Abstracts (In order of presentation)

Presenting Residents

Title: A comparison of sentinel lymph node identification between lymphoscintigraphy and sentinel lymph node dissection in patients with vulvar cancer
Author: Laura L. Holman, MD
Preceptors: Katina M. Robison, MD; Richard G. Moore, MD
Other authors: Vrishali V. Lopes, MS; Margaret Steinhoff, MD

Objective: The purpose of this study is to determine if the number of sentinel lymph nodes (SLN) seen on preoperative lymphoscintigraphy (LSG) predicts the number of SLN found intraoperatively in women with vulvar cancer.

Methods: An institutional review board approved retrospective chart review of patients undergoing a SLN dissection for vulvar cancer between January 2004 and June 2009 was performed. Data on patient demographics, surgical records, pathology, and LSG was collected. Additionally, the original LSG studies were evaluated by three surgeons who were blinded to the SLN dissection results. The findings of these surgeons were then compared with the number of SLN harvested at surgery.

Results: Forty-nine patients met inclusion criteria. In 48 patients, at least 2 of the 3 clinicians agreed on the number of SLN identified on LSG. One case had no agreement among reviewers and was not included in further analysis. One or more SLN was noted on LSG in 40 patients giving a false positive rate of 0% and a false negative rate of 9%. The sensitivity and specificity for LSG was 91% and 100%, respectively. The number of SLN identified by LSG was equal to the number of SLN found intraoperatively in 33% of patients, but differed by 2 or more in 38%. When comparing LSG with only the number of hot lymph nodes found intraoperatively, there was no difference in 27% of patients and a difference of 2 or more in 42%. The Spearman correlation coefficient of the difference between total SLN identified in surgery from LSG was 0.25, corresponding to a low correlation.

Conclusion: Lymphoscintigraphy does not improve SLN identification and SLN’s can be adequately identified with Tc-99m and methylene blue dye injections alone. Therefore, the cost and time associated with LSG can be omitted.

Title: Anemia and chorioamnionitis at term
Author: Karen L. Archabald, MD
Preceptor: Brenna L. Anderson, MD, MSCR
Other authors: Vrishali V. Lopes, MS

Objective: Chorioamnionitis at term is associated with cerebral palsy as well as increased risk of maternal and fetal morbidity. Our objective is to examine the association of anemia at the time of the diabetic screen with chorioamnionitis at term.

Methods: We conducted a case control study of women with and without chorioamnionitis who presented to a single tertiary care institution in spontaneous or induced labor at 37’0 weeks of gestation or greater between December 2007 and June 2009 via chart abstraction. The primary outcome measure was the development of chorioamnionitis, defined as fever ≥38 degrees and placental pathology consistent with histologic chorioamnionitis. The primary exposure was anemia, defined by CDC guidelines as Hgb <10.5 in the 2nd trimester or <11.0 in the 3rd trimester. Controls were matched for care provider and were chosen in a 2:1 ratio by random number generator. Categorical variables were compared by Chi-square or Fishers exact tests, continuous variables were compared using t-test or Wilcoxon rank sum test. Multiple logistic regression was used to calculate Odds Ratios.

Results: 101 cases and 197 controls were identified. Demographics for the two groups were significant only for a higher frequency of primiparity (p<0.0001) and lower frequency of Rh negative status (p=0.01) in the
chorioamnionitis group. Prevalence of anemia at the time of the diabetic screen was significantly higher in the chorioamnionitis group (36.36%) compared to the controls (46.23%) (p=0.02). This finding persisted after adjusting for known risk factors for chorioamnionitis at term including duration of labor, number of cervical exams, GBS status, meconium, duration of ruptured membranes, use of internal fetal monitors, and parity as well as RH status which was identified as a significant variable in this study (Adjusted OR 2.15; 1.01-4.60).

Conclusion: Our case control study detected an increased prevalence of anemia at the time of the routine diabetic screen in women who developed chorioamnionitis at term. Anemia may be a modifiable risk factor for the prevention of chorioamnionitis at term.

Title: Association between maternal-fetal attachment and quitting smoking with pregnancy recognition
Author: Julie A. Baker, MD PhD
Preceptor: Maureen G. Phipps, MD, MPH

Objective: To assess whether maternal-fetal attachment is associated with a decision to quit smoking during pregnancy.
Methods: Preliminary analysis of the first 111 women from an ongoing prospective cohort study of pregnant women presenting for their first prenatal appointment at the Women’s Primary Care Center who have smoked in the past year. Maternal-Fetal attachment was assessed using both the Cranley Maternal-Fetal Attachment Scale (MFAS) and Condon’s Maternal Antenatal Attachment Scale (MAAS), with participants categorized as having low or high attachment levels based on median scores in the overall cohort (median MFAS score 80, range 47-102; median MAAS score 79, range 46-95).
Results: Among the 111 women in this cohort, 42% quit smoking completely prior to the initial prenatal visit. Women with depression or anxiety were less likely to change their smoking habits; and women who had felt fetal movement were more likely to quit or decreasing their cigarette use. Maternal fetal attachment level was not associated with quitting smoking as measured by either the MFAS (OR 0.98, 95% CI 0.46-2.08) or MAAS (OR 0.92, 95% CI 0.43-1.96). Results did not differ when stratified on fetal movement, ultrasound use, or pregnancy intention.
Conclusion: Women who felt fetal movement were more likely to change their smoking habits, however, higher levels of maternal-fetal attachment was not associated with quitting smoking early in pregnancy.

Title: An observational study of pain with IUD insertion
Author: Molly S. Carey, MD
Preceptor: Rebecca H. Allen, MD, MPH
Other authors: Christina A. Raker, ScD

Objective: The intrauterine device (IUD) is a long-acting, highly effective, reversible contraceptive that may be underutilized due to fear of pain during insertion. In order to better counsel women on what to expect, we sought to measure pain scores at the time of IUD insertion in a United States clinic population and to estimate the effect of prior vaginal delivery.
Methods: This is an observational cohort study that was conducted at the Women’s Primary Care Center among women seeking IUD insertion. English-speaking women over the age of 18 with no prior IUD use were enrolled. Baseline data was collected including age, race/ethnicity, BMI, OB/GYN history, self-assessment of pain tolerance, State-Trait Anxiety Inventory, and ratings of anticipated and acceptable levels of pain on the visual analog scale (VAS). Pain during speculum placement and IUD insertion was measured on the VAS as well as procedure time and insertion difficulty. Twenty minutes post-insertion, side effects, pain score, and acceptability of pain during insertion were measured. The study is powered to detect a 15mm difference in pain scores on the 0 to 100mm VAS between women with and without prior vaginal delivery.
Results: Over 9 months, 52 participants of the needed 98 have been enrolled. 58% of eligible subjects participated. Of the 52 subjects, 37 have a prior vaginal delivery and 15 have no prior vaginal delivery. The average age of the study population is 26 with 48% Hispanic, 19% black, 19% white, 8% multiracial, and 6% other. 58% of the insertions were postpartum, 2% postabortion, and 40% interval. Of 52 subjects, 41 (79%) chose the levonorgestrel IUD. Women with prior vaginal delivery reported mean pain scores of 39.3 (SD of 32.2) during IUD insertion and 14.3 (SD 19.2) twenty minutes post-procedure. For women with no history of vaginal delivery, the mean pain score was 55.5 (SD 27.4) during IUD insertion and 20.2 (SD 21.6) twenty minutes post-procedure.

Conclusion: To date, recruitment has been limited by study staff availability. Recruitment is ongoing and the study has been incorporated well into clinic flow. We anticipate final results to be presented at a national meeting in 2011.

Title: A novel biomarker for the management of patients with epithelial ovarian cancer

Author: Amanda L. Jackson, MD
Preceptor: Richard Moore, MD
Other authors: M. Craig Miller, BS, Elizabeth Eklund, Geralyn Messerlian, PhD,

Objective: CA125 is the gold standard biomarker for monitoring women with epithelial ovarian cancer (EOC). Human epididymal protein 4 (HE4) is a novel biomarker that has been shown to be elevated in 80% of EOC and in 50% of patients where CA125 is not elevated. Our objective is to show serial change in HE4 is not inferior to serial change in CA125 for monitoring response to chemotherapy in EOC.

Methods: This was an IRB approved retrospective trial. Longitudinal serum samples from histologically proven EOC were obtained from residual samples drawn for serum CA125. Sera were drawn at 3-5 week intervals to monitor response to therapy. Serum CA125 and HE4 levels were analyzed at each time point and a velocity of change over each treatment regimen was calculated and correlated with clinical status determined by standard clinical measure such as physical exam, biomarkers and imaging. The null hypothesis was tested using concordance and a two sided Fisher’s exact test.

Results: Forty-four patients with 47 treatment regimens were identified with a total of 306 serum samples. There were 10 (23%) patients with stage I disease, 3 (7%) stage II, 28 (63%) stage III and 3 (7%) stage IV. Twenty seven (61%) patients were receiving first line therapy, 8 (18%) second line and 9 (21%) third line or greater. Using a velocity of change cut point of >4 to indicate progressive disease (PD), HE4 had a sensitivity of 64.3% (CI 95%: 35.1-87.2%), specificity of 97.0% (CI 95%: 84.2-99.9%), a PPV of 90.0% (CI 95%: 55.5-99.7%), a NPV 86.5% (CI 95%: 71.2%-95.5%) and an overall accuracy of 87.2% (CI 95%: 74.3-95.2%). Using a velocity of change cut point of >1 to indicate PD, CA125 had a sensitivity of 57.1% (CI 95%: 28.9-82.3%), specificity of 97.0% (CI 95%: 84.2-99.9%), a PPV of 88.9% (CI 95%: 51.8-99.7%), a NPV 84.2% (CI 95%: 68.7-94.0%) and an overall accuracy of 85.1% (CI 95%: 71.7-93.8%). Concordance comparison of overall agreement for HE4 and CA125 velocities for PD and non-PD resulted in a ratio (HE4/CA125) of 1.025 (p=1.000). HE4 and CA125 agreement with clinical status was not significantly different. At least one of the biomarkers agreed with clinical status in 97.7% of cases.

Conclusion: Our results show that HE4 is equivalent to CA125 for monitoring patients with EOC while on chemotherapy. HE4 compliments CA125 and together the majority of EOC patients will have a marker to help manage their disease.
Title: Effect of surgical therapy on improving physical activity levels in women with stress urinary incontinence

Author: Nadine Kassis, MD
Preceptor: Vivian Sung, MD, MPH
Other authors: Felisha Marques, BA, Ann Meers, RN, Christina A. Raker, ScD

Objective: To estimate the effect of midurethral slings on increasing physical activity in women with stress urinary incontinence.

Methods: This is a prospective, observational, repeated measures study evaluating the effect of midurethral slings for stress urinary incontinence on improving physical activity and physical functioning 6 months postoperatively. Women under age 65 undergoing midurethral slings who described improved physical activity as a goal are recruited through the Division of Urogynecology. Physical activity levels are measured using the International Physical Activity Questionnaire (IPAQ). Responses are categorized into low-moderate or high activity levels based on standard IPAQ guidelines. Physical functioning was measured using the physical function domain of the NIH Patient-Reported Outcomes Measurement Information System (PROMIS). Subjective severity of incontinence was measured using the Pelvic Floor Distress Inventory (PFDI-20) and Pelvic Floor Impact Questionnaire (PFIQ-7). All measures are collected at baseline and 6 months postoperatively. Demographics, clinical characteristics, physical findings are also collected. With a two-sided alpha of 0.05, we estimate that 67 women will be needed to detect a 25% difference with 80% power.

Results: To date, 38 women have enrolled; however no women have undergone their six month postoperative evaluation. The mean age of enrolled patients is 48.8 +/- 8.6 yrs, mean parity of 2 (0-6), mean BMI 31.6 +/- 8.9. Based on IPAQ scores, 12% of women were categorized as low activity, 41% moderately active and 47% highly active. There was no statistically significant difference between groups in regards to age, race, parity, menopausal status, BMI, prolapse severity, or duration of incontinence. In addition, when comparing highly active women to low-moderately active women, scores on the Urinary Impact Questionnaire-7 were similar (mean score 39.9 vs. 40.8, p=0.9) as were scores on the Urogenital Distress Inventory-6 (mean score 50.8 vs. 55.0, p=0.6). When comparing highly active women to low-moderately active women, there was no difference in physical functioning score, mean of 3.6 vs. 3.9, p=0.2. There has been one intra-operative complication, a bladder perforation.

Conclusion: Recruitment and follow-up are ongoing. Improvement in physical activity levels and physical functioning is a common goal in women undergoing surgical treatment of stress urinary incontinence.

Title: Neurologic Outcomes Associated with Polyhydramnios

Author: Mollie A. McDonnold, MD
Preceptor: Barbara M. O’Brien, MD
Other Authors: Vrishali V. Lopes, MS, Christina A. Raker, ScD

Objective: Several studies have evaluated the etiology and risk of perinatal mortality associated with polyhydramnios, but the risk of abnormal neurologic outcomes in infants has not been evaluated. As central nervous system anomalies and neuromuscular disorders are potential causes of increased amniotic fluid, abnormal neurologic outcomes would be expected in a percentage of cases. The objective of this study was to evaluate the neurologic outcomes after delivery in cases diagnosed with polyhydramnios compared to those cases with normal fluid indices.

Methods: A retrospective chart review was performed evaluating cases of polyhydramnios, as defined by an AFI greater than 24.1, as compared to those pregnancies with normal fluid indices. Neurologic outcomes were evaluated using a composite score of abnormal tone, alertness, abnormal reflexes, neonatal seizures, respiratory distress, and feeding difficulty. Assuming a rate of abnormal outcomes of 1% in the normal population, a sample size of 121 patients per group is required to detect a 10% rate of abnormalities in the polyhydramnios group, with an alpha of 0.05 and power of 80%.
Results: 198 cases of polyhydramnios were identified and compared to 175 controls. Of these cases, 39 (19.6%) were associated with diabetes, 32 (16%) were explained by findings of genetic or structural abnormalities, and 127 (64%) were unexplained. Overall, 27% of the infants in the polyhydramnios group had a composite outcome score > 0, as opposed to 9% of those in the normal group (p < 0.0001). However, this difference does not persist when only those infants with unexplained polyhydramnios were compared to the normal group. When comparing mild and severe polyhydramnios (AFI greater than 30), there were more abnormal composite scores (22% vs. 59%, p < 0.0001) and more genetic or structural abnormalities of the newborn (2% vs. 27%, p < 0.0001) in the severe group.

Conclusion: Increased rates of abnormal neurological findings are associated with polyhydramnios, primarily due to the increased rates of genetic disorders and structural defects. However, in the absence of concomitant finding to explain polyhydramnios, there does not appear to be an increased risk the infant will have neurologic abnormalities at birth.

Title: The effect of obesity on perioperative outcomes of laparoscopic hysterectomy
Author: Megan D. McMahon, MD
Preceptor: Kristen A. Matteson, MD, MPH
Other authors: Christina A. Raker, ScD

Objective: To compare perioperative outcomes between obese and non-obese women who underwent laparoscopic hysterectomy

Methods: A retrospective chart review was performed of 192 women who underwent laparoscopic hysterectomy between July 2006 and January 2009 at Women and Infants Hospital. Patients who underwent a total laparoscopic or laparoscopic supracervical hysterectomy at our institution during the study period were eligible and identified by the health information management department. This study is Institutional Review Board approved and data collection is ongoing. We collected data from the medical records. The independent variable, 'obese', was defined as body mass index greater than or equal to 30 kilograms per meter squared. The dependent variable, 'major surgical complications', was defined as having a bowel injury, blood vessel injury, trocar site hernia, pelvic hematoma, vaginal non-healing, need for reoperation, pelvic infection, sepsis, or thromboembolic event within 3 months of surgery. Data were analyzed using SAS 9.0.

Results: Our preliminary analyses identified 63 patients who had a total laparoscopic hysterectomy (33%) and 129 patients who had a laparoscopic supracervical hysterectomy (67%). The mean uterine weight was 185 grams, estimated blood loss was 150 milliliters and operative time was 125 minutes. Twenty three percent of patients (n=45) were obese. Obese and non-obese patients were similar in terms of indication for hysterectomy, estimated blood loss, and operative time. Major surgical complications occurred in 1.4% of non-obese patients and 6.7% of obese patients (n=2 and n=3, respectively, p=0.09). Though there appears to be a trend, this difference was not statistically significant.

Conclusion: Determining risk of complications associated with obesity for laparoscopic hysterectomy could facilitate patient counseling on risks of complications. Although this study was underpowered, a trend toward increased risk of complications from laparoscopic hysterectomy was found when comparing obese women to non-obese women. Data collection is ongoing to clarify the significance of these findings.
Title: Should we excise all breast core-biopsy proven papillary lesions?
Author: Sonali Pandya, MD  
Preceptors: Don Dizon, MD; Jennifer Gass, MD  
Other authors: Katrine Hansen, MD; Christina A. Raker, ScD

Object: The primary objective of our study is to determine the clinical outcome of patients with core-biopsy proven papillary lesions. In the surgical excision cohort, we wanted to determine whether there is concordance between core-biopsy findings and final pathology. In the surveillance group, we wanted to determine if the patients had a second-breast event.

Methods: We performed a retrospective chart review of patients diagnosed with core-biopsy proven papillary lesions between January 2001 and August 2009. In the surgical group, we compared their core-biopsy findings to their final surgical excision. In the surveillance group, we monitored for a second breast event. All patients who had core-biopsy proven papillary lesions were included in the study, as well as concurrent ADH. We excluded patients with invasive carcinoma, DCIS or LCIS. Benign core-biopsy included intraductal papilloma and papillomatosis. Papillary neoplasm or any lesion with atypia was categorized as non-benign core-biopsy.

Results: We had a total of 142 patients whose core-biopsies were reviewed retrospectively. The final cohort was 124 (12 had unknown outcome, final surgical pathology not known in 4 and 2 in the surveillance group were lost to follow-up). We had 94 in the surgical cohort and 30 in the surveillance cohort. The NPV (if benign core then benign final pathology) was 97.6% (95% CI: 87.1 – 99.9%). The sensitivity was 90.9% (the probability of having malignant final pathology given non-benign core biopsy). The PPV was 18.9% (non-benign core biopsy resulted in malignant final pathology). In our surveillance benign-core biopsy group (n = 30), 6 failed surveillance, of which 5 had benign final pathology. We had 1 who was upgraded to invasive carcinoma (developed interval bloody nipple discharge). The median follow-up in the surveillance group was 24 months. We had 12 in the entire cohort with malignant final pathology (11 in the surgery group and 1 in the surveillance group). In the surgery group (n = 94), 1 had malignant final pathology in the benign-core biopsy group with a 2.4% rate of malignancy, and 10 with malignant final pathology in the non-benign core biopsy group with a 18.9% rate of malignancy (80% of patients with malignancy had atypia on their core-biopsy).

Conclusion: There is significant concordance between benign core-biopsy and surgical excision pathology (NPV 97.6%). The presence of atypia or a papillary lesion on core-biopsy will lead to DCIS or invasive carcinoma in 18.9% of surgical excisions. The development of bloody nipple discharge should prompt surgical intervention. Surveillance of core-biopsy proven intraductal papilloma and papillomatosis is a reasonable alternative to surgical excision.

Title: Developing an integrated genomic approach to explore the antitumor activity of vitamin D and derivatives to treat ovarian cancer
Author: Ashley Stuckey, MD  
Preceptor: Laurent Brard, MD, PhD  
Other authors: Kyu Kwang Kim, Rakesh K. Singh, Anna Ritz, Andrew Fischer, Sara Hillenmeyer, Ben Raphael, Alexander S. Brodsky

Objective: We aim to understand the mechanism of action of MT19C, a Vitamin D derivative, and to understand the genetic changes occurring in ovarian tumors treated with MT19C in a mouse xenograft model.

Methods: SKOV-3 cells were cultured to 80% confluence then harvested. Cells were suspended in 0.1 ml of Matrigel and inoculated subcutaneously into the flank of 4-6-week-old immunodeficient nude mice (Charles River Laboratories, Wilmington, MA) with 2 million cells/inoculate. When tumor volume reached
6-10 mm (2-3 weeks), the mice were treated intraperitoneally every other day in 3 groups (Calcitriol, MT19C, control) of 16 animals per group. Tumor was retrieved and we measured mRNA expression levels using Affymetrix Human Gene microarrays. We determined which genes were significantly up and down regulated comparing all the treated and control samples. Complementing these expression studies, we examined possible structural rearrangement and copy number changes using Agilent 188K microarrays of isolated DNA.

**Results:** Tumors treated with MT19C typically decreased in size or did not grow while control tumors grew steadily. MT19C treated xenograft tumors showed lower expression levels for genes involved in energy metabolism including both oxidative phosphorylation and glycolysis. Interestingly, specific chromosomal regions revealed strong differences in expression between treatment and control. These regions appeared to correlate with copy number changes by array-CGH analysis. We observed specific amplifications in control tumors but not in treated tumors suggesting that treatment selected for a specific cell population.

**Conclusion:** MT19C shrinks tumor cells by affecting key metabolic pathways. By examining treated versus control xenograft tumors, we can identify genes critical for cancer cell survival. In addition, we are comparing expression and copy number changes to those seen in primary ovarian tumors. These approaches will provide insight into key factors mediating tumor growth and drug sensitivity in ovarian cancer.

**Title:** Mersilene versus Ethibond suture efficacy and cerclage
**Author:** Julie M. Johnson, MD
**Preceptor:** Brenna L. Anderson, MD, MSCR
**Other authors:** Christina A. Raker, ScD

**Objective:** We sought to evaluate the risk of preterm birth between women who received a cerclage with Mersilene® versus Ethibond®.

**Methods:** This was a retrospective cohort study of 200 pregnancies with McDonald cerclage placement from 1998-2008 comparing pregnancy outcomes between the two suture types. Maternal demographics and clinical data were collected. The primary outcome was preterm birth at less than 37 weeks gestation. Secondary outcomes included gestational age at delivery, chorioamnionitis, and PPROM. Data were analyzed using a two-tailed t-test and logistic regression as appropriate. Assuming a preterm birth rate of 40% based on prior data, a sample size of 100 patients in each group was required to detect a 20 % difference in the preterm birth rate with a power of 80% and a significance level of 0.05 with 2-sided t-test.

**Results:** There were 100 women in each suture group. Maternal age, ethnicity, and gravidity did not differ significantly between the Mersilene® and Ethibond® groups. The median gestational age at placement of cerclage was 13.9 versus 13.6 weeks. Of the 200 patients studied, the indication for cerclage was cervical insufficiency in the majority (65%). There was no difference in preterm birth among the entire study population (OR 0.65, 95% CI 0.36-1.2). The median gestational age at delivery was 36.5 versus 37 weeks, p=0.07. The results were similar when analyzing only the group with cervical insufficiency (OR 0.61, 95%CI 0.30-1.24). No difference was found in the rate of PPROM or chorioamnionitis.

**Conclusion:** Mersilene® is not associated with an increased risk of preterm birth when used for McDonald cerclage. Suture type should be determined by physician preference.

**Title:** The association between regional anesthesia and acute postoperative urinary retention in women undergoing outpatient midurethral slings.
**Author:** Kyle J. Wohlrab, MD
**Preceptor:** Vivian Sung, MD MPH
**Other authors:** Elisabeth A. Erekson, MD, Nicole B. Korbly, MD, Calin D. Drimbarean, MD, Charles R. Rardin, MD

**Objective:** To estimate the association between regional anesthesia and acute postoperative urinary retention in women undergoing outpatient midurethral sling procedures.
**Method:** We performed a retrospective cohort study of women undergoing outpatient midurethral sling procedures. Exposure was defined as the type of anesthesia, categorized as regional (spinal or combined spinal/epidural) or non-regional (general endotracheal, monitored anesthesia care with sedation, or local). Outcome, acute postoperative urinary retention, was defined as a failed voiding trial prior to discharge.

**Results:** A total of 131 women meet our inclusion criteria. Forty-two (32%) women had regional anesthesia and 89 (68%) women had non-regional anesthesia. Overall, 48 (36.6%) women had acute postoperative urinary retention. Women who had regional anesthesia had an increased odds (Adjusted OR=4.84, 95% CI 2.17, 10.8) of acute postoperative urinary retention compared to women receiving non-regional anesthesia.

**Conclusion:** Regional anesthesia is a risk factor for acute postoperative urinary retention following outpatient midurethral slings.