

blinded to the final diagnosis. In addition, serum levels of human chorionic gonadotropin ( $\beta$ hCG) on the day of sonographic testing were compared within these groups as well as with these sonographic parameters.

**Materials and Methods:** The evaluation of 64 women with possible ectopic pregnancy included a serum quantitative  $\beta$ hCG and a transvaginal sonogram. The  $\beta$ hCG was measured using the Access Immunoassay method on a Sanofi Diagnostics Pasteur machine (Chaska, MN). Pelvic sonogram was performed with a 7 MHz transvaginal probe using an Acuson 128 XP sonogram machine (Mountainview, CA). Endometrial thickness was obtained from the standard longitudinal view and defined as the width of the hyperechoic region marked by margins set at the abrupt transition to hypoechoic area. The final diagnosis was reached by either a dilatation and curettage (D&C) or by laparoscopy/laparotomy. The EP and the IUP groups were identified by finding chorionic villi in the adnexal or the curetting specimens respectively.  $\beta$ hCG levels, endometrial thickness values and presence or absence of free fluid were correlated and compared in both groups.

**Results:** 1) The mean age in both EP and IUP groups was similar ( $30.7 \pm 5.6$  and  $28.7 \pm 6.1$  respectively,  $P = 0.17$ ). 2) The mean endometrial thickness in the EP group was  $8.9 \pm 4.8$  mm and in the IUP group  $14.9 \pm 5.6$  mm. This difference was significant ( $P = 0.0001$ ). 3) The mean serum  $\beta$ hCG in the EP group ( $5364 \pm 9642$  mIU/ml) was not significantly different from the mean serum  $\beta$ hCG in the IUP group ( $5393 \pm 8668$  mIU/ml) ( $P = 0.9$ ). 4) Free fluid was seen in 40.5% of the EP vs. 22.2% of the IUP patients (not significant by Fisher exact test,  $P = 0.19$ ). 5) Only in one patient with EP did the thickness exceed 17 mm, for a specificity of 97.3% and sensitivity of 29.6%. 6) Serum  $\beta$ hCG was directly correlated to the endometrial thickness in both EP and IUP groups ( $r=0.39$ ,  $P=0.02$  and  $r=0.48$ ,  $P=0.015$  respectively).

**Conclusions:** Mean endometrial thickness is significantly smaller in women with EP, and therefore may be helpful in the sonographic diagnosis of EP. For our patient population, a cut off value of 17 mm was better than the previously reported 13 mm for the exclusion of this diagnosis. The presence of free fluid alone was a poor predictor for the diagnosis of EP, consistent with other studies. Endometrial thickness was positively correlated to  $\beta$ hCG levels in both groups.

## P-008

**Treatment of Menorrhagia with Tranexamic Acid.**<sup>1</sup> J. Y. Lee, R. L. Reid, J. P. Van Dijk. Dept. of OB/Gyn, Queen's University, Kingston, ON.

**Objective:** Tranexamic acid is an antifibrinolytic used for treatment of menorrhagia with good efficacy and safety. Its efficacy and safety in the treatment of both fibroid associated menorrhagia and non-fibroid associated menorrhagia were investigated.

**Design:** An uncontrolled prospective clinical trial was used in the non-fibroid associated menorrhagia (NFAM) study and a double-blind, placebo-controlled crossover clinical trial was used in the fibroid associated menorrhagia (FAM) study.

**Materials and Methods:** Patients were recruited into the study by newspaper ads or referral by another physician. Inclusion criteria included: ages 18–45, regular ovulatory periods, and baseline menstrual blood loss of greater than 80 ml per cycle. Baseline and treatment menstrual cycle blood loss was assessed by pictorial based assessment charts (PBAC) in the NFAM study and by alkaline hematin extraction in the FAM study. As well a symptom questionnaire delineating the impact of menstrual bleeding and cramps on the patient's social life and ability to work was completed and scored after each cycle. Baseline blood loss and questionnaire scores were then compared to treatment scores and p-values were calculated using a Student's T-test. Side effects were monitored with regular telephone follow-up.

**Results:** Treatment with tranexamic acid induced a 51% average reduction in PBAC scores between baseline and treatment cycles in the 12 patients enrolled in the NFAM study. Questionnaire scores were reduced by 62%. Only one patient reported a significant GI side effect (nausea) and no serious side effects were noted by any of the subjects. At this time, only 4 patients had completed the FAM study but preliminary data suggest neither the reduction in menstrual blood loss nor questionnaire scores was as great as in patients without fibroids.

**Conclusion:** Tranexamic acid is a safe, effective therapy for reducing both menstrual blood loss and the negative impact of menorrhagia on patients' lives. Its role in the treatment of fibroid associated menorrhagia is not clear.

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## P-009

**Glandular Developmental Arrest (GDA): A Unifying Model of Reproductive Endometrial Pathology.**

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**Objectives:** We evaluated the possibility that endometrial dating using histologic criteria alone may miss defects in the biochemical differentiation of the endometrial glands that could be critical for optimal endometrial receptivity.

**Design:** MAG mucin and progesterone receptor (PR) immunohistochemistry were performed on endometrial biopsies. The patterns of MAG and PR epithelial staining were compared to standard histologic dating criteria.

**Materials and Methods:** Endometrial biopsies were collected from over 300 patients, many of which were biopsied on d16 and d25 and in two or more cycles. Biopsies were fixed in formalin, paraffin embedded and immunohistochemically stained for MAG (AJP, 146:166-181, 1995), ABO blood group antigens, MUCI (+ control), and NMA (- control). Over 100 biopsies were also stained for PR. Hematoxylin and eosin sections were used for endometrial dating of the stroma and glands according to the criteria of Hendrickson and Kempson.

Results: Four patterns of immunostaining were identified: 1) Normal: MAG and PR were positive in the follicular phase, but negative after d20; 2) Delayed: MAG and PR were expressed only during the luteal phase; 3) Prolonged: MAG and/or PR were expressed in both follicular and luteal phases; 4) Absent: MAG was absent at all times (this pattern was not seen for PR).

Conclusions: We propose a novel model to unify the complex patterns we have observed. Our model is based on the concept that the differentiation of the glands and of the stroma through the menstrual cycle are related, but can be completely dyssynchronous such that a particular endometrial biopsy may show stromal differentiation typical of cycle d25, but the glands may have only developed to d4 or d15. We interpret this as glandular developmental arrest (GDA) and would label the above examples as GDA4 and GDA15. This model allows us to unify the various endometrial defects that we and others have identified in endometrial biopsies. The cause of GDA is unknown, but comparison of patterns of MAG and PR staining in biopsy series from patients during natural cycles and HRT cycles has suggested that appropriate hormonal stimulation, possibly acting through an endometrial cytokine/growth factor network, is critical for normal synchronous glandular and stromal maturation through the menstrual cycle. Some patients unfortunately never show glandular development-in spite of large doses of  $E_2$  and P-suggesting that these patients may have a more fundamental stromal-glandular cytokine/growth factor network dysfunction.

## P-010

**The Correlation of Luteal Phase Serum Hormone Levels and Sonographic Echo Patterns.** C. Dietterich, J. H. Check, D. Lurie. UMDNJ, Robert Wood Johnson Med. School at Camden, Cooper Hosp./Univ. Med. Cntr., Dept. OB/GYN, Div. Repro. Endo. & Infertility, Camden, NJ.

Objectives: Previous research has demonstrated that women who fail to progress to the homogeneous hyperechogenic (HH) echo pattern by the mid-luteal phase have a reduced pregnancy rate (PR). The objective of this study was to evaluate the correlation between mid-luteal phase serum estradiol ( $E_2$ ) and progesterone (P) levels, as well as sonographic measurements of the endometrial echo pattern to determine if those women who fail to progress to the HH pattern have different  $E_2$  or  $E_2/P$  levels. Furthermore, the correlation of luteal phase serum levels and results of the endometrial biopsy was evaluated.

Design: Comparative observational study in which 291 women presenting for treatment for luteal phase defect and/or ovulatory dysfunction were monitored in the mid-luteal phase. The women were stratified into these groups based on treatment modality: P supplementation only (n = 139), clomiphene citrate (CC) and P supplementation (n = 106), or human menopausal gonadotropin and P (n = 46).

Materials and Methods: One week post peak follicular maturation, i.e.,  $E_2 > 200\text{pg/mL}$  and a dominant follicle  $> 17\text{mm}$ , serum hormone levels of  $E_2$  and P were obtained

together with a sonographic assessment of echo patterns. Echo patterns were classified as trilaminar (TL), intermediate (IE) or HH. A subset (n = 169) of these women had endometrial biopsies performed in the late luteal phase of the cycle and the hormone levels were compared by the result of the biopsy. Since the distributions of serum  $E_2$  and P were positively skewed, a logarithmic transformation of the data was used. The ratio of  $\log(P)/\log(E_2)$  was also computed. Analysis of variance was used to compare the mean sera hormone levels by echo pattern within each treatment modality. All tests were done with a p value of .05.

Results: Within each treatment modality, there was no correlation found between the mid-luteal serum hormone levels of P,  $E_2$ ,  $P/E_2$ , and echo pattern. The geometric mean of  $E_2$  for HH pattern was 2.04 in the P only group, 2.26 in the CC/P group and 2.38 in the hMG/P group. For non-HH patterns, the respective geometric means were 2.09, 2.35, and 2.27. The geometric mean of the  $P/E_2$  ratio for HH pattern and treatment group were .67, .66, and .64, respectively; for non-HH patterns .65, .63, and .74, respectively. There was no difference in the mid-luteal phase hormone levels by phase of biopsy.

Conclusions: Mid-luteal phase serum levels of  $E_2$  and P were not found to be associated with endometrial development as measured by echo pattern. These measures do not provide a clinical marker for identifying patients with possible luteal phase defects or reduced fecundity.

## P-011

**Selection of Contrast Media for Hysterosalpingography: Results of a Community Survey and Cost Analysis.** K. R. Hammond, R. E. Blackwell, M. P. Steinkampf. Dept. of OB/GYN, University of Alabama at Birmingham, Birmingham, AL.

Objectives: The choice of contrast media for hysterosalpingography (HSG) in infertile patients remains a controversial topic. While there are technical advantages to both oil- and water-based media, it has been reported that most facilities consider water-soluble media safer and less expensive. However, a recent meta-analysis (Watson A. et al., 1994) found that subsequent pregnancy rates were significantly higher when oil-based dye was used (odds ratio 1:9;  $p < 0.00001$ ). The purpose of our study was to determine the current status of HSG media use in our community, and to calculate the number and costs of additional pregnancies if all HSG's were performed with oil-based contrast media.

Design: Community survey and cost analysis.

Material and Methods: A telephone survey of radiology departments in all hospitals and outpatient imaging facilities in the Birmingham metropolitan (Bham-MA) was performed. Information obtained included the annual number of HSGs performed, the contrast media used, and the reason for media selection. The proportion of HSGs performed for infertility evaluation was estimated by reviewing the records of all HSGs performed at the University of Alabama Hospital over the last 12 months. Cost calculations were made using the average wholesale price (AWP) of HSG