O-4

Basal Follicle-Stimulating Hormone as a Predictor of Fetal Aneuploidy. J.A.M. Massie, R.O. Burney, A.A. Milki, L.M. Westphal, R.B. Lathi. Department of Obstetrics and Gynecology, Stanford University School of Medicine, Stanford, CA.

Background: The majority of cases of fetal aneuploidy are thought to originate from genetic errors in oocyte development. A prevalent hypothesis predicts that meiotic error rates in oocytes are higher in women with diminished ovarian reserve, regardless of whether the reduction in the oocyte pool is physiologic or pathologically premature. Studies evaluating this hypothesis using karyotypes collected at amniocentesis risk missing a significant number of aneuploid conceptions which spontaneously abort in the first trimester.

Objective: To determine whether elevated basal FSH concentration is an independent predictor of fetal aneuploidy, as measured in spontaneous abortions.

Materials and Methods: We reviewed the charts of all women with karyotypes of chorionic villi isolated from first trimester spontaneous miscarriages at the time of dilation and curettage (D&C) from 1999 to present. The highest basal FSH level within one year of D&C was recorded. Statistical analysis consisted of Student's *t*-test or chi-square tests, with FSH and maternal age evaluated both as continuous and as categorical variables. Logistic regression was used to estimate the odds ratios and 95% confidence intervals relating aneuploidy to each predictor variable.

Results: A total of 177 spontaneous miscarriages with karyotypes (70 euploid and 107 aneuploid) were identified, of which 52% were conceived via in vitro fertilization. Due to a higher than expected (61%) ratio of XX karyotypes in the euploid cohort and the potential for maternal contaminant to confound interpretation, we considered only 46 XY karyotypes (n = 27) in the euploid group. The aneuploid cohort consisted of trisomic (87%), tetraploid (9.3%), and monosomic (3.7%) gestations.

Variable	XY (n = 27)	Aneuploid (n = 107)	p value
Maternal Age (years)	36.7	38.0	NS
Age > 35	55.6%	73.8%	0.064
CD 3 FSH (mIU/mL)	9.2	8.6	NS
CD3 FSH ≥ 14	18.5%	5.6%	0.029
CD3 E2 (pg/mL)	29.3	33.4	NS

Logistic regression analysis (basal FSH and maternal as continuous variables) revealed neither to be independently predictive of an aneuploid gestation in our dataset.

Conclusions: This study is the largest to date, evaluating an association between elevated basal FSH and fetal aneuploidy in spontaneous abortions. Our data do not appear to support the hypothesis that a reduced oocyte pool is associated with an increased meiotic error rate. Clinically, an elevated basal FSH does not predict an increase in fetal aneuploidy.

O-5

Effects of Estradiol and Medroxyprogesterone Acetate on Vascular Function in Young Women. P.F. Kaplan, J.R. Meendering, C.T. Minson. Department of Human Physiology, University of Oregon, Eugene; Department of Obstetrics and Gynecology, Oregon Health and Sciences University, Portland, OR.

Background: It has been established that estrogen improves endothelial function, but the effects of progestins are less clear. Medroxyprogesterone acetate (MPA) is a commonly prescribed progestin used in combination hormone replacement therapy for postmenopausal women and contraception for young women. However, the effects of MPA on vascular health are unclear.

Objective: To determine the acute affects of MPA alone and in combination with estradiol (E2) on conduit and resistance vessel responsiveness in young women.

Materials and Methods: We suppressed endogenous estrogens and progesterone in 14 subjects using a gonadotropin-releasing hormone antagonist (GnRHa) for 10 days. On days 4–10 of GnRHa, *Group 1* (n = 10) was administered 0.1 mg transdermal E2 (GnRHa + E2), and on days 7–10 administered 5.0 mg oral MPA (GnRHa + E2 + MPA). *Group 2* (n = 2) was given 0.1 mg transdermal E2 beginning on day 4 (GnRHa + E2) and continued through day 10 (GnRHa + E2). *Group 3* (n = 2) used GnRHa only for 10 days. On days 4, 7, and 10 of GnRHa administration, wall tracking of high-resolution ultrasound images of the brachial artery were used during flow-mediated dilation (FMD) and nitroglycerin (NTG) administration to test endothelium-dependent and endothelium-independent vasodilation, respectively. In addition, resistance vessel function was assessed in 2 subjects by measuring forearm blood flow (venous occlusion plethysmography) and calculating forearm vascular conductance (FVC) during intra-arterial infusions of acetylcholine and sodium nitroprusside.

Results: There was no difference in baseline brachial artery diameter, shear rate, or dilation to NTG between hormone treatments ($p > .05$). In *Group 1*, FMD was greater during treatment with GnRHa + E2 than with GnRHa alone ($p < .05$). FMD decreased with GnRHa + E2 + MPA and was not significantly different from GnRHa alone ($p > .05$). In group 2, FMD increased from treatment with GnRHa alone to treatment with E2; and stayed elevated with continued E2 treatment. FMD did not change across hormone treatments in Group 3. MPA administration resulted in an attenuated rise in FVC in response to acetylcholine.

Conclusions: These preliminary data support previous evidence that E2 increases endothelium-dependent vasodilation, and expand upon this finding to suggest that acute MPA administration attenuates the effects of E2 on endothelium-dependent vasodilation.

O-6

Paternal Factors, Specifically Low Sperm Motility, and High Levels of Moderate DNA Damage Predict Increased Rates of Aneuploidy in Embryos from Egg Donor Cycles. C. Adams, L. Anderson, S. Wood. Reproductive Sciences Center, La Jolla, CA.

Background: Aneuploidies, numerical chromosome errors, are common in human embryos and are associated with increasing maternal age. Although sperm aneuploidy rates have been shown to be elevated in infertile men with very poor sperm quality, the effect of paternal influences (age, semen quality, and sperm DNA fragmentation) on the frequency of aneuploidy in embryos is less well known.

Objectives: The aim of this study was to evaluate the relationship between sperm quality, as defined by conventional semen parameters and measurements of sperm DNA integrity, and incidence of chromosomally abnormal embryos. To eliminate any effect of maternal age, only embryos obtained from egg-donation cycles were examined.

Materials and Methods: A retrospective study of 23 egg-donation cycles (mean age of donors: 24 ± 3.1) with preimplantation genetic diagnosis (PGD) performed in a private infertility clinic. Semen analyses and sperm DNA evaluation using the Sperm Chromatin Structure Assay (SCSA) were performed on all semen specimens prior to processing for insemination. Multicolor fluorescent *in situ* hybridization (FISH) for chromosomes 13,18, 21, X, and Y (Vysis) was applied on single cells biopsied from day 3 embryos that had cleaved to ≥5 cells (n = 200). Embryos were considered aneuploid if the PGD result indicated monosomy, trisomy, complex abnormal, haploidy, or polyploidy. Statistical analysis was performed using Spearman's rank correlation coefficient.

Results: Male age (mean: 41 ± 5.7 years) did not correlate with aneuploidy rate (mean: 37%, range 0–80%). There was no relationship between the total DNA Fragmentation Index (DFI, percent of sperm cells containing damaged DNA) and aneuploidy rate. Interestingly, however, there was a significant correlation between the percentage of sperm with moderate DNA fragmentation (moderate % DFI) and rate of aneuploidy ($p < .05$). Percentage sperm motility was significantly negatively correlated with embryo aneuploidy rate ($p < .05$). There was no association between HDS (percent of sperm with immature chromatin), sperm concentration, or percentage normal morphology and aneuploidy rate.

Conclusions: This preliminary study suggests that two indicators of poor sperm quality, reduced sperm motility, and increased levels of moderate DNA fragmentation are related to higher aneuploidy rates in preimplantation embryos. In both situations, ICSI may not select out the sperm of highest quality for oocyte injection. This data lends support to previous studies, suggesting a paternal influence on embryo development, possibly mediated through centrosomal defects, mitochondrial dysfunction, or abnormal oocyte activation.