 143 (50.8%) women in the IVM group and 136 (46.8%) in the IVF group successfully completed at least one cycle with embryos transferred. A total of 138 (51) women in the IVM group and 154 (56) in the IVF group became pregnant. The rates of ongoing pregnancies were similar in the IVM and IVF groups (20% vs 21%, respectively, p=0.7). The rates of OHSS were also similar in the IVM and IVF groups (3% vs 3%, respectively, p=0.9). There was improvement across all domains of the IIEF scores in erectile function, libido, intercourse satisfaction, orgasm, and overall sexual satisfaction as well as improvement in questions related to energy in the IIEF. Secondary endpoints were summarized in Table 1. There were no significant differences in any of the secondary endpoints between the IVM and IVF groups. Conclusions: IVM appears to be a safe and effective treatment for men with hypogonadism who wish to preserve fertility. SUPPORT: Ayu Biosciences provided drug free to patients.
releasing hormone ( GnRH ) antagonist protocol and oocytes were retrieved 36 h after GnRH agonist trigger. In both groups, mature oocytes were fertilized using intracytoplasmic sperm injection, and all embryos were frozen on day 3: ≤2 embryos were transferred in a subsequent frozen cycle. The primary outcome was live birth after first embryo transfer of the started treatment cycle. The planned sample size was 546, assuming an expected live birth rate of 45% in the IVF group, a noninferiority margin of −10%, 90% power and 15% loss to follow-up. While follow-up for live birth is ongoing, we report ongoing pregnancy in this abstract.

RESULTS: Between January 2018 and December 2018, we randomized 546 women (273 in each group). Baseline characteristics were comparable (mean ± SD, associated quartiles and reference intervals were calculated in alignment with CLSI guidelines). The effect of menstrual status with respect to rising AMH in childhood. This contributes to the limited literature on normative AMH values throughout childhood and adolescence. This study presents reliable reference ranges, from a single batched assay on healthy children. This is also the largest series of its kind using a kind using an automated AMH assay. These normative values for AMH will be a major adjunct to counseling pediatric cancer patients and their families who require or have completed fertility damaging therapies. SUPPORT: AMH assay kits were provided by Beckman Coulter (Lot 971017).

CONCLUSIONS: Our results demonstrate comparable trends to other studies with respect to rising AMH in childhood. This contributes to the limited literature on normative AMH values throughout childhood and adolescence. This study presents reliable reference ranges, from a single batched assay on healthy children. This is also the largest series of its kind using an automated AMH assay. These normative values for AMH will be a major adjunct to counseling pediatric cancer patients and their families who require or have completed fertility damaging therapies.

Menstrual status did not significantly impact AMH serum concentrations (p=0.787). Similarly, ethnicity did not significantly impact AMH concentrations (p=0.0965).

**O-270**

**DAMAGED SPERM PARAMETERS AND SPERMATION FAILURE IN VENLAFAXINE-TREATED RATS: A CORRELATION WITH HIGH TESTICULAR ARomatase IMMUNOEXPRESSION AND REDUCED EPIDIDYMIAL V-ATPASE.** Estela Sasso-Cerri, PhD, Fabiane de Santi, Master degree, André A. S. da Silva, Under graduate, student, Beatriz M. Rodrigues, Under graduate, student, Flávia L. Beltrame, PhD, Paulo C. C. P. "São Paulo State University - UNESP, Araraquara, Brazil; "São Paulo Federal University - UNIFESP, Morphology and Genetics, São Paulo, Brazil.

OBJECTIVE: The antidepressant venlafaxine (Serotonin Norepinephrine Reuptake Inhibitor-SNRI) has impaired sexual function in male patients. We investigated the impact of this SNRI on sperm parameters, relating them to testicular and epididymal histophysiological markers. The recovery of sperm and testicular changes was also evaluated following the interruption of treatment.

DESIGN: Adult male rats were grouped: Venlafaxine-35 days (VFG-35; n = 6) and Venlafaxine-65 days (VFG-65; n = 6) received venlafaxine (30mg/kg BW) by gavage for 35 days; Control-35 days (CG-35; n = 6) and Control-65 days (CG-65; n = 6) received saline. After treatment, the animals from CG-35 and VFG-35 were killed while the animals from CG-65 and VFG-65 were maintained without treatment for 30 days to evaluate reversibility of changes. In these groups, sperm parameters were evaluated in association to seminiferous epithelium integrity, steroidogenesis, testicular aromatase and epididymal V-ATPase immunoeexpression.

MATERIALS AND METHODS: Rats received 30mg/kg (therapeutic dosage) of venlafaxine for 35 days (minimal period for the antidepressant effect). The concentration, morphology and mitochondrial cytochemical activity (MCA) of sperm from cauda epididymis were analyzed. In epididymal and testicular sections, the following parameters were evaluated: epididymal duct diameter, frequency of tubules with spermiation failure, number of Sertoli cells (NSC), viability of germ cells by TUNEL, Leydig cells nuclear diameter (LCn), StAR immunoexpression (steroidogenesis), testosterone levels were observed. Venlafaxine also impaired the epididymal V-ATPase immunoeexpression. Except for the tail changes and MCA, sperm concentration and testicular parameters were improved following the interruption of treatment.

CONCLUSIONS: Venlafaxine stimulates LC steroidogenesis and increases aromatase levels, impairing spermiation and sperm concentration and quality. Therefore, the evaluation of fertility together with a careful analysis of spermato genesis and hormonal status of patients treated with SNRI is useful. The changes in sperm parameters may also be associated with disturbances in the acid/basic milieu of epididymal lumen due to reduction in V-ATPase. The improvement of sperm parameters following the interruption of treatment is, at least in part, due to recovery of aromatase/estrogen levels and the restoration of spermiation process.


**O-271**

**THE AGE TAX: OCOCYTE CRYOPRESERVATION (OC) AGE-BASED COST ANALYSIS.** Bat-Sheva L. Maslow, MD, MSCTR, Kristen Mancinelli, MSPh, Jennifer Nicole Lannon, BS, Sidonia R. Swarn, BS, Joshua U. Klein, MD "Extend Fertility, New York, NY; "FreezeHealth, Miami, FL.

OBJECTIVE: The degree to which OC costs increase with age is not known. Data regarding OC outcomes and associated costs are limited. With increasing demand for OC, there is a need for evidence-based counseling tools for age-related costs. The primary aim of this study is to quantify relative age-based increase in OC costs with an evidence-based cost evaluation model of OC cost, incorporating age, medication, oocyte yield, and potential for LB. DESIGN: Cost analysis. Nested retrospective cohort study.

MATERIALS AND METHODS: All women undergoing OC at Extend Fertility Medical Practice from 4/2016-12/2018 were included in the cohort. Demographic and cycle data were abstracted from the electronic medical record. Cycle and storage fees were calculated for 135 U.S. practices from FreezeHealth’s public dataset. Medication pricing was calculated using first 15 listings in a national online database (fertilitydrugcalculator.com).

Mathematical model for cost per cryopreserve MII oocyte and cost per potential LB were developed with age, MII oocyte per cycle, total cycles, total medication utilization, mean national cycle and medication fees, and per oocyte potential LB rates from Doyle et al. Using the <34 group as a reference, relative increase in median cost per MII and cost per potential LB were calculated as multiples of the median (MoM) and 25-75%tiles. Associations were analyzed using ANOVA and Kruskall-Wallis, where appropriate.

RESULTS: 1241 subjects with a total of 1791 cycles were included. Mean age = 35.6±6.3, mean # cycles 14.5±10.79, mean MII cryopreserved oocytes = 16.19±9.34, median cost per MII oocyte cryopreserved = $1170.99 ($708.19-2051.69) and median cost per potential LB = $17,041.34 ($9589.29-33,253.79).

CONCLUSIONS: The relative cost of OC significantly increases with age.

**TABLE 1.** demonstrates significant increase in relative costs per MII oocyte and potential LB with age. In our model, per cost potential LB at 30-32 is 2.18x less the cost at 37-39 and 1.28x less the cost at 34-36 (p<0.001). The difference equals 6-12 years of storage.

<table>
<thead>
<tr>
<th>Age Group</th>
<th># Cycles</th>
<th>MIs</th>
<th>GND (IUs)</th>
<th>Relative increase: Cost per MII</th>
<th>Relative increase: Cost per potential LB</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤34 N=415</td>
<td>1.28±0.60</td>
<td>1.46±0.77</td>
<td>1.60±0.93</td>
<td>1.76±0.97</td>
<td>2.29±1.49</td>
</tr>
<tr>
<td>35-37 N=524</td>
<td>18.16±9.52</td>
<td>16.18±9.06</td>
<td>13.88±8.43</td>
<td>12.35±10.7</td>
<td>11.23±9.99</td>
</tr>
<tr>
<td>38-40 N=234</td>
<td>42.54±3302.98</td>
<td>5473.56±3830.88</td>
<td>6293.91±4238.65</td>
<td>7703.92±5061.78</td>
<td>7998.53±6590.56</td>
</tr>
<tr>
<td>41-42 N=51</td>
<td>1.34 (0.80-2.23)</td>
<td>1.78 (1.13-2.78)</td>
<td>2.71 (1.35-5.46)</td>
<td>3.70 (1.83-6.13)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>&gt;42 N=17</td>
<td>1.51 (0.90-2.50)</td>
<td>3.25 (2.01-5.07)</td>
<td>8.89 (4.36-17.91)</td>
<td>12.13 (6.01-20.12)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

**O-272**

**MENSTRUAL CYCLE REGULARITY AND LENGTH AND RISK OF MORTALITY: A PROSPECTIVE COHORT STUDY.** Yixin Wang, MD, Mariel Arvizu, MD, ScD, Bernard Rosner, PhD, Jennifer J. Stuart, ScD, Janet Rich-Edwards, PhD, JoAnn E. Manson, MD, DrPh, An Pan, PhD, Jorge E. Chavarro, MD, ScD, "Harvard T.H. Chan School of Public Health, Boston, MA; "Brigham and Women’s Hospital and Harvard Medical School, Boston, MA; "Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

OBJECTIVE: To prospectively assess the associations of menstrual cycle characteristics in adolescence and adulthood with risk of all-cause and cause-specific mortality.

Women considering OC should be counseled about the drastic increase in cost with age. This study represents the most robust analysis to date of OC costs with data collected from OC cycles.

References: Successful elective and medically indicated oocyte vitrification and warming for autologous in a vitro fertilization, with predicted birth probabilities for fertility preservation according to number of cryopreserved oocytes and age at retrieval. Doyle, Joseph O. et al. Fertility and Sterility, Vol. 105, Issue 2, 459-466.e2

**CONCLUSIONS: The relative cost of OC significantly increases with age.**

---

**testicular aromatase (Cyp19) and epididymal V-ATPase immunofluorescent intensity. Serum and testicular testosterone levels were also measured. Data were submitted to two-way ANOVA with Tukey post-hoc test.**

RESULTS: In VFG-35, the epididymal duct diameter, sperm concentration and MCA decreased, and a high frequency of sperm tail abnormalities was found. Changes in seminiferous epithelium and high frequency of post-spermiation tubules with retained spermatozoids were found. The NSC decreased whereas the number of TUNEL-positive germ cells and Cyp19 immunoeexpression increased in this group. In VFG-35, LCns were larger than CG; a high immunoeexpression of StAR and elevated serum and testicular testosterone levels were observed. Venlafaxine also impaired the epididymal V-ATPase immunoeexpression. Except for the tail changes and MCA, sperm concentration and testicular parameters were improved following the interruption of treatment.

CONCLUSIONS: Venlafaxine stimulates LC steroidogenesis and increases aromatase levels, impairing spermiation and sperm concentration and quality. Therefore, the evaluation of fertility together with a careful analysis of spermato genesis and hormonal status of patients treated with SNRI is useful. The changes in sperm parameters may also be associated with disturbances in the acid/basic milieu of epididymal lumen due to reduction in V-ATPase. The improvement of sperm parameters following the interruption of treatment is, at least in part, due to recovery of aromatase/estrogen levels and the restoration of spermiation process.

Sengers, MD, a Lucille M. Little, BS, a Ravi Gada, MD, b Laura Lawrence, MD, b Jean Marc Ayoubi, MD, PhD, b Emre Seli, MD, a Jason M. Franasiak, MD, a Richard Thomas Scott, Jr., MD a IVI-RMA New Jersey, Basking Ridge, NJ; bHospital FOCH, Paris, France; cFoundation for Embryonic Competence, Basking Ridge, NJ.

OBJECTIVE: RIF is one of the more challenging areas of reproductive medicine. Despite a significant interest in RIF, its definition has not yet been agreed upon, and etiologic factors responsible for RIF have not been fully characterized. One of the most common causes of pregnancy failure is chromosomal abnormality of the embryos. Therefore, it is likely that a number of RIF cases are due to aneuploidy. Other potential causes of RIF include immune and endometrial factors; however, the relative contribution of these factors to RIF have not yet been established. In this study, we aimed to determine the true prevalence of RIF in women undergoing successive SET.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: To answer this question we analysed all patients (n=4,515) with up to three consecutive euploid frozen SETs taking place from January 2012 to July 2018, excluding cycles with donor eggs or gestational carriers. We analysed the cumulative outcomes from these cycles in order to determine what percentage of them had causes of RIF that were not related to the ability to achieve a euploid blastocyst. All embryos underwent PGT-A at the blastocyst stage using qPCR or NGS-based platforms. All embryos were vitrified at the blastocyst stage after a trophoderm (TE) biopsy was performed. Endometrial preparation was achieved with oral E2 and intramuscular progesterone supplementation with transfer of a single euploid blastocyst performed on the 6th day of progesterone exposure. The primary endpoint was implantation as determined by the presence of a gestational sac with fetal cardiac activity. A logistic regression model was employed to assess the differences of outcomes between first, second, and third euploid SET and a Kaplan-Meier curve as utilized to analyze cumulative implantation rate.

RESULTS: The mean age of the patients included in the study was 35.4±4.2. The implantation rates of the first, second and third euploid SET were 69.4%, 59.3%, and 59.2% per transfer, respectively. Of those who failed to achieve implantation after the first euploid SET (n=1381), 799 (57.9%) underwent a second euploid SET and of those who failed to achieve implantation after the second euploid SET (n=325), 142 (43.7%) patients underwent a 3rd euploid SET. The second (OR=0.638, 95% CI 0.547-0.746) and third (OR=0.627, 95% CI 0.446-0.886) frozen euploid SET provided a slightly decreased implantation when compared to the first frozen euploid SET. The cumulative implantation rates after up to three consecutive frozen euploid SET was 94.9% (95% CI: 93.7%-95.9%).

CONCLUSIONS: Our findings suggest that true RIF is rare. For those patients with the ability to make euploid blastocysts, 94.9% would achieve clinical pregnancy with 3 embryos transferred. The implantation rates decline minimally with increasing transfers, but the fact that they remain high

---

### Table 1: Treatment and outcomes

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n</th>
<th>Age (Average)</th>
<th>Exposure Time to Embryo Glue (Hours) (Average)</th>
<th>Embryos Transferred (Average)</th>
<th>Clinical Pregnancy Rate</th>
<th>Implantation Rate</th>
<th>Ongoing Pregnancy Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>26</td>
<td>33</td>
<td>0</td>
<td>1.2</td>
<td>46%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>47%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>45%&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>One-hour</td>
<td>26</td>
<td>33</td>
<td>1.3</td>
<td>1.3</td>
<td>54%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>48%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>46%&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Two-hour</td>
<td>31</td>
<td>33</td>
<td>2.2</td>
<td>1.3</td>
<td>68%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>60%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>59%&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Three-hour</td>
<td>36</td>
<td>34</td>
<td>3.3</td>
<td>1.2</td>
<td>81%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>73%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>75%&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a,b</sup> Different superscripts within columns indicate significant differences (P<0.05)
O-275

A SINGLE INJECTION OF LONG ACTING GNRH-ANTAGONIST: DEGARELIX—DOWNREGULATES HYPOTHYSIS DURING OVARIAN STIMULATION. A RANDOMIZED CONTROLLED TRIAL.

Tatiana Chartomatsidou, MSc,a Robert Najdecki, MD, PhD,a Fotini Choulia, MD, MD,a Eirini Asouchidou, MD, PhD,a Sofia Bouchlariotou, MD, PhD,a Evangelos Mumbas, MD, PhD, b Lazaros Konstantinios Karagianidis, MD, b Nikolaos Nikolaou, MD, PhD,a Evangelos Papankolou, MD, PhD,a b Assisting Nature, Center of Assisted Reproduction and Genetics, Thessaloniki, Greece; b Medical Department, Aristotle University of Thessaloniki, Thessaloniki, Greece; Medical Department, Democritus University of Thrace, Alexandroupolis, Greece.

OBJECTIVE: Study’s objective was to examine if the use of a novel long acting, single dose GnRH antagonist, Degarelix, can cause efficient pituitary downregulation during ovarian stimulation in oocyte donors.

RESULTS: No LH rise or any OHSS was noticed in any groups. Mean age ≥ 35yrs) between January 2017-January 2019 in Assisting Nature, Centre of Assisted Reproduction and Genetics, Thessaloniki, Greece. Two groups of patients were examined; the first group (study group) received a single Day-6 follicular dose of degarelix (Firmagam, Ferring Pharmaceuticals); the second group (control group) received daily 0.25mg of ganirelix as is the standard antagonist protocol. Study Group (Degarelix group) consisted of 80 women, who followed the new protocol, whereas, 93 donors followed the classical fixed Day6 GnRH-antagonist protocol.

MATERIALS AND METHODS: Ovarian stimulation was initiated on cycle Day2 or 3 with gonadotropins 225 IU (200-300), daily, in both groups. In Control group 0.25 mg of antagonist ganirelix was administered daily from stimulation Day6 in a fixed manner. In the new study group, on the same day, day-6, a single bolus injection of 0.1 ml Degarelix was administrated subcutaneously. Agonist triggering (Triptorelin 0.3ml) was employed for all and OPU performed at 36h. Fresh or frozen blastocyst-only transfer was performed following recipient endometrial estrogen and progesterone priming.

RESULTS: No LH rise or any OHSS was noticed in any groups. Mean age (27.1 vs 27.9 years), mean AMH (4.1 vs. 3.6ng/ml) and total gonadotropin dose (2400 vs 2508 IU) of participants were not different among Control-group and Study-group respectively. Similar number of oocytes retrieved (18.1 vs.17.1, p>0.05) with degarelix short antagonist group, and similar number of blastocysts produced in both groups (6.6 in Control-group-A vs. 6.9 in Study-group). All recipients underwent 2 blastocysts transfer. Pregnancy is expressed per donor. Initial positive HCG per donor was significantly higher (p<0.05) in the Degarelix Short Antagonist (Study-Group) 78.7% (63/80) as compared with 65.5% (n=61/93) in classic short antagonist (Control-Group). Cumulative delivery rate was higher 60.0% (48/80) in the new single shot Degarelix short antagonist group as compared to 50.5% (n=47/93) in classic antagonist group, however not significant (p>0.05).

CONCLUSIONS: The new long-acting GnRH antagonist in a single bolus dose of 0.1 mg carries no risk for LH, produce mature oocytes and achieve comparable pregnancy outcome to the classical short multiple dose antagonist protocol. This new protocol is first described by us, it is more patient friendly decreasing the number of injections that a patient receives. This is an ongoing study, dose of degarelix was arbitrarily chosen by our team, and more degarelix doses can be tested in future studies.
AUTHOR INDEX: ORAL, POSTER, AND VIDEO SESSIONS

Aasted, H., P-182
Abali, R., O-263
Abbas, A. M., O-19, O-20, O-21, O-72, O-127, O-206, P-249, P-263, P-491, P-496, P-499, P-622, P-770, P-775, P-784
Abd Ellah, N. H., P-491, P-496
Abdalla, K. A., O-194
Abdalla, N. K., O-194
Abdalmageed, O. S., O-135, P-770
Abdel-Aleem, M. A., P-784
Abdelaal, I. I., P-532
Abdelaleem, A. A., P-249, P-622
Abdelhajy, M., P-229
Abdelhakim, A. M., P-263, P-775
Abdelhail, M., P-496
Abdelmagied, A. M., O-20, O-135, P-499, P-770
Abdelnaby, E. A., P-406
Abdulhasan, M. A., P-461
Abdullah, N., P-647, P-774
Abern, L., P-633
Abittan, B., O-116, P-646
Abo Markb, A., P-532
Abohashem, E. M., P-284
Abo-Taleb, H. A., O-135
Aboughura, M. A., P-286
Abravom, R., P-91, P-334, P-337
Abravonova, N., P-290
Abu Maizat, A. M., P-112
Abu-Elhassan, A., O-20
Abu-Musa, A., O-68
Abu-Rafea, B., P-201
Abu-Soud, H., O-180
Abubakirov, A., P-58, P-382, P-448
Achariya, C. R., O-192
Achariya, K. S., O-192, P-465
Achilli, C., O-69
Acton, A. J., O-107
Adashi, E., O-99
Adelaye, A., P-632, P-634
Adhikari, D., P-357
Adler, A., P-5
Adriaanse, H. M., P-59, P-62
Adriaenssens, T., O-182, P-199
Adsit, J., O-38
Afeiche, M. C., P-524
Afman, N., P-583
Afrin, S., P-600, P-601, P-607
Agameya, A., P-236
Agarwal, A., O-227, P-425, P-433, P-641, P-649, P-676, P-679
Agarwal, S., P-709
Agarwal, S., O-165, P-778
Aggarwal, R., P-459
Aghajanova, L., O-143, P-6, P-572, P-756, P-760
Aglan, A. D., P-776, P-783
Aglan, D. M., P-776
Aglan, D. M., P-783
Aguilar, J., O-12
Aharon, D., O-198, P-168
Aherm, D., O-38
Ahmad, K., P-584
Ahmady, A., P-103
Ahmed, H., O-72
Ahn, J., P-96
Aijun, S., O-252
AinMelk, Y., P-269
Ajarapu, A. S., P-727
Akcins Alagöz, O., P-437
Akimoto, S., P-432
Akin, N., O-182, P-199
Akoines, A., P-139
Akopians, A. L., O-125, P-100, P-149, P-156
Aksakal, E., P-263
Al-Hendy, A., O-205, O-209, O-243, P-603, P-604, P-606, P-717, P-792
AL-Zubaidi, U. I., P-357
Albert, A. Y., P-597, P-746
Albert, C., O-109
Albertini, D. F., P-30, P-324
Albertsen, H. M., O-189, O-190, P-556
Albobaghli, A., P-284
Aldo, P., O-253
Alegre, L., O-9, O-12, O-109, O-184, P-39, P-125, P-175, P-332, P-415, P-439, V-6
Alegretti, J., P-44
Alexa, S. T., P-567
Alexander, C. J., P-71, P-100, P-149
Alexander, V., P-618
Algergawy, a. a., O-86
Alhahlawy, a. a., O-86
Alhiili, M., V-11
Ali, A., O-72
Ali, M., P-604, P-606
Ali, M. K., O-20, O-206, P-499, P-770
Ali, S., O-206, P-249, P-491
Ali, Y., O-127, O-206
Aljassar, R., P-201
Alkhader, H. A., P-425, P-428, P-433
Alkhalaf, F., O-34, O-61, O-64
Alkon, T., O-70, O-221, P-244
Aliaire, C., P-597
Allen, R., O-165
Allen-Brady, K., P-715
Alligoll, A., P-224
Almeida, C. P., P-193
Almeida, F. D., P-709
Almuzeni, A. A., O-57
Alouf, C. A., P-326
Alouf, C. A., P-331
Al rashid, K., P-699
Alsaid, S., P-641, P-643, P-649, P-661
Altun, A., P-731
Alur-Gupta, S., O-93, O-105
Alvarado, S., O-260
Alvarez, A. V., P-226
Alvarez, I. P., P-563
Alvarez Sedo, C. R., P-665
Alvero, R. J., O-235, P-628
Alviggi, C., P-67
Aly, J., O-65, P-608
Amadoz, A., P-516
Amargant Kiera, F., P-352, P-369
Amari, S., P-18
Amer, A., P-286
Amidi, F., P-763
Amighi, A., O-57
Amin, A. F., O-135
Amin, R. K., P-63, P-261
AmirIannatt, N., P-786
Amita, M., P-139
An, R., O-178
Andaloussi, A. E., P-792
Anderson, A., P-137
Anderson, D., P-735, P-799
Anderson, E., P-124
Anderson, K., P-209
Anderson, R. E., P-73
Anderson, S. H., P-200
Ando, M., P-282
Andreeva, A., P-95
Andriessen, V. C., O-34, O-36, O-61, O-64, P-483
Angun, B., P-225
Anira, R. B., P-15, P-84
Ansari, S., P-179, P-734
Antes, R., P-91, P-334, P-337
Antoniasia, M. P., P-671, P-680
Antonova, E., P-389
Aono, N., A. K., P-127, P-278
Aparicio-Ruiz, B., O-12, O-109
Applebee, D. M., P-610
Aquilante, C. L., O-22
Arafa, M., P-641, P-643, P-649, P-661
Araki, Y., P-243
Araki, Y., P-753
Araki, Y., P-86
Aradujo, P. B., P-226
Arce, J., P-182
Archer, D. F., O-6, O-24, O-179
Arisnend, J., P-608
Arjunan, A., P-384
Armstrong, A. A., P-266
Arnam, P. A., P-119
Aronne, A., O-25
Arora, H., P-270, P-666
Arya, S., O-106, O-193
Asada, H., P-432
Asada, Y., O-128, V-4
Asai-Sato, M., P-602
Asano, R., P-602
Ascher-Walsh, C., O-198
Ashkinadze, E., P-614
Ashraf, M., P-178
Ashraf, R., P-178
Aston, C. E., P-726
Aston, K. I., P-577, P-668
Ata, M. B., O-263, P-225, P-235
Atheleye, A., P-709
Athanasiou, A., P-346
Athevala, D. M., P-387, P-392
Atrio, J. M., P-750
Attar, E., P-731
Attaran, M., P-37, P-109
Au, J. K., P-138
Au, Y., P-632, P-634
Augello, F. S., P-388
Austing, C. M., P-37, P-109
Hata, K., P-429
Hatch, E. E., O-4, P-586, P-663, P-701
Hatch, N., P-580
Hatipoglu, B., P-625
Hattori, H., P-127
Hauschildt, J., P-492
Hauser, R., O-35, O-207, P-211
Havelock, J., P-138
Hawkins, K. C., P-526
Haworth, L., P-98, P-779
Hayden, R. P., O-60, O-225, P-247
Hayon, S., O-58
Hayward, B., P-179, P-734, P-737, P-743
Haywood, M. E., O-170, O-177, P-707
He, P., O-91
He, Q., P-766
He, Q., P-696
He, X., P-306, P-317
Heagerty, A. L., P-703
Healey, M., P-252, P-253
Healy, M. W., P-99
Heiser, P. W., O-133, P-282
Heller, D., O-195
Hellwege, J. N., P-593
Hemalal, S., O-144
Henderson, S., O-259, P-11
Hendrick, N., P-270
Henkel, R., P-406, P-407, P-408, P-425, P-433, P-676
Hennebold, J. D., O-104, P-509
Henessy, D., O-19
Henschke, M. R., P-475
Herbemont, C., P-26
Hernandez, J. O., O-87
Hernandez-Nieto, C., O-70, O-117, O-221, P-85, P-147, P-242, P-244, P-248, P-279
Hernández-Vargas, P., P-521
Herndon, C. N., O-6, P-756, P-760
Herraz, P., O-787
Herreros, J. P., O-112, P-65
Hershlag, A., O-116
Hershlag, A., O-239, O-240, P-28, P-77, P-646
Hervas, L., P-439
Hesla, J. S., P-338
Hess, A., P-698, P-700
Hewitt, W., P-29
Hibray, C., P-328
Hickman, C., O-91, O-184, P-455
Hidalgo, J. P., P-277
Hinckley, M. D., P-177
Hipp, H. S., O-152, P-7, P-123, P-285, P-682
Hirooka, K., P-416, P-434
Hirsch, S. A., P-260
Hirschberg, C., O-172
Hirschberg, C., O-172
Hirshfeld-Cytron, J. E., P-105
Ho, H., O-202, P-718
Ho, J., O-101, P-6, P-101, P-103, P-154, P-474, P-480, P-689, P-697, P-756
Hocaoglu, M., O-731
Hoffman, A., P-83
Hoffman, A. R., P-83
Hoffman, J. R., P-6, P-756
Hohos, N. M., O-175, P-702
Hoidal, J. R., P-577
Holman, D., P-83
Holmes, R., O-114, P-405
Holå, M., P-656
Honig, S., O-148, P-639
Honjo, K., P-422, P-447
Hood, B. L., O-209, P-603
Horikawa, T., P-86
Horiuchi, T., P-24, P-423
Hornick, J. E., P-369
Hornstein, M. D., P-322, P-552
Horowitz, R., O-131
Horton, M., O-490
Hotaling, J., O-2, O-50, O-51, O-52, O-54, O-56, O-380, P-577, P-668
Hou, D., P-354
Houten, A., O-83
Howard, B., O-23, P-497
Howard, K. L., O-38
Howards, P. P., P-780
Howles, C. M., O-227
Hoyos, L. R., P-266, P-730
Hozayen, W. G., O-194
Hoyzen, M. M., O-428
Hsieh, A., P-662
Hsu, A. L., P-507, P-540
Hsu, J. Y., P-722, P-752
Hsu, Y., O-291
Huc, C., O-138
Hu, R., P-454
Huang, C., O-202, P-273
Huang, D., O-43, P-714
Huang, H., O-291
Huang, J., P-218, P-584
Huang, L., P-520
Huang, S., P-291
Huang, T. T., P-462
Huang, T. P., P-273
Huang, W., P-553
Huang, X., P-553
Huber, W. J., P-768
Huber, W. J., O-122
Hubert, G., O-237, P-559
Huddleston, H. G., O-229, P-714, P-723, P-724
Hudgens, J. L., V-14
Hudgens, S., O-595
Huecksteadt, T., P-577
Huete Ferriz, H., O-229
Humes, L. P., O-201
Humaïdan, P., P-67
Humberstone, A., O-16, P-539
Humphreys, M., O-226
Humphries, L. A., O-251
Hurd, M., O-720
Hunn, C., O-774
Hunsche, E., O-595
Hunter Cohn, K., P-478
Hunter, K. L., O-38
Hu, R., O-234
Huyet, E. G., P-498
Hurst, B. S., O-234
Hurtado, S. M., O-205
Hussein, R. S., O-135
Hussain, B., P-780
Hussain, A., O-83, P-261
Hussain, B., O-780
Hussein, R. S., O-135
Hutchinson, A., O-115, P-484, P-561, P-741
Huttler, J., O-551
Huttler, J., O-548
Huynh, H. T., P-36
Hwang, J., O-273
Hwang, S. S., O-14
Hynes, J. L., O-465
Iaconelli, A., O-21
Osès, R. J., P-75
Ostermeier, G. C., P-398, P-435, P-631
Ota, K., P-187, P-754
Othman, E. R., P-532
Outo, E., P-40
Otsuro, H., O-219, P-403
Otsubo, T., O-80
Ottosen, L., P-145, P-471
Oubiña, A., P-390
Ouidir, M., P-578
Ouyang, Y., O-130, O-212, P-208, P-482, P-489, P-696, P-773
Owens, C. D., O-6, O-205
Oyugi, T., O-176
Ozbek, I. Y., P-67
Ozcan, P., P-437
Ozel, B., O-196
Özmann, O., P-642
Ozmen, A., P-547, P-560
Pace, A., P-478
Pacheco, A., O-81
Padmanabhan, V., O-139
Pae, S., P-23
Païdas, M., O-253
Pais, R. J., P-421
Pak, K., P-96
Pakes, C. L., P-164
Pal, L., O-253
Palgamskar, J., P-709
Pall, M., O-108
Pallavi, P., O-244
Palmerola, K. L., P-51
Palumbo, A., O-87
Pan, W., P-412
Panagiotis, P., O-11
Panecheva, M., P-46
Pandurangi, M., P-238, P-257, P-789
Panner Selvam, M., O-227, P-676, P-679
Panaplia, M. M., P-659
Papanikolaou, E., P-126
Papayannis, M., P-490
Papier, S. D., P-15, P-84
Papit, C. M., P-626
Papini, A., P-415
Papini, A., P-143
Parigian-Alvarez, L., O-131, P-771
Pereira, N., O-90, O-132, P-299, P-506
Perez, M., O-60
Perez, I., O-59, P-52
Perez-Villaroya, D., P-519
Perin, J., O-44, P-74
Perkins, N. J., O-1, O-2, O-36, O-61, O-63, O-64, O-65, O-197, P-483, P-579
Perlman, B. E., O-195, P-114, P-180
Persily, J. B., P-657
Perugini, D., P-329
Perugini, M., P-329
Pesant, M., P-269
Pessone, F., P-466, P-479
Petersdorf, K., P-591
Petersen, B., O-40, P-374, P-376, P-431, P-674
Petersen, C. G., O-40, P-374, P-376, P-431, P-674
Petersen, C., O-2, P-715
Petraco, A., P-475
Petrini, A. C., O-90, P-256
Petrozza, J. C., P-755
Peura, T., O-9
Peyser, A., P-28
Pfeifer, S., P-755
Pham, V., P-104
Phan, V., P-542
Phillips, S., P-132
Picou, A., O-172, P-329
Pieper, C. F., P-307, P-758
Pike, J., P-70
Pilgrim, J., P-608
Piña, Y., P-511
Pinho de França, P., P-94
Pini, T., O-170, P-265
Pinkerton, K. E., O-31
Pinson, K., O-160, O-161, P-10
Pirkevi Cetinkaya, C., P-772
Pirrollo, L. M., O-87
Pirrie, A., P-345
Pirte, A., P-214
Pisarska, M. D., O-108, P-149, P-716
Plant, T., P-767
Platt, L. D., P-42
Plowden, T. C., O-61
Pollack, A. Z., O-34
Pollack, C. C., P-610
Polland, M., O-57
Polotsky, A. J., O-75, O-258
Polyakov, A., P-164
Pool, G., P-455
Poonawala, R., O-167, O-168, O-185, P-409, P-410, P-411
Porchia, L. M., P-713
Portela, S., O-134
Post, M. D., O-258
Powe Dillon, J. \_\_\_\_\_\_, P-618
Poza, O. R., P-687
Pratt, P. F., P-568
Preaubert, L., P-132
Price, T. M., P-295
Prien, S. D., P-218, P-419, P-584
Pritchard, M. T., P-352, P-369
Proença, L. A., P-475
Propst, A. M., O-172
Protopsaltis, S., P-316
Prusinski Fernung, L., P-606
Pryzhkov, M. V., P-790
Psathas, P. S., O-11
Puga Molina, L. C., P-240
Pujol Masana, A., O-217
Pundir, J., O-69
Purdue-Šmite, A. C., O-17, O-34, O-61, O-63, O-64, O-73, P-336
Purkiss, S., P-748
Purswani, H., O-196
Puscheck, E. E., O-6, P-137, P-461
Pushparaj, P. N., O-227
Qian, Y., P-210
Qiao, J., P-438
Qin, W., P-443
Qin, Y., P-128
Qiu, J., P-694
Qiu, S., P-133
Quake, S., P-605
Quinn, G. P., O-126
Quinn, M. M., O-37, O-42, O-140, P-6, P-156, P-237, P-266, P-559, P-612, P-756
Quinn, M., P-714
Quint, E. H., O-157, P-626
### AUTHOR AND SPOUSE/PARTNER DISCLOSURES INDEX: ORAL, POSTER, AND VIDEO SESSIONS

All oral, poster, and video presenters at the 2019 ASRM Scientific Congress were required to complete a disclosure form. Each abstract or video author is listed below along with any relationships their partners/spouses disclosed.

<table>
<thead>
<tr>
<th>Author</th>
<th>Spouse/Partner</th>
<th>Disclosure Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aasted, H.</td>
<td></td>
<td>Ferring Pharmaceuticals$^3$</td>
</tr>
<tr>
<td>Aboulghar, M. A.</td>
<td></td>
<td>Ferring$^8$ (travel expenses to attend conference covered by the company); IBSA$^8$ (travel expenses to attend conference covered by the company)</td>
</tr>
<tr>
<td>Abramova, N.</td>
<td></td>
<td>Merck Healthcare KGaA$^3$</td>
</tr>
<tr>
<td>Adeleye, A.</td>
<td></td>
<td>Natera$^3$</td>
</tr>
<tr>
<td>Adsit, I.</td>
<td></td>
<td>Nestle Research Center$^3$</td>
</tr>
<tr>
<td>Afriache, M. C.</td>
<td></td>
<td>Natera, Inc.$^2,3$</td>
</tr>
<tr>
<td>Ahern, D.</td>
<td></td>
<td>Shiyurigaoka general hospital$^3$</td>
</tr>
<tr>
<td>Akimoto, S.</td>
<td></td>
<td>abb-vie$^6$; Bayer$^6$; Myovant$^6$</td>
</tr>
<tr>
<td>Al-Hendy, A.</td>
<td></td>
<td>Center for Human Reproduction$^6$; EMD Serono$^6$; Springer Nature$^5$</td>
</tr>
<tr>
<td>Albertini, D. F.</td>
<td></td>
<td>Juneau Biosciences, LLC$^{1,2,3}$</td>
</tr>
<tr>
<td>Albertsen, H. M.</td>
<td></td>
<td>Abbvie$^5$; Allergan$^5$</td>
</tr>
<tr>
<td>Allaire, C.</td>
<td></td>
<td>Merck Healthcare KGaA$^2,3$</td>
</tr>
<tr>
<td>Allignol, A.</td>
<td></td>
<td>Invitae$^6$ (PGT clinical specialist)</td>
</tr>
<tr>
<td>Alouf, C. A.</td>
<td></td>
<td>Igenomix SL$^3$</td>
</tr>
<tr>
<td>Amador, T.</td>
<td></td>
<td>Animated Dynamics, Inc.$^{1,2,3}$</td>
</tr>
<tr>
<td>Anderson, D.</td>
<td></td>
<td>FertilityIQ$^7$</td>
</tr>
<tr>
<td>Ando, M.</td>
<td></td>
<td>Ferring$^5$</td>
</tr>
<tr>
<td>Arce, J.</td>
<td></td>
<td>Ferring Pharmaceuticals$^3$</td>
</tr>
<tr>
<td>Archer, D. F.</td>
<td></td>
<td>Abbvie$^6,8$; Agile Therapeutics$^6,8$ (Stock Options); Bayer Healthcare$^4,6$; Endocutics$^4,6$; Exelixis$^5$; Innovaya$^2,3$; Merck$^4$; Myovant$^4$; ObsEva$^3,5$; Shionogi$^5$; TherapeuticsMD$^4,6$</td>
</tr>
<tr>
<td>Arjuman, A.</td>
<td></td>
<td>Merida Women’s Health$^3$</td>
</tr>
<tr>
<td>Ascher-Walsh, C.</td>
<td></td>
<td>Expert Alternatives$^4$</td>
</tr>
<tr>
<td>Ata, M. B.</td>
<td></td>
<td>Bayer$^4,6$; Merck KGaA$^4,6$</td>
</tr>
<tr>
<td>Augello, F. S.</td>
<td></td>
<td>Celmatix$^3$</td>
</tr>
<tr>
<td>Awwad, J.</td>
<td></td>
<td>Merck Serono$^5$; Rovi Pharmaceutical$^4$</td>
</tr>
<tr>
<td>Azziz, R.</td>
<td></td>
<td>Ansh Lab$^6$; Martin PET Imaging$^{3,8}$ (Advisory Board); Medtronic$^8$; Spruce Biosciences$^8$</td>
</tr>
<tr>
<td>Babu, R. T.</td>
<td></td>
<td>SpOvum Technologies Private Limited$^1$</td>
</tr>
<tr>
<td>Bachmann, G.</td>
<td></td>
<td>Medscape$^1$; prestige consumer health care$^2$; Up to date$^4$</td>
</tr>
<tr>
<td>Baldwin, K.</td>
<td></td>
<td>California Cryobank$^3$</td>
</tr>
<tr>
<td>Baldwin, M.</td>
<td></td>
<td>Medicines 360$^3$ (Research Co-I)</td>
</tr>
<tr>
<td>Ball, G.</td>
<td></td>
<td>EMD Serono$^6$</td>
</tr>
<tr>
<td>Ball, G. D.</td>
<td></td>
<td>Serono EMD$^6$</td>
</tr>
<tr>
<td>Barad, D. H.</td>
<td></td>
<td>Edwards Life Sciences$^2$; Fertility Nutriceutical$^6$ (Receive Royalty based on Patent); Merck Manual$^6$ (Editorial)</td>
</tr>
<tr>
<td>Barnhart, K.</td>
<td></td>
<td>Barnhart, K. T.</td>
</tr>
<tr>
<td>Beckers, F. P.</td>
<td></td>
<td>Bedawi, M. A.</td>
</tr>
<tr>
<td>Behr, B. R.</td>
<td></td>
<td>Benavent, M.</td>
</tr>
<tr>
<td>Bendikson, K.</td>
<td></td>
<td>Bennett, N. E.</td>
</tr>
<tr>
<td>Berga, S. L.</td>
<td></td>
<td>AMAG Pharmaceuticals$^5$; Ava AG Advisory Meeting$^3$; Lupin Women’s Health Advisory Board$^5$; UpToDate$^5$</td>
</tr>
<tr>
<td>Bhargav, S.</td>
<td></td>
<td>Dibimed$^6$; GE Healthcare$^6$; MedSoftware$^2$</td>
</tr>
<tr>
<td>Bhandari, H. M.</td>
<td></td>
<td>TherapeuticsMD$^{1,2,3}$</td>
</tr>
<tr>
<td>Bhandari, K.</td>
<td></td>
<td>ObsEva$^{1,2,3}$</td>
</tr>
<tr>
<td>Bhargav, S.</td>
<td></td>
<td>Bolognia$^4,7$; Gedeon-Richter$^4,6$; Medtronic$^4,7$; Norgine$^4,7$; Roche$^4,7$; SmithKline$^4,7$; UpToDate$^4,7$</td>
</tr>
<tr>
<td>Bhargav, S.</td>
<td></td>
<td>Bayer$^4,7$; Gedeon-Richter$^4,6$; Medtronic$^4,7$; Norgine$^4,7$; Roche$^4,7$; SmithKline$^4,7$; UpToDate$^4,7$</td>
</tr>
<tr>
<td>Bhargav, S.</td>
<td></td>
<td>Bayer$^4,7$; Gedeon-Richter$^4,6$; Medtronic$^4,7$; Norgine$^4,7$; Roche$^4,7$; SmithKline$^4,7$; UpToDate$^4,7$</td>
</tr>
<tr>
<td>Bhargav, S.</td>
<td></td>
<td>Bayer$^4,7$; Gedeon-Richter$^4,6$; Medtronic$^4,7$; Norgine$^4,7$; Roche$^4,7$; SmithKline$^4,7$; UpToDate$^4,7$</td>
</tr>
<tr>
<td>Bhargav, S.</td>
<td></td>
<td>Bayer$^4,7$; Gedeon-Richter$^4,6$; Medtronic$^4,7$; Norgine$^4,7$; Roche$^4,7$; SmithKline$^4,7$; UpToDate$^4,7$</td>
</tr>
<tr>
<td>Bhargav, S.</td>
<td></td>
<td>Bayer$^4,7$; Gedeon-Richter$^4,6$; Medtronic$^4,7$; Norgine$^4,7$; Roche$^4,7$; SmithKline$^4,7$; UpToDate$^4,7$</td>
</tr>
<tr>
<td>Bhargav, S.</td>
<td></td>
<td>Bayer$^4,7$; Gedeon-Richter$^4,6$; Medtronic$^4,7$; Norgine$^4,7$; Roche$^4,7$; SmithKline$^4,7$; UpToDate$^4,7$</td>
</tr>
<tr>
<td>Bhargav, S.</td>
<td></td>
<td>Bayer$^4,7$; Gedeon-Richter$^4,6$; Medtronic$^4,7$; Norgine$^4,7$; Roche$^4,7$; SmithKline$^4,7$; UpToDate$^4,7$</td>
</tr>
<tr>
<td>Bhargav, S.</td>
<td></td>
<td>Bayer$^4,7$; Gedeon-Richter$^4,6$; Medtronic$^4,7$; Norgine$^4,7$; Roche$^4,7$; SmithKline$^4,7$; UpToDate$^4,7$</td>
</tr>
<tr>
<td>Author</td>
<td>Company/Institution</td>
<td>Notes</td>
</tr>
<tr>
<td>--------</td>
<td>---------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Estes, S. J.</td>
<td>Abbvie</td>
<td>(research support); Obseva (research support)</td>
</tr>
<tr>
<td>Estes, S. C.</td>
<td>Gedeon-Richter</td>
<td>; Merck</td>
</tr>
<tr>
<td>Farland, L. V.</td>
<td>Merck &amp; Co.; Smith &amp; Nephew</td>
<td></td>
</tr>
<tr>
<td>Faulkner, N.</td>
<td>Invitae</td>
<td></td>
</tr>
<tr>
<td>Fernández-Sánchez, M.</td>
<td>Ferring Pharmaceuticals</td>
<td></td>
</tr>
<tr>
<td>Ferrando, C. A.</td>
<td>Fertlity1,2,3; Sequence46</td>
<td>2</td>
</tr>
<tr>
<td>Ferrando, M.</td>
<td>Anecova; Ferring; Gedeon Richter; IVI Clinics; Merck</td>
<td>(Congresses attendance)</td>
</tr>
<tr>
<td>Fidler, M. B.</td>
<td>Insight Medical Genetics</td>
<td>1b,2b,3b</td>
</tr>
<tr>
<td>Fields, R. A.</td>
<td>Bayer AG</td>
<td></td>
</tr>
<tr>
<td>Filonenko, A.</td>
<td>Ferring</td>
<td></td>
</tr>
<tr>
<td>Fischer, K.</td>
<td>MERCK</td>
<td></td>
</tr>
<tr>
<td>Fleischer, K.</td>
<td>ferring; goodlife (fee for lecture); merck-serono</td>
<td></td>
</tr>
<tr>
<td>Flores, V. A.</td>
<td>Abbvie; Society of Reproductive Investigation-Bayer Discovery Grant 4,8 (This is a grant given to Yale University to support my research)</td>
<td></td>
</tr>
<tr>
<td>Flores-Saiffe Farias, A.</td>
<td>New Hope Fertility Center</td>
<td>3</td>
</tr>
<tr>
<td>Forman, E. J.</td>
<td>Ferring Pharmaceuticals</td>
<td>1</td>
</tr>
<tr>
<td>Foster, E. D.</td>
<td>Ferring Pharmaceuticals</td>
<td>3</td>
</tr>
<tr>
<td>Fox, J. T.</td>
<td>Lehigh University</td>
<td>4</td>
</tr>
<tr>
<td>Gada, R.</td>
<td>ReUnite Rx</td>
<td>2a,3b</td>
</tr>
<tr>
<td>Garbarini, W. N.</td>
<td>TMRW Life Sciences, Inc.</td>
<td>1,2,3</td>
</tr>
<tr>
<td>Garcia, C. M.</td>
<td>Texas Fertility Center</td>
<td></td>
</tr>
<tr>
<td>Garcia-Peiró, A.</td>
<td>cimab and DXnow</td>
<td>2a</td>
</tr>
<tr>
<td>Garcia-Velasco, J. A.</td>
<td>Merck, MSD, Ferring, Gedeon Richter, Theramex</td>
<td></td>
</tr>
<tr>
<td>Gardner, D.</td>
<td>VitroLife AB</td>
<td></td>
</tr>
<tr>
<td>Gemzell-Danielsson, K.</td>
<td>Bayer, Merck/MSD, Gedeon Richter, Azanta, Exelixis, HRA-Pharma, Natural Cycles</td>
<td></td>
</tr>
<tr>
<td>Gerlinger, C.</td>
<td>Bayer AG</td>
<td></td>
</tr>
<tr>
<td>Gershman, S. T.</td>
<td>Massachusetts Cancer Registry (Staff)</td>
<td></td>
</tr>
<tr>
<td>Gillispie, V.</td>
<td>AbbVie; Lecture6 (Royalties for USMLE Step 1 Preparation Lectures)</td>
<td></td>
</tr>
<tr>
<td>Ginsburg, E. S.</td>
<td>Advance Medical; Biomed Central; Sanders and Parks; Upto Date</td>
<td></td>
</tr>
<tr>
<td>Glass, S.</td>
<td>Invitae</td>
<td></td>
</tr>
<tr>
<td>Gleicher, N.</td>
<td>Fertility Nutraceuticals, LLC</td>
<td>2,8 (Receives patent loyalty); OvaNova, LLC2,8 (Co-owner); US patents2 (Listed as co-inventors on a number of US patents); Various pharma and medical device companies2,8 (Received research support, travel funding and lecture fees)</td>
</tr>
<tr>
<td>Go, K. J.</td>
<td>TMRW Life Sciences</td>
<td>2,6</td>
</tr>
<tr>
<td>Goldberg, J.</td>
<td>Myriad Women’s Health</td>
<td></td>
</tr>
<tr>
<td>Goldring, G.</td>
<td>Natera</td>
<td></td>
</tr>
<tr>
<td>Gomez, C.</td>
<td>Igenomix SL</td>
<td>3</td>
</tr>
<tr>
<td>Gonzalez-Monfort, M.</td>
<td>Igenomix S.L. (Part-time employed)</td>
<td>8</td>
</tr>
<tr>
<td>Göthberg, M.</td>
<td>Ferring</td>
<td>3b</td>
</tr>
<tr>
<td>Gotteland, J.</td>
<td>ObsEva1,2,3</td>
<td></td>
</tr>
<tr>
<td>Graham, S.</td>
<td>TherapeuticsMD3,8 (Stock Options)</td>
<td></td>
</tr>
<tr>
<td>Grainger, D. A.</td>
<td>AbbVie</td>
<td>7</td>
</tr>
<tr>
<td>Greenberg, R.</td>
<td>TMRW Life Sciences</td>
<td>2,6</td>
</tr>
<tr>
<td>Greenwood, E. A.</td>
<td>EMD Serono</td>
<td>4</td>
</tr>
<tr>
<td>Grifo, J. A.</td>
<td>Inception Fertility</td>
<td></td>
</tr>
<tr>
<td>Grill, E. A.</td>
<td>Aliz LLC (Co owner); Donor Egg Meeting; FertilCalm (Co owner); FertilStrong (Co owner); Merck</td>
<td></td>
</tr>
<tr>
<td>Gris, J.</td>
<td>Ferring laboratory</td>
<td>6</td>
</tr>
<tr>
<td>Groenewoud, E.</td>
<td>Guedes, S.</td>
<td></td>
</tr>
<tr>
<td>Ha, S.</td>
<td>Haahr, T.</td>
<td></td>
</tr>
<tr>
<td>Haerlan, C.</td>
<td>Hacker, M.</td>
<td></td>
</tr>
<tr>
<td>Han, C. S.</td>
<td>Hamaki, A.</td>
<td></td>
</tr>
<tr>
<td>Hamanah, S.</td>
<td>Hatzinikolaou, B.</td>
<td></td>
</tr>
<tr>
<td>Hawlak, J.</td>
<td>Healey, M.</td>
<td></td>
</tr>
<tr>
<td>Hayward, B.</td>
<td>Heiser, P. W.</td>
<td></td>
</tr>
<tr>
<td>Hendon, N.</td>
<td>Herreros, J.</td>
<td></td>
</tr>
<tr>
<td>Hesla, J. S.</td>
<td>Hill, M. J.</td>
<td></td>
</tr>
<tr>
<td>Hirshfeld-Cytron, J. E.</td>
<td>Hoidal, J. R.</td>
<td></td>
</tr>
<tr>
<td>Honig, S.</td>
<td>Hornstein, M. D.</td>
<td></td>
</tr>
<tr>
<td>Hund, M.</td>
<td>Hustine, E.</td>
<td></td>
</tr>
<tr>
<td>Hunter Cohn, K.</td>
<td>Hurley, E. G.</td>
<td></td>
</tr>
<tr>
<td>Hurtado, S. M.</td>
<td>Huynh, H. T.</td>
<td></td>
</tr>
<tr>
<td>Iles, R. K.</td>
<td>Ishihara, O.</td>
<td></td>
</tr>
<tr>
<td>Istock healthcare</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Merck Healthcare KGaA</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Pfizer</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Merck KGaA; Osel Inc.</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Bayer AG</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Novo Nordisk (Medical Advisory Board)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prestige Consumer Healthcare, Inc.</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Life Whisperer; Presagen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shinyurigaoka general hospital</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Ferring, Gedeon Richter</td>
<td>4,5</td>
<td></td>
</tr>
<tr>
<td>Jubel Health</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EverNow (Medical Advisor)</td>
<td>Kitazato; Merck</td>
<td>5</td>
</tr>
<tr>
<td>merck; nonovonicnic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obs EVA 5.8 (Phase 3 new drug study)</td>
<td>Center for Innovative GYN Care</td>
<td>6</td>
</tr>
<tr>
<td>EMD Serono, Inc.</td>
<td>Monash IVF</td>
<td>2a</td>
</tr>
<tr>
<td>Ferring Pharmaceuticals</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>IVFMD</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>IVIRMA</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>NewEra Pharmacy; ORM</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Fertility1,2,3; Sequence46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apricity; Cooper surgical, Apricity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hamilton Thorne, vitrolife, Ferring, Merck Serono, TMRW, Attieh Medical, Parallabs, Cook, Spectrum, Salveappp1,6,7,8 (Advisory Board); TMRW (Advisor)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ohana Biosciences (Research Advisor)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natera</td>
<td>3,8 (option to hold stock)</td>
<td></td>
</tr>
<tr>
<td>ContraVae (Owned stock)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gedeon Richter; Theramex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Applied medical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVI RMA</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>ObsEva SA</td>
<td>2,3</td>
<td></td>
</tr>
<tr>
<td>Roche Diagnostics</td>
<td>2,3</td>
<td></td>
</tr>
<tr>
<td>Myovant Sciences GmbH</td>
<td>3,8 (Stock Options Holder)</td>
<td></td>
</tr>
<tr>
<td>Celmatis</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Innoviva, Inc</td>
<td>2a; Theravance</td>
<td></td>
</tr>
<tr>
<td>Biopharma, Inc</td>
<td>2a</td>
<td></td>
</tr>
<tr>
<td>Abbvie; Novartis, Pfizer, Sanofi; genzyme regeneron</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Andrio360; Boston Scientific</td>
<td>6,7</td>
<td></td>
</tr>
<tr>
<td>ENDO pharmaceuticals; Nanoc; StreamDx</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Evofem Biosciences</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natera, Inc.</td>
<td>3,8 (option to hold stock)</td>
<td></td>
</tr>
<tr>
<td>ContraVae (Owned stock)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gedeon Richter; Theramex</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Applied medical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVI RMA</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>ObsEva SA</td>
<td>2,3</td>
<td></td>
</tr>
<tr>
<td>Roche Diagnostics</td>
<td>2,3</td>
<td></td>
</tr>
<tr>
<td>Myovant Sciences GmbH</td>
<td>3,8 (Stock Options Holder)</td>
<td></td>
</tr>
<tr>
<td>Celmatis</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Innoviva, Inc</td>
<td>2a; Theravance</td>
<td></td>
</tr>
<tr>
<td>Biopharma, Inc</td>
<td>2a</td>
<td></td>
</tr>
<tr>
<td>Abbvie 5,7,8 (Research Principal Investigator); Allergen</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>(Research Principal Investigator) ; Bayer8 (Research Principal Investigator); Femasys8 (Research Principal Investigator); Merk5,7,8; Myovant 8 (Research Principal Investigator); Obseva 8 (Research Principal Investigator)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LifeAire Systems (Partner and Part-time Employee)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAP Sciences</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ferring; Merck Serono</td>
<td>6,7</td>
<td></td>
</tr>
</tbody>
</table>
Isley, L. California Cryobank
Jahangiri, S. CReATe Fertility Centre
Jalalian, L. UCSF Center for Reproductive Health
Jalas, C. Foundation for Embryonic Competence
Jasper, M. J. PerkinElmer Health Sciences (Australia) Pty Ltd
Jasulaitis, S. EMD Serono
Jenkins, T. G. Nanonc
Jensen, J. T. AbbVie (research support to OHSU); Bayer (research support to OHSU); Celmatix (Scientific Advisory Board- No financial compensation); Ferring; Hanzhou first hospital of Zhejiang University (Travel Costs); Shanghai General Hospital and Shanghai Andrology Society (Travel costs); Suzhou University IVF and fertility center (Travel costs)
Jian, L. DIAsource ImmunoAssays SA, Belgium (This company provided the assay kit)
Jimenez-Almazán, J. Igenomix
Johanputra, V. FEC (Consultant)
Johansen Taber, K. Myriad Women’s Health
Johnson, R. Progenity
Johnson, S. SPD Development Company Ltd
Jonker, D. M. Ferring Pharmaceuticals
Jukic, A. Theralogix (Vitamin D supplements from this company were donated for a clinical trial of which I am PI.)

Kadoch, I. Yadtec
Kalaghan, L. CCRM Boston
Kaneshiro, B. Gynuity Health Projects, Merck Sharp & Dohme; Mithra Pharmaceuticals; National Institutes of Health; Sebela Pharmaceuticals; Uptodate
Kaseniit, K. E. Myriad
Kashanian, J. A. Roman Health
Kavoussi, P. K. AYTU Biosciences
Kavoussi, S. K. AbbVie
Keefe, D. L. Illumina; March of Dimes; Origio
Khair, A. F. Ferring Pharmaceuticals
Kiehl, M. Natera, Inc
Kijacic, D. Natera
Kim, J. J. Ferring Pharmaceuticals
Lamb, D. J. 2019 5th PuJiang Reproductive Medicine Forum (Travel costs)

Kloos, B. Androvia LifeSciences (Part Time Employee)

Knowles, T. G. Fertility Focus Ltd (Receive royalties from the Company, co-founded the Company)
Knox, K. Coppe Healthcare Solutions
Knudtson, J. Bayer; Endometriosi Foundation of America; Merck
Kodaman, P. Ferring
Korevaar, T. Berlin Chemie, Goodlife Healthcare, Quidel
Kostaras, K. Ioditiko iatreio Konstantinos E Kostaras & SIA Iatrik E.E.
Kadesia, R. Progyno; Simple Health
Labarta, E. Ferring; FINOX; IBSA/Angelini; MSD; OvaScience

Lambalk, C. B. Lambalk, N. B.
Lanes, A.
Langley, M.
Langlois, M.
Lannon, J. N.
Lauffer, M. R.
Laven, J. S.
Lazorwitz, A.
Leahey, J.
Leahey, C.
Lecomte, V.
Lee, B.
Lee, M. S.
Legro, R. S.
Leppert, P.
Lazorwitz, A.
Leahey, J.
Leahey, C.
Lecomte, V.
Lee, B.
Lee, M. S.
Legro, R. S.
Leppert, P.
Lazorwitz, A.
Leahey, J.
Leahey, C.
Lecomte, V.
Lee, B.
Lee, M. S.
Legro, R. S.
Leppert, P.
Lazorwitz, A.
Leahey, J.
Leahey, C.
Lecomte, V.
Lee, B.
Lee, M. S.
Legro, R. S.
Leppert, P.
Lazorwitz, A.
Leahey, J.
Leahey, C.
Lecomte, V.
Lee, B.
Lee, M. S.
Legro, R. S.
Leppert, P.
Lazorwitz, A.
Leahey, J.
Leahey, C.
Lecomte, V.
Lee, B.
Lee, M. S.
Legro, R. S.
Leppert, P.
Lazorwitz, A.
Leahey, J.
Leahey, C.
Lecomte, V.
Lee, B.
Lee, M. S.
Legro, R. S.
Leppert, P.
Lazorwitz, A.
Leahey, J.
Leahey, C.
Lecomte, V.
Lee, B.
Lee, M. S.
Legro, R. S.
Leppert, P.
Lazorwitz, A.
Leahey, J.
Leahey, C.
Lecomte, V.
Lee, B.
Lee, M. S.
Legro, R. S.
Leppert, P.
Lazorwitz, A.
Leahey, J.
Leahey, C.
Lecomte, V.
Lee, B.
Lee, M. S.
Legro, R. S.
Leppert, P.
Lazorwitz, A.
Leahey, J.
Leahey, C.
Lecomte, V.
Lee, B.
Lee, M. S.
Legro, R. S.
Leppert, P.
Lazorwitz, A.
Leahey, J.
Leahey, C.
Lecomte, V.
Lee, B.
Lee, M. S.
Legro, R. S.
Leppert, P.
Duchesnay USA, Hologic Inc., KaNDy/NeRRe Therapeutics Ltd., Mitsubishi Tanabe; AbbVie, Inc., AMAG Pharmaceuticals, Inc., Duchesnay USA, Novo Nordisk, Shionogi Inc., TherapeuticsMD, Sermonix Pharmaceuticals.

Simpson, A. J. Androvia LifeSciences
Singh, S. S. AbbVie; Investigator for Elagolix trials; Allergan (Investigator for UPA trials (Venus)); Bayer (Investigator for the Vilaprisan trials); Cooper Surgical (Trial for Endosee Device); Hologic

Sinha, A.
Ferring Pharmaceuticals Inc

Smeenk, J. M.
Mojo inc.

Smith, Y. R.
UpToDate (Receive royalties)

Soliman, A. M.
AbbVie Inc.

Soma, J.
Advance Biofactures Corporation

Sommer, G.
Sandstone Diagnostics

Stratton, P.
Allergan (Toxin and funds for study monitoring are provided by Allergan through a clinical trials agreement with NIH)

Stuart, G. S.
Sufen, C.
DIAsource ImmunoAssays

Stull, P.
Bath Fertility UK; Capex; CARe Fertility - TX; Care Fertility UK; Ferring Pharmaceuticals; Fertility Dynamics; Reproductive Medicine Institute; Seattle Reproductive Medicine; Shady Grove Fertility

Suimin, Z.
DIAsource ImmunoAssays S.A. (Belgium)

Surrey, E. S.
AbbVie; Ferring

Sutcliffe, A. G.
Zogenix Inc (member of IDMSC)

Swarm, S. R.
Freeze Health

Tal, R.
Celmatix

Talebi, A.
Tehran university of medical sciences

Tan, Y.
Reproductive and Genetic Hospital of CITIC-Xiangya

Tanrikut, C.
Ferring Pharmaceutical Advisory Board; New England Cryogenic Center (Medical Director)

Taske, H.
Care Fertility UK; Center for Assisted Reproductive Endocrinology; Ferring; Reproductive Medicine Institute; Seattle Reproductive Medicine; Shady Grove Fertility

Tay, L.
PKI

Taylor, H. S.
AbbVie; Dot (Unpaid consultant); Onseva

Taylor, R. N.
AbbVie; Ferring; ObsEva

Teal, S.
Bayer Healthcare; Medicines360; Merck & Co.

Terhaar, C.
Progenity, inc

Terrill, P.
Cytel Inc

Terry, K. L.
CapsuleTech

Teruel, J.
Thomas, E.
Thomas, M. A.

Tirado, E. E.
Tournaye, H.
Traversa, M. V.

Travis, A. J.
Trawick, E. C.
Trent, M.

Tulandi, T.
Ubaldi, F. M.
Udoff, L.

Ulas, T.
Uren, P. J.
Urrutia, A. R.

Van Hecke, E.
Vasilepoulos, Y.

Vazquez-Pacheco, S.
Verhoeve, H.

VerMilyea, M. D.
Walters-Sen, L.
Ward, K.

Warren, K.
Watson, A.
Weddell, S.

Wells, D.
Welty, L. J.

Wemmer, N.
Wessels, C.

Westhoff, C. L.
Westhoof, C. L.

Weyand, A. C.

Wild, R. A.
Williams, S. Z.

Wilk, J.
Yamashita, H.

Yang, H.

Yang, L.

Yao, M. W.

Yu, A.

Zhang, J.

Zayed, A.

Zdrojewski, E.

Zhang, F.

Zhang, S.

Zhou, Y.

Zhu, H.

Zhao, L.

Zhao, Z.

Zhong, Y.

Zhao, X.

Zhao, W.

Zhang, Y.

Zhang, W.

Zhang, L.

Zhou, L.

Zhang, J.

Zhou, H.

Zhang, Z.

Zhang, X.

Zhang, G.

Zhang, Y.

Zhang, X.

Zhang, J.

Zhang, W.

Zhou, Y.

Zhang, H.

Zhou, Z.

Zhang, J.

Zhang, X.

Zhang, J.

Zhang, W.

Zhou, M.

Zhang, L.

Zhou, X.

Zhang, J.

Zhang, W.

Zhou, Y.

Zhang, H.

Zhou, Z.

Zhang, J.

Zhang, W.

Zhou, M.

Zhang, L.

Zhou, X.

Zhang, J.

Zhang, W.

Zhou, Y.

Zhang, H.

Zhou, Z.

Zhang, J.

Zhang, W.

Zhou, M.

Zhang, L.

Zhou, X.

Zhang, J.

Zhang, W.
<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young, S. L.</td>
<td>Abbvie Pharmaceuticals; Ferring</td>
</tr>
<tr>
<td></td>
<td>Pharmaceuticals</td>
</tr>
<tr>
<td>Younis, A. H.</td>
<td>Assuit university (Co author)</td>
</tr>
<tr>
<td>Yurttas Beim, P.</td>
<td>Celmatix</td>
</tr>
<tr>
<td>Zambelli, F.</td>
<td></td>
</tr>
<tr>
<td>Zhan, Y.</td>
<td></td>
</tr>
<tr>
<td>Zhang, J. J.</td>
<td></td>
</tr>
<tr>
<td>Clinica Eugin</td>
<td>Foundation for Embryonic Competence</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>New Hope Fertility Center</td>
</tr>
</tbody>
</table>