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1 A Decision Support Tool for Optimized Personalized Drug Dosage Profiles for Superovulation in In-Vitro Fertilization with Early Clinical Trial Results

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OBJECTIVE: Superovulation is a drug-induced method that enables multiple ovulation per menstrual cycle and is a vital component of a successful IVF cycle. Although there are general guidelines for dosage, the dose is not optimized for each patient, and complications, such as overstimulation, can occur.

To overcome the shortcomings of the current IVF practice of dosage profile determination by trial and error, a mathematical procedure and a decision support tool was developed which can provide a customized model of this stage regarding the size distribution of follicles obtained per cycle as a function of the chemical interactions of the drugs used and the conditions imposed on the patient during the cycle. Uncertainty and risk are modeled and included in optimal drug dosage decisions. This talk describes the theory, model, the optimal control procedure, and the decision support tool for improving outcomes of IVF treatment for both antagonist and agonist protocols used in real practice. We present preliminary results of the results of early clinical trials carried out in India in last three months.

MATERIALS & METHODS: In our earlier work, we developed models for agonist and antagonist protocols based on analogy between superovulation and the particulate process of batch crystallization. It was shown that the model could be customized for each patient using the two two days of follicular data (day 1 and day5 or 6) from that patient. It was found that the model predictions are reasonably accu-rate for most of the patients. The optimal control method is then applied to optimize the dosage profile for each patient. The primary outcome measures studied include the proportion of women with an appropriate number of retrieved oocytes), total hormonal dosage employed during the cycle, and serum oestradiol concentrations on rHCG day, % follicles retrieved, % MIIs in follicles, Number of MIIs.

RESULTS: The validation of the procedure was performed using retrospective as well as data from clinical trials from more than 100 patients. Customized patient-specific model parameters are obtained by using initial day1 and day5 data for each patient and validated. The model is then used for predicting the customized optimal drug dosage for each patient on days 5 through the trigger day.

Preliminary results from the trials show that the dosage predicted by using the model is 40% less than the suggestion made by the IVF clinicians using their standard orotocols. The testing and monitoring requirements for patients using optimized drug dosage is reduced by 72%. For most of the patients, this approach resulted in optimal number of MII follicles.

CONCLUSIONS: A mathematical-based approach to dosage profile determination results in optimal mature follicles with reduced dosage and need for testing.

FINANCIAL SUPPORT: No external support.

2 Can Artificial Intelligence Predict Good Eggs From Bad? Comparing Oocyte Assessment Tool Violet To Current Egg Freezing Predictors

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BACKGROUND: Future Fertility's Violet is an artificial intelligence image analysis egg assessment tool for patients seeking elective oocyte preservation. The technology is used to identify the relative viability of mature eggs to tailor a personalized treatment plan for each patient. The software detects patterns in oocytes in order to better understand egg quality. It may be particularly impactful for older patients who are known to have problems related to egg quality, especially given the fact that they may have less opportunities to undergo multiple cycles. While we currently have methods for assessing sperm quality and embryo quality, there are very limited guidelines for determining successful oocytes. Violet is currently the only objective assessment tool for predicting egg quality. Current research suggests Violet is superior to trained embryologists by more than 20%, with 100% reproducibility1. More data is needed to assess the viability of Violet to better assess the value it provides in improving IVF outcomes.

OBJECTIVE: We sought to compare predictions of live birth rate between Violet and a currently utilized egg freezing predictor, which takes into account age and number of mature oocytes.

MATERIALS & METHODS: A retrospective chart review was performed at a private multi-site infertility center from March 2020 to April 2022. All patients undergoing elective egg vitrification who opted to get oocyte assessment results from Violet were included, for a total of 154 patients. Patients under the age of 24 or over the age of 44 were excluded as the calculator is not recommended in those age groups. All patients underwent controlled ovarian stimulation and subsequent retrieval and mature oocyte vitrification. Likelihood of one live birth was given as a percentage by the Violet report. These results were compared to the Brigham & Women's Hospital Egg Freezing Counseling Tool (BWH EGCT) calculator per MDCalc. An unpaired t-test was performed to compare the mean percentages. Given differences in egg quality with relation to age, we also sought to determine if there was a difference in results by age (age groups: 27-32, 33-38, and 39-44 years old).

RESULTS: The probability of one live birth was assessed using Violet as well as the BWH EGCT for 154 patients. Mean AMH of patients included was 2.42. Mean age at retrieval was 36, with a range of 27-44. The mean likelihood of one live birth rate using Violet as an assessment tool was 47.60%, while the conventional method gave a mean likelihood of one live birth of 49.14% (p=0.6079). There was no significant difference in predictions by Violet versus the conventional method by age, though the results did approach signficance (p=.12 for 27-32, p=.24 for 33-38, and p=.13 for 39-44).

CONCLUSIONS: This is the largest study to our knowledge assessing the viability of Violet compared to conventional methods for assessing egg quality. Our results suggest there is no significant difference between the AI oocyte assessment tool Violet and conventional methods for prediction using age and number of mature oocytes. Additionally, there is no signficant difference when comparing results by age group. This suggests that Violet is able to individually visually assess oocytes for quality and likelihood of success. Violet provides a non-invasive approach and a comprehensive breakdown of the quality of each oocyte. Though these results suggest Violet is similar to existing predictors, it adds value by determining the individual quality of each oocyte. This allows for stratification that can guide fertility decision-making. A limitation of the study is the fairly low number of patients given this is a new technology. As more patients utilize the Violet assessment tool, there will be greater numbers of oocytes that undergo thaw, insemination, and transfer. This will provider greater data regarding fertilization, blastocyst development, and ultimately live birth rate. Though this technology is still in its relative infancy, there is an exciting future ahead for artificial intelligence in assessing oocyte quality and predicting IVF success.

FINANCIAL SUPPORT: None.

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3 Content Analysis of COVID- 19 Vaccine and Infertility Tweets: The Etiology of a Misinformation Pandemic

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OBJECTIVE: To understand misinformation surrounding infertility and the COVID19 vaccine on Twitter by analyzing the prevalence and content of this misinformation.

DESIGN: This study involves content analysis of tweets from a public dataset to identify the etiology of misinformation.

MATERIALS & METHODS: Tweets included were from key points in the COVID19 vaccine discourse (July 2021 and December 2021) and contained at least one word related to COVID19 vaccination and one word related to fertility. Relevant tweets were analyzed for factuality. Descriptive statistics on followers, verification status, and engagement were obtained. Differences between the factual and misinformation groups were examined using ANOVA or Chi-square tests. Rates of factual vs misinformation tweets were compared to US COVID19 case counts and the most common hashtags and words were determined. Sentiment analysis was used to determine if tweets were positive, neutral, or negative.

RESULTS: Misinformation tweets rose from 29.9% in July 2021 to 45.1% in December 2021. The proportion of misinformation in July 2021 fell as daily COVID19 cases rose ($r=-0.50$, $p = 0.01$), while relevant tweets mirrored cases ($r = 0.53$, $p < 0.001$). Accounts sharing factual information had more followers ($p<0.001$) and verified users were more likely to share factual tweets ($p =< 0.001$). Factual and misinformation tweets had similar engagement. Common hashtags in factual tweets included #getvaccinated and #vaccineswork, compared to #vaccinesideeffects and #vaccineskillingunbornbabies in misinformation tweets. Sentiment analysis found factual tweets were more positive and misinformation tweets more negative ($p < 0.001$).

CONCLUSIONS: Misinformation about the COVID19 vaccine and infertility is a threat to vaccine uptake in patients desiring future fertility. Understanding the content, sentiment, and reach of tweets is vital to combat misinformation.

SUPPORT: Association for Healthcare Social Media and Cochrane Healthcare Social Media Grant.

4 Elevated Anti-Müllerian Hormone Level Is Associated with Lower Live Birth Rate in Patients Undergoing Fresh Embryo Transfer

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OBJECTIVE: Anti-Müllerian hormone (AMH) is a reliable predictor of ovarian response in IVF. However, its role as a prognostic marker of pregnancy outcome is conflicting. Traditionally, high AMH level is considered a marker of optimal ovarian reserve, but higher AMH level in patients with PCOS was found to corelate with poor IVF outcomes. Therefore, we propose to investigate the association between severely elevated AMH level and live birth rate (LBR) in young patients undergoing IVF for different etiologies.

MATERIALS & METHODS: A retrospective analysis of the Society of Assisted Reproductive Technology Clinic Outcome Reporting System Database (SART CORS) was performed using data from 2012-2016. All fresh autologous IVF cycles followed by fresh embryo transfer in women <35 years old were included (n=113,643). Based on AMH level, cycles were stratified into 3 groups; Low (<0.6 ng/mL, 10th percentile value), intermediate (0.6-7.88 ng/mL), high (>7.88 ng/mL, 90th percentile). Cycle characteristics and pregnancy outcomes were compared between the groups.

RESULTS: Women in the high AMH group were younger (31 ± 2.9 years) than the intermediate and low AMH group ($p < 0.001$) and required lower doses of gonadotropins (1800 IU, $p < 0.001$) for stimulation. In the high AMH group, 74.6% of the patients had a primary infertility diagnosis other than PCOS. The fertilization rate was significantly higher in the high AMH group as compared to the intermediate and low AMH group (12 vs. 8 vs. 3 oocytes). LBR was significantly higher in the intermediate AMH group (36.4%) as compared to high AMH (31.1%) and low AMH (22.2%; $p < 0.01$). When compared between two groups, LBR was higher in the intermediate AMH group than high AMH group [$p < 0.01$, OR 1.26 (1.22 - 1.32)]. The area under the curve for AMH for LBR was 0.52 in intermediate AMH and 0.47 in high AMH group.

CONCLUSION: In young women undergoing IVF for different indications, severely elevated AMH levels (>7.88 ng/mL) are associated with higher fertilization but lower LBR after fresh embryo transfer.

IMPACT STATEMENT: The result of this study underscores the fact that severely elevated AMH level does not translate into better pregnancy outcome in young women undergoing fresh transfer. This information is useful for patient counselling and individualization of IVF cycle for optimal outcome.

5 Ideal Number of Days of Ovarian Stimulation Based on Anti-Mullerian Hormone Level: Can the Live Birth Rate Be Improved?

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OBJECTIVE: To determine if the relationship between the anti-Mullerian hormone (AMH) level and in vitro fertilization (IVF) stimulation cycle length predicts success of a live birth with a fresh autologous embryo transfer.

DESIGN: A retrospective descriptive study of patients diagnosed with infertility at the University of Cincinnati (UC) Health, Center for Reproductive Health from January 2012 to December 2019 was performed. Autologous IVF cycles with fresh embryo transfers were included. Patients with an AMH reported as zero ng/ml were excluded from the study. Patients with a live birth were compared to patients who did not experience a live birth in relation to their AMH level and stimulation cycle length.

MATERIALS & METHODS: De-identified data was queried through the Society for Assisted Reproductive Technology Clinical Outcomes Reporting System (SART CORS). The outcomes examined were live birth and number of oocytes retrieved. The analysis included T-test, Shapiro-Wilk, and Mann-Whitney U tests using Program R. A value of $p < 0.05$ was assumed to be significant.

RESULTS: A total of 460 IVF stimulation cycles were included. No clear relationship was observed between AMH, number of days of ovarian stimulation, and live birth rate. However, an increased AMH (4.51 ng/ml versus 2.92; $p < 0.001$), lower age (32.6 years versus 34.2; $p<0.001$), larger number of oocytes retrieved (16.5 oocytes versus 12.9; $p < 0.0001$), and lower FSH dosage (1342 IU versus 1745; $p = 0.0205$) were associated with a higher birth rate.

CONCLUSION: There is not an ideal duration of stimulation, based on AMH level, that is associated with an improved chance of a live birth with a fresh autologous embryo transfer. Therefore, adjusting the stimulation cycle length to obtain appropriate oocyte growth should not have a detrimental effect on live birth rate in women with a high AMH.

SUPPORT: None.

6 Impact of Adoption of Radio Frequency Identification (RFID) Witnessing System on Workflow, Organization, and Quality Management in the IVF Laboratory

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OBJECTIVE: To evaluate the impact of using a RFID based electronic witnessing system, RI Witness on workflow, organization, and quality management in the IVF laboratory.

DESIGN: An 11-question anonymous self-administered online survey was developed using Qualtrics software.

MATERIALS & METHODS: 58 respondents were recruited to complete the survey. Individuals were eligible if working at an IVF clinic in the United States. Using a Likert scale survey recipients were asked their opinion on several statements, including how an electronic witnessing system impacted the workflow, organization, and quality management in the IVF laboratory.

RESULTS: Embryologists made up 64% of respondents and andrologists 21%. Electronic witnessing increased efficiency in the laboratory of 83% respondents, but in clinics working with the system over 2 years all clinics reported increased efficiency. Furthermore, among respondents who identified as managerial level the majority (90%) reported increased efficiency. Improved quality management was recognized by 79% of all respondents, and 90% of mana

gerial level embryologist. Only 64% of respondents agreed that electronic witnessing provided time savings, this was increased to 90% when evaluating respondents who identified as managerial level. When examining how electronic witnessing helps to streamline and standardize workflows, improvement rose from 74% to 89%, 2 or more years after installation. Agreement that electronic witnessing ensured adherence to SOPs was also highest 2 years or more post installation at 89% as opposed to 68% among all respondents. Overall, 73% of respondents were not likely to return to manual double witnessing, and this increased to 89% after working with the system for 2 years or more.

CONCLUSION: This research demonstrates a consensus among respondents that the electronic witnessing system had a positive impact on organization, workflow, and quality management in the IVF laboratory. The experience of management level embryologists and those working with the witness system for over 2years were highest. These findings may acknowledge the greater role that managerial level embryologists have in quality control and laboratory organization. Overall, the electronic witnessing system increased efficiency, improved quality management and provided time savings for most respondents.

SUPPORT: CooperSurgical

7 Impact of Personal Experience with Abortion on Obstetric and Gynecology Residents' Intention to Provide Family Planning Following Residency

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OBJECTIVE: This study aims to determine if an Obstetrics and Gynecology (Ob/Gyn) resident's personal experience influence practice patterns.

DESIGN: Voluntary online multiple-choice survey sent to all Ob/Gyn residents in the United States.

MATERIALS & METHODS: The IRB approved survey was completed by 409 residents with 383 responding to the question on personal history of abortion (PHA). Data regarding demographics, religious affiliation, residency program metrics and training experience was gathered and analyzed. Chi-square test was performed on descriptive statistics and ANOVA testing was performed on continuous variables with $p<0.05$ considered significant.

RESULTS: Those with a personal history of abortion were older ($p=0.007$), politically democrat ($p=0.016$), sought out additional training in family planning ($p=0.009$), considered it extremely important that their program offer abortion training ($p<0.001$) and were more likely to intend to provide abortions post-residency ($p<0.001$).

CONCLUSION: Personal experiences do affect a physician's plans on abortion provision post residency. Programs must remain aware of biases and establish an open environment where residents can provide family planning to the degree that they find comfortable.

SUPPORT: This research was supported by an NIH-K12 grant.

8 Impact of the Use of Radio Frequency Identification (RFID) Electronic Witnessing System on the IVF Laboratory Staff and Patient Experience

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DOI: 10.54053/001c.37557

OBJECTIVE: To explore the utilization of RI Witness ™, a radio frequency identification (RFID) based electronic witnessing system, on the experience of laboratory staff and their perceptions of patient experience.

DESIGN: An 11-question anonymous self-administered online survey was developed using Qualtrics software.

MATERIALS & METHODS: 58 respondents were recruited to complete the survey. Individuals were eligible if

working at an IVF clinic in the United States. Using a Likert scale survey, recipients were asked their opinion on several statements, including how the electronic witnessing system agreed that electronic witnessing provided time savings, this was impacted their daily work experience and quality of patient care. Responses were analysed using descriptive statistics and Chi-square automatic interaction detection in SPSS.

RESULTS: Embryologists made up 64% of respondents and andrologists 21%. Of embryologists surveyed, 92% agreed that the electronic witnessing system was easy to use. Most respondents found the system intuitive (90%), with 97% of embryologists agreeing. Job related stress was reduced in 72% of all respondents, with higher agreement among junior embryologists and embryologists (87%). RI Witness increased confidence in all junior embryologists and embryologists that they had not made any potential errors; this was slightly lower in the overall study population at 91%. Most respondents agreed patients were aware their clinic was using an electronic witnessing system. Further evaluation of this subpopulation demonstrated respondents believe patient experience was enhanced by the witnessing system. Patients were more likely to have treatment at their clinics (100%), were reassured the risk of mistakes were reduced (100%) and had greater confidence in the clinic due to the use of witnessing system (100%).

CONCLUSION: This research demonstrates laboratory staff find the RFID electronic witnessing system intuitive and easy to use. Use of this system was shown to positively impact overall work experience, with embryologists collectively more strongly impacted than other groups. Witness has an important role to play in increasing confidence that procedures have been performed correctly, while reducing job-related stress. There was overwhelming agreement that when patients are aware that the electronic witnessing system is being used, that the patient experience was positively impacted and that it plays a role in patient clinic selection.

SUPPORT: CooperSurgical

9 Inclusion of Human Growth Horomone in IVF Stimulation Cycles Reduces Total Gonadotropin Usage and Cycle Cost

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OBJECTIVE: The use of human growth hormone (HGH) treatment in ovarian stimulation (OS) for IVF may increase the number of oocytes retrieved and decrease the total dose of gonadotropins needed during OS. However, neither a cost effectiveness analysis nor a paired comparison between OS cycles with and without HGH in the same patient have been performed. The objectives of this study were to investigate if the inclusion of HGH as an adjuvant in OS reduces the total gonadotropin usage, is more cost effective, and impacts oocyte and blastocyst yield.

MATERIALS & METHODS: This IRB-approved study identified patients who used HGH in their OS at an academic fertility practice between January 2020 and October 2021 after a previous OS without the inclusion of HGH. A retrospective chart review was performed and paired t-tests using GraphPad Prism (v 8.0) were used for statistical analysis with $p<0.05$ considered significant.

RESULTS: A total of 20 patients who had paired OS cycles with and without HGH were included in this study. Study participants had an average age of 36.3 years, BMI of 25.3, and AMH of 1.58. Total gonadotropin dose, length of stimulation, and total cost of stimulation were lower for OS with HGH but were not statistically significant. The number of oocytes retrieved, number of 2PNs, and number of blasto-

	OS without HGH (n=20)	OS with HGH (n=20)	P-value
Total Gonadotropin Dose	3990 (1759.3)	3793 (1554.6)	0.71
Length of Stimulation	12.1 (2.9)	11.8 (2.1)	0.71
Cost of Stimulation	$1330 (609.3)	$1312 (540.4)	0.88
Number of Oocytes Retrieved	8 (6.3)	19 (7.8)	0.38
Number of 2PNs	5.0 (4.2)	6.8 (5.7)	0.28
Number of Blastocysts	2.5 (1.8)	3.6 (3.1)	0.16

(Table 1) Cycle characteristics and outcomes.
Shown as mean (SD)

cysts were higher for OS with HGH but were not significantly different (Table 1).

CONCLUSION: Our study is the first to compare OS cycles with and without HGH in the same patient. This study found that when HGH is used, the total dose of gonadotropin and length of stimulation are decreased. Even with the additional cost of HGH, the overall cycle cost is lower for the cycles that included HGH compared to those that did not. However, these results did not demonstrate statistical significance; and a larger sample size is required to rule out a Type II error. This pilot study described important trends that require further study.

SUPPORT: None

10 Is IVF making more male embryos and does maternal AMH play a role in this?

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STUDY QUESTION: Does a high maternal AMH environment during oocyte maturation affects in vitro preimplantation embryo development resulting in a sex skew toward male live births

STUDY ANSWER: Increasing AMH levels correlate with an increased trend for male births after in vitro conception (IVF) but not with in vivo (intrauterine insemination, IUI) conception.

WHAT IS ALREADY KNOWN: A sex skew toward male neonates after IVF has been described, but it is unclear why this skew exists[1]. This phenomenon may be related to speed at which a male embryo develops to the blastocyst stage leading to an increase in their selection for transfer. We propose that maternal AMH also plays a role in early embryonic development. AMH is known for its role in sexual differentiation and as a marker for ovarian reserve. AMH receptor has been heavily identified in male placentae and fetal membranes and likely impacts early embryonic development[2].

STUDY DESIGN, SIZE, DURATION: Retrospective data analysis of live births from IUI and IVF cycles between January 2015 to December 2021 at an academic institution in the United States. Primary outcome was the rate of male versus female live birth analyzed by maternal AMH. Exclusion criteria included use of donor oocytes, cycle cancellation, missing AMH values, fetal loss and PCOS diagnosis.

PARTICIPANTS/MATERIALS, SETTING METHODS: The IVF and IUI dataset included women ages 27 - 44 with an AMH level drawn within one year of treatment. Results were analyzed by AMH level within quartiles and as a continuous variable.

MAIN RESULTS AND THE ROLE OF CHANCE: The IUI population consisted of 1089 live births, after exclusions 325 live births were analyzed. AMH levels were similar between males and females born after IUI (median [IQR]: female 3.0 [1.6, 4.5] and male 2.6 [1.4, 4.3], p 0.29). AMH analyzed continuously had an OR 0.99 (95%CI 0.97, 1.01) and compared to those below the 75%ile those with maternal AMH above the 75th percentile (AMH 5ng/mL) had an OR 0.92 (95%CI 0.79, 1.07) for male live birth. The odds rations were adjusted for maternal age, BMI, and sperm type (fresh vs frozen). The IUI population did not show a correlation with AMH and male neonates at birth.

The IVF population had 698 live births, after exclusions 406 were analyzed. AMH levels did differ significantly between male and female live births (median [IQR]: female 2.7[1.55, 4.4] and male 3.5 [1.6, 5.8], p=0.012). Odds for male live birth increased with increasing levels of AMH, both when analyzed as a continuous variable with an adjusted OR 1.12 (95%CI 1.04, 1.13, p<0.05) and when analyzed as quartile increment, [AMH above the 75%ile (AMH 5ng/mL) had an adjusted OR2.06 (95%CI 1.30,3.25, p<0.05)]. Adjustments were made for maternal age, BMI, number of fertilized oocytes and cycle type (fresh vs frozen).

LIMITATIONS, REASONS FOR CAUTION: This is a retrospective review of ART data from a single center, more work is needed to elucidate how AMH exposure of the oocyte may affect subsequent and development of male vs female embryos.

WIDER IMPLICATIONS OF THE FINDINGS: AMH levels are correlated with increased odds for male live birth after IVF, but the mechanism for why this occurs is unclear. Further investigation is warranted to understand sex differences in embryo development so as not to artificially skew the sex ratio when selecting embryos for transfer.

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11 Case Report of Acute Encephalopathy Due to Bilateral Tubo-Ovarian Abscesses Following Frozen Embryo Transfer

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OBJECTIVE: To describe a patient with endometriosis who developed acute encephalopathy and sepsis attributed to bilateral tubo-ovarian abscesses (TOAs) after a frozen embryo transfer (FET).

DESIGN: Case Report

MATERIALS & METHODS: A patient with stage IV endometriosis with significant sequelae developed bilateral TOAs following FET resulting in sepsis with acute encephalopathy. TOAs after fertility treatment such as oocyte retrievals or intrauterine inseminations have been documented and are characterized by a more severe clinical presentation than TOAs not associated with fertility treatment [1] . TOAs following embryo transfer are rarely reported in the literature and the clinical pregnancy rate following embryo transfer in cycles complicated by TOA is dismal [2,3] . The complication of sepsis and acute encephalopathy from TOAs adds an additional complexity to the case presented.

RESULTS: The patient is a 40 year old G1P0010 with stage IV endometriosis and a history of two prior exploratory laparotomies for extensive endometriosis excision resulting in a colostomy who underwent in vitro fertilization (IVF) and subsequent FET. Two weeks after her FET, she presented to the hospital with seizure-like activity, altered mental status, abdominal pain, and tachycardia. She was admitted with septic shock and acute encephalopathy attributed to bilateral TOAs identified on CT scan. While hospitalized in the intensive care unit, she was aggressively fluid resuscitated and placed on broad spectrum antibiotics. Interventional radiology placed bilateral percutaneous drains with purulent output that grew Escherichia coli in culture. The patient stabilized, transitioned to oral antibiotics, and was discharged home on hospital day five. The embryo transfer was unsuccessful. After sufficient recovery, she underwent another FET with ampicillin, gentamycin and clindamycin prophylaxis. The transfer did not result in pregnancy, however, the patient did not have a recurrent infection.

CONCLUSIONS: Acute encephalopathy resulting from sepsis due to bilateral TOAs is an uncommon complication of FET. Stage IV endometriosis with significant surgical history increased the risk of this rare outcome. A subsequent embryo transfer was safely performed with surgical prophylaxis.

SUPPORT: None.

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12 Euploid Rates Do Not Decrease Following Re-Biopsy of an Undetermined Embryo

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OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) is being performed more readily in patients undergoing in-vitro fertilization (IVF). However, a small percentage of biopsies, up to 5-6%, return with undetermined results, which have been difficult to interpret. Previous studies had suggested that these embryos were more likely to be aneuploid after re-biopsy, as they were thought to have poor quality DNA. This study aims to determine if the euploid rate is decreased after re-biopsy of previously uninformative results.

DESIGN: The design of this study is a retrospective chart review of patients who underwent embryo biopsy for PGT-A which then returned with indeterminate results. Those that chose to undergo re-biopsy were evaluated.

MATERIALS & METHODS: This study was performed at a private fertility practice. Samples underwent whole genome amplification followed by next generation sequencing, consistent with practice protocols. A two-sided chi-square test was used to compare initial and re-biopsy euploid rates.

RESULTS: A total of 33 embryos were re-biopsied and analyzed. Only 1 (3%) did not survive thawing. Another 9% (3/33 samples) returned again with no results. 15 of the 33 samples (45%) resulted with euploid PGT-A after re-biopsying due to no results on the first biopsy, 42% were aneuploid. The euploid rates for the re-biopsy specimens were not significantly different compared the practice's initial biopsy euploid rate of 53% (P=0.39). 9 of the 15 embryos that were euploid after re-biopsy have been transferred, with 7 resulting in clinical pregnancies.

CONCLUSIONS: With increased use of PGT-A in patients undergoing IVF, a larger number of patients in which initial undetermined results can be expected. While previous literature has suggested these embryos are more likely to be aneuploid, this analysis refutes that statement. Almost half of the samples analyzed in this study were found to be euploid on repeat biopsy, which was not statistically different from the initial euploid biopsy rate. Additionally, only one embryo did not survive the thawing process. Of the re-biopsied embryos that have been transferred, 7 of 9 have resulted in clinical pregnancies, suggesting likely minimal structural damage. Therefore, re-biopsy should be offered to all individuals who receive initially indeterminate results.

SUPPORT: None.

13 Gonadotropin Dose in Young IVF Population with Low Anti-Mullerian Hormone Level: A SART Data Study

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INTRODUCTION: Most common cause for female infertility is diminished ovarian reserve (DOR). AMH plays a key role in determining ovarian reserve, with level <1.05 ng/mL associated with DOR. Young IVF population even with DOR have modest clinical outcome, however information on the stimulation regimen is limited. The aim of this study was to investigate Gonadotropin dose required in young IVF patients with low AMH to achieve optimal clinical response.

METHODS: This is a retrospective cohort study based on SART database between 2012-2016. The study population included 23,001 fresh autologous IVF cycles in women <35 years old with AMH level <1.05 ng/mL. Based on AMH level, women were stratified into 3 groups: low (<1.05-0.4 ng/mL), very low (<0.4-0.16 ng/mL) and ultralow (<0.16 ng/mL). Student t test was used to compare continuous variables and chi-square test to compare pregnancy groups.

RESULTS: Mean population age was 32.4 ± 2.4 and BMI 25 ± 5.9. Women with ultralow AMH had lowest number of oocytes retrieved (5.2 ± 0.4), followed by very low (6.1 ± 0.1) and low AMH (9.4 ± 0.07), p<0.001. The total gonadotropin dose required was significantly lesser in the low AMH group (4086 ± 13.9IU) than very low (4446.5 ± 28.3IU) and ultralow (4319.34 ± 66.6IU), AMH group (p<0.00). Median days of stimulation was 12 in all cycles. Live birth rate was significantly higher in the low AMH (4735/16290,19.1%), followed by very low (1131/5375,21%) and ultralow AMH (159/1336,11.9%).

CONCLUSION: AMH is an independent predictor of live birth. It can be used as a guide to estimate Gonadotropin dosage in young IVF population with DOR.

14 Intrauterine Devices And Its Effects On Anti-Müllerian Hormone Levels And Egg Quantity

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OBJECTIVE: This study sought to investigate how previous intrauterine device (IUD) usage in patients with low Anti-Müllerian hormone (AMH) levels (<1), affects the amount of oocytes retrieved in relation to antral follicle count (AFC).

DESIGN: Retrospective chart review at a private multi-site infertility center.

MATERIALS & METHODS: All IVF and cryopreservation cycle outcomes were reviewed for patients who received treatment between June 2017 and April 2022. Patients were split into two groups, those who self-reported using/having an IUD and patients who reported other or no form of contraception prior to treatment. Data on antral-follicle counts and corresponding number of oocytes retrieved was collected and analyzed to determine if there were any differences between the two patient groups. T-tests and confidence interval analysis were used to analyze the data using R-studio.

RESULTS: A total of 44 patients were included in the study. Average difference in AFC to egg count in the group of patients who reported IUD usage prior or during treatment was 2.8. Average difference in AFC to egg count in the group of patients who did not report IUD usage prior or during treatment was 3.4. There was no statistically significant difference found between these groups ($p > .05$).

CONCLUSIONS: Preliminary data showed no significant difference in average AFC to egg count between patients who reported IUD use prior or during treatment and patients who did not report IUD use prior or during treatment. These results are encouraging for patients searching for types of contraception to use that will not impact their egg count or quality. With more individuals undergoing diagnostic testing and treatment while utilizing IUDs, further research regarding potential effects of IUDs on post-retrieval outcomes in relation to AMH levels and egg quantity is needed.

SUPPORT: None.

15 Legal Case Study Of Severe IVF Incidents Worldwide: Causes, Consequences, And High Emotional, Financial, And Reputational Costs To Patients And Providers

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OBJECTIVE: To determine the causes of lawsuits against ART/IVF providers and ways to prevent them.

DESIGN: Detailed descriptive analysis.

MATERIALS & METHODS: The Lexis Nexis, Westlaw, Bloomberg Law, and CaseLaw databases, newspaper and magazine articles, legal reviews, journals, and online publications were used for U.S. IVF incidents. For international cases, HFEA reports, and industry and online publications were queried. The search was not time restrained.

RESULTS: One hundred eighty-four IVF incidents (89.7% U.S., 3.3% U.K., 7.0% other), excluding large-scale tank and alarm failures and blackouts, which affected 264 people (86.0%, 3.8%, 10.2%) and 225 specimens (88.8%, 3.1%, 8.1%), resulting in 59 lawsuits (71.2%, 10.2%, 18.6%) were identified worldwide, and categorized by error types. Specimen mix-ups were the most prevalent type (91.0%). Meanwhile, the nine failed storage and alarm incidents caused most damage, affecting >1800 patients and >8100 specimens, and resulting in 181 initial lawsuits.

CONCLUSIONS: Overreliance on manual protocols, irregular/skipped audits, and human error led to IVF incidents reviewed. Damaged, destroyed, or lost embryos and embryo transfer to the wrong recipient have lifelong devastating effects on patients, for many of whom IVF was their last chance for parenthood because of cancer treatment, infertility, and/or age. Moreover, embryo mix-ups led to custody disputes over the newborn child(ren), as in Manukyan v. CHA Health Systems, and loss of identity in children and parents in sperm mix-up cases. U.S. babies born to embryo mix-ups are reunited with their genetic parents, followingthe legal precedent of Perry-Rogers v. Fasano. In many coun-

tries, however, the law protects birth parents. Most lawsuits are dismissed or settled because of outdated/missing laws concerning IVF procedures, reproductive specimens, health insurance, and patient bill of rights, and absent/relaxed regulation. Hence, we can only make educated estimates about the true scope of the issue and its financial cost to ART/IVF providers, which might range from thousands to millions of USD. Lawsuits also come at a great reputational cost for patients and providers, so the latter might benefit from embracing automation, robotics, and AI as a new standard of care in their practice and to avoid lawsuits.

16 Rethinking Follicular Maturation: The Incorporation of Luteal Phase Stimulation In IVf Patients With Diminished Ovarian Reserve

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OBJECTIVE: Studies suggest that a single ovarian cycle actually consists of several "waves" of follicular maturation. Therefore, the study aimed to optimize ovarian stimulation through the utilization of both follicular and luteal phase stimulation in IVF patients with diminished ovarian reserve (DOR).

DESIGN: Chart review of patients with a diagnosis of DOR was conducted at a multisite fertility practice in the United States. DOR was defined by pre-stimulation AMH level < 1 ng/ml.Patients underwent either DuoStim or Microdose Flare (MDF) protocol. DuoStim protocol consisted of follicular phase stimulation (FPS) by antagonist stimulation protocol, hCG trigger and oocyte retrieval, immediately followed by microdose leuprolide flare with recombinant FSH, hCG trigger, and oocyte retrieval. MDF protocol consisted of one ovarian stimulation cycle with microdose leuprolide and recombinant FSH with hCG trigger, and oocyte retrieval.

MATERIALS & METHODS: Outcomes were quantified as total number of oocytes retrieved, fertilization rate, and total number of embryos frozen per cycle. Outcomes of three cycle types (DuoStim FPS, DuoStim LPS, and MDF cycle) were statistically compared via one-way ANOVA. Unpaired t-test then compared the same outcome parameters between complete DuoStim cycles (FPS + LPS) and MDF cycles. Statistical analyses were performed using Graph Pad, LLC.

RESULTS: Statistical analysis suggested no significant difference in outcome parameters between DuoStim FPS, DuoStim LPS, and MDF groups (p=0.29, p=0.62, p=0.1; see Table 1). There was no significant difference in outcome parameters between a complete DuoStim cycle (FPS + LPS) and MDF cycle (p=0.12, 0.71, 0.74; see table 1). Of note, there was no significant difference in the outcome parameters between DuoStim FPS and DuoStim LPS (p=0.21, 0.22, 0.78; see table 1).

CONCLUSIONS: This study compared cycle outcomes in DOR patients who underwent IVF with DuoStim and MDF protocols. Whereas trends indicated that DuoStim resulted in a greater number of oocytes retrieved than MDF, this trend was statistically insignificant. Further, there was no significant difference in fertilization rate or number of embryos frozen between the two groups. These preliminary results suggest that DuoStim cycles, which can be costly, may not improve cycle outcomes in patients with DOR.

SUPPORT: None.

	Oocytes Retrieved	Fertilization Rate	Embryos Frozen
DuoStim FPS	4.4	0.45	0.40
DuoStim LPS	5.5	0.33	0.60
DuoStim Total (FPS+LPS)	9.70	0.38	0.90
MDF	6.82	0.42	1.08

(Table 1)

Mean number of oocytes retrieved, mean fertilization rate, and mean number of embryos frozen in DuoStim FPS, DuoStim LPS, DuoStim Total (FPS+LPS), and MDF cycles (p-values as noted in Results section).

17 The Contribution of Clomiphene Citrate To Birth, And Perinatal Death, In a Population Cohort

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BACKGROUND: Over 55 years of clinical success and optimism have made clomiphene citrate the first line treatment for anovulatory infertility globally, despite there never being a prospective study of patient safety as requested by the FDA in the '60's. Further, CC escaped routine surveillance and thereby its contemporary contribution to population fertility, multiplicity, and risk of lethal adverse perinatal outcomes remains uncertain.

OBJECTIVE: The objective is to describe the contribution of CC to total births, and perinatal deaths, including stillbirth and neonatal death.

DESIGN: This is a whole of population cohort of 150,713 women and their 241,561 pregnancies. Records of births ≥20 weeks' gestation, including still birth and deaths in the first 28 days, for South Australia from July 2003 to December 2015 were linked to records of dispensed medications held by the Australian government. Linkage was achieved for 97.9% of women. A pregnancy was designated as exposed to CC if a prescription was dispensed from 90 days before to the end of a defined conception window. For singletons, multivariable logistic regression models were used to examine perinatal death.

RESULTS: In South Australia, 1.6% of pregnancies (1 in 60) of at least 20 weeks' gestation were conceived proximal to CC dispensing. Of these, 5.7% were multiple pregnancies. IVF plus CC now accounts for 6% of all births.

Among all singletons, the prevalence of stillbirth was 6.6 per 1,000 pregnancies, with neonatal deaths of 2.1 per 1,000 live births. Among the 3,632 singletons (3,595 live births) conceived with CC, stillbirth and neonatal death were elevated, prevalence of 10.2 and 3.1 per 1,000, respectively. For the combined outcome of perinatal death, the odds ratio was 1.54, 95% confidence interval (1.15, 2.07), stable upon adjustment for potential biological and social confounders.

CONCLUSIONS: With CC, the prevalence of all medically assisted conceptions was 6%. Multiple pregnancy from CC is now higher than from IVF. Receiving CC was associated with a significantly increased risk of perinatal death. This was not due to major known maternal confounding factors, However, we cannot exclude a degree of residual confounding from some currently unknown factor(s).

SUPPORT: Research funding was received from the Medical Research Future Fund (MRFF), National Health and Medical Research Council (NHMRC), Australia Research Council (ARC), Heartkids Australia, and the National Heart Foundation (NHF).

18 The Effect of Human Growth Hormone In IVF Cycles On Miscarriage Rates

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OBJECTIVE: To determine the effect of adding human growth hormone to IVF protocols on the rate of miscarriage after frozen embryo transfers (FET).

DESIGN: Retrospective chart reviews were conducted in patients who underwent FETs at a private, multi-site fertility center.

MATERIALS AND METHODS: Patients were divided into two groups: One group typically received a total dose of 200 units of human growth hormone in their IVF cycle, while another age-matched control group did not receive any. The pregnancy outcome after the FET was then charted. Only transfers with PGT normal embryos were included. We defined miscarriages based on ACOG guidelines as the loss of a pregnancy within the first trimester, including biochemical pregnancies. A two-sample proportion t-test was run to determine statistical significance.

RESULTS: 221 patients were included in this study, with an average age of 40.5 years in both groups. 166 patients took human growth hormone during their IVF cycle, with an overall miscarriage rate of 15% and biochemical pregnancy rate of 6.6%. 55 patients did not take human growth hormone during their IVF cycle, with an overall miscarriage rate of 33% and a 16.3% biochemical pregnancy rate. Our results demonstrate that the incorporation of human growth hormone in IVF treatment protocols may significantly reduce the likelihood of miscarriage ($p = 0.004$).

CONCLUSIONS: Human growth hormone is frequently incorporated into IVF protocols for patients with a poor IVF response, such as women of advanced reproductive age or with a diminished ovarian reserve. Research supports how adding human growth hormone increases the number of oo-

cytes retrieved, the number of embryos available to transfer, and the clinical pregnancy rate. Previous research conducted by our clinic found improved Blastocyst Quality Scores (BQS) in IVF cycles with human growth hormone. However, there are few studies on whether human growth hormone significantly affects miscarriage rates. Our results suggest that human growth hormone may significantly reduce the likelihood of miscarriage in these poor ovarian responder patients in their subsequent frozen embryo transfer. Additional studies are necessary to further evaluate this effect, controlling for other variables such as overall IVF treatment protocol and total number of IVF cycles.

SUPPORT: None

19 Ultrasound Guided Polypectomy: Evaluation of A Novel Technique To Remove Endometrial Polyp In The Office

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BACKGROUND: Endometrial polyps are present in 13-50% in women with abnormal uterine bleeding (AUB). Hysteroscopy is currently the method of choice for definitive diagnosis and treatment, which has some limitations. Hence, we propose a novel technique which allows ultrasound-guided office-based polypectomy. It avoids general anaesthesia, is inexpensive and allows single point of care.

OBJECTIVE: The purpose of this study was to evaluate a novel technique of endometrial polyp removal in the office and pain scores associated with that procedure.

MATERIALS AND METHODS: Prospective trial conducted at an academic hospital after Institutional Review Board approval over a period of 12 months. Women with AUB had saline infusion sonogram (SIS) to delineate the polyp. Then under ultrasound guidance, the universal grasping forceps (2.5 mm X 25 cm) was introduced through the cervix into the uterus to remove the polyp. It was an off-label use of the instrument. The goal of the study was to evaluate the patients' post-procedure pain and satisfaction score. The secondary outcomes were confirmation of complete removal of polyp by assessing resolution of patients' symptoms and performing SIS at 3 months interval.

RESULTS: There were 30 patients. Mean age and BMI was 54.8 ± 11 and 30.6 ± 10 respectively. Average polyp volume was 1.26 cm3 and mean time taken for polypectomy was 11 minutes 50 seconds. The median pain score was in Visual Analogue Scale (VAS) was 5. The median satisfaction score post procedure was 10. Adequate pathology sample was obtained for 100% of cases and 2 returned as malignancy. For 3 months follow-up, 16 patients returned. Among them 13 (81%) had no evidence of polyp on SIS and 14 (87%) reported complete symptom resolution.

CONCLUSIONS: This technique can be used safely and effectively to remove endometrial polyp in appropriately selected patient population in an outpatient setting. In times of COVID-19, this technique can be helpful in reducing the number of cases which needs to be performed under anesthesia.

SUPPORT: The authors did not receive any funding for this study.

20 Vitamin D Deficiency And Uterine Fibroids: A Systematic Review

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OBJECTIVE: To evaluate the relationship between vitamin D deficiency and uterine fibroids.

DESIGN: Systematic literature review.

MATERIALS AND METHODS: Studies evaluating the relationship between vitamin D and uterine fibroids in humans were identified by searching Cochrane Library, Embase, PubMed, Scopus, and Web of Science in accordance with the PRISMA guidelines in collaboration with an experienced medical librarian. Any English-language publication evaluating the relationship between vitamin D and uterine fibroid in humans was included.

RESULTS: The initial search yielded a total of 1602 arti cles. A total of 642 duplicates were removed, leaving 960

unique citations. After screening the title and abstract of the 960 articles identified, 163 articles were considered for full review. A total of 89 studies met complete inclusion criteria, 25 of which were clinical articles evaluating the relationship between fibroids and vitamin D deficiency. Fourteen clinical studies (n=3535 participants) assessed serum vitamin D level in women with ultrasound-proven fibroids and all found an inverse correlation between serum vitamin D level and presence of fibroids. These studies took place in diverse demographic groups and multiple geographic settings. Vitamin D deficiency approximately doubles the risk of uterine fibroids. Five clinical studies (n=472 patients) evaluated treatment of fibroids with vitamin D in women with deficiency. Four of five studies showed vitamin D significantly inhibited fibroid growth. One well-designed pilot study (n=109 patients) of vitamin D for secondary prevention of fibroids demonstrated a lower risk of recurrence and smaller recurrent fibroids in the treated group.

CONCLUSIONS: The association between uterine fibroids and hypovitaminosis D exists across racial groups and geographic locations with remarkably consistent findings between studies. Some evidence suggests that vitamin D may be beneficial for the treatment of uterine fibroids. Routine vitamin D supplementation for women with insufficiency might provide effective treatment or prevention of this prevalent and costly disease.

SUPPORT: This research was supported in part by the Howard and Georgeanna Jones Endowment.

21 Use of Telehealth Services to Improve Access to Fertility Preservation Consultations In Patients Diagnosed With Cancer

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OBJECTIVE: Currently available strategies for fertility preservation are well established once a patient meets with an expert, however, obtaining access to that initial consult with an expert can be difficult. Only 15-29% of female reproductive-age patients with cancer have at least one fertility consultation which demonstrates a need to focus not only on treatment options but also initial access to care [1,2] . We investigated the utility of telehealth services to improve access to fertility consultations in patients diagnosed with a malignancy referred to our institution.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: this was a single institution prospective study of all patients who were referred for a fertility preservation consultation to our reproductive endocrinology and infertility (REI) clinic from Nov. 2020 to July 2021. Our prior policy was an in-person consultation for all referred patients but given logistical considerations, the policy changed to a phone consultation followed by a telehealth consultation if desired. The phone consultation was not billed and was done by a REI fellow who reviewed risks of cancer treatment to ovarian reserve, fertility treatment options, and costs. Demographics along with fertility counseling outcomes were collected for each patient.

RESULTS: A total of 45 patients were referred to our REI center during the study time, majority for breast, hematologic or endometrial cancer. Ninety one percent of patients had a phone consultation, 31.1% had a zoom consultation and 20% proceeded with oocyte or embryo cryopreservation. Of patients who did not proceed with treatment, commonly cited reasons were time to delay treatment (33.3%) and financial constraints (17.8%).

CONCLUSIONS: In our study, access to fertility consultations was drastically higher than previously published literature with 91.1% of patients having a phone call to discuss fertility preservation options. This strategy allows patients to make an informed decision about proceeding before paying potential out-of-pocket costs for a formal telehealth consultation or treatment. Most large cancer institutions are part of academic centers with trainees such as residents or fellows who can provide these services to patients and increase access to fertility consultations.

SUPPORT: None.

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