Jennifer Botte, MD

Embryo transfers, does the use of phenazopyridine decrease discomfort?
J. P. Botte, MD; G. Frishman, MD

Objective: To determine if a single dose of phenazopyridine prior to embryo transfer reduces patient discomfort during the procedure. Embryo transfer requires a full bladder to facilitate ultrasound guidance of the transfer catheter. Patients often state that the discomfort of the distended bladder causes more discomfort than the transfer procedure itself. Phenazopyridine acts as a bladder anesthetic. There are no trials using phenazopyridine during embryo transfer.

Methods: A double blinded, randomized, placebo controlled trial was conducted. 85 patients undergoing embryo transfer in the W&I division of reproductive endocrinology and infertility between September, 2004 and April, 2005 were recruited. Patients with an allergy to phenazopyridine or liver or kidney disease or G6PD deficiency were excluded. Patients were randomized to receive placebo or phenazopyridine through a computer generated block randomization schedule. The medication was taken at least one hour prior to transfer. Patients completed a visual analogue pain scale several weeks prior to their transfer (baseline), immediately prior to the transfer, and following transfer. Both the physician and nurse involved in the transfer also assessed patient discomfort. T-tests, chi-square, and Fisher exact test were used.

Results: There was no difference in pain scores between groups. Pain scores during the procedure in the placebo group were 2.95, and in the active medication group 3.03 (p=0.89). (t-tests) Study groups were similar in age, ethnicity, BMI, history of pelvic pain, cystitis, frequent UTI, and voiding habits. There were no significant differences in pregnancy outcomes (33% vs. 39% clinical pregnancy rate).

Conclusion: Phenazopyridine used a single dose prior to embryo transfer does not affect patient discomfort. However, the study is not powered to detect a 20% difference in pain, and patients will continue to be recruited.

Jeannine Connolly, MD

Recurrent lobular breast cancer and the association with lobular carcinoma in situ.
J. C. Connolly, MD; M. Phipps, MD; D. Giri, MD; M. R. Quddus, MD; P. Hirway, MD; M. Chung, MD.

Objective: To investigate the association between the presence of lobular carcinoma in situ (LCIS) at the specimen margin in patients with invasive lobular carcinoma (ILC) and local recurrence.

Methods: This is a retrospective cohort study of 42 consecutive patients diagnosed with ILC who were followed for a minimum of 5 years post initial diagnosis. All women were treated at Women and Infants Hospital or Rhode Island Hospital between January 1990 and May 2000. Patients were identified by the cancer registry at each hospital and medical records were reviewed to confirm the diagnosis. Patients with concurrent invasive ductal carcinoma, incomplete medical records or less than 5 years of follow-up information were excluded. Patients were treated initially with breast conservation surgery or mastectomy. The main
exposure was LCIS at the specimen margin and the outcome of interest was local recurrence of ILC. Binomial probability tests to assess differences were calculated using STATA.

**Results:** Of the 42 patients in our cohort, 19% had a 5 year local recurrence of ILC. The median follow-up for the cohort was 8.9 years. There was a higher local recurrence rate of ILC for patients with LCIS at the margins (36.4%) compared with those patients who had no LCIS at the margins (12.9%, p=0.044). The median time for recurrence was 2.9 years.

**Conclusion:** In our study, LCIS at the specimen margin was associated with an increased recurrence of ILC. Our results support the hypothesis that LCIS associated with ILC is a pre-neoplastic lesion and suggest that an attempt to obtain LCIS negative margins should be made in patients diagnosed with ILC.

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**Carla DiGirolamo, MD, PhD**

**Telomerase deficiency impairs differentiation of mesenchymal stem cells**

C. M. DiGirolamo, MD; L. Liu, MD; P. A. A. S. Navarro, MD; M. A. Blasco, MD; D. L. Keefe, MD.

**Objective:** Expression of telomerase activity is involved in maintaining self-replication and the undifferentiated state of stem cells. Adult mouse bone marrow mesenchymal stem cells (mMSCs) are multi-potential cells capable of differentiating into a variety of lineage cell types including adipocytes and chondrocytes. The goal of this study is to investigate the role of telomerase activity in the *in vitro* differentiation of mouse mMSC’s.

**Methods:** Primary cultures of mMSCs were obtained from telomerase knockout (mTR-/-) and wild type (WT) mice. Cells were directed down various differentiation pathways *in vitro* using lineage-specific growth media additives. Differentiation was determined with standard assays for adipocyte and chondrocyte cell types. Cell senescence was evaluated using a standard beta-galactosidase assay and chromosomal instability demonstrated with fluorescence in-situ histochemistry (FISH).

**Results:** MSCs isolated from mTR-/- mice failed to differentiate into adipocytes and chondrocytes whereas WT MSCs were capable of differentiation. Consistent with other cell types, late passage cells from mTR-/- mice underwent senescence and were accompanied by telomere loss and chromosomal end-to-end fusions.

**Conclusion:** These results suggest that in addition to its known role in cell replication, telomerase is required for differentiation of mMSCs in vitro. This work may contribute understanding of the significance of telomerase expression in the process of cell differentiation.

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**Katherine Eastwood, MD**

**Resident Training in Abortion.**

K. L. Eastwood, MD; L. A. Boardman, MD; J. E. Kacmar; J. Steinauer, MD; S. Weitzen, PhD.

**Objective:**

1. To evaluate whether abortion training is in accordance with the ACGME Guidelines of 1996.
2. To describe characteristics of residents who plan to provide abortions, and the residencies that trained them.

**Methods:** This is a cross-sectional, descriptive study using investigator-designed questionnaires to elicit information on abortion training in US OBGYN residency programs. Collected data included demographic information and characteristics of abortion training. Residents were questioned regarding plans to receive abortion training, and to provide abortions. Data were analyzed to determine trends in abortion training on the individual, program and regional level. Characteristics of residents who plan to provide abortions
following residency were determined, as well as characteristics of the residency programs at which they trained.

**Results:** Response rates varied from 43% to 63%. According to program directors, 50% of programs provide routine training, 36% provide optional training, and 14% offer no abortion training. Of programs offering training, a strong trend in location and religious affiliation emerged, with programs in New England, Mid Atlantic and Pacific regions being most likely to offer training. From the resident data, no age or sex differences emerged between those planning to provide/not provide abortions. The 38% of residents planning to provide abortions were more likely to be unmarried and without children. Training at university and non-religious programs, with support from the chair or director were strongly associated with providing abortions.

**Conclusion:** Of the 161 US program respondents, 86% currently offer abortion training. Strong institutional support, university programs, and non-religious affiliations were associated with increased likelihood of ongoing abortion provision.

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**Rachel Friedman, MD**

**Diagnostic Properties and Use of Fetal Fibronectin (fFN) at Women & Infants Hospital.**  
R. Friedman, MD; J. F. Peipert, MD; P. Hirway, MD; V. Swiatkowski, MD.

**Objective:** To evaluate the test properties of Fetal Fibronectin (fFN) at Women & Infants Hospital and describe its use over time.

**Methods:** We conducted a retrospective cohort study of 432 patients evaluated at Women & Infants triage for preterm labor from 2000 to 2002. ICD-9 codes for preterm labor or preterm contractions were used to obtain charts of patients presenting between 24 and 35 weeks gestation. We excluded patients with multifetal pregnancies, ruptured membranes, fetal anomalies, and nonreassuring fetal status. We collected data on demographics, obstetric and medical history, current pregnancy, triage evaluation, and delivery. Chi-square, and student t-tests were used to compare groups.

**Results:** Of 432 total patients, 187 (43%) underwent fFN testing. The groups tested and not tested were similar with respect to age, parity, clinical service, insurance status, presence of contractions and initial cervical exam. The sensitivity of fFN for delivery within 14 days was 29%, specificity was 88%, and the negative predictive value was 97% (95% CI = 93.0%, 99.0%). The use of fFN testing at WIH increased over time from 19% in 2000 to 48% in 2002 (p<0.0001).

**Conclusion:** The test properties of fFN at Women & Infants Hospital are similar to those reported in the literature. Use of fFN at WIH has increased over time. Given its excellent negative predictive value, clinicians should consider more routine use of fFN in patients presenting with symptoms and signs of preterm labor.
Karin Fuchs, MD  
**Management of high-grade cervical neoplasia in adolescents.**  
K. Fuchs, MD; S. Weitzen, PhD; L. Wu; M. G. Phipps, MD, MPH; L. A. Boardman, MD, ScM.  
**Objective:** To evaluate regression rates among adolescents with high-grade cervical disease managed expectantly and to determine the rate of high-grade disease documented on cone biopsy of those undergoing immediate treatment.  
**Methods:** Using a colposcopic database of over 2,300 women, we identified 86 adolescents with evidence of high-grade disease by cytology and/or histology (adolescents with CIN 3 were excluded). Since 1999, adolescents fitting these criteria were offered two options: immediate treatment or repeat colposcopy in 4-6 months. For those managed expectantly, disease was classified as regressed if subsequent cytology and/or biopsies demonstrated normal or mildly abnormal results. Demographic information, including sexual risk behaviors and smoking history, was assessed to determine possible associations with disease regression. Descriptive characteristics and odds ratios with 95% confidence intervals were calculated where appropriate.  
**Results:** Of the 86 adolescents, 20 (23%) were found to have a non-confirmatory biopsy following referral for HSIL and 66 (77%) were found to have CIN 2. Forty-five underwent immediate treatment with conization, while 39 were followed colposcopically. Of those treated, high-grade disease (≥CIN 2) was found in 29 (64%), while 9 (20%) had negative specimens. Of those followed conservatively, regression was documented in 28 (72%), persistence in 9 (23%), and progression in 2 (5%). Factors associated with regression included younger age (≤16 years vs 17-19 year olds; OR 2.5, 95% CI (0.5-14.3) and referral for HSIL smear with non-confirmatory biopsy (82% vs. 64% for those with CIN 2; OR 2.7, 95% CI (0.9-12.5).  
**Conclusion:** Based on significant regression of high-grade disease among adolescent women, conservative management should be considered for this population.  

Lindsay Madom, MD  
**Negative cone biopsies: predictors and clinical significance.**  
L. M. Madom, MD; L. A. Boardman, MD; S. Weitzen, PhD.  
**Objective:** The significance of the absence of neoplasia in a cone biopsy performed for treatment of cervical disease is uncertain. Livasy found that patients with negative cone biopsies were as likely to have residual disease as were women with neoplasia on cone specimens, with rates in both populations approximating 25%. The goal of our study was to determine the rate of residual disease among a population of women with negative cone biopsies and to evaluate potential factors associated with the finding of a disease-free cone biopsy.  
**Methods:** Using a colposcopic database of over 1,700 women, we identified 244 who underwent a cone biopsy between 1999 and 2004. Residual disease was defined as the presence of any degree of cervical intraepithelial neoplasia (CIN) on follow-up biopsy or the presence of a high-grade abnormality on cytology. Potential factors associated with the outcome of interest (e.g., smoking, indication for cone) were also assessed. Differences between those with negative and positive cones were analyzed using appropriate statistical tests (e.g. t-test for differences in means, chi-square test of independence).  
**Results:** Of the 244 women treated, 36 (15%) were found to have negative cones. Twenty-two (61%) underwent adequate follow-up with cytology, and in the majority of cases, colposcopically-directed biopsy. One woman had repeated evidence of CIN1 after 15 months of follow-up, while the remaining 21 (95%) had no evidence of residual disease. Neither age, smoking, colposcopic adequacy or lesion size were associated with a finding of a negative
Those treated for CIN1 or HSIL without confirmatory biopsy were more likely to have negative cone biopsies than were those treated for ≥CIN2 (22% vs. 13%, p=.09).

**Conclusion:** Clinically significant residual disease was not encountered among women with negative cone biopsies. The indication for treatment was marginally associated with the finding of disease on the final specimen.

**Kristen Page, MD**

**In vitro fertilization may overcome the negative effects of smoking on fertility.**

K. L. Page, MD; J. R. Trimarchi, PhD; J. Allesworth; D. Keefe, MD

**Objective:** We retrospectively evaluated the effect of smoking on pregnancy rate and other measures of IVF outcome in a large, diverse socioeconomic population located in a state where IVF coverage is mandated by law.

**Materials and methods:** We retrospectively analyzed cycle data from 404 patients who had undergone either their first attempt at IVF treatment or their first cycle of IVF following a clinical pregnancy. Outcomes of the stimulation response, egg and embryo number and quality, pregnancy and live birth rates were assessed in patients reported as never smokers, past smokers and current smokers. The sample size was nearly twice that needed to have 80% power to detect a 5% effect of smoking on pregnancy outcome, based on preliminary data indicating a 26% smoking incidence. Categorical variables were compared using a chi-square tests and Fisher’s exact tests were used to compare small sample sizes. Continuous variables were compared using PROC ANOVA. Relative risks for association with positive pregnancy and live birth were estimated using a log-binomial regression model estimated using PROC GENMOD.

**Results:** 9.3% of patients reported current smoking, and 12.1% reported a history of smoking. Smoking status did not significantly affect peak estradiol levels, number of oocytes retrieved, egg maturity, log mean ovarian volume, fertilization rate, cleavage rate, embryo quality, percent of 6 cell embryos, pregnancy rate or live birth rate in women < 35 or ≥ 35 years old. Outcomes were then evaluated controlling for FSH, number of oocytes retrieved and embryo quality score. The relative risk of smoking continued to have no significant impact on pregnancy rate or other fertility outcomes when controlling for these factors.

**Conclusion:** 21.4% of IVF patients in this study had past or present exposure to cigarette smoking with no measurable effect on IVF outcome. It is possible that the aggressive controlled ovarian hyperstimulation employed with ART overcomes the negative effects of smoking on fertility, and that the relative paucity of vascular supply to primordial follicles may protect them from the detrimental effects of smoking.

**Beth Plante, MD**

**A multiple marker model to predict pregnancy viability.**

B. J. Plante, MD; N, M. Phipps, MD; J. Blume, PhD; G. Messerlian, PhD; R. Shackelton; J. Canick, PhD.

**Objective:** To develop a clinically useful model for predicting pregnancy viability in the first nine weeks of gestation.

**Methods:** Between February, 2002 and March, 2004, we conducted a prospective cohort study of 256 symptomatic women in the first 9 weeks of pregnancy. Clinical information as well as serum samples for progesterone, inhibin A, and human chorionic gonadotropin (hCG) were collected at presentation. Each predictor was evaluated alone using univariate statistics and in conjunction with other variables using Receiver Operator Characteristic (ROC) curves. To develop the most clinically useful model, the cohort was separated into two subgroups based on whether the progesterone was at the “extremes” (less than 5 ng/mL or greater than
25 ng/mL) or in the “grey zone” (between 5 ng/mL and 25 ng/mL) and further analyses were performed.

**Results:** Among single biomarkers, progesterone had the greatest diagnostic accuracy for predicting viability (area under the ROC curve (AUC) = 0.891 (95% CI 0.852-0.930)). At the “extremes,” progesterone was highly accurate (AUC = 0.991 (95% CI 0.976-1.00)). In the “grey zone,” progesterone was less accurate (AUC = 0.707 (95% CI 0.618-0.795)). Including hCG, symptoms, and ultrasound findings in the “grey zone” improved the AUC (0.772 (95% CI 0.692-0.851)). We then developed a Multiple Marker Model that included progesterone for all patients, and additional information for those participants in the “grey zone” (AUC = 0.904 (95% CI 0.867-0.940)).

**Conclusion:** A Multiple Marker Model has the potential to be clinically useful for predicting pregnancy viability at a single visit with an overall accuracy of 90%.

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**Aaron Shafer, MD**

**The association of microvessel density counts and the risk for inguinal lymph node metastases in patients with squamous cell carcinoma of the vulva.**

A. Shafer, MD; M. M. Steinhoff, MD; C.O. Granai, MD; R. G. Moore, MD.

**Objective:** To determine if microvessel density (MVD) counts in the primary tumor of patients with squamous cell carcinoma of the vulva is associated with inguinal lymph node metastases.

**Methods:** This was an IRB approved retrospective study of patients diagnosed with primary squamous cell carcinoma of the vulva. Microvessel density counts were examined in each patient’s primary tumor and then correlated with the patient inguinal lymph node status for metastasis. We hypothesized that microvessel density counts are predictive of lymph node metastasis in patients with vulvar carcinoma. A search of the Women and Infants/Brown University tumor database was performed to identify all patients diagnosed with a primary squamous cell carcinoma of the vulva from 1990 to 2004. Available tissue blocks were recovered and all slides were reviewed for accuracy of diagnosis. From each tissue block new slides were prepared with 5micron sections and stained with Factor-VIII related antigen immunohistochemical stain using a Dako automated staining processor. The most densely staining regions on the slide were examined under 200X and a microvessel density count was performed. Two of the investigators separately performed MVD counts and a mean MVD count was obtained for each patient. Four control slides of vulvar skin without carcinoma were also stained and MVD counted in the same manner. The mean MVD of the control slides were also calculated. Patient charts were reviewed for demographics and pathology results for presence or absence of groin lymph node metastases, tumor size and depth of invasion. The mean MVD count for patients with and without groin node metastases were calculated.

**Results:** Forty-five patients were identified that had all of the clinical and pathologic material available to carry out the study. Thirty-two patients had groins negative for metastasis and 13 had inguinal metastasis. The mean MVD count (SD) for patients without groin node metastases was 89.22 (39.64) and the mean MVD count (SD) for patients with LN mets was 91.69 (34.55). The p value was 0.86. The mean age was 78.4 in the group with metastasis, and 73.4 in the group without metastases. Groin node metastases were associated with depth of invasion and tumor size.

**Conclusion:** There is no association between microvessel density counts in the primary tumors of patients with squamous cell carcinoma of the vulva and the risk for inguinal lymph node metastases.
Valerie Swiatkowski, MD

Estimating the prevalence of chlamydia and gonorrhea infection in patients at risk for preterm labor.

V. Swiatkowski, MD; R. Friedman, MD; J. F. Peipert, MD; P. Hirway, MS.

Objective: To estimate the prevalence of Chlamydia trachomatis and Neisseria gonorrhoeae infection in women presenting to Women and Infants’ Hospital triage area with signs and symptoms of preterm labor.

Methods: This study was a retrospective chart review of patients presenting to Women and Infants’ Hospital for preterm labor evaluation between January 2000 and December 2002. We included patients presenting with a singleton gestation between 24 to 35 weeks. Data were extracted from 433 patient charts to determine the frequency of testing for and prevalence of two sexually transmitted diseases (C. trachomatis and N. gonorrhoeae) using the BDPRobeTec™ amplified DNA assay. The prevalence of each STD and the respective 95% confidence intervals (CI) were calculated.

Results: Of the 433 patients presenting during the study period, 271 (63 percent) of patients were screened with the amplified DNA assay. The prevalence of C. trachomatis within the screened population was 1.1 percent (95% confidence interval 0.2% - 3.2%). The prevalence of N. gonorrhoeae was 0.4 percent (95% confidence interval 0.0% - 0.2%).

Conclusion: The prevalence of C. trachomatis and N. gonorrhoeae in a patient population presenting at risk for preterm labor is extremely low. Routine testing during evaluation for preterm labor may not be useful or cost effective in all patients presenting with signs and symptoms of preterm labor. Further research should be performed to determine if selected screening based on risk factor stratification may be more useful.

Emily White, MD

Fears about not being able to get pregnant among pregnant adolescents.

E. White MD; M. Phipps MD, MPH; S. Weizen PhD; A. Meers; C. Rosengard, PhD.

Objective: To examine demographic and health history differences between pregnant adolescents who had fears that they would not be able to get pregnant and those without these fears.

Methods: This is part of a cohort study assessing attitudes about pregnancy among 300 pregnant adolescents presenting for their first prenatal visit. Inclusion criteria: delivery prior to 20th birthday, English speaking, less than 24 weeks gestation at first visit, and informed consent which included the guardian’s consent if the participant was a minor. The dependent variable was a positive response to the question “Did you have any fears that you wouldn’t be able to get pregnant?” Independent variables included medical history and demographic variables.

Results: Fear about not being able to get pregnant was expressed by 42% of study participants. There was no statistical difference in fear of infertility by age when examined by year. There were also no differences in previous STD rates, age at first intercourse, or number of partners between adolescents with fear about infertility and those without this fear. There were a higher proportion of spontaneous abortions among those who expressed fear compared with those without fear (56% vs. 32%, p=0.02). Although not statistically significant, birth control use among adolescents who had fears was lower than the comparison group (17% vs. 26%, p=0.09).

Conclusion: A considerable number of adolescents presenting for their first prenatal visit expressed fear that they would not be able to get pregnant. Further investigation is needed to explore the cause of this fear and the association with adolescent pregnancy and contraceptive use.
Nurit Winkler, MD

Antimullerian hormone – marker of follicle number or quality?
N. Winkler, MD; E. Sabo, MD; J. E. Allsworth, MD; D. L. Keefe, MD.

Objective: Anti-mullerian hormone (AMH), a peptide secreted by pre- and early antral follicles, is a promising biomarker of oocyte aging, since it predicts response to outcome after IVF, but little is known about what ovarian factors determine AMH levels in women. Are AMH levels determined by ovarian reserve, i.e. number of follicles, or by their “quality”?

Methods: Cross sectional study of AMH levels from serum obtained on the day of oophorectomy, and follicle number counted in ovaries after histological staining. Ovaries were obtained from women, ages >18 and <45, undergoing oophorectomy if their pathological process did not preclude ovarian histology for follicle count. AMH serum levels were measured from specimens drawn at day of surgery, and serum stored at -20° Celsius until assay. An ultra-sensitive immuno-enzymometric assay kit was used to determine AMH concentration (Diagnostic Systems Laboratories, Inc. CV <15%). One sample of ovarian cortex was cut from each ovary, fixed in formalin, dehydrated in 70% ethanol, serial sectioned (5 μm thick), and stained with hematoxylin/eosin. Counting follicles only in every tenth slide avoided double counting. A fractionator stereological sampling technique, assisted by a digital image analysis system connected to an inverted microscope, was used for follicle counts. The examinee that performed the follicle counts was blinded to the AMH serum concentrations. Pearson and the Winsorized tests estimated correlations between number of preantral and total follicle numbers, age and AMH concentration.

Results: Ovaries were examined from 42 women of median age 38.8 years (range 23-45 years). Median section area analyzed was 151.0 mm/sq (range 14.37-405.8 mm/sq), median volume of ovaries was 7.55 mm/cube (range 0.718-20.29 mm/cube), and median AMH level was 0.65 ng/ml (range 0.02-3.6). Age negatively correlated with number of preantral follicles (R= -0.80, p = < 0.001), as well as with total number of follicles per mm² (R = -0.80, p = <0.001). AMH serum concentration did not correlate with age (R = 0.02, p = 0.91), number of preantral follicles (R= 0.05, p = 0.84) or total number of follicles per mm² (R = 0.03, p = 0.92). These findings were robust with respect to the influence of outliers.

Conclusion: Age correlated with the number of preantral follicles, as previously shown. AMH serum concentration, however, did not correlate either with number of preantral follicles or total number of follicles, suggesting that this bio-marker of ovarian aging must affect follicle quality rather than quantity.

Presenting Fellows

Laurent Brard, MD

Iron chelators deferoxamine and diethylene triamine pentaacetic acid induce apoptosis in gynecologic cancer cell lines.
L. Brard, MD, PhD; C. O. Granai, MD; N. Swamy, MD.

Objective: Iron chelators have traditionally been used in the treatment of iron overload conditions. The critical role of iron (Fe) in cell proliferation makes it a potential target for cancer therapy. Recent studies suggest that iron chelators may have potential in the treatment of cancer. The goal of this study was to explore the anti-proliferative effects of iron chelators in gynecologic cancer cell lines and more specifically ovarian cancer.

Methods: Human ovarian (CaOV-3), endometrial, cervical, vulvar, and rat ovarian (NuTu-19) cancer cell lines were treated with deferoxamine (DFO) and diethylene triamine pentaacetic acid (DTPA). Non-cancerous cell lines (rat fibroblast and human granulosa) were also tested. All cell lines were treated with 50 to 800 μM of iron chelator for 24-96 hours. Cell viability was measured by MTT colorimetric assay and cell
proliferation was determined by BrdU incorporation. Apoptosis was analyzed by DNA fragmentation, Hoechst staining and caspase-3, 8, and 9 activities. Cell cycle analysis was performed by flow cytometry.

**Results:** Iron chelators DFO and DTPA demonstrated anti-proliferative effects in all gynecologic tumor cell lines. Minimal effects were noted in the non-cancerous cell lines. Cytotoxic effects were chelator-, dose-, time-, and cell line-dependent. At doses of 50-μM, both chelators demonstrated significant anti-proliferative activity against NuTu-19 cells (<30% viability at 96 hours) compared to other cell lines (50-95% viability). Diminished cell proliferation in the presence of iron chelators was further demonstrated by significant reduction of BrdU incorporation, corroborating cell viability assays. Cell proliferation inhibition was due to DNA synthesis arrest. Cell cycle analysis of NuTu-19 and CaOV-3 treated with DFO or DTPA revealed a G0/G1- and S-phase block with increased apoptosis. DNA fragmentation analysis and Hoechst staining confirmed apoptosis. Apoptotic caspase-3, 8, and 9 activities were increased 2.4 times in DFO and DTPA treated cells over controls.

**Conclusion:** Treatment of gynecologic cancer cells with iron chelators causes significant decrease in cell viability. Iron chelators arrest ovarian cancer cell growth through inhibition of proliferation, cell cycle block, and apoptosis. Therefore, iron chelators can be potentially developed as novel therapeutic agents against ovarian cancer.

**Amy Kirkpatrick Brown, MD**

_The effect of protocol inclusion on the outcomes of ovarian cancer patients receiving first line chemotherapy._

A. Brown, MD, MPH; S. DonFrancesco; C.O. Granai, MD; P. DiSilvestro, MD.

**Objective:** Clinical trials are the gold standard for evidence based medicine. Despite this, only 2% of cancer patients enroll in clinical trials. Recent data has shown improved outcomes with protocol treatment in a variety of cancers. We investigated the outcomes of patients receiving first line chemotherapy for ovarian cancer on or off protocol.

**Methods:** Subjects were identified from the Women and Infants’ tumor registry. Cases were those receiving first line chemotherapy on protocol, and controls were those eligible for inclusion in any ongoing protocol at this institution but who chose not to participate. The primary end-point was progression free survival (PFS). Secondary endpoints were cycle delays, hospital admissions and overall survival (OS). Kaplan-Meier analysis was performed for recurrence free and overall survival. Continuous variables were compared with t-test, and categorical variables with Chi-square or Fisher’s exact tests where appropriate.

**Results:** There was no difference in PFS between the two groups, 21 months vs 23 months on or off protocol respectively. An improved PFS and OS in suboptimally debulked patients was found (p<.05) in those treated on protocol. There was no difference in OS or hospital admissions between those treated on or off protocol. Delay of at least 1 cycle occurred in 53% on protocol vs 62% off protocol (NS). On multivariate analysis, optimal debulking was the only factor significantly associated with either recurrence or survival.

**Conclusion:** Enrollment in a randomized trial had no adverse impact on the outcomes of patients receiving first line chemotherapy for ovarian cancer. Suboptimally debulked patients may benefit more from protocol therapy.

**Michelle Russell, MD**

_Evaluation of postpartum glucose tolerance assessment after gestational diabetes mellitus._

M. Russell, MD; M. Phipps, MD, MPH; P. Hirway, MS; C. Olsen; M. Carpenter, MD.

**Objective:** To determine the risk factors associated with lack of postpartum glucose tolerance assessment after gestational diabetes mellitus (GDM).
Methods: A retrospective cohort study was performed. Women with GDM receiving prenatal care in the Diabetes In Pregnancy clinic during 2001-2004 were included. Women with pregestational diabetes mellitus (DM) and referral from a source precluding determination of outcome were excluded. Statistical analyses utilized Student’s t-test and Pearson’s Chi square.

Results: Of 354 women, 156 (44%) had postpartum testing. Of Tested, 44 had abnormal glucose tolerance (AGT) and 12 had suspected DM.

Conclusion: 56% of women with GDM do not have postpartum testing for AGT. Welfare/Medicaid insurance, fasting plasma glucose (FPG) on pregnancy OGTT, absence of and location of postpartum visit are associated with lack of testing. Of Tested, 36% had AGT and 8% had suspected DM. The FPG on the pregnancy OGTT is associated with persistent AGT in Tested. The mean FPG on the pregnancy OGTT in the Not Tested was similar to the mean FPG in the Tested with AGT.