OBJECTIVE: Access to reproductive tissues is critical for development of new therapies in reproductive care. To optimize research utilization of reproductive tissues generated during IVF cycles, an IRB protocol was designed to encourage and maximize patient participation.

DESIGN: Descriptive Study.

MATERIALS AND METHODS: An IRB protocol was designed to allow patients to donate several types of reproductive tissue generated by IVF. A consent for research is presented to couples in advance of treatment listing five statements to which the couple may agree or disagree. The statements include donation of 1) normally discarded cellular material and 2) normal embryos in excess of clinical need. Participants also consent to or refuse 1) usage for research of infertility or inherited genetic disease and 2) usage for future research to learn about, prevent, or treat any other health problems. The fifth option allows Mayo investigators to release material to outside institutions for collaborative research.

RESULTS: Of 316 couples offered participation, nineteen (6%) declined any participation. Of the consenting 297 couples, all but one (99.7%) agreed to research on discard-type material while 20% of patients were uncomfortable donating excess embryos. Interestingly, 15% of couples were uncomfortable with their tissues going to outside institutions. See distribution of results in the following table.

<table>
<thead>
<tr>
<th>Statement</th>
<th>Agree (%)</th>
<th>Disagree (%)</th>
<th>Decline Participation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donation of normally discarded cellular material generated during an IVF cycle</td>
<td>296 (93.7%)</td>
<td>1 (0.3%)</td>
<td>19 (6.0%)</td>
</tr>
<tr>
<td>Donation of excess embryos following a maximum 10 year storage period</td>
<td>237 (75.0%)</td>
<td>60 (19.0%)</td>
<td>19 (6.0%)</td>
</tr>
<tr>
<td>Storage for future research of infertility or inherited genetic disease</td>
<td>295 (93.4%)</td>
<td>2 (0.6%)</td>
<td>19 (6.0%)</td>
</tr>
<tr>
<td>Storage for future research to learn about, prevent or treat any other health problems</td>
<td>292 (92.4%)</td>
<td>5 (1.6%)</td>
<td>19 (6.0%)</td>
</tr>
<tr>
<td>Allow sharing of anonymous material with outside institutions</td>
<td>253 (80.1%)</td>
<td>44 (13.9%)</td>
<td>19 (6.0%)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The majority of couples agreed to participate in donation indicating strong patient support of research. This type of inclusive IRB protocol allows for the storage of multiple types of reproductive tissue. As research projects are identified, specific IRB protocols are submitted for use of the previously stored materials. This prospective generalized consent process is a flexible method of obtaining research materials that can be used for a wide range of research to further advance fertility care.

Supported by: None.

P-470

A DOSE FINDING STUDY OF RECOMBINANT HUMAN FOLLICLE-STIMULATING HORMONE (r-hFSH; FOLLITROPIN ALFA) IN JAPANESE PATIENTS UNDERGOING OVULATION INDUCTION.

D. R. Tredway, Y. Taketani, T. Yanaihara, M. Irahara, H. Saito on behalf of the Japanese r-hFSH OI Study Group. Clinical Development, EMD Serono Inc., Rockland, MA; Department of Obstetrics and Gynecology, Faculty of Medicine, University of Tokyo, Tokyo, Japan; Department of Obstetrics and Gynecology, School of Medicine, Showa University, Kamakura, Japan; Department of Obstetrics and Gynecology, Institute of Health Biosciences, University of Tokushima Graduate School, Tokushima, Japan; Division of Reproductive Medicine, National Center for Child Health and Development, Tokyo, Japan.

OBJECTIVE: In Japan, purified human FSH (u-hFSH-HP) is registered for use in patients with polycystic ovary syndrome (PCOS). Compared to u-hFSH, recombinant human FSH (r-hFSH, follitropin-alfa) offers a greater purity and consistency in composition, higher specific activity and a reduced risk of immunogenicity. A dose finding study was conducted in Japan using follitropin alfa in patients undergoing ovulation induction.

DESIGN: Double-blind, randomized, multi-center study.

MATERIALS AND METHODS: Study objectives were to assess safety and time to achieve a dominant follicle of 18 mm diameter. The study was conducted at 22 sites and enrolled patients with amenorrhea I or anovulatory cycles, with or without PCOS. Patients’ age was 20–39 years, and BMI was 17–28 kg/m². Patients were randomized to a starting dose of 37.5 IU (Group L), 75 IU (Group M) or 150 IU (Group H) follitropin-alfa. The daily dose was increased by 37.5 IU if the dominant follicle was <11 mm on Day 8.

RESULTS: Clinical pregnancy was associated with younger recipient age (41.5 vs. 42.1 years; P=0.02). Interestingly, increased recipient age was associated with reduced pregnancy odds when controlling for confounding factors (figure). A younger paternal age was observed among those achieving pregnancy (42.0 vs. 43.0 years; P=0.01). Paternal age negatively correlated with pre-wash semen concentration (P<0.03); ICSI use resulted in lower pregnancy odds compared to IVF (OR:0.746; P<0.01). The use of frozen embryos (P<0.01) and increased cycle number (P<0.04) also negatively impacted pregnancy. However, logistic regression modeling found no difference in pregnancy odds with increasing paternal age when controlling for these factors (OR:0.987; P=0.18).

CONCLUSIONS: Contrary to our expectation, increasing recipient age negatively impacted pregnancy odds. This decrease occurred among recipients between the ages of 25 and 38 years, and remained stable thereafter. Increasing paternal age did not seem to significantly reduce pregnancy odds despite its association with lower pre-wash semen concentration. These results suggest that recipient age-dependent factors are involved in reduced pregnancy odds independent of oocyte quality. Further studies should focus on age-dependent uterine factors.

Supported by: This research was supported in part by RBMB/NICHID/NIH, Bethesda, MD and UCLA, Los Angeles, CA.

P-469

RECIPIENT AGE, NOT PATERNAL AGE, REDUCES PREGNANCY RATE IN OOCYTE DONATION CYCLES.

K. M. Brennan, E. Levens, A. Huang, K. Richter, D. Hill, S. Kipersztock. Obstetrics and Gynecology, University of California Los Angeles, Los Angeles, CA; Southern California Reproductive Center Medical Group, Beverly Hills, CA; Reproductive Biology and Medicine Branch, National Institute of Child Health and Human Development, NIH, Bethesda, MD; Shady Grove Fertility Reproductive Science Center, Rockville, MD.

OBJECTIVE: To determine the influence of recipient and paternal age on pregnancy rate (PR) in oocyte donation cycles.

DESIGN: Retrospective cross-sectional analysis.

MATERIALS AND METHODS: Analysis of data from 1777 women undergoing 1843 donor oocyte cycles at two bicoastal fertility centers from 2002 to 2006 were retrospectively analyzed. Variables assessed were paternal age, recipient age, semen parameters (pre- and post-wash concentration and motility), use of frozen embryos, use intracytoplasmic sperm injection (ICSI) or in vitro fertilization (IVF), cycle number, and number of embryos transferred. Wilcoxon rank sum and χ² test were used for continuous and categorical variables. The relationship of recipient and paternal age on PR was analyzed using an additive logistic regression model.

RESULTS: Clinical pregnancy was associated with younger recipient age (41.5 vs. 42.1 years; P=0.02). Interestingly, increased recipient age was associated with reduced pregnancy odds when controlling for confounding factors (figure). A younger paternal age was observed among those achieving pregnancy (42.0 vs. 43.0 years; P=0.01). Paternal age negatively correlated with pre-wash semen concentration (P<0.03); ICSI use resulted in lower pregnancy odds compared to IVF (OR:0.746; P<0.01). The use of frozen embryos (P<0.01) and increased cycle number (P<0.04) also negatively impacted pregnancy. However, logistic regression modeling found no difference in pregnancy odds with increasing paternal age when controlling for these factors (OR:0.987; P=0.18).

CONCLUSIONS: Contrary to our expectation, increasing recipient age negatively impacted pregnancy odds. This decrease occurred among recipients between the ages of 25 and 38 years, and remained stable thereafter. Increasing paternal age did not seem to significantly reduce pregnancy odds despite its association with lower pre-wash semen concentration. These results suggest that recipient age-dependent factors are involved in reduced pregnancy odds independent of oocyte quality. Further studies should focus on age-dependent uterine factors.

Supported by: None.
15 or 22. Follitropin alfa was administered until the dominant follicle reached 18 mm, but not for longer than 28 days.

RESULTS: 184 subjects received follitropin alfa (62 in Group L, 62 in Group M and 62 in Group H). There was a clear dose-response relationship around the median time length to achieve a dominant follicular diameter of 18 mm was in the order of 14.0 days (Gr. L); >10.0 days (Gr. M) and 8.0 days (Gr. H). Patients achieving a dominant follicular diameter of 18 mm were 87.7% in Gr. L; 98.4% in Gr. M and 94.5% in Gr. H. Ovulation rates were 86.0% in Gr. L; 95.1% in Gr. M and 50.9% in Gr. H. Total follitropin alfa doses administered were 697 ± 559 IU in Gr. L; 871 ± 588 IU in Gr. M and 1105 ± 227 IU in Gr. H. The bCG cancellation rates were 0.0% in Gr. L; 3.3% in Gr. M and 38.2% in Gr. H. Pregnancy rates were 15.8% in Gr. L; 18.0% in Gr. M and 9.1% (5/55) in Gr. H. Moderate or severe adverse events tended to occur in Gr. H and were therefore attributed to the study drug. Most adverse events observed in groups L and M were mild, confirming the safety of these doses.

CONCLUSIONS: The results suggest that the 75 IU starting dose is the most appropriate starting dose for ovulation induction in Japanese patients. The results of the ongoing comparison study will hopefully lead to lower IVF drop out rates.

P-471
A PATIENT CENTERED APPROACH FOR IVF UNDERSTANDING THE BURDEN OF CONTROLLED OVARIAN STIMULATION (COS) AS EXPERIENCED BY PATIENTS. M. Brod, C. Wiebinga, E. Hoomans. The Brod Group, Mill Valley, CA; Global Health Economics & Strategic Pricing, NV Organon, Oss, Netherlands; Global Venture Team Fertility, NV Organon, Oss, Netherlands.

OBJECTIVE: The impact of COS for women is significant. Understanding the patient and clinician perceptions of this burden is key in developing a patient centered approach for IVF treatment.

DESIGN: A qualitative study to assess the burden profile of COS from a clinician and patient perspective.

MATERIALS AND METHODS: Nine clinicians and 48 patients from 3 countries (US, UK, France) were interviewed. The individual statements were categorized by applying a coding system. These coding themes were compared with data from an independently conducted survey of the attitudes of 170 fertility physicians/nurses in 8 countries (Italy, France, Germany, Turkey, US, UK, Japan, Spain).

RESULTS: The clinicians had on average 16 years of ART experience and treated more than 250 women a year. The average patient was age 35, had 2 children and 26% had successful IVF. In the perception of clinicians and patients, COS is a burdensome process with daily injections perceived as contributing to this burden. Patients estimated the degree of stress due to daily injections higher than the clinicians. Clinicians felt that a successful IVF outcome would negate the negative impact of COS on daily functioning, work and social relationships. The women reported that their previous distressing experiences were not completely offset by a successful IVF outcome. Most clinicians did not realize that many patients believed they had made a wrong decision and administration errors during COS. Improving the patient process of care were considered of paramount importance by patients, psychologists and nurses. The clinician attitude survey supported the observed differential perception of clinicians and patients.

CONCLUSIONS: All patients regard COS as a distressing component of IVF and are overwhelmed/negatively impacted by the IVF process. Clinicians and patients have differential perceptions around burden and impact of COS. Understanding the burden of COS as experienced by the women may contribute to the development of a patient centered approach that reduces the negative impact of IVF on the well being of the patients and hopefully lead to lower IVF drop out rates.

Supported by: NV Organon.

P-472
PREDICTION OF ICSI OUTCOME BY SPERM CHROMATIN PARAMETERS. R. Mahfouz, M. Elsahfei, S. Kandil, R. Sharma, A. Fatih, A. Agarwal. Reproductive Research Center, Glickman Urological Institute and Department of Obstetrics/Gynecology, Cleveland Clinic, Cleveland, OH; Department of Clinical Pathology, Meno thyra University Hospital, Shbib Elkom, Meno thyra, Egypt.

OBJECTIVE: A variety of assays are available to evaluate the sperm chromatin status. Sperm DNA cytometry can differentiate cells into sub-haploid damaged, mature condensed haploid and immature sperm chromatin subpopulations. In addition, Aniline blue test can detect defects in the histones/proteins replacement. Intracytoplasmic sperm injection (ICSI) is an important option for the treatment of severe cases of male infertility. The aim of our study was to evaluate if parameters of sperm chromatin assay may help in predicting ICSI outcome in patients with male infertility.

DESIGN: Prospective study.

MATERIALS AND METHODS: Semen samples were collected from 42 infertile men with no female factor infertility. Routine semen analysis was done and one aliquot of semen used for sperm DNA cytometry and aniline blue test. Another aliquot used for ICSI. Pregnancy test was done after 2 week from the embryo transfer to the female partner. Receiver operating curve (ROC) were calculated for sperm DNA cytometry and aniline blue test to predict pregnancy following ICSI.

RESULTS: For detection of pregnancy and outcome of ICSI: % of condensed chromatin sperm showed a cutoff value of (22.7%) with area under the curve (AUC, 0.85), sensitivity (94.7%) and specificity (65.2%). The % aniline blue non-stained sperm showed a cutoff of (73.5%) with AUC (0.57), sensitivity (63%) and specificity (52.2%). Patients with % of haploid sperm below the cutoff value showed a higher incidence of sperm DNA fragmentation as expressed by high sub-haploid sperm percentage compared to patients with % of haploid sperm above the cutoff (P<0.001) (Table).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Below haploid cutoff (%)</th>
<th>Above haploid cutoff (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA cytometry</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Haploid cells (condensed chromatin)</td>
<td>11.5 ± 1.8</td>
<td>45.7 ± 3.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% Sub-haploid cells (apoptotic bodies)</td>
<td>81.7 ± 2.8</td>
<td>38.9 ± 3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aniline blue staining</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>stained sperm (%)</td>
<td>5.5 ± 1.4</td>
<td>5.9 ± 1.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Abnormal chromatin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unstained sperm (%)</td>
<td>73.1 ± 3.7</td>
<td>73.5 ± 3.2</td>
<td>0.9</td>
</tr>
</tbody>
</table>

P<0.05 was significant for below and above haploid cutoff groups using Student’s t-test.

CONCLUSIONS: Mature condensed haploid sperm chromatin is the best predictor for ICSI outcome. Men show severe sperm DNA damage when the damage is below the haploid cutoff value.

Supported by: None.

P-473
ACCESS TO ASSISTED REPRODUCTIVE TECHNOLOGY (ART) CENTERS IN THE USA. ARE ART CENTERS RATIONALLY LOCATED? A. K. Nangia, D. S. Likosky, D. Wang. Section of Urology and Ob/Gyn, Dartmouth-Hitchcock Medical Center, Lebanon, NH; Department of Surgery, Dartmouth Medical School, Hanover, NH; Center for Evaluative Sciences and Community & Family Medicine, Dartmouth Medical School, Hanover, NH.

OBJECTIVE: To describe the spatial disparity of ART centers based on their location in relation to the populations in the reproductive years. To identify an association between state-mandated coverage for infertility services and number and location of ART centers.

DESIGN: Cross sectional study.

MATERIALS AND METHODS: 2000 U.S. Census estimates by sex and age groups for population in the reproductive years (women 20–44 and men 20–49) were calculated. ART centers registered with the Society for Assisted Reproductive Technology (SART) in 2005 were retrieved (sart.org). Sixty minute travel distances from the ART addresses were calculated and graphed using Geographic Information Systems software (ArcGIS 9.1). Populations within the 60 min catchment area served by in-state and neighboring state ART centers were calculated. Proximity of the study populations to ART centers was stratified by gender, female age, and 2005 state-mandated coverage for ART.

Supported by: None.