

7th Annual
**Bruce K. Young, MD
Research Retreat**



**Department of Obstetrics and Gynecology
November 20th, 2009**





Welcome to the 7th Annual
Bruce K. Young, MD
Research Retreat

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<i>Family Planning and Reproductive Choice</i>	28
<i>General Gynecology</i>	29-32





Schedule of Events

- 8:30 - 9:00am** **Registration and Continental Breakfast**
- 9:00 - 9:10am** **Welcome and Opening Remarks**
David L. Keefe, MD, *Chairman*
Frederick Naftolin, MD, PhD, *Director, Research in Reproductive Biology*
Steven R. Goldstein, MD, *Facilitator*
- 9:10 - 9:25am** **Global Women's Reproductive Health**
Moderator: Robert F. Porges, MD
- 9:10 - 9:25am A Holistic Approach to Reduce Maternal/Neonatal Mortality in Rural Uganda
Robert F. Porges, MD
- 9:25 - 9:55am** **Epidemiology**
Moderator: Paolo Toniolo, MD
- 9:25 - 9:40am Human Chorionic Gonadotropin and Maternal Risk of Breast Cancer
Paolo Toniolo, MD
- 9:40 - 9:55am Characterization and Validation of Genomic Signature of Pregnancy
Alan Arslan, MD
- 9:55 - 10:40am** **Gynecologic Oncology**
Moderator: John Curtin, MD
- 9:55 - 10:10am The Mammalian Target of Rapamycin Pathway in Endometrial Adenocarcinoma: An Interim Analysis
Sarah Czok, MD
- 10:10 - 10:25am A Comparison of Post-operative Pain Among Robotic and Laparoscopic Gynecologic Surgery
Tarah Pua, MD
- 10:25 - 10:40am Healthcare Disparities in Gynecologic Oncology at NYU School of Medicine: *Is Care Different at BHC and Tisch?*
Leslie Boyd, MD
- 10:40 - 10:55am** **Coffee Break**



Schedule of Events

10:55 - 11:40am Reproductive Endocrinology and Infertility

Moderator: James Grifo, MD, PhD

10:55 - 11:10am The Effect of Thyroid Autoimmunity in the Older, Infertile IVF Population
Andrea Reh, MD

11:10 - 11:25am Comparison of Pregnancy Outcomes in Elective Single (eSBT) versus Double-Blastocyst Transfer (2BT) Stratified by Age
Christine Mullin, MD

11:25 - 11:40am Time-lapse Imaging of Murine Embryogenesis: Surprise Observation Providing Insight into Early Reproductive Processes
Yael Kramer, MS

11:40am - 12:10pm Stem Cell and Regenerative Medicine

Moderator: Bruce K. Young, MD

11:40 - 11:55am Generation of Disease-specific Human Embryonic Stem Cells from Genetically Abnormal Embryos
Christoph Hansis, MD, PhD

11:55am - 12:10pm Cytokine Profiling of the Maternal and Fetal Response to LPS *in vitro*
Doris B. Tse, PhD

12:10 - 1:10pm Lunch

Will be provided outside Farkas Auditorium

1:10 - 1:55pm Ultrasound

Moderator: Ilan Timor-Tritsch, MD

1:10 - 1:25pm Comparison Between Fetal 2D/3D Neurosonography and Magnetic Resonance Imaging Findings in a Selected Population: Do We Need Both?
Christine L. Proudfit, MD

1:25 - 1:40pm Basic as well as Detailed Neurosonogram can be Performed by an Off-line Analysis of 3D Fetal Brain Volumes
Eran Bornstein, MD



Schedule of Events

- 1:40 - 1:55pm Conservative Management of Cervical Scar Pregnancies with Serial 3D Power Doppler Assay of Vascularization after Transvaginal US Guided Injection of MTX
Elizabeth Rodgers, MD
- 1:55 - 2:10pm Pelvic Reconstructive Surgery and Urogynecology**
Moderator: Scott W. Smilen, MD
- 1:55 - 2:10pm Role of Urodynamic Testing in Patient Care at Bellevue Hospital
Arash Rahi, MD
- 2:10 - 2:40pm Reproductive Biology**
Moderator: Frederick Naftolin, MD, PhD
- 2:10 - 2:25pm Membrane-Actin Cytoskeleton Linking Protein Expression by Human Post-Operative Adhesions and Fibroblasts
Kui Huang, PhD
- 2:25 - 2:40pm Expression of Ezrin and Estrogen Receptors by Human Cervical Cancer
Seung Do Choi, MD
- 2:40 - 2:55pm Break**
- 2:55 - 3:40pm Maternal Fetal Medicine**
Moderator: Ana Monteagudo, MD
- 2:55 - 3:10pm Prediction of Preterm Birth in Asymptomatic Twin Pregnancies: Fetal Fibronectin, Cervical Length, and the Change in Cervical Length Over Time
Nathan S. Fox, MD
- 3:10 - 3:25pm Anti-Factor Xa Plasma Levels in Pregnant Women Receiving Low Molecular Weight Heparin Thromboprophylaxis
Nathan S. Fox, MD
- 3:25 - 3:40pm Brain Development in Fetuses with Congenital Heart Disease
Ashwin Jadhav, MD



Schedule of Events

- 3:40 - 3:55pm** **Family Planning and Reproductive Choice**
Moderator: Livia Wan, MD
- 3:40 - 3:55pm A Multicenter, Open-Label Study on the Efficacy, Cycle Control and Safety of a Novel Contraceptive Vaginal Ring (CVR)
Livia Wan, MD
- 3:55 - 4:55pm** **General Gynecology**
Moderator: Julian Mierlak, MD
- 3:55 - 4:10pm The Relationship Between Labrum Tears of the Hip and Generalized Unprovoked Vulvodynia
Deborah Coady, MD
- 4:10 - 4:25pm When Abnormal Uterine Bleeding is the Main Complaint in Pre-menopausal Women Diagnosed with Endometrial Polyps, is Surgical Polypectomy an Effective Treatment?
Autumn Edenfield, MD
- 4:25 - 4:40pm Increased Endometrial Thickness at Baseline is Associated with Decreased Success in IVF
Rachel Weinerman, MD
- 4:40 - 4:55pm Is Obesity a Risk Factor for the Development of Pre-malignant or Malignant Lesions in Endometrial Polyps?
Lydia Garcia, MD
- 4:55 - 5:00pm** **Closing Remarks - David Keefe, MD**
- 5:00 - 6:00pm** **Cocktail Reception**
Will be held outside Farkas Auditorium



Research Retreat Committee Members

Frederick Naftolin, MD, PhD - Chair

Erica Berliner

Latoya Bishop

Beverly Ginsberg

Ronald Maddock

Online Resources

This program and other information related to the 2009 Bruce K. Young, MD Research Retreat can be found on the Department's intranet site:

<http://www.nyumc.net/obgyn>

Main Department Website

<http://obgyn.med.nyu.edu>

NYU Fertility Center Website

<http://www.NYUFertilityCenter.org>

National Ovarian Cancer Early Detection Program Website

<http://www.med.nyu.edu/nocedp>

To learn more about government-sponsored debt forgiveness programs for research trainees and young scientists contact Dr. Naftolin at frederick.naftolin@nyumc.org or (212) 263-2823 or go online:

<http://www.training.nih.gov/careers/careercenter/debt.html>



A Holistic Approach to Reduce Maternal/Neonatal Mortality in Rural Uganda

Presented By: Robert F. Porges, MD

Robert F. Porges, MD, Principal Investigator, Professor, Division of Global Reproductive Health, Department of Obstetrics and Gynecology, New York University School of Medicine; Harry Strulovici, MD, MPH, Co-Investigator, Director, International Maternal Health Initiative, Assistant Professor, Division of Global Reproductive Health, Department of Obstetrics and Gynecology, New York University School of Medicine

The purpose of this project is to implement a cost-effective, replicable, and sustainable pilot program to reduce maternal/neonatal mortality in rural Uganda through a holistic approach. This will be accomplished by the recruitment and training of health professionals and community health workers (incorporating a mobile phone network linked to a computer data base at the Level IV Health Facility); improvement of the health facility; promotion of health literacy and gender equity; enabling transport for women and families and also family planning counseling. This project will be utilized be examined by the Ministry of Health as a case study to determine lessons learned and obstacles encountered to increasing access to health care services (health system strengthening). This pilot program will be initiated in the sub-district of Mwera in Mityana, 70 km from Kampala, Uganda and by working in concert with private and local partners, ultimately, this model will be expanded to other districts.

Notes:



Human Chorionic Gonadotropin and Maternal Risk of Breast Cancer

Presented By: Paolo Toniolo, MD

P. Toniolo¹, A. Lukanova², E. Lundin³, T. Chen², K. Grankvist³, P. Lenner³, H. Schock², A. Zeleniuch-Jacquotte¹
1New York University School of Medicine; 2German Cancer Research Center, Heidelberg, Germany; 3University of Umeå, Sweden.

Objectives: Childbearing confers the mother lifetime protection from breast cancer. The epidemiological evidence supporting the protective association is large and consistent across populations, but not all women benefit from such protection. For those who delay first pregnancy beyond age 30-35, pregnancy increases the risk for up to 10-15 years following pregnancy. Despite the weight of evidence, there is limited understanding of the biological determinants of the effect of pregnancy on breast cancer. Research in rodents shows unequivocally that pregnancy inhibits carcinogen-induced mammary tumors and that the same effect could be achieved by administering hormones of pregnancy (estradiol, estradiol+progesterone, hCG) to virgin animals, although no experimental model offer clues concerning the transient post-pregnancy increase in risk. Thus, there is evidence that the hormones that are most relevant to the progression of pregnancy are also implicated in the profound changes in the breast that occur during pregnancy and, in turn, may be determinants of both the lifetime protection of the gland from carcinogenic transformation and, when specific conditions apply, of the transient increase in risk following pregnancy.

Methods: A case-control study (237 cases, 445 controls) was nested within the North Sweden Maternity Cohort, with access to first-trimester serum specimens obtained from over 150,000 pregnancies. Only first full-term pregnancies leading to the delivery of a singleton offspring were considered. HCG was determined using Immulite 2000 analyzer. Odds ratios (OR) and 95% confidence intervals (CI) were estimated through conditional logistic regression.

Results: There was a protective association of breast cancer with increasing hCG (upper tertile OR=0.67 (0.46-0.99); ptrend=0.04), which appeared to be stronger for pregnancies occurring before age 25 (upper tertile OR=0.52 (0.29 - 0.94); ptrend=0.03). In subgroup analyses by age at diagnosis elevations in hCG were associated with maximum protection from cancers diagnosed about or after menopause. The upper tertile OR for diagnoses \geq age 50 was 0.37 (0.16 - 0.88; ptrend=0.02). No protection was observed for cancers diagnosed before age 40.

Conclusions: These observations offer intriguing new evidence suggesting that elevated hCG during the first trimester of a first full-term pregnancy might be an important determinant of the long-observed lifetime protection from breast cancer among parous women. HCG does not appear to be a factor in cancers diagnosed at young age.

Notes:



Characterization and Validation of Genomic Signature of Pregnancy

Presented By: Alan Arslan, MD

Alan A. Arslan, Ilana Belitskaya-Levy, Anne Zeleniuch-Jacquotte, Eric Ross, Irma Russo, Suraj Peri, Per Lenner, Göran Hallmans, Pal Bordas, Jose Russo, Paolo Toniolo

Pregnancies early in life afford mothers lifetime protection against breast cancer, which subsequent pregnancies further enhance. The reasons for such protection are unknown, but research suggests that hormones sustaining pregnancy help the breast become resistant to cancer by making fully mature its constituent cells, which until a first delivery remain immature and, thus, susceptible to carcinogens.

This multi-disciplinary, collaborative international research (funding: Avon Foundation) is rooted on the preliminary evidence from one of the participating laboratories that giving birth may confer a genetic signature detectable in breast cells and different from that of women who never experienced pregnancy. The goal is to characterize and validate the proposed genomic signature of pregnancy in fine-needle breast biopsies obtained from volunteers in a manner independent of previous observations. The program involves 136 postmenopausal women (90 with a history of pregnancies and 46 without) part of an ethnically homogeneous region in northern Sweden. Gene expression analyses have been performed at the Fox Chase Cancer Center using the Affymetrix U133 2 plus human array.

Preliminary results indicate that the breast of postmenopausal women is characterized by a specific genomic signature determined by early reproductive events. Compared to nulliparous women, breast of parous women demonstrated significant up-regulation of genes involved in lactation (OXTR, PRLR), cell adhesion (SC3, ERBB3, ALCAM, MGP, MYBPC1, HSPB11, AZGP1, EZR, ANXA9), nutrient response (HMGCS2, AQP3, MGP, OGT), tissue development (DHCR24, IRF6, KRT5, KRT14, KRT15, KRT17, MGP, MREG, UGCG), epithelial cell differentiation (FOXA1, KCNE1, KRT14, SHROOM3), tumor necrosis factor-mediated signaling pathway (KRT8, KRT18), and neural tube development (HES1, SHROOM3, OVOL2, BBS4). To date, a total of 245 up-regulated genes and 261 down-regulated genes were identified for validation in an independent set of postmenopausal women.

These observations may lead to a better understanding of the unknown biological determinants of the well-established lifetime protection from breast cancer that a pregnancy confers to the mother. The project represents the first step in preparation for a more complex multi-institutional program seeking to develop biomarkers reflecting the genomic and physiological changes in the breast associated with pregnancy for applications in epidemiological research and chemopreventive interventions aiming at reducing the impact of breast cancer.

Notes:



The Mammalian Target of Rapamycin Pathway in Endometrial Adenocarcinoma: An Interim Analysis

Presented By: Sarah Czok, MD

S. Czok, P.S. Shukla, K.B. Mittal, R. Arju, S.V. Blank, R.J. Schneider; New York University Medical Center, New York, NY

Objectives: The mammalian target of rapamycin (mTOR) is a serine-threonine protein kinase of the phosphatidylinositol 3-kinase (PI3K)/Akt signaling pathway that controls protein synthesis, and has been shown to be involved in endometrial cancer. We sought to identify which mRNA translational and regulatory factors in this pathway have altered expression or activity in endometrial adenocarcinoma, and whether expression or activity differs between endometrioid subtype and type II tumors. Currently rapamycin, an mTOR inhibitor, is being used in clinical trials to treat recurrent endometrial adenocarcinoma, and we sought to identify alterations in the mTOR-dependent translational control pathway that may be informative of rapamycin sensitivity and resistance to enable individualized treatment strategies.

Methods: Fifty-four specimens have been evaluated to date: 33 endometrioid endometrial adenocarcinoma, eight type II tumors, and 13 normal controls. Immunohistochemical staining was performed for the following proteins: Akt, Akt-P, mTOR, mTOR-P, PTEN, eIF4E, eIF4G, 4E-BP1, 4E-BP1-P, TSC2. Protein expression was scored by a gynecologic pathologist on a three-point scale (0= no staining; +1= <25% staining, +2= 25-50% staining, and +3= >50% staining). Differences in expression were then analyzed using the Chi-square test and pairwise analysis.

Results: The proteins mTOR, eIF4E, 4E-BP1, 4E-BP1-P, and TSC2 showed significant over-expression in endometrial adenocarcinomas compared to normal endometrial controls. The proteins Akt, Akt-P, and eIF4G showed a trend toward over-expression in endometrial adenocarcinomas, although were not statistically significant. PTEN showed a non-significant trend toward reduced-expression in endometrial adenocarcinoma compared to normal endometrial controls. There was no difference in expression between endometrioid and type II tumors.

Conclusions: These preliminary results suggest that several of the translational and regulatory proteins in the mTOR pathway may be significantly over-expressed in endometrial adenocarcinoma. These may possibly be differentially expressed between endometrioid and type II tumors, however our sample size of eight type II tumors was too small to find a significant difference. While other translational and regulatory proteins showed a trend toward over-expression, and PTEN showed a trend toward reduced-expression, these findings may also be non-significant due to a small sample size. Further study with a larger sample size is necessary to delineate if these trends are truly significant. If substantiated by an ongoing larger analysis, the increased expression of mTOR in endometrial adenocarcinoma would be the first report of any human cancer demonstrating increased mTOR expression.

Notes:



A Comparison of Post-operative Pain Among Robotic and Laparoscopic Gynecologic Surgery

Presented By: Tarah Pua, MD

Tarah L Pua, MD; Kimberly Ferrante, MD; Akiva Novetsky, MD; Rajat Jain, Stephanie V Blank, MD; Leslie R Boyd MD; John P Curtin, MD; Bhavana Pothuri, MD.

Background: Minimally invasive surgical techniques in gynecologic oncology have become increasingly important in recent years. Numerous studies have shown that laparoscopic techniques are safe, feasible and efficacious, with less postoperative pain than open techniques. With the advent of robotic surgery as a new operative tool in gynecologic oncology, more comparisons are being made between traditional laparoscopy and robotics. Advantages of robotic surgery when compared to traditional laparoscopy include a faster learning curve, wrist like range of motion, and 3-dimensional imaging of the operative field. The level of postoperative pain experienced by patients has yet to be evaluated. Given the concept of the remote center utilized in robotic surgery, it is theorized that patients experience less post-operative pain. In this study, we assess the difference in pain experienced by patients after robotic versus laparoscopic surgery through the utilization of analgesics post-operatively.

Methods: Women who underwent a robotic gynecologic procedure at our institution from 2008-2009 were identified and compared to laparoscopic controls matched for procedure type. Pain scores, as assessed by the visual analog pain scale obtained by nursing staff, were collected in all cases as well as the type and quantity of pain medication used. Cases that were converted to laparotomy or those that did not have adequate documentation of pain were excluded. Comparative analysis of pain was performed using Pearson's chi-square test and logistic regression.

Results: 34 robotic and 28 laparoscopic procedures were identified. There was no difference found between the two groups in the immediate postoperative (score 0 vs 3, $p=0.31$), 1hr (score 3 vs 4, $p = 0.27$) or discharge pain scores (score 1 vs 0, $p = 0.49$). There was also no difference in the type and quantity of pain medications used. After controlling for type of surgery (minor versus major), patients who underwent laparoscopic surgery were 5.84 (CI 1.17-29.3) times more likely to used intravenous (IV) and intramuscular (IM) pain medications in the recovery room.

Discussion: While pain scores and the absolute use of postoperative analgesics did not differ between robotic and laparoscopic gynecologic surgeries. After controlling for type of surgery, women who underwent robotic surgery required less IV/IM pain medications implying that the quality of the pain experienced by those who underwent robotic surgery may be less severe. Additional prospective studies with other pain assessment tools are necessary to verify this finding.

Notes:



Intraperitoneal Chemotherapy: Who, What, When and How in Diverse Academic Settings

Presented By: Leslie Boyd, MD

L.R. Boyd, A.P. Novetsky, T.L. Pua, B. Pothuri, J.P. Curtin, R.C. Wallach, and S.V. Blank

Objective: When GOG 172 showed a clear benefit to intraperitoneal (IP) chemotherapy as frontline treatment for advanced ovarian cancer, our division adopted IP as the preferred method for administering front-line treatment at both a public and a private hospital setting. We sought to determine what factors impact in decision-making for IP port placement and use for patients (pts) with advanced ovarian cancers.

Methods: A chart review was undertaken from January 2005 to May 2009. All pts with a diagnosis of advanced (stage III or IV) epithelial ovarian, fallopian tube or primary peritoneal cancer were included. Operative reports and chemotherapy records were reviewed. ASA class was utilized as a surrogate for overall health status. Statistical analysis was performed using chi-square analyses.

Results: A total of 108 pts were identified for inclusion in the study. Of these, 90/108 (83%) were optimally debulked and were evaluated for IP port placement. 37% of pts received an IP port at the time of cytoreductive surgery. An additional 16% of patients received an interval IP port via laparoscopic insertion, for a total of 53% of eligible patients receiving IP ports. Pts aged ≤ 60 were more likely to have an IP port placed ($P < .04$) than pts over age 60. Hospital type (public or private) did not affect the rate of IP port placement, although pts at the public hospital were less likely to undergo optimal cytoreduction ($P = .04$). Race/ethnicity and ASA class were not associated with likelihood of IP port placement. The rate of IP port placement increased over time, with more ports placed in the latter years of our series ($P = .003$). 26/40 (65%) of pts with IP ports received ≥ 4 cycles of chemotherapy, while 5/40 (13%) received no IP chemotherapy. The most common reasons for failed completion include: grade 3 toxicity (4 pts); patients' fear of toxicity (3 pts); and port malfunction (3 pts).

Conclusions: Despite a concerted institution-wide effort to implement IP therapy as standard treatment for patients with optimally debulked ovarian cancer, a substantial percentage of pts do not receive IP ports. This percentage is improving over time. The rate of IP port placement was similar in both a public and private hospital setting. Although placement will likely increase with surgeons' comfort, refinements are needed to decrease the toxicities associated with the 172 regimen, while maintaining its successful outcome.

Notes:



The Effect of Thyroid Autoimmunity in the Older, Infertile IVF Population

Presented By: Andrea Reh, MD

Reh A, Chaudhry S, Im S, Amarosa A, Berkeley AS, Krey L, Levitz M, Grifo J, Danoff A.

Background: Thyroid autoimmunity is more common in older women and has been cited as a potential etiology for infertility, miscarriage, failed fertilization, and/or IVF failure, although most studies were done in patients <35 years old. Studies have shown that fertile patients with thyroid autoimmunity appear to have a diminished thyroid functional reserve during early pregnancy, suggesting that both ovarian hyperstimulation and autoimmune thyroid disease are factors that can attenuate the normal thyroid response necessary for maintaining an ongoing pregnancy after assisted reproductive technologies.

Objective: Part 1) To determine if there is a greater association of anti-thyroid antibody (TPO Ab) and anti-thyroglobulin antibody (TG Ab) in IVF patients ≥ 38 years old without a baby from IVF versus those with a live birth from IVF. Part 2) To describe the effect of gonadotropin stimulation and early pregnancy on the thyroid profile. We hypothesize that patients with thyroid autoimmunity will have an attenuated thyroid response to the IVF cycle and early pregnancy.

Design: Case-control study of patients ≥ 38 years old who have undergone a fresh in-vitro fertilization (IVF) cycle using stored frozen serum samples (IRB H#6902)

Materials and Methods: Patients were divided into 4 groups, based on their outcome from their first IVF cycle at NYUFC from 2005-2008: 1) Miscarriage; 2) Singleton pregnancy with singleton delivery; 3) No pregnancy; 4) Biochemical pregnancy. Each patient was tested for (Part 1) Thyroid autoimmunity (TPO Ab and TG Ab); and (Part 2) Thyroid function testing (thyroid stimulating hormone (TSH), free thyroxine (F4), thyroid binding globulin (TBG), and total thyroxine (TT4). Thyroid function testing was performed at four points in the IVF cycle: a) Start of IVF cycle, "day 2"; b) Two days prior to the egg retrieval, "day of HCG"; c) First pregnancy test, "day 28"; d) Second pregnancy test, "day 35". Demographic information and medical history, including BMI, pregnancy, and history of thyroid disease and/or thyroid medication, were obtained through a comprehensive chart review (IRB # 10-00052).

Results: Part 1: A total of 369 euthyroid patients were assayed for thyroid autoimmunity with a mean age of 40.8 ± 2 years, range 38-47. Overall, 11.1% (41) were positive for TPO Ab, 4.1% (15) were positive for TG Ab, 2.4% were positive for both, and 12.7% (47) were positive for either TPO Ab or TG Ab. There was no difference in the proportion of patients testing positive for either antibody with a singleton delivery versus no baby (13.0% vs. 12.6%, OR 1.03, $p=0.93$), nor in those with a singleton delivery versus a miscarriage (13.0% vs. 15.7%, OR 0.80, $p=0.62$). There was no difference in the proportion of patients with either antibody with a history of a prior pregnancy (12.2%) versus no prior pregnancies (14.4%, OR 1.21, $p=0.56$). There was no difference in age, gravity, parity, day 2 FSH, total gonadotropin dosage, or individual fertilization rates between the thyroid antibody positive and negative groups. The 42 patients with clinical hypothyroidism were excluded from this preliminary analysis and will be analyzed at a future time. Part 2: Data collection and statistical analysis are ongoing at the time of abstract submission.

Conclusions: While the incidence of thyroid autoimmunity in our euthyroid population is consistent with previous studies, the absence of an association of thyroid autoimmunity and pregnancy outcomes contradicts previous studies in younger patients. Ongoing research aims to determine the effect of thyroid autoimmunity on the thyroid response during an IVF cycle and early pregnancy by comparing those with and without thyroid autoimmunity to those with thyroid disease.

Notes:



Comparison of Pregnancy Outcomes in Elective Single (eSBT) versus Double-Blastocyst Transfer (2BT) Stratified by Age

Presented By: Christine M. Mullin, MD

Christine M. Mullin MD, M. Elizabeth Fino MD, Sheeva Talebian MD, Lewis C. Krey PhD, Frederick Licciardi MD, Jamie A. Grifo MD, PhD

Objective: To determine if there is a difference in pregnancy outcomes, stratified by maternal age, between women undergoing elective single blastocyst transfer (eSBT) versus those undergoing double-blastocyst transfer (2BT)

Design: Retrospective analysis

Setting: University IVF Center

Patients: 1141 non-donor IVF cycles in women <40 years of age from January 2004-March 2007.

Main Outcome Measure(s): Eggs retrieved, Embryos cryopreserved, Implantation Rates, Clinical Pregnancy Rates, Live Birth Rates, Spontaneous Abortion Rates

Results: Pregnancy outcomes in 52 cycles of women <40 years of age who underwent eSBT were compared to 1086 cycles of women who underwent 2BT in fresh IVF cycles from January 2004 to March 2007. Overall, the eSBT was associated with a statistically significant 92% reduction in the twinning rate (from 25% to 2%) while maintaining a high clinical pregnancy rate (63% in the eSBT group versus 61% in the 2BT group).

Conclusions: Women who are < forty years of age undergoing non-donor fresh IVF cycles can electively choose to transfer a single blastocyst for the purpose of significantly reducing their risk of multiples without compromising their pregnancy rate.

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Notes:



Time-Lapse Imaging of Murine Embryogenesis: Surprise Observation Providing Insight into Early Reproductive Processes

Presented By: Yael Kramer, MS

Nicole Noyes MD, M. Elizabeth Fino MD, Yael Kramer MS, Lewis Krey PhD, Caroline McCaffrey PhD, Kristin Gunsalus PhD

This video was presented at the annual meeting of the American Society of Reproductive Medicine October 20, 2009. It was awarded honorable mention for technical achievement in video: assisted reproductive technology. This work is supported by an RO1-NIH grant: Principal Investigators – Nicole Noyes MD and Kristin Gunsalus PhD

Objective: Time lapse microscopy allows in depth study of early embryologic processes. Scientific experimentation requires the use of healthy, disease free animals to achieve reproducible results. For the past 2 years, we have studied early mouse embryogenesis through repeated 4-day time-lapse capture from the zygote to the blastocyst stage of development.

Methodology: Time-lapse microscopy is achieved using a unique stage-top incubator capable of achieving culture conditions similar to those of standard laboratory CO₂ incubation systems. The stage-top incubator is affixed to a high-definition microscope and embryo image capture is performed using a quantitative, digital camera with accompanying computer software. Images are recorded and stored, then converted to video for subsequent analysis. Our experiments are performed weekly using young CB6F1 superovulated female mice that are mated 1:1 with stud males housed in the NYUSOM animal facility. Resultant zygotes are harvested, evaluated and then cultured in the stage-top incubator. Two months prior to making the video being shown, we noted consistent, aberrant microscopic findings in the retrieved zygotes that were associated with decreased embryo development and survival. Seven weeks later, we were provided a clue as to what may have contributed to the embryonic changes.

Conclusions: Our time-lapse videos show reproducible, highly specific early embryonic alterations. These data provide new and important insight into the understanding of early murine reproductive processes.

Notes:



Generation of Disease-specific Human Embryonic Stem Cells from Genetically Abnormal Embryos

Christopher Hansis, MD, PhD

Chris Hansis, Christine Rice, Jamie Grifo, Ruth Lehmann

Background: For many human diseases, a model system for studying their nature and exploring new treatment strategies is lacking. This is because there is no appropriate animal model and no primary cell culture from patients which can properly reflect the disease. To overcome this problem, specific disease models based on human embryonic stem (hES) cells can be generated from in vitro fertilized embryos diagnosed by preimplantation genetic diagnosis (PGD) to harbor genetic abnormalities. Single cells of the cleavage-stage embryo can be biopsied for this purpose. Over the past 15 years, PGD has been used to screen embryos for more than 300 diseases related to single gene defects (e.g., cystic fibrosis), abnormal numbers of chromosomes (e.g., Down syndrome), or chromosome structure defects (e.g., Robertsonian translocation).

Objectives: The goal of this IRB-approved study is to generate new disease models based on hES cells from genetically abnormal embryos. This will aid in enhancing the understanding of diseases as well as finding new therapeutic approaches such as by drug screening.

Materials and Methods: Zona-free human blastocysts previously assessed by PGD for genetic conditions were transferred onto feeder cells and cultured in DMEM-based media. Stem cell colonies were mechanically subcultured onto fresh feeder cells. Pieces of the colonies were frozen by liquid nitrogen vitrification with cryoprotectants propylene glycol, DMSO, and acetamide and subsequently thawed. Differentiation of hES cells was achieved by colony overgrowth or embryoid body formation. Embryonic and control cells were subjected to marker gene and protein analysis for pluripotency, differentiation and disease-specific mutations by reverse transcription PCR and immunofluorescence, respectively.

Results: Colonies could be established and maintained which showed the typical morphological features of hES cells such as compact colony formation. Colonies were derived from seven affected embryos (one each of cystic fibrosis, trisomy X, 18, 21, 22, Tay-Sachs disease, two each of alpha thalassemia X-linked mental retardation syndrome, unbalanced translocation long arm chromosomes 8, 15), from five embryos tested inconclusively (one each of cystic fibrosis and BRCA1, three of Tay-Sachs disease), and from three normal control embryos. Marker gene and protein expression as well as growth pattern analysis suggest that the colony cells harbor disease-specific mutations, retain their undifferentiated state in culture as well as after vitrification and thawing and that they can be differentiated into a variety of cell types, including the tissues most affected by the conditions.

Conclusions: These newly established protocols for the derivation, maintenance, and differentiation of novel disease-specific hES cells should enable the efficient generation of new disease models. This will provide new tools to study diseases as well as to develop new therapeutic approaches.

Notes:



Cytokine Profiling of the Maternal and Fetal Response to LPS *in vitro*

Presented by: Doris B. Tse, PhD

*Doris B. Tse*¹, *Xiao Li*¹, *Igor Eyzner*¹, *Alexander Ha*¹, *Bruce K. Young*²; ¹*Division of Infectious Disease and Immunology, Department of Medicine;*

²*Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, New York University School of Medicine, New York, NY*

Rationale: Cytokines and chemokines play a central role in mediating infection-related preterm parturition.

Objectives: The aim of this study is to investigate the effects of *in vitro* endotoxin exposure on the production of numerous cytokines and chemokines by maternal and neonatal blood leukocytes to correlate maternal and fetal biomarkers that may be descriptors of the fetal inflammatory response associated with infection-related preterm labor.

Methods: Paired maternal and fetal whole blood samples (N=7) were studied, with corresponding paternal blood samples, when available (N=2). One hundred microliters of heparinized whole blood were incubated in the absence or presence of *E. coli* lipopolysaccharide (LPS) at 6 different concentrations (10⁻¹, 100, 10¹, 10², 10³, 10⁴ ng/mL) at 37 °C with 5% CO₂ for 18-24 hrs. Afterwards, the samples were diluted with 400 µL RPMI and centrifuged. Supernatants were collected, stored at -85°C and subsequently assayed for proinflammatory cytokines, anti-inflammatory cytokines and chemokines, using multiplex analyte detection on a Luminex 200.

Measurements and Results: We could not detect changes in IFN- γ expression following LPS treatment at all concentrations. IL-1Ra (IL-1 Receptor antagonist), IL-8 and IL-12p40 levels increased by <10-fold with increasing concentrations of LPS, while G-CSF, IL-1 β , IL-6, IL-8, IL-10, MIP-1 α and TNF- α levels increased by 10- to 100-fold. A plateau was reached for IL-1 β , IL-6, IL-8, IL-10, IL-12p40, and TNF- α , at 10 ng/mL LPS. In contrast, both IL-1Ra and MIP-1 α levels reached a plateau at 1 ng/mL LPS. Maternal and fetal responses were significantly correlated. With the exception of IL-1Ra, IL-12p40, and TNF- α , fetal blood leukocytes produced significantly higher levels of cytokines and chemokines. Different levels of production between different maternal/paternal and fetal pairs were observed.

Conclusion: Cytokines and chemokines produced by maternal blood leukocytes can be useful indicators of the fetal inflammatory response to endotoxin for predicting the risk of preterm labor.

Notes:



Comparison Between Fetal 2D/3D Neurosonography and Magnetic Resonance Imaging Findings in a Selected Population: Do We Need Both?

Presented by: Christine L. Proudfit, MD

A Monteagudo†, M. del Río††, C Proudfit†, S Milla ‡, I Timor Tritsch†.

Department of Obstetrics and Gynecology†, Department of Radiology ‡ New York University. School of Medicine

Department of Ob/Gyn University of Barcelona, Spain††

Objective: To compare fetal neurosonography using both 2D/3D transabdominal and/or transvaginal sonography with magnetic resonance imaging (MRI) findings in fetuses with suspected brain anomalies.

Methods: 24 fetuses were included. 2D and 3D fetal neurosonography was performed transabdominally and transvaginally following the ISUOG Guidelines by experienced operators.

Cases where MRI proved to be more accurate (n=4)				
Referral indication	US finding	Wk	MRI finding	Wk
Bilateral VM	Suspected IVH	35.	Ruled out IVH	35
Bilateral VM	Suspected LH vs schizencephaly.	30.	Confirmed bilat. open lip schizencephaly.	30
Hydrocephaly	Suspected LH	21.	Ruled out LH	21
Absence CSP	LH vs SOP	21	Visualized OC	21
Cases where US and MRI were in agreement (n= 16)				
Suspected diagnosis				N
Normal evaluation				2
Isolated ventriculomegaly				5
Cerebellar or posterior fossa anomaly				5
IVH				1
Others (thrombus torcular herophili, occipital meningocele, schizencephaly				3
Cases where US proved to be more accurate (n=4)				
Referral indic.	US finding	Wk	MRI finding	Wk
Mild VM	2 cases of small QC, arachnoid cysts	22.6 19	No cysts seen	24 19
CPC	Large bilat.CPC	18.2	No cysts seen	19
High mat. AFP	Small lumbar NTD	19	No NTD seen	19

VM, ventriculomegaly; IVH intraventricular hemorrhage; LH, lobar holoprosencephaly; OC optic chiasm; CSP cavum septum pellucidum; SOP septo optic dysplasia; QC, quadrigeminal cistern; NTD neural tube defect.

Conclusions: In our small series fetal neurosonography using both 2D/3D transabdominal and transvaginal approaches provided equal results to MRI in the diagnosis of most, but not all fetal brain anomalies. MRI supplied important clinically useful information in selected cases of brain anomalies. Therefore, both diagnostic tools can and probably should be used to complement each other.

Notes:



Basic as well as Detailed Neurosonogram can be Performed by an Off-line Analysis of 3D Fetal Brain Volumes

Presented by: Eran Bornstein, MD

Eran Bornstein, Ana Montegudo, Rosalba Santos, Irina Strok, Tanya Tsymbal, Erez Lenchner, Ilan E Timor-Tritsch. Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, New York University School of Medicine, New York, NY, USA.

Objectives: To evaluate the feasibility and the processing time using off-line analysis of 3D brain volumes to perform basic as well as detailed, targeted, fetal neurosonogram

Methods: 3D fetal brain volumes were obtained in 103 consecutive healthy fetuses that underwent routine anatomical survey at 20 to 23 post menstrual weeks. Transabdominal gray scale and power Doppler volumes of the fetal brain were acquired by one of three experienced sonographers (average of 7 volumes per fetus). Acquisition was first attempted in the sagittal and coronal planes. When fetal position did not enable easy and rapid access to these planes, axial acquisition at the level of the biparietal diameter was performed. Off-line analysis of each volume was performed by two of the authors in blinded fashion. A systematic technique of "volume manipulation" was used to identify a list of 25 brain structures comprising a complete basic evaluation, intra-cranial biometry as well as detailed targeted fetal neurosonogram. The feasibility and reproducibility of obtaining diagnostic quality images of the different structures was evaluated and processing times recorded by the two examiners.

Results: Diagnostic quality visualization was feasible in all of the 25 structures with excellent visualization rate (85%-100%) reported in 18 structures, good visualization rate (69%-97%) in 5 structures, and low visualization rate (38%-54%) reported in 2 structures by the two examiners. Average of 4.3 and 5.4 volumes were used to complete the examination by the two examiners with a mean processing time of 7.2 and 8.8 minutes, respectively. The overall agreement rate for diagnostic visualization of the different brain structures between the two examiners was 89.9%, with a Kappa coefficient of 0.5 ($p < 0.001$).

Conclusions: In experienced hands, off-line analysis of 3D brain volumes is a reproducible modality that can identify all of the structures necessary to complete both basic and detailed second trimester fetal neurosonogram.

Basic CNS Examination Structures	Visualization by 1st / 2nd examiner (%)	Detailed Fetal Neurosonogram Structures	Visualization by 1st / 2nd examiner (%)
Biparietal diameter	100% / 98%	Corpus callosum	99% / 93%
Occipito-frontal diameter	100% / 98%	Quadrigeminal plate	100% / 88%
Head circumference	100% / 98%	Quadrigeminal cistern *	99% / 88%
Cerebellum	98% / 93%	Cisterna ambiens *	97% / 80%
Cisterna magna	96% / 94%	Vermis (sagittal view) *	96% / 79%
Nuchal fold	53% / 38%	Tela choroidea *	99% / 92%
Choroid plexuses	100% / 99%	Site of torcular *	78% / 69%
Lateral ventricles	99% / 98%	4th ventricle	84% / 77%
Cavum septi pellucidi	99% / 96%	Anterior horn	96% / 89%
Thalami	100% / 98%	Posterior horn	99% / 91%
Falx	100% / 100%	Evaluate 3rd ventricle	99% / 85%
		Vein of Galen *	42% / 54%
		Pericallosal artery *	96% / 94%
		Orbits	76% / 77%

*Accepted for publication: Ultrasound Obstet Gynecol
Oral presentation at the 2009 AIUM Annual Convention, New York.*

Notes:



Conservative Management of Cervical Scar Pregnancies with Serial 3D Power Doppler Assay of Vascularization after Transvaginal US Guided Injection of MTX

Presented by: Elizabeth Rodgers, MD

Timor-Tritsch IE, Monteagudo A, Del Rio M, Rodgers E

Division of Ob/Gyn Ultrasound. Department of Ob/Gyn, New York School of Medicine, NY

Introduction: One in 3 deliveries in the USA & other countries is by cesarean section (CS). A subsequent pregnancy implanting in the CS scar niche may present significant risk in the form of pathologically adherent placenta and/or C/S scar pregnancy (CSP). We offer a semi-invasive management & follow-up of such ectopic pregnancies.

Material: 8 cases of CSPs were injected by methotrexate (MTX) by transvaginal ultrasound directed needle puncture. The message of this abstract is the follow up by serial surveillance of: 1. chorionic sac vascularization by 3D power Doppler angiography defined using the quantitative Vascularity Index (VI), 2. using its volume, and 3. β hCG. Ages ranged between 6-13 wks. Initial β hCG levels were between 101,000 - 7,600 IU. Initial sac volumes were between 119 - 5. None of the cases required surgical interventions. Follow up of four cases ranged from 63-154 days.

Results: Three observations were clear: 1. After injection, before the decrease, there is an initial increase in the volume of the sac. 2. The same is true for the VI, 3. There is poor correlation between vascularity and the declining β hCG.

Conclusion: Local and subsequent parenteral injection of MTX with follow up of the vascularization of the chorionic sac is a reasonable approach for the increasing number of 1st trimester CSPs. Following volume, vascularity & β hCG. seems to be important in the management.

Notes:



Role of Urodynamic Testing in Patient Care at Bellevue Hospital

Presented by: Arash Rahi, MD

Arash Rahi, MD; Robert Porges, MD; Scott Smilen, MD

Introduction: Urodynamic testing has been used frequently in managing women with urinary incontinence but its impact on treatment recommendations has not been shown.

Aims: 1. To show whether urodynamic findings correlate with patients' complaints of urinary symptoms.
2. Evaluate the prevalence of different types of urodynamic diagnoses among the patients undergoing urodynamic testing at the urogynecology clinic within Bellevue Hospital.

Methods: A retrospective chart review will be performed on all women undergoing urodynamic testing at the mentioned facility between July 2004 and August 2009. The review included urodynamic tracings, patients' clinic notes and the clinic log. For this preliminary presentation 30 charts are selected at random and reviewed and the correlation between the patient's history and the findings on urodynamic testing is evaluated.

Results: 89% of patients with complaints of stress urinary incontinence without any urge incontinence were found to have genuine stress incontinence on urodynamic testing. Only 38% of those with chief complaint of urge incontinence had evidence of detrusor overactivity or incontinence.

Discussion: In patients with a history indicating stress urinary incontinence urodynamic testing may not be necessary to offer treatment options. A larger scale study is warranted to further demonstrate potential utility of urodynamic testing and also to better evaluate the prevalence of urinary symptoms in this population.

Notes:



Membrane-Actin Cytoskeleton Linking Protein Expression by Human Post-Operative Adhesions and Fibroblasts

Presented by: Kui Huang, PhD

Kui Huang, PhD1, Ghassan M Saed, PhD2, Jonathan Crispino1, Joon Song, MD, PhD1, Seung Do Choi, MD1, Michael Diamond, MD2 and Frederick Naftolin, MD, PhD1. 1Obstetrics and Gynecology, New York University, New York, NY, United States, 10016 and 2Obstetrics and Gynecology, Wayne State University, Detroit, MI, United States.

Rationale: Although they are major complications, the basis of adhesions is poorly understood. The present methods of prevention/treatment are physical barriers and careful technique. We studied the possible role of membrane-cytoskeleton linker proteins (MERM; moesin, ezrin, radixin, Merlin) in post-operative adhesions.

Experimental: Immunohistochemistry was used to examine expression of immunoreactive estrogen receptors (ERa & ERb) and MERM in adhesions from surgical patients and in cultured adhesion fibroblasts. The effect of estradiol (10-8M) and/or tamoxifen(10-6M) was tested by 24h culturing with fibroblasts from adhesions and from retroperitoneal fibroblasts from the same patients.

Results: All four MERM were expressed in adhesion and non-adhesion fibroblasts, and, in surgically removed adhesion tissues. There were strong differences in expression (ezrin>>>moesin>>radixin and Merlin). Estradiol induced shape changes (ruffles, stellate shape and processes) and proliferation in cultured fibroblasts; but there was not an increase in immunoreactive ezrin. Tamoxifen induced more ezrin and less shape changes. Combining estradiol with tamoxifen reduced the overall estrogen effect.

Conclusions: The presence of ER and MERM in established adhesions supports the activity of this signaling pathway and cellular response in adhesions. The expression of MERM in fibroblasts involved in adhesion formation indicates a fundamental role for these molecules, especially ezrin and moesin, in the biology of wounding and response that results in adhesions. This implies that ER-active molecules may play a role in adhesion formation. Therefore, strategies based on ER-MERM interactions may be developed to inhibit adhesion formation.

Reference: Song J, Fadiel A, Edusa V, Chen Z, So J, Sakamoto H, Fishman DA, Naftolin F. Estradiol-induced ezrin overexpression in ovarian cancer: a new signaling domain for estrogen. *Cancer Letters* 220:57-65, 2005.

Notes:



Expression of Ezrin and Estrogen Receptors by Human Cervical Cancer

Presented by: Seung Do Choi, MD

Seung Do Choi, MD1,2, Kui Huang, PhD1, Emma Steinberg, BA1, Dong Han Bae, MD2 and Frederick Naftolin, MD, PhD1. 1O/G, New York University, New York, NY, United States, 10016 and 2O/G, Soonchunhyang University, Cheonan, Chung-Nam, Korea.

Rationale: Ezrin is an estrogen-sensitive actin cytoskeleton-membrane protein that is present in cervical epithelium and cancer. Estrogen receptors (ER) are present in normal cervical epithelium but diminished in invasive cervical cancer. In this study the expression of both types of molecule was examined in progressively more disordered cervical lesions.

Experimental: Individual histological sections from each of ten patients with one of the following progressively increasing cytologically classified cervical lesions (normal, CIN I-III, invasive epithelial cancer) were studied by immunocytochemistry for ERa, ERb or ezrin. H testing was applied for semi-quantitative evaluation of the expression of each protein at the transition zone.

Results: All three proteins were expressed. The H score increased progressively until in situ cancer was present. Expression of immunoreactive ER and ezrin was less in invasive cancer than in CIN I-III. ($p < 0.05$)

Conclusions: Ezrin is an estrogen receptor-regulated protein. Since the progression of malignant transformation paralleled the changes in ER and ezrin until in situ disease was reached, but not in invasive lesions, it may be that ER-response and ezrin are involved in malignant transformation but not in the invasive phenotype of cervical cancer.

Reference: Song J, Fadiel A, Edusa V, Chen Z, So J, Sakamoto H, Fishman DA, Naftolin F. Estradiol-induced ezrin overexpression in ovarian cancer: a new signaling domain for estrogen. *Cancer Letters* 220:57-65, 2005.

Notes:



Prediction of Preterm Birth in Asymptomatic Twin Pregnancies: Fetal Fibronectin, Cervical Length, and the Change in Cervical Length Over Time

Presented by: Nathan S. Fox, MD

Fox NS, Saltzman DS, Klauser CK, Peress D, Gutierrez, CV, Rebarber A.

Objective: To evaluate combined fetal fibronectin (fFN) and cervical length (CL), and the change in cervical length over time, as predictors of spontaneous preterm birth in asymptomatic twin pregnancies.

Methods: Historical cohort of 155 twin pregnancies with routine fFN and CL testing performed in one maternal-fetal medicine practice from 2005-2008.

Results: A positive fFN between 22-32 weeks or a CL <20mm increased the risk of spontaneous preterm birth <37 weeks, <34 weeks, <32 weeks, <30 weeks, and <28 weeks. The combination of a positive FFN and CL<20mm had a significantly higher positive predictive value for delivery at all gestational ages than either positive test alone. Patients whose CL shortened 20% or more over consecutive CL measurements at least 2 weeks apart starting at 18-24 weeks had a significantly higher rate of spontaneous preterm birth <28 weeks, <30 weeks, <32 weeks, and <34 weeks. This remained true even when excluding patients with a short CL (≤ 25 mm) on the repeat CL.

Conclusions: In asymptomatic twin pregnancies, fFN and CL testing as well as the change in CL over time can identify pregnancies at significantly increased risk for preterm birth including deliveries earlier than 28 weeks gestation.

Notes:



Anti-Factor Xa Plasma Levels in Pregnant Women Receiving Low Molecular Weight Heparin Thromboprophylaxis

Presented by: Nathan S. Fox, MD

Fox NS, Laughon SK, Bender SD, Saltzman DS, Rebarber A.

Objective: To report the incidence of prophylactic, subprophylactic, and supraprophylactic anti-factor Xa activity in pregnant patients receiving low molecular weight heparin for venous thromboembolism prophylaxis, and to evaluate whether maternal weight, body mass index, age, gestational age, or the low molecular weight heparin dose correlated with anti-factor Xa levels.

Methods: We reviewed 321 anti-factor Xa levels in 77 patients from one Maternal-Fetal Medicine faculty practice. All patients were administered low molecular weight heparin that subsequently was adjusted based upon serial assessment of peak plasma (at 4 hours postinjection) anti-factor Xa levels at less than 36 weeks gestation. Targeted prophylactic range of peak plasma anti-factor Xa level was 0.2-0.4 units/mL.

Results: Only 59% of anti-Xa concentrations were in the prophylactic range, whereas 26% were subprophylactic, and 15% were supraprophylactic. Anti-Xa values were not significantly more likely to be prophylactic in early compared with late pregnancy, obese compared with nonobese patients, or in patients receiving a weight-based minimal dose compared with patients receiving less than a weight-based minimal dose. Anti-factor Xa levels did not correlate with maternal age, weight, body mass index, or gestational age, but there was a positive correlation with the percent of the minimal weight-based dose.

Conclusion: Even with enhanced low molecular weight heparin dosing, 26% of patients have subprophylactic anti-factor Xa levels. Serial anti-factor Xa assessment for dose adjustment should be considered for all pregnant women receiving low molecular weight heparin.

Obstet Gynecol 2008;112:884-9

Notes:



Brain Development in Fetuses with Congenital Heart Disease

Presented by: Ashwin R. Jadhav, MD, MS

Maria Del Rio, MD, Ashwin R. Jadhav, MD, MS, Christina Proudfit, MD, Ana Monteagudo, MD, Ilan E. Timor-Tritsch, MD

Introduction: Congenital Heart Disease is a well known cause of childhood morbidity. However, several studies have shown that many children with CHD survive with fine motor, visuospatial, behavioral, social, and academic problems that impair their progress in school. Changes to in utero cerebral blood flow patterns and proportion of oxygenated blood in cerebral circulation causing chronic hypoxia could be one of the pathophysiological mechanisms behind the neurodevelopmental outcomes. To date, no study has determined the fetal neurodevelopmental status in fetuses with CHD and none has studied the relationship between fetal and pre-operative neonatal neuroimaging findings.

Hypothesis: During fetal life CHD may be associated with changes in cerebrovascular blood flow distribution and blood flow resistance compared to normal fetuses. Thereby, fetuses with CHD are at increased risk of both gray and white matter injury and these preoperative fetal central nervous system lesions are related to neonatal neurodevelopmental outcome impairment.

Methods: This is a prospective case-control collaborative study between Division of MFM and Department of Pediatric cardiology. Cases are from pregnant women referred with diagnosis of fetuses with CHD and controls will be equally matched pregnant women with fetuses with normal cardiac anatomy. The study variables include, evaluation for presence of structural brain lesions by two dimensional (2D) and three dimensional (3D) ultrasound imaging by study of brain volume evaluated by 3D imaging and Virtual Organ Computer-aided Analysis (VOCAL) and also Doppler ultrasound parameters of fetal brain circulation measured in cerebral arteries at the level of circle of Willis (Anterior, Middle, Posterior), vein of Galen and Transverse sinus. The cardiac and extracardiac measurements include evaluation of Doppler velocity waveform across all cardiac valves, aortic isthmus and Pulmonary veins and Ductus venosus by advanced fetal echocardiography following the International Society of Ultrasound in Obstetrics and Gynecology Guidelines 2008. At this time there are 7 cases enrolled in the study. The analysis of the cases will be presented.

Conclusion: Our ongoing study aims to determine fetal neurodevelopmental status in fetuses with CHD. In light of the evidence provided by recent studies, it seems that brain ultrasound and brain MRI studies in the fetus with CHD may provide objective and early information on brain injuries such as global hypoxia-ischemia, white matter injury and structural lesions. This information might greatly contribute to our understanding of cerebral injury and may help to stratify patients into risk categories even before surgery.

Notes:



A Multicenter, Open-Label Study on the Efficacy, Cycle Control and Safety of a Novel Contraceptive Vaginal Ring (CVR)

Presented by: Livia Wan, MD

*Sponsored By: NICHD/NIH Contraceptive Clinical Trial Network (CCTN) & Population Council
Principal Investigator: Livia S. Wan, MD; Sub-Investigators: Machelles Allen, MD, Miriam Cremer, MD, Maria Gloria Mulima, RN; Study Coordinator: Anna Davis, BS*

Objective:

- The effectiveness of the new one year Contraceptive Vaginal Ring (CVR).
- The side-effects and acceptance of the new CVR

Study Sites:

12 Centers in United States and 8 Centers around the world.

Subjects:

- Age: 18-39 healthy sexually active women with normal menstrual pattern who desired contraception
- BMI: <29 (changed from <33 to <29 in the middle of the study).
- No contraindication for hormonal contraceptives

Product Studied:

One year Contraceptive Vaginal Ring containing Nesterone(NES) 150ug/Ethinyl Estrodiol(EE) 15ug

Protocol:

- CVR was inserted day 1-5 of the first menstrual cycle and stay in vagina for 21 days.
- CVR stayed out for 7 days and then was reinserted for another 21 days.
- The 21 days in and 7 days out schedule were kept for 13 cycles (12 months).
- Subjects were followed at enrollment, cycles 3, 6, 9, 13 and one month after Ring removal.

Results:

- A total of 159 subjects were screened and 92 were enrolled.
- 32 completed the study; 56 were early termination for various reasons.
- 4 subjects became pregnant during the study.
- No serious side effect except one subject had persistent bleeding which required surgery.
- One subject dropped out due to repeated Ring expulsion.

Conclusions:

- One year CVR is an effective contraceptive method with minimal side effect
- It is convenient, less expensive method than the one month Ring available now on US market.

Future Studies:

To use the Ring continuously for three month and remove for 5-7 days for endometrium shedding.

Notes:



The Relationship Between Labrum Tears of the Hip and Generalized Unprovoked Vulvodynia

Presented by: Deborah Coady, MD

Deborah Coady, M.D., New York University- Langone Medical Center; Stacey Futterman, M.P.T., BCIA-PMDB, Beyond Basics Physical Therapy; Dena Harris, M.D., New York-Langone Medical Center; Meeta Shah, B.A.; and Struan Coleman, M.D., Hospital for Special Surgery, New York, New York, USA

Introduction: The objective of this study is to investigate the relationship between labrum tears of the hip and generalized unprovoked vulvodynia.

Study Design: In this ongoing prospective observational study, women with unprovoked vulvodynia, referred to a private vulvology practice between 2005 and 2009, were assessed for concurrent hip pain or mechanical hip symptoms, in addition to pelvic floor abnormalities. Those women with hip complaints, findings, or suggestive history were evaluated with high spatial resolution magnetic resonance imaging (MRI) of the hip cartilage and labrum (using 2.5 mm slice sagittals and in-plane resolution of 350 microns), as well as dedicated pelvic floor high spatial resolution studies. Women found to have labrum tears, cartilage splits, synovitis, intralabral ossifications, soft tissue ganglion cysts, iliopsoas tendonosis, or other findings associated with inflammation of pincer forms of hip impingement, were identified. Orthopedic evaluations were performed and women were advised of available treatment options of physical therapy, differential joint injections under fluoroscopic or ultrasound guidance, and/or arthroscopic repair. Outcomes were assessed by type of hip MRI findings and, if applicable, surgical findings, and focused on vulvodynia pain measures, and improvements in pelvic floor muscle abnormalities and symptoms. Benefits to associated bowel and bladder symptoms were also assessed.

Results: As of the time of the preparation of this poster presentation, 40 of 41 women with unprovoked vulvodynia and suspected hip pathology were found to have anterior labrum tears on MRI. All had previously undergone numerous treatments for vulvodynia over an average of 4 years without adequate relief. The average age was 40 years with an age range of 26 to 74 years. 50% had right-sided hip abnormalities and 50% had pain worse on one side. 28% had concomitant vestibulodynia and 10% clitorodynia. 13/33 (39%) have improved with hip focused physical therapy. 9 so far have undergone surgical repair, with 7 resulting in moderate to marked improvement in vulvar pain as well as their hip pain. 8 are currently planning surgical repair.

Conclusion: This prospective observational study is ongoing. Preliminary results suggest that, in a subset of women with chronic vulvar pain of unknown cause, previously unrecognized hip labrum tears may be an etiologic trigger for their vulvar pain. Assessment for hip disorders is thus an important component of all vulvodynia evaluations. The pathophysiology that may be responsible include several possible mechanisms. Hip capsule restriction and impingement may result in an increase in surrounding muscle protective tension, and thus cause neural restriction along the course of or at the branches of the ipsilateral and/or contralateral pudendal nerve, referring pain to the vulva. Chronic low grade hip discomfort may provoke postural compensations and gait changes that put stretch or torsion on the hip rotators such as the obturator internus and thus the pudendal nerve. An inflammatory reaction in the injured hip joint may spread to the pelvic floor, and cause secondary inflammation of the ipsilateral pudendal nerve, again referring pain to the vulva. This study will continue, and will follow these women and others newly diagnosed with labrum tears, in order to further clarify which women need MRI imaging, as well as hip interventions and clinical outcomes, in this under-appreciated condition associated with vulvodynia.

Abstract Presentation at the International Society for the Study of Vulvovaginal Disease World Congress, Edinburgh, Scotland, September 2009

Poster Presentation at the International Pelvic Pain Society Annual Meeting, Phoenix, Arizona, October 2009

Notes:



When Abnormal Uterine Bleeding is the Main Complaint in Pre-menopausal Women Diagnosed with Endometrial Polyps, is Surgical Polypectomy an Effective Treatment?

Presented by: Autumn Edenfield, MD

Lydia Garcia, M.D., Autumn Edenfield, M.D., Molly Cason, B.A., Amisha Shah, B.A., Kate Raisler, B.A. Erin Fitzgerald, B.A., Elizabeth Maxwell, B.A. and Ming C. Tsai, M.D.

Objective: To evaluate the effect of hysteroscopic polypectomy on the symptoms of abnormal uterine bleeding in patients diagnosed with endometrial polyps.

Methods: Endometrial polyps were diagnosed via saline infusion sonogram in 54 pre-menopausal women (age 22-56 years) presenting with abnormal uterine bleeding who subsequently underwent hysteroscopic polypectomy between year 2007-2008. Patient survey and retrospective analysis was performed in these 54 consecutive cases of endometrial polyps treated with hysteroscopic polypectomy at Bellevue Hospital, Department of Obstetrics & Gynecology.

Results: Of the 95 consecutive cases analyzed during this period, 54 patients were eligible for this study. The survey form was completed and returned in 33 patients (61%). In 21 patients (38%) the survey was not completed due to change of address or incorrect contact information. For those patients who participated in the survey, 27.2%, 24.4% and 48.5% presented with pre-operative complaint of metrorrhagia, metromenorrhagia and menorrhagia, respectively. Of the surveyed patients, 75.8% reported significant improvement of their bleeding symptoms and in 87% of these patients, the result can be observed immediately after the surgical procedure. In the remaining 24.2% of patients surveyed, surgical polypectomy was ineffective to reverse the bleeding symptoms. Interestingly, 75% of them were found to have underlying systemic diseases or uterine anatomic pathology in addition to the endometrial polyp, possibly accounting for their persistent bleeding.

Conclusion: In the absence of other uterine anatomic lesion, surgical polypectomy appears to be an effective treatment of the abnormal uterine bleeding in pre-menopausal women diagnosed with an endometrial polyp. Further studies with larger number of patients are needed to confirm our result.

Oral presentation at American Association of Gynecologic Laparoscopists 38th Global Congress of Minimally Invasive Gynecology, November 2009

Notes:



Increased Endometrial Thickness at Baseline is Associated with Decreased Success in IVF

Presented by: Rachel Weinerman, MD

*R. Weinerman¹, S. Missmer², T. Ceyhan², E. Yanushpolsky², K. Jackson², C. Racowsky²
1New York University Medical Center, New York, NY. 2Brigham and Women's Hospital, Boston, MA.*

Objective: To test the hypothesis that increased endometrial thickness at baseline compromises clinical IVF success rates.

Design: Retrospective cohort study of fresh cycles of IVF or ICSI with day 3 embryo transfer.

Methods: All fresh non-donor IVF and ICSI cycles using a down-regulated protocol with day 3 embryo transfer performed at our institution in 2005 and 2006 were reviewed for inclusion. Patients who had a transvaginal ultrasound performed at baseline and who did not have uterine factor infertility or uterine anomalies were included in the study (n=1443). Each patient had only one cycle included in the final dataset (n=1098 cycles). Patients were started on oral contraceptive pills and/or a GnRH agonist for down-regulation. Baseline endometrial thickness (mm) was measured by transvaginal ultrasound after completion of down-regulation. If patients were adequately suppressed (estrogen level < 30 pg/mL), patients were started on rFSH, hMG, or both. hCG was given when ≥ 2 follicles had a mean diameter ≥ 18 mm. Endometrial thickness was measured again on the day of hCG administration. Oocyte retrieval and insemination via IVF or ICSI was performed, with assisted hatching performed on selected embryos. Embryo transfer was performed on day 3. Multivariable logistic and linear regression analyses were performed to assess the association of endometrial thickness at baseline or at hCG administration with implantation rate, early loss rate, and live birth rate. Wald p-values are two-sided.

Results: Mean patient age was 35.6 and mean attempt number was 1.5. Mean endometrial thickness at baseline was 5 mm (SD 2.3, range 0.6-16.8 mm). Mean endometrial thickness on the day of hCG administration was 11.5 mm (SD 2.6, range 1.1-21.9 mm). Baseline endometrial thickness was inversely associated with both implantation and live birth rates; for every millimeter increase in baseline endometrial thickness, the implantation rate decreased by 1.1% (p=0.02) and the live birth rate decreased by 6% (p=0.03). However, baseline endometrial thickness was not associated with early loss rate. Of note, endometrial thickness on the day of hCG administration was not associated with any of the evaluated IVF outcomes.

Conclusions: The present data support the hypothesis that increased baseline endometrial thickness is negatively associated with IVF outcome. However, the results failed to show an association between endometrial thickness on the day of hCG and clinical IVF success rates.

Poster Presentation at the American Society for Reproductive Medicine Annual Meeting, San Francisco, CA, November 2008

Notes:



Is Obesity a Risk Factor for the Development of Pre-malignant or Malignant Lesions in Endometrial Polyps?

Presented by: Lydia Garcia, MD

1Lydia Garcia, M.D., 1Akiva P. Novetsky, M.D., 1Meghana Gowda, M.D., 1Elizabeth Maxwell, B.A., 2Khusbbakhat Mittal, M.D., and 1Ming C. Tsai, M.D.; 1Department of Obstetrics and Gynecology, 2Department of Pathology, New York University School of Medicine, New York, New York, USA.

Study Objective: To evaluate for an association between body mass index (BMI) and development of pre-malignant or malignant lesions in endometrial polyps. Design: Retrospective chart review of all endometrial polyps in one institution diagnosed either on routine hysteroscopic polypectomy or hysterectomy.

Setting: University-based tertiary teaching hospital, Department of Obstetrics & Gynecology and Department of Pathology.

Patients: Two hundred fifty seven charts were reviewed. Of those, 181 women underwent hysteroscopic polypectomy and 76 women who had endometrial polyp diagnosed on their hysterectomy specimen.

Intervention: Hysteroscopic polypectomy, dilation and curettage, or hysterectomy. Measurements and Main Results: Benign pathology, endometrial hyperplasia without atypia, atypical endometrial hyperplasia and endometrial cancer were found in endometrial polyp specimens in 218 (84.8%), 11 (4.3%), 12 (4.7%) and 16 (6.2%) patients, respectively. The total combined percentage of pre-malignant (atypical hyperplasia) and malignant polyps was 10.9%. There were 105/257 (40.8%) patients with a BMI >30 and 124/257 (48.3%) of them were post-menopausal. Multi-variate logistic regression demonstrated that menopausal status is associated with an increased risk of developing pre-malignant or malignant lesions in endometrial polyps [OR: 4.57 (95% C.I.: 1.78, 11.68)] while BMI >30 was not associated with a similarly increased risk. [OR: 1.69 (95% C.I.: 0.75, 3.83)].

Conclusion: Patient menopausal status, but not the BMI, is associated with an increased risk of pre-malignant and malignant lesions in endometrial polyps. Due to its relatively high incidence and current lack of a reliable predictor or screening test for pre-malignant and malignant polyps, universal polypectomy for tissue diagnosis should be considered especially in post-menopausal women.

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