Title: Patient preferences for uterine preservation and hysterectomy in women with pelvic organ prolapse

Presenter: Nicole B. Korbly, MD  
Preceptor: Vivian W. Sung, MD, MPH  
Other authors: Nadine C. Kassis, MD, Meadow M. Good, DO, Monica L. Richardson, MD, MPH, Nicole M. Book, MD, Sallis Yip, MD, Docile Saguán, MD, Carey Gross, MD, Janelle Evans, MD, Vrishali V. Lopes, MS, Heidi S. Harvie, MD, MSCE, MBA

Objectives: Describe patient preferences for uterine preservation and hysterectomy in women with pelvic organ prolapse symptoms and describe predictors of preference for uterine preservation.

Methods: This multi-center, cross-sectional study evaluated patient preferences for uterine preservation versus hysterectomy in women with prolapse symptoms presenting for initial urogynecologic evaluation. Prior to meeting the physician, women completed a questionnaire asking them to indicate their prolapse treatment preference (uterine preservation versus hysterectomy) for scenarios in which the efficacy of treatment varied. Patient characteristics associated with preferences were determined and predictors for uterine preservation preference were identified using multivariable logistic regression.

Results: 213 women participated. Assuming outcomes were equal between hysterectomy and uterine preservation, 36% preferred uterine preservation, 20% preferred hysterectomy, and 44% had no strong preference. If uterine preservation was superior, 46% preferred uterine preservation and 11% preferred hysterectomy. If hysterectomy was superior, 21% still preferred uterine preservation despite inferior efficacy. On multivariable logistic regression, women in the South had decreased odds of preferring uterine preservation compared to women in the Northeast [OR 0.17, 95% CI 0.05-0.66]. Women with at least some college education [OR 2.87, 95% CI 1.08-7.62] and those who believed the uterus was important for their sense of self [OR 28.2, 95% CI 5.00-158.7] had increased odds for preferring uterine preservation.

Conclusion: Many women with prolapse symptoms presenting for urogynecologic evaluation preferred uterine preservation. Geographic region, education level, and belief that the uterus is important for sense of self were predictors of preference for uterine preservation.
Title: Impact of 17α-hydroxyprogesterone caproate on risk of infection at preterm delivery

Presenter: Alexandra D. Mainiero, MD, MPH
Preceptors: Brenna L. Anderson, MD, MSCR; Dwight J. Rouse, MD, MSPH
Other authors: Vrishali Lopes, MS; Alexander Kuczmarski

Objective: To evaluate whether exposure to 17α-hydroxyprogesterone caproate (17P) is associated with the rate of peripartum infection in women who deliver preterm.

Methods: This is a retrospective cohort study of patients who delivered prior to 37 weeks gestational age at Women and Infants Hospital between July 1st, 2005 and December 31st, 2012. Subjects were matched for gestational age and date of delivery. The primary outcome was a composite infection rate comprising histologic and clinical chorioamnionitis, endometritis, and early-onset neonatal sepsis. To detect a 15% difference in the rate of the primary outcome between subjects exposed to 17P and those unexposed, with an alpha = 5% and Power = 80%, 183 subjects per group were required.

Results: Composite infection rate was 33% in both subjects exposed to 17P and those unexposed (p=1.0). There was no significant difference between subjects exposed to 17P and those unexposed in rates of clinical chorioamnionitis (1.6% vs 1.1%, p=1.0), histologic chorioamnionitis (30.3% vs 31.4%, p=0.82), endometritis (2.7% vs 2.2%, p=1.0), or early-onset neonatal sepsis (2.7% vs 1.1%, p=0.45). Logistic regression was performed to control for the potential confounding variables history of prior spontaneous preterm birth and exposure to betamethasone. Adjusted odds ratio for composite infection rate in women exposed to 17P compared to unexposed is 0.55 (95% confidence interval 0.24-1.24).

Conclusion: Exposure to 17P does not increase the risk of peripartum infection among women who deliver preterm.
**Title:** A Comparison of Antiemetics Used to Treat Acute Exacerbations of Nausea/Vomiting of Pregnancy in the Emergency Room

**Presenter:** Elizabeth A. Mayhall, MD
Preceptors: Kristen A. Matteson, MD, MPH; Robyn Gray, DO
Other Authors: Vrishali Lopes, MS

**Objectives:** To compare time from medication administration to patient disposition between women treated for acute exacerbations of nausea and vomiting of pregnancy with ondansetron to women treated first with other medications.

**Methods:** We performed a retrospective cohort study of women who presented between December 2009 and December 2011 to the Women and Infants Hospital Emergency Room (WIH ER) with a diagnosis of nausea and vomiting of pregnancy at or before 13 weeks gestation. We collected data on patient demographics, medical history, antiemetics used, and time to disposition. The main independent variable was type of antiemetic administered first to the patient (ondansetron versus metoclopramide versus promethazine or prochlorperazine). The main dependent variable, “time to disposition” was defined as the time from antiemetic administration to placement of patient discharge/admission order. Multivariable logistic regression was used to calculate adjusted odds ratios.

**Results:** Among 500 women who presented with acute exacerbations of nausea and vomiting during pregnancy, 52% (n=261) received ondansetron, 35% received metoclopramide (n=175), and 12% received either promethazine or prochlorperazine (n=64) as a first line agent. Age, parity, prior history of nausea and vomiting in pregnancy, vital signs, ketonuria, and disposition did not differ between the women administered the different antiemetics. Women treated first with ondansetron were more likely to have prior WIH ER visits for nausea and vomiting than women treated with metoclopramide or promethazine/prochlorperazine. Mean “time to disposition” was greatest for the ondansetron group. [122 minutes versus 103 minutes (metoclopramide) versus 97 minutes (promethazine/prochlorperazine), p=0.02]. Controlling for confounding factors (nausea and vomiting in a prior pregnancy, prior WIH ER visit for nausea and vomiting, and on antiemetics at the time of presentation), we found that, compared to patients who received any other first line therapy, patients who received ondansetron first line had 1.86 time the odds of having a “time to disposition” at or above the 75th percentile (168 minutes) (aOR 1.86, 95%CI 1.2 – 2.9).

**Conclusions:** Compared to the use of other medical therapies, use of ondansetron as the first line treatment for acute exacerbations of nausea and vomiting of early pregnancy was associated with increased time to disposition in the emergency room setting.
Effects of labor on placental fatty acid beta oxidation

Presenter: Hector Mendez-Figueroa, M.D.

Preceptor: Edward K Chien, M.D.

Other authors: Huiling Ji, M.D., Ph.D., Nicole L. Nesbitt, Sivakama S. Bharathi, PhD, Eric Goetzman, PhD

Objective: To measure the effect labor exerts on fatty acid (FA) oxidation in term human placentas, and to compare enzymes expression and activity between placenta and liver.

Methods: Placental samples were collected: a) scheduled non-labored cesarean section (n=9) and b) normal vaginal delivery at or beyond 37 weeks (n=9). Long and medium-chain FA oxidation were measured using $^3$H-labeled FA, ATP concentration was measured via commercial kit. Activity and expression levels of 11 FA enzymes were measured and results compared to both human and mouse liver.

Results: Placental palmitate oxidation was significantly decreased with labor, 1.57 vs. 2.51 pmole/mg/h, p=0.04. Placentas undergoing labor also had significantly decreased ATP levels (0.61 vs. 0.41 nmoles ATP/mg, p<0.01). Octanoic acid oxidation was 10-fold higher than palmitic acid oxidation. No difference in expression or activity level was detected between the groups.

Conclusion: Term human placentas express all the enzymes required to oxidize FA, at a rate 20-fold lower than liver. FA Oxidation is not likely an important placental energy source during labor. Further work is needed to determine the functionality of this pathway in placenta.
**PT19C, a novel vitamin D2 derivative, demonstrates in vitro and in vivo activity in an epithelial ovarian cancer model.**

**Presenter:** Nada M Kawar, MD

**Preceptors:** Rakesh K. Singh, PhD. and Richard G. Moore, MD

**Other authors:** Shannon MacLaughlan, MD, Timothy C. Horan, BS, Kyu-Kwang Kim, PhD, Christina A. Raker, ScD, Thilo S. Lange, PhD

**Objective:** To evaluate the anticancer efficacy and calcemic effects of PT19C, a novel vitamin D derivative, in an epithelial ovarian cancer model.

**Methods:** Ergocalciferol (vitamin D2) was modified to generate PT19C, a heterocyclic derivative. Cytotoxicity of PT19C against a panel of cancer and reference cell lines was assessed using the MTS based ELISA assay and further evaluated through the NCI Development Therapeutics Program (DTP) NCI60 cancer cell lines. Morphologic and apoptotic responses of SKOV-3 cells were studied by fluorescence microscopy. Changes of the mitochondrial transmembrane-potential and cell cycle progression were studied by FACS analysis. VDR agonistic or antagonistic properties of PT19C were determined via a VDR–coactivator binding assay. Molecular docking simulation was carried out using the AutoDock 4.0 program with the structure of PT19C and calcitriol-liganded VDR. For in vivo analysis, SKOV-3 cells were xenografted into nude female mice and randomly assigned to control (vehicle, n=10) or PT19C treatment groups (10mg/kg bwt, n=10). Calcemic effects of PT19c were assessed by measuring the serum calcium levels in drug treated animals. Acute toxicity studies (400, 200, 100mg/kg bwt PT19c, IP, day 0, one mouse each) and Hollow Fiber Assay were performed by the NCI DTP.

**Results:** PT19C reduced the cell-viability of the cancer cell-lines evaluated (IC50<5uM), and showed dose dependent growth inhibition (GI) of NCI60 cell lines including six platinum refractory ovarian cancer cell lines (log10GI50~-4.05 to -6.73). In a representative ovarian cancer cell line (SKOV-3), PT19C induced apoptosis, displayed TUNEL positive DNA nicks, collapsed mitochondrial depolarization potential, and arrested cells in S-phase. PT19C showed a weak vitamin-D receptor (VDR) antagonism in a cell-based VDR reporter and VDR binding assay. Molecular docking simulation revealed that PT19C acquired an inverted spatial accommodation in the VDR-ligand binding domain, and did not enact classical calcitriol/VDR-like interactions. In SKOV-3 xenografts, PT19C reduced the growth of tumors (p<0.05) at 10mg/kg bwt at 35 days (study endpoint) without causing hypercalcemia. No acute toxicity was observed at 400mg/kg bwt in animals at 13 days. PT19C showed efficacy in the NCI hollow fiber assay.

**Conclusion:** PT19C is a non-hypercalcemic vitamin D2 derivative that exhibits antitumor effects in vitro and in a xenograft ovarian cancer model.
Abstract

Title: Sexual function and the surgical management of breast cancer

Presenter: Michaela Onstad, MD, MPH

Preceptor: Jennifer Gass, MD

Other authors: Erin Kunkel, Melissa A. Clark, PhD, Vrishali Lopes, MS

Objective:
Women diagnosed with early stage breast cancer may be managed surgically with lumpectomy followed by radiation, mastectomy alone, or mastectomy with reconstructive procedures, all demonstrating equal survival outcomes. Prior research has shown that sexual dysfunction among women with breast cancer is common, however the association between the type of surgery a woman undergoes and her sexual function has not been well studied. We aim to evaluate the association between each of these surgical modalities and a woman’s sexual function, as measured by the Female Sexual Function Index (FSFI).

Methods:
This study involves women who underwent breast cancer surgery at Women and Infants Hospital between the years 2000-2010 and receive follow up care at the Breast Health Center. We excluded patients less than 21 years old at surgery and women with a known diagnosis of a sexual disorder prior to surgery. The study involves a survey and a retrospective chart review. The survey includes the FSFI and investigator-generated questions. Demographic and medical data are extracted from the medical record to explore for potential confounders.

The primary outcome is the numeric FSFI score. Secondary outcomes include subdivided FSFI category scores and responses to investigator-generated questions. Assuming an FSFI score of 20 for patients undergoing lumpectomy, in order to detect a score difference of 2 points, with power set at 80%, the sample size needed is 50 patients.

Results:
Final results are to be presented at time of presentation. Preliminary data demonstrates a mean FSFI score of 18.9 for patients who underwent lumpectomy, 27.8 for patients who underwent mastectomy alone, and 2.2 for patients who underwent mastectomy with reconstruction. These values are not statistically significant, and they represent a small portion of respondents with remaining data collection still underway.

Conclusion:
There may be an association between surgical modality for early breast cancer and sexual function. If such an association exists, this would be valuable in counseling patients about surgical options.
Title: Increased False Positive Rate of the Integrated Screen in the HIV Positive Population

**Presenter:** Andrea B. Rollins, MD

Preceptor: Brenna Anderson, MD (add Brenna’s other degrees)

Other author: Vrishali Lopes, MS

Objective: Based on prior study results evaluating other aneuploidy screening tests, we hypothesize that HIV positive pregnant women will have an increased risk of false positive rate on integrated screening compared to HIV negative women.

Methods: A retrospective chart review of HIV-positive pregnant women, who underwent integrated screening as part of their prenatal care is being performed. Patient demographic and clinical data as well as postnatal fetal evaluations is being collected. Variables are being compared by chi-square, Fishers exact test, T-test or nonparametric Wilcoxon sum rank test. Odds ratios and 95% confident intervals will be calculated for the outcomes and multivariable logistic regression will be used to adjust for any potential confounders. Assuming a false positive baseline rate of 5% among HIV negative pregnant women a sample size of 112 HIV positive pregnant women and 224 controls are required for the study to detect a three-fold increase in the false positive rate in this population. A two sided alpha of 5% and power of 80% are being used.

Results: So far 18 HIV positive pregnant women and 20 controls have been entered in the study database. Preliminary data analysis has demonstrated a statistically significant difference in age, BMI and race between the two groups, with controls being younger (25 vs. 30 years old), having lower BMIs (23.3 vs. 31.4) and being predominantly Hispanic and Caucasian vs. black non-Hispanic. So far no controls and only 2 subjects have had abnormal aneuploidy screening results and of those that screened positive, 100% have had confirmed postnatal abnormalities.

Conclusion: The statistically significant differences observed between groups are likely secondary to the small sample size. To date very few abnormal aneuploidy screening results and no false positives have been observed in either one of the groups. While a larger sample size is required to fully analyze our hypothesis, the results from this study can potentially alter the current aneuploidy screening recommendations in the HIV positive pregnant population.
Title: Women with advanced epithelial ovarian cancer requiring gastrostomy tubes for bowel obstruction: The role of best supportive care versus further chemotherapy and parenteral nutrition.

Presenter: Erin J. Saks, MD
Preceptor: Carolyn McCourt, MD
Other Authors: Greg J. Dubel, MD, Vrishali Lopes, MS

Objective: To determine the impact of chemotherapy or parenteral nutrition on overall survival, and the proportion of days of life spent in an acute care facility, following gastrostomy tube placement for malignant bowel obstruction from advanced ovarian cancer.

Methods: This was a retrospective cohort study. Women treated at Women and Infants Hospital 2005 to 2011 requiring gastrostomy tubes for bowel obstruction due to epithelial ovarian, primary peritoneal or fallopian tube cancer were included. Survival from the time of gastrostomy tube placement was the primary outcome.

Results: Of the 47 women who met inclusion criteria, 20 had both chemotherapy and TPN, 20 had neither, and 7 had only TPN. There was a documented plan to continue chemotherapy in the 7 women who received only TPN. The cohort was divided into those who received neither chemotherapy nor TPN and those who received one of these treatments. There were no statistically significant differences between the two groups in age (median 63 at time of gastrostomy), time since original diagnosis (median 29 months), and number of previous chemotherapy regimens (median 4), and stage at diagnosis. Median survival from the time of gastrostomy tube placement to death was 29.0 days versus 92.5 days, p 0.006, for the group that received no treatment versus the group that received either chemotherapy or TPN. Percentage of days of life spent in the hospital was 12% for the no treatment group, and 24% for the either chemotherapy or TPN group, p 0.3. The group that received either chemotherapy or TPN was more likely to die at home, 60% versus 30%, p 0.02.

Conclusion: The survival following the need for gastrostomy tube placement for ovarian cancer is poor. There is a role for palliative chemotherapy in the setting of malignant bowel obstruction if the patient’s functional status is adequate to withstand treatment.
Title: Interval Surgical Sterilization and Obesity: How does BMI affect complication rates in hysteroscopic versus laparoscopic sterilization?

Presenter: Rachel R. Shepherd, MD

Preceptor: Rebecca H. Allen, MD, MPH

Other authors: Kristen A. Matteson, MD, MPH, Christina A. Raker, ScD, ScM, Nan Du, BMS

Objective: To compare the complication rate of hysteroscopic tubal occlusion to interval laparoscopic tubal sterilization across BMI classes

Methods: We performed a retrospective cohort study of all women undergoing interval tubal sterilization via laparoscopic approach (LTL) or Essure device between 2007 and December 2011 at Women and Infants Hospital. Data collected included demographics, BMI class, complications, surgical time, recovery time, and estimated blood loss. The chi-square or Fisher’s exact test was used for categorical variables and the T test or Wilcoxon rank-sum test was used for continuous variables. Odds ratios and 95% confidence intervals were used to summarize associations between occlusion type and complications. All p-values presented are two-tailed with p < 0.05 considered statistically significant.

Results: A total of 429 charts have been reviewed to date including 282 LTLs and 147 Essures. The LTL group had lower number of co-morbidities (41.8% versus 46.9%, p =0.4) and lower BMI (mean 28.1 versus 29.8, p= 0.04). Surgical time was significantly higher in the LTL group, with the median surgical times being 30 minutes for LTL versus 15 minutes for Essures (p<0.0001). There was no significant difference in major complications with 12 (4.3 %) major complications in the LTL group and 2 (1.4%) in the Essure group (p = 0.2). There was a significant difference in the minor complication rate (LTL n = 74, 26.2% versus Essure n= 25, 17%, p=0.04). Preliminary analysis also indicates that the rate of any complication (major or minor) is higher with a BMI of 30 or higher for LTLs compared to Essure (n = 25, 29.8% versus n = 4, 6.9%, OR 0.17, 95% CI 0.06-0.51) .

Conclusion: While the data collection is not complete, it appears that complication rates are lower with hysteroscopic sterilization especially in patients with a BMI of 30 or higher.
Title: Factors associated with treatment failure of global endometrial ablation

Presenter: Katelyn Smithling, MD
Preceptor: Kristen A. Matteson, MD, MPH
Other author: Christina A. Raker, ScD

Objective(s): (1) To compare, among women who underwent endometrial ablation for heavy menstrual bleeding, risks of treatment failure and subsequent gynecologic interventions between women with irregular bleeding and women with regular bleeding prior to their procedure and (2) To determine other patient characteristics associated with risk of treatment failure.

Methods: We performed a retrospective cohort study of women who underwent endometrial ablation for heavy menstrual bleeding between January 2007 and July 2009. Bleeding pattern was defined as "irregular" or "regular" based on history recorded in notes or the operative report. Treatment failure was defined as reablation or hysterectomy. Subsequent gynecological interventions included endometrial biopsy, dilation and curettage, hysteroscopy, re-ablation, or hysterectomy. Prevalence and odds of treatment failure and subsequent gynecologic intervention were calculated using Chi-square or Fisher's exact test and multiple logistic regression, respectively.

Results: Nine hundred sixty-nine women had endometrial ablations for heavy bleeding during the study period. One hundred sixty-nine women were classified as having regular bleeding (17%), 264 had irregular bleeding (27%), and the pattern could not be specified for 474 women (49%). Comparing women with regular and women with irregular bleeding, we found no differences in treatment failure (13% versus 13.4%, p = 1.0) or re-intervention (20.7% versus 22.6%, p = 0.7). When we controlled for confounding variables, women with irregular bleeding were not at increased odds of treatment failure compared to women with regular bleeding [aOR 1.1, (0.6 - 2.02)]. Women with dysmenorrhea preoperatively had increased odds of treatment failure and re-intervention when compared to women without dysmenorrhea [aOR 3.22 (1.95 – 5.33) and aOR 2.39 (1.53 - 3.75), respectively]. Similarly, women with previous tubal ligation and women with a higher BMI were at increased odds for treatment failure [aOR 2.05 (1.37 – 3.07) and aOR 1.05 (1.02 - 1.08), respectively] and re-intervention [aOR 1.69 (1.22 - 2.33) and aOR 1.05 (1.03 - 1.07), respectively].

Conclusion: We did not find a difference in failure or intervention rate after endometrial ablation between women with regular and irregular bleeding, however data collection are ongoing. Preoperative dysmenorrhea, tubal ligation, and increased BMI were associated with both failure and gynecologic intervention after endometrial ablation.
**Title:** The effect of topical lidocaine on pain scores during manual vacuum aspiration for nonviable pregnancies  
**Presenter:** Amanda M Tower, MD  
Preceptors: Roxanne A. Vrees, MD and Jared Robins, MD  
Other author: Vrishali Lopes, MS

**Objective:** To compare pain scores on a visual analogue scale during manual vacuum aspiration for treatment of first trimester nonviable pregnancies between women who are treated with topical lidocaine gel or placebo on the cervix. The hypothesis is that patients treated with topical lidocaine gel will have lower pain scores on a visual analogue scale during intracervical block, tenaculum placement, cervical dilation and aspiration during manual vacuum aspiration for first trimester nonviable pregnancies.

**Methods:** Study design is a double-blinded, randomized, controlled trial. Subjects are women being treated at the Women & Infants Center for Reproduction and Infertility or at the Women and Infants Triage/Women’s Emergency Department who have experienced a first trimester missed abortion, inevitable abortion, incomplete abortion or other nonviable pregnancy and are being treated with a manual vacuum aspiration. They are randomized to receive 9 mL of 2% topical lidocaine gel or 9 mL of placebo gel applied to the cervix prior to the procedure. Measured outcomes are pain scores on a visual analogue scale during tenaculum placement, intracervical block, cervical dilation, and uterine aspiration, as well as demographic information, pertinent medical history, and complications. Assuming an alpha of 0.05, 80% power, and a standard deviation of 21 mm, 32 subjects are required per arm to be able to detect a 15 mm mean difference between groups on the 100 mm visual analogue scale.

**Results:** At this time, 16 patients have been enrolled. The randomized groups do not differ in terms of age, parity, gestational age, history of depression, anxiety or pelvic pain, or pre-procedure pain level. Preliminary analysis fails to show any difference in pain scores during MVA between the two groups, but there may be a trend toward less pain during tenaculum placement.

**Conclusion:** More time is needed to complete recruitment before final conclusions can be made, but the results so far do not support use of topical lidocaine to reduce pain during manual vacuum aspiration.