



# **The American College of Obstetricians and Gynecologists**

## **Papers on Current Clinical and Basic Investigation**

**Monday, May 4, 2009  
Chicago, IL**

# Contents

## *Papers on Current Clinical and Basic Investigation*

*Monday, May 4, 2009*

**2:00pm – 2:10pm**

**Simultaneous Administration of Mifepristone and Misoprotol for Early Medical Abortion**

*Melissa A. Strafford, Julie Mottl-Santiago, Olivera Vragovic, Lynn Borgatta*

**2:10pm – 2:20pm**

**Evaluation of an Instructional Video on the Repair of 4th Degree Lacerations: A Randomized**

**Trial** *Tamara T. Chao, George D. Wendel Jr, Shayzreen M. Roshanravan, Donald D. McIntire,*

*Marlene M. Corton*

**2:20pm – 2:30pm**

**Adhesion Formation and Morbidity after Repeated Cesarean Deliveries**

*Togas Tulandi, Mohammed Agdi, Afsoon Zare, Louise Miner, Vanja Sikirica*

**2:30pm – 2:40pm**

**Reduced Impact of Heavy Menstrual Bleeding on Physical and Social Activities of Women Using XP12B-MR**

*Andrea Lukes, Bryan Hecht, Scott Eder, George Attia, Gary Shangold, Keith Moore*

**2:40pm – 2:50pm**

**Longitudinal Validation of the Premenstrual Symptoms Impact Survey (PMSIS)**

*Aaron S. Yarlas, Min Yang, Geoffrey C. Hammond, Richard Lynen, Joseph Gricar*

**2:50pm – 3:00pm**

**Efficacy and Responder Analyses of Divigel® (Estradiol Gel) 0.1% for the Treatment of Menopause**

*William Koltun, Richard E. Hedrick, Michelle Zachman*

**3:00pm – 3:10pm**

**Transvaginal Ultrasonography to Predict Preterm Birth in Women with Uterine Anomalies**

*Joan MG Crane, Heather Scott, Wendy Whittle, Sujata Chandra, Donna Hutchens*

**3:10pm – 3:20pm**

**A Comparison of Estimated and Calculated Blood Loss in Postpartum Hemorrhage**

*Anjali Rozario, Dena Goffman, Hye Heo, Cynthia Chazotte, Robert C. Madden, Peter S. Bernstein*

**3:20pm – 3:30pm**

**Effect of Mode of Delivery on Infant Mortality in Late-preterm and Term Infants**

*Erol Amon, Nicholas Ruthmann, Daniel M. Rubalcava, Terry Leet*

**3:30pm – 3:40pm**

**Gestational Sac Size, Yolk Sac Size and Fetal Cardiac Activity are Related to Miscarriage Risk**

*Soyoung Bae, Joseph V. Karnitis*

**3:40pm – 3:50pm**

**The Genetics of Premature Rupture of Membranes and Preterm Delivery**

*Heather Byers, JC Murray, Cesar Saleme, Keegan Kelsey, Viviana Consentino*

**3:50pm – 4:00pm**

**Regression of Cervical Lesions Is Associated with CD8 T-Cell Responses to HPV 16 E6 but not**

**E7**

*William W. Greenfield, Sushil Gupta, Hannah Coleman, Matthew Sellers, Joseph Banken, Mayumi Nakagawa*

## **Simultaneous Administration of Mifepristone and Misoprotol for Early Medical Abortion**

*Melissa A. Strafford, MD*

Boston Medical Center, Boston, Massachusetts

*Julie Mottl-Santiago, CNM, MPH, Olivera Vragovic, MBA, Lynn Borgatta, MD, MPH*

**OBJECTIVE:** Medical abortion is typically performed using a combination of mifepristone and misoprostol. While earlier studies showed that simultaneous administration is effective, outcome data are limited.

**METHODS:** We conducted a retrospective review of women undergoing medical abortion with mifepristone and misoprostol from 2005-2007. If a woman had more than one medical abortion, only the first was considered. Non-viable pregnancies were excluded.

**RESULTS:** There were 1223 medical abortions; 550 women had simultaneous administration (Group 1) and 673 women had misoprostol 24 hours after mifepristone (Group 2). The groups had similar demographic and obstetrical histories. Forty-three (7.8%, 95% confidence interval [CI] 5.6 - 10.6%) women in group 1 required intervention (uterine aspiration) compared to 29 (4.3%, 95% CI 2.8 - 5.8%) in Group 2. For Groups 1 and 2, intervention was done for request in 2 (0.4%, 95% CI 0.1-0.9%) and 10 (1.5%, 95% CI 0.6-2.4 %) women, respectively. Intervention for bleeding/incomplete abortion was done for 39 (7.1%, 95% CI 5.0-9.2%) women in Group 1 and 16 (2.4%, 95% CI 1.8-3.0%) in Group 2. There were 3 interventions for continuing pregnancies and 2 for other reasons. Twenty-nine (5.3%) women in Group 1 and 45 (6.7%) in Group 2 received additional misoprostol, resulting in completed medical abortion. Nine women in each group received additional misoprostol, but subsequently had uterine aspiration. Loss to follow up for Groups 1 and 2 was 15.4% and 12.0%, respectively.

**CONCLUSION:** Simultaneous administration of mifepristone and misoprostol is associated with increased rates of uterine aspiration, primarily for bleeding and incomplete abortion.

## Evaluation of an Instructional Video on the Repair of 4th Degree Lacerations: A Randomized Trial

*Tamara T. Chao, MD*

University of Texas Southwestern Medical Center at Dallas, Dallas, Texas

*George D. Wendel Jr, MD, Shayzreen M. Roshanravan, MD, Donald D. McIntire, PhD, Marlene M. Corton, MD*

**OBJECTIVE:** To assess the effectiveness of an instructional video on anatomy and repair of fourth-degree obstetrical lacerations for OB/GYN residents.

**METHODS:** In this randomized trial, 71 of 72 UT Southwestern residents were given an 18-question multiple choice test and 14-item survey regarding fourth-degree lacerations to assess baseline knowledge and perceptions in July 2007. Test question categories included anatomy, antibiotics, anesthesia, repair methods, complications, post-operative care, and risk factors. In June 2008, residents who completed the test and survey were randomized into DVD (presented at 2008 ACOG ACM) and non-DVD (control) groups. The same tests were given three weeks later.

**RESULTS:** Of 71 participants, 67 (94%) were randomized into DVD (n=34) and non-DVD (n=33) groups. All but one resident completed the post-test and survey. In the DVD group, mean scores on the pre-test vs post-test by class were: 65% vs 74% for PGY-1 (p=0.09), 72% vs 83% for PGY-2 (p=0.06), 67% vs 83% for PGY-3 (p=0.01), and 75% vs 87% for PGY-4 (p=0.0006). In the non-DVD group, mean scores did not change significantly for any class level. The increase in score from pre-test to post-test is significantly different between assignment groups, independent of class (p=0.0006). The DVD group improved significantly compared to the control group in anatomy (p=0.005) and repair methods (p=0.042) subscales. Test results were analyzed using repeated measures ANOVA.

**CONCLUSION:** Our newly developed video is an effective teaching tool in improving resident understanding of fourth degree lacerations. Further studies are needed to elucidate if this translates into improved surgical competency.

## Adhesion Formation and Morbidity after Repeated Cesarean Deliveries

*Togas Tulandi, MD, MHCM*  
McGill University, Montreal, Quebec

*Mohammed Agdi, MD, Afsoon Zare, MD, Louise Miner, MD, Vanja Sikirica, PharmD*

**OBJECTIVE:** To evaluate development and outcomes of intra-abdominal adhesions after repeated cesarean deliveries (CS).

**METHODS:** We examined the records of 1,486 women who had undergone CSs (1st: CS: 203, 2nd: 955, 3rd: 255, or 4th+: 73 patients) at the Sir Mortimer B. Davis, Jewish General Hospital, a McGill University teaching hospital. Primary outcome measures were incidence and extent of adhesions (scored 0-2 per site as none, filmy or dense), incision-delivery interval, and operating time. The secondary outcome measures were intra- and post-operative complications, and Apgar score.

**RESULTS:** No patient used adhesion reducing substance. Women with 1st CS were devoid of adhesions. Compared to those with 2nd CS (24.4%), significantly more women developed adhesions after 3 CSs (42.8%, 95% CI: 0.84-0.99), and  $\geq 4$  CSs (47.9%, CI: 0.91-0.98). Adhesion scores after 2, 3, and  $\geq 4$  CSs were  $1.8 \pm 0.1$ ,  $2.1 \pm 0.1$ , and  $1.9 \pm 0.1$ , respectively. The sites of adhesions were predominantly between the uterus and abdominal wall (range: 41.7-54.5%) or the bladder (range: 25.9-36.4%). Compared to 1st CS ( $7.7 \pm 0.3$  min), the delivery time was significantly longer at subsequent CSs (2nd:  $9.4 \pm 0.1$ , CI 1-2, 3rd:  $10.6 \pm 0.3$ , CI 2-4;  $\geq 4$  CSs:  $10.4 \pm 0.1$  min., CI 1-2). The operating time became significantly longer after 2 CSs ( $P < 0.001$ , 3rd CI 4-9, 4th CI 3-12). Despite these, 5-minute Apgar scores for all newborns were similar (8.9-9.0). Rates of hysterectomy, post-partum hemorrhage (PPH), and wound dehiscence were similar among all groups of women.

**CONCLUSIONS:** Increased adhesion development and longer delivery time are found with each subsequent caesarean delivery.

## **Reduced Impact of Heavy Menstrual Bleeding on Physical and Social Activities of Women Using XP12B-MR**

*Andrea Lukes, MD, MHSc*

Carolina Women's Research and Wellness Center, Chapel Hill, North Carolina

*Bryan Hecht, MD, Scott Eder, MD, George Attia, MD, Gary Shangold, MD, Keith Moore, PharmD*

**OBJECTIVE:** To determine the impact of the investigational product XP12B-MR (tranexamic acid – modified release) on the physical and social or leisure activities of women.

**METHODS:** This randomized, placebo-controlled, parallel group study was conducted at 40 sites within the United States. Women, 18-49 years of age, with HMB defined using a validated alkaline hematin method with a mean menstrual blood loss of  $\geq 80$  mL during 2 baseline cycles were included in the study. Subjects were randomized to either XP12B-MR (3.9 g/day PO for up to 5 days starting at the onset of HMB) or placebo. Limitations on physical (walking, exercise, sports, etc.) and social or leisure (dancing, dining out, camping, etc.) activities during menstruation were assessed at baseline and over 6 menstrual cycles using 2 items on a validated patient reported outcome instrument, the Menorrhagia Impact Questionnaire (MIQ).

**RESULTS:** A total of 187 subjects (XP12B-MR with n=115, placebo with n=72) were included in the modified intent-to-treat population. Mean scores of the XP12B-MR group were significantly reduced from baseline ( $P \leq .0001$ ) on both MIQ items compared with the placebo group indicating improvement in physical and social or leisure activities of subjects treated with XP12B-MR. Treatment-related adverse events of interest occurred in the following percentages (XP12B-MR/placebo): nausea (8.6 vs 6.9), headache (8.6 vs 11.1), abdominal pain (4.3 vs 1.4), vomiting (1.7 vs 0), and dizziness (0.9 vs 2.8).

**CONCLUSION:** Women with HMB treated with XP12B-MR experienced significant improvement in physical and social or leisure activities. In addition, XP12B-MR was well tolerated.

## Longitudinal Validation of the Premenstrual Symptoms Impact Survey (PMSIS)

Aaron S. Yarlas, PhD

QualityMetric, Inc., Lincoln, Rhode Island

Min Yang, MD, PhD, Geoffrey C. Hammond, PhD, Richard Lynen, MD, MBA, Joseph Gricar, MS

**OBJECTIVE:** To validate the Premenstrual Symptom Impact Survey (PMSIS), a newly developed patient-reported outcomes instrument.

**METHODS:** Adult females (18-45 years old) participated in a two-wave 4-week apart non-interventional study (Wave1: N=1100, Wave2: N=770). At each wave, participants completed the following online questionnaires: PMSIS, SF-12v2, and retrospective criteria from the ACOG and DSM-IV-TR to identify women in the Premenstrual Syndrome (PMS) or Premenstrual Dysphoric Disorder (PMDD) groups. Responses on the PMSIS at each wave were analyzed for internal consistency reliability, convergent and discriminant/known-group validity, while responses across waves were analyzed for test-retest reliability.

**RESULTS:** The PMSIS showed good internal consistency at each wave (alphas greater than or equal to 0.88), and adequate test-retest reliability across waves (intra-class correlation: 0.74). PMSIS scores correlated significantly ( $p$  less than 0.001) with SF-12 Physical Component Summary (PCS) and Mental Component Summary (MCS). At each wave, PMSIS scores discriminated well across presence/absence of PMS and PMDD (all  $F$ 's greater than 100, all  $ps$  less than 0.001), and between low/medium/high PCS and MCS groups (all  $F$ 's greater than 24,  $ps$  less than 0.001), indicating known-group discriminant validity. Receiver operating characteristics analyses showed satisfactory values for areas under curves (greater than or equal to 0.78) in detecting women with PMS and/or PMDD at each time. Group (Wave1/Wave2) Wave1 Wave2 Mean SD Mean SD PMS(n=377/251) 54.3 17.4 52.0 18.2 Non-PMS(n=723/519) 32.4 19.8 28.3 19.6 PMDD(n=164/109) 59.0 15.6 55.0 14.9 Non-PMDD(n=936/661) 36.5 20.8 32.8 21.5

**CONCLUSION:** The PMSIS demonstrates satisfactory internal consistency, test-retest reliability, and convergent and discriminant validity at and across two time-points.

## **Efficacy and Responder Analyses of Divigel® (Estradiol Gel) 0.1% for the Treatment of Menopause**

*William Koltun, MD*

Medical Center for Clinical Research, San Diego, California

*Richard E. Hedrick, MD, Michelle Zachman, PharmD*

**OBJECTIVE:** To investigate the safety, efficacy, and response rates of 3 doses of estradiol gel 0.1% (Divigel®) for the treatment of symptoms associated with menopause.

**DESIGN:** Postmenopausal women were evaluated in a 12-week study investigating the efficacy and patient response of estradiol gel 0.1% at daily doses of 1 g, 0.5 g, and 0.25 g. Efficacy endpoints included change from baseline in frequency and severity of moderate to severe vasomotor symptoms (MSVMS) at weeks 4 and 12. A responder was defined as a woman who experienced  $\geq 50\%$  reduction in the frequency of MSVMS from baseline. Safety analyses included the incidence of adverse events (AEs) and clinical laboratory evaluations.

**RESULTS:** Treatment with estradiol gel 0.1% decreased the frequency and severity of MSVMS compared to placebo at weeks 4 and 12. The percent of women considered responders was significantly greater for women treated with estradiol gel 0.1% than for women treated with placebo. The percent of responders was highest at Week 12: 90% (1 g/day), 72% (0.5 g/day), 68% (0.25 g/day). All were significantly different from placebo (48%;  $P \leq 0.05$ ). The most frequently reported AEs were breast tenderness and metrorrhagia; no remarkable changes in clinical laboratory values following treatment with estradiol gel 0.1% were reported.

**CONCLUSIONS:** Estradiol gel 0.1% (Divigel®) is a safe and well-tolerated estrogen therapy that significantly reduces vasomotor symptoms associated with menopause. Responder analysis indicates that Divigel, even at the lowest dose, significantly decreased frequency of MSVMS, with a 68% rate of response.

## Transvaginal Ultrasonography to Predict Preterm Birth in Women with Uterine Anomalies

*Joan MG Crane, MD, MSc*

Memorial University, Eastern Health, St. John's, Newfoundland

*Heather Scott, MD, Wendy Whittle, MD, Sujata Chandra, MD, Donna Hutchens, RN, BN*

**OBJECTIVE:** To estimate whether cervical length(CL) measured by transvaginal ultrasonography(TVUS) in women with uterine anomalies predicts spontaneous preterm birth(SPTB).

**METHODS:** Women with a uterine anomaly who were pregnant with singleton gestations and delivered August2000-April2008 were compared with a low-risk control group. TVUS CLs were performed 16-30weeks gestation. Primary outcomes included CL and SPTB<35weeks. Secondary outcomes were SPTB<37weeks, SPTB<32weeks, low birthweight, maternal and neonatal outcomes. ROC curves were generated to identify the best CL cut-off.

**RESULTS:** Women with a bicornuate uterus(N=37), didelphus uterus(N=17) or septum resected(N=9) had shorter cervical lengths(3.40cm,3.72cm,2.80cm) than the low-risk control group(N=122,4.32cm,P<0.0001). Women with a bicornuate or didelphus uterus, compared with low-risk women, had higher rates of SPTB<35weeks(8.1% and 35.3% versus 0.8%, P=0.040 and P<0.0001), NICU admission(25.0% and 52.9% versus 7.5%, P=0.004 and P=0.001) and composite neonatal morbidity(30.6% and 64.7% versus 8.3%, P=0.001 and P<0.0001). Using a cutoff of 3.0cm, TVUS CL in women with a bicornuate uterus predicted SPTB<35weeks(PPV=33.3%, NPV=100%), birthweight <2500g(PPV=44.4%, NPV 96.4%) and RDS(PPV=33.3%, NPV=100%). Women with a resected uterine septum did not have an increased risk of SPTB<35weeks(81% power to see 25% SPTB<35weeks).

**CONCLUSION:** The implications of TVUS CL measurements for women with a uterine anomaly depend on the type of anomaly, and whether it has been surgically resected. Women with a history of septum resected, bicornuate or didelphus uterus have shorter CLs than low-risk controls. Bicornuate and dildelphus uterus are associated with SPTB<35weeks, but resected uterine septum is not. TVUS CL predicts SPTB<35weeks, low birthweight and neonatal morbidity in women with a bicornuate uterus.

## A Comparison of Estimated and Calculated Blood Loss in Postpartum Hemorrhage

Anjali Rozario

Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, New York

Dena Goffman, MD, Hye Heo, MD, Cynthia Chazotte, MD, Robert C. Madden, PhD, Peter S. Bernstein, MD, MPH

**OBJECTIVE:** To determine whether estimated blood loss correlates with hematocrit drop, an objective measure of blood loss, in women diagnosed with postpartum hemorrhage (PPH).

**METHODS:** Patients diagnosed with PPH during a 6-month time period were identified using ICD9 codes and charts were reviewed. Data was extracted including: demographics, mode of delivery, estimated blood loss (EBL), PPH etiology, blood transfusion, admission hematocrit, nadir hematocrit. Calculated blood loss (CBL) was based on hematocrit drop, adjusted for transfusion, and this value was compared with EBL. EBL was considered accurate if within 20% of CBL. Cohen's kappa statistics were calculated to test for agreement between EBL and CBL.

**RESULTS:** PPH occurred in 113 (4%) of 2,693 deliveries in a 6-month period. Median estimated blood loss was 1100cc (range 300-5000cc). Etiology of hemorrhage included: atony 71 (63%), retained products 11 (10%), laceration 10 (9%), accreta 4 (4%), surgical complication 4 (4%), abruption 3 (3%), bleeding disorder 2 (2%), previa 1 (1%), and unknown 7 (6%). Twenty-nine patients (26%) received a blood transfusion as a result of PPH. EBL was underestimated in 65 (58%), overestimated in 23 (20%) and accurate in 25 (22%) of patients. Poor agreement between EBL and CBL was found, especially in the intermediate blood loss categories (see table).

**CONCLUSIONS:** Current clinical methods for estimating blood loss are poor. Improved strategies for accurate blood loss assessment are necessary to ensure prompt and appropriate response to hemorrhage.

### Agreement between EBL and CBL

EBL (cc)	N	Kappa (SE)
<500	6	0.227 (0.131)
500-999	31	0.047 (0.090)
1000-1499	41	0.107 (0.092)
1500-1999	17	0.014 (0.093)
≥2000	18	0.297 (0.099)
Overall	113	0.131 (0.053)

## **Effect of Mode of Delivery on Infant Mortality in Late-preterm and Term Infants**

*Erol Amon, MD*

Saint Louis University, Saint Louis, Missouri

*Nicholas Ruthmann, Daniel M. Rubalcava, MD, Terry Leet, PhD*

**OBJECTIVE:** To determine the effect of mode of delivery on infant mortality risk (IMR) for late-preterm versus term infants.

**METHODS:** We conducted a population-based cohort study of a 10% random sample of all births during 2000-2002 using the U.S. linked infant birth/death cohort dataset. Multiple gestations and stillborns were excluded. Gestational age (GA) was classified as late-preterm (34-36 wks) or term (37-41 wks). Delivery mode was classified as vaginal (VD) or cesarean. A proxy variable for the presence of labor was used. Logistic regression was used to assess for confounding bias from other maternal and infant characteristics and to determine if mode of delivery with and without labor modified the overall effect of gestational age on IMR. Odds ratio (OR) and 95% confidence intervals (CI) were computed.

**RESULTS:** 1,040,685 births were studied. Late-preterm infants had a 3-fold higher IMR than term infants. Among cesarean births the IMR of late-preterm and term infants were 12.9/1000 versus 3.4/1000 infants. Among vaginal births, IMRs were 6.1/1000 versus 2.2/1000 infants. Compared to term infants, the OR and CI for infant mortality was 2.83 (2.53-3.16) and 3.87 (3.38-4.42) times higher for late-preterm infants delivered vaginally and by cesarean, respectively. Among late-preterm infants delivered by cesarean, the IMR for those experiencing labor was 8.1/1000 versus 13.4/1000 for those without labor.

**CONCLUSION:** Late-preterm infants have a higher IMR than term infants. Among late-preterm infants, the IMR is highest for infants delivered by cesarean without labor and lowest for those delivered vaginally.

### ***THIRD PRIZE***

#### **Gestational Sac Size, Yolk Sac Size and Fetal Cardiac Activity are Related to Miscarriage Risk**

*Soyoung Bae, MD*

University of Toledo Medical Center, Toledo, Ohio

*Joseph V. Karnitis, MD*

**OBJECTIVE:** To identify ultrasound markers in early pregnant patients with a known date of conception that predict a live-birth success.

**METHODS:** 1092 early pregnancies were evaluated in a retrospective case-control study. We examined the relationship of the presence of fetal cardiac activity, gestational sac diameter and yolk sac diameter by ultrasound on post-conception day 33 to 36 --- on the main outcome of ongoing pregnancy greater than 20 weeks of gestation. The majority of these pregnancies were conceived using infertility treatments, and the date of conception was clearly known. Odds ratio (OR) of gestational sac diameter, yolk sac diameter and presence of fetal cardiac activity were analyzed by chi-square test. Additional risk factors of age and history of recurrent pregnancy loss were also examined.

**RESULTS:** Ongoing pregnancy rate was 90.4% for those pregnancies having early fetal cardiac activity (OR=69.5,  $P<0.001$ ). Gestational sac diameter 12mm and above was associated with ongoing pregnancy rate of 91.9%. Conversely, small gestational sac diameter less than 8mm was associated with high miscarriage rate, 86.1% (OR=69.95, 12mm and above versus less than 8mm,  $p<0.001$ ). Success rate for yolk sac diameter less than 2mm, 2 to 6mm and greater than 6mm were 20.5% , 89.2% and 20% respectively (OR=32, 2 to 6mm versus less than 2mm; OR=33, 2to 6mm versus greater than 6mm,  $p<0.001$ ).

**CONCLUSION:** On post-conception day 33-36, gestational sac diameter 12mm and above, yolk sac diameter between 2 and 6mm, and the presence of fetal cardiac activity were all significantly related to the successful pregnancy outcome.

## **SECOND PRIZE**

### **The Genetics of Premature Rupture of Membranes and Preterm Delivery**

*Heather Byers, BA*

University of Iowa Carver College of Medicine, Iowa City, Iowa

*JC Murray, MD, Cesar Saleme, MD, Keegan Kelsey, BA, Viviana Consentino, MD*

**BACKGROUND:** Premature births are a major health challenge resulting in 3 million deaths per year. It is estimated that genetics underlie 40% of preterm births.

**OBJECTIVE:** We hypothesize that variation in genes that encode collagenases in the decidual and fetal membranes contribute to preterm births particularly those resulting from PROM.

**METHODS:** DNA samples (from cord blood, whole blood or saliva) were collected in Argentina from 2005-08 for a total of 1536 unique DNA samples from 359 families consisting of baby, mother, father and maternal grandparents. One gender-matched control (term baby) was collected per case. 13 SNPs were genotyped from 4 different genes (MMP1, MMP3, MMP9 and SERPINH1) using PCR technology. A Family Based Association Test (FBAT) was used for linkage disequilibrium analysis.

**RESULTS:** One SNP (rs679620) from a highly conserved region of MMP3 showed significant linkage disequilibrium ( $p=0.005$ ) across the entire study population. This SNP encodes a non-synonymous protein change from glutamate to lysine. None of the SNPs within MMP9, MMP1 or SERPINH1 were statistically significant for PTD.

**CONCLUSION:** MMP3 encodes stromelysin-1, a zinc-dependant enzyme in the decidua that degrades a wide array of ECM substrates within the decidua, fetal membranes and cervical ECM. The non-synonymous protein change was highly significant for association with PTD. MMP3 plays a key role in the proteolytic pathway and degrades a wide array of ECMs. This study linked a SNP in MMP3 to preterm delivery with disrupted gene functioning resulting in weakened decidua or fetal membranes, causing early delivery.

## ***FIRST PRIZE***

### **Regression of Cervical Lesions Is Associated with CD8 T-Cell Responses to HPV 16 E6 but not E7**

*William W. Greenfield, MD*

University of Arkansas for Medical Sciences, Little Rock, Arkansas

*Sushil Gupta, PhD, Hannah Coleman, Matthew Sellers, MD, Joseph Banken, PhD, Mayumi Nakagawa, MD, PhD*

**OBJECTIVE:** The goal was to examine the role CD8 T-cell responses to HPV 16 in regression of cervical lesions.

**METHODS:** Women being followed but untreated for abnormal Pap smear results were enrolled. HPV-DNA testing using the Linear Array HPV Genotyping Test (Roche Diagnostics, Indianapolis, IN) and enzyme-linked immunospot (ELISPOT) assay using the HPV 16 E6 and E7 peptides were performed. The subjects were categorized into three groups: regressor (n=32), persistor/progressor (n=33), or indeterminate (n=20) based on comparisons of pathological diagnoses (Pap smear or biopsy) between the last clinic visit and the current clinic visit at which blood sample was collected.

**RESULTS:** There was a higher rate of CD8 T-cell responses to the HPV 16 E6 antigen in the regressor group (17 of 32 or 53.1%) compared to the persistor/progressor group (8 of 33 or 24.2%) (p=0.0225) but not for the E7 antigen (4 of 32 or 12.5% for the regressor group and 4 of 33 or 12.1% for the persistor/progressor group, p=1.0000). The results were the same when the analyses included only subjects who were HPV 16-positive (n=27), HPV 16-related positive (n=48) or high-risk HPV positive (n=64), but not low-risk HPV positive (n=19).

**CONCLUSION:** CD8 T-cell immune responses to the HPV 16 E6 antigens but not to E7 antigens are associated with SIL regression, and such responses appear to be cross-reactive to other high risk HPV types. These data support the use of HPV 16 E6 antigens in the development of therapeutic vaccines for prevention and treatment of cervical cancer.