

35 POLYMORPHISM IN THE INTERLEUKIN 1 GENE COMPLEX AND PRETERM DELIVERY MEHMET GENÇ¹, STEFAN GERBER², MIRJANA NESIN³, STEVEN WITKIN²; ¹Brigham and Women's Hospital, Obstetrics and Gynecology, Boston, MA; ²Weill Medical College of Cornell University, Obstetrics and Gynecology, New York, NY; ³Weill Medical College of Cornell University, Pediatrics, New York, NY

OBJECTIVE: We hypothesized that polymorphisms in cytokine genes may determine the severity of inflammatory responses by fetal and maternal tissues and, thereby, susceptibility to spontaneous preterm labor and delivery. To test this hypothesis, we examined the association between preterm delivery and polymorphisms at position +3953 of the interleukin-1 beta gene (IL1B+3953) and in intron 2 of the interleukin 1 receptor antagonist gene (IL1RN).

STUDY DESIGN: This was a case-control study involving 52 pregnancies that resulted in preterm delivery before 34 weeks' gestation and 197 pregnancies that resulted in birth at term. Cells from the buccal mucosa collected from mothers and their children were tested by polymerase chain reaction (PCR) to amplify regions including IL1B+3953 and IL1RN polymorphisms. PCR products for IL1B+3953 were further digested with Taq I restriction endonuclease.

RESULTS: Maternal and fetal carriage of the less common alleles, i.e., IL1B+3953 allele 2 and IL1RN allele 2, either alone or in various combinations were not associated with an increased risk of spontaneous preterm delivery in the entire study population. However, subgroup analysis revealed significant differences in the carrier rates of these alleles among subjects of different ethnic groups. In fetuses of African descent, homozygous carriage of IL1B+3953 allele 1 was associated with a risk of spontaneous preterm delivery ($P = .033$). Fetuses of Hispanic descent, carrying IL1RN allele 2 were found to be at an increased risk for preterm and premature rupture of membranes and subsequent spontaneous preterm delivery (odds ratio: 6.5, 95% confidence interval: 1.25-37.7).

CONCLUSION: The carriage rates of IL1B+3953 and IL1RN alleles vary by ethnic group. There are associations of spontaneous preterm delivery with fetal carriage of IL1B+3953*1 and IL1RN*2 alleles in African and Hispanic populations, respectively.

37 THE MEMPHIS PRETERM BIRTH PROJECT: PREDICTION AND PREVENTION OF PRETERM BIRTH IN EXTREMELY HIGH RISK WOMEN DOROTHY BEAZLEY¹, BRIAN MERCER², NORMAN MEYER¹, TERESA CARR³; ¹University of Tennessee Health Science Center and The Prematurity Center, Obstetrics and Gynecology, Memphis, TN; ²Case Western Reserve University, Obstetrics and Gynecology, Cleveland, OH; ³University of Tennessee Health Science Center and The Prematurity Center, Department of Obstetrics and Gynecology, Memphis, TN

OBJECTIVE: To prospectively evaluate a program of weekly nurse contact and identify risk factors for preterm birth (PTB) in women at high risk.

STUDY DESIGN: This is randomized prospective trial of weekly contact (WC) versus routine care for prevention of PTB in women with risk factors. Women <32 weeks gestation underwent a baseline clinical evaluation including detailed history, examination, vaginal cervical ultrasound (USC_x), and bacterial vaginosis (BV) screen. Perinatal outcomes were determined concurrently. The primary outcomes PTB before 37 weeks (PTB), and spontaneous PTB (SPB) were evaluated, $P < .05$ considered significant.

RESULTS: 218 women have been recruited and delivered, with 42.2% PTBs and 32.1% SPBs. There was no decrease in the incidence of PTB or SPB in the WC group (43 vs. 41%, 35 vs. 30% respectively). Women with prior SPB, Bishop score >4 cervix >1 cm dilated, BV, recent contractions, vaginal bleeding, work in pregnancy, were not at increased risk for PTB or SPB. Women with twin gestations were at increased risk for PTB (64 vs. 40%, $P = .02$) and those with cervical effacement $\geq 50\%$ were at increased SPB (64 vs. 31%, $P = .04$). Those with an USC_x <25, <30 or <35 mm were at increased risk for PTB and SPB, particularly with screening before 24 weeks (see Table).

CONCLUSION: While weekly contact did not prevent PTB or SPB in this extremely high risk population, transvaginal cervical imaging early in gestation appears to play a role in identifying those at further increased risk for PTB and SPB. However, in this population, women with a reassuring cervical length remain at high risk for preterm and spontaneous preterm birth.

Table
Risk of PTB and SPB based on ultrasound cervical length before 24 weeks (N = 128)

	SPB (%)	P	PTB (%)	P
<25 vs. ≥ 25 mm	71 vs. 33	.10	86 vs. 41	.04
<30 vs. ≥ 30 mm	71 vs. 31	.006	79 vs. 40	.009
<35 vs. ≥ 35 mm	50 vs. 29	.03	63 vs. 36	.006

36 MID-TRIMESTER METRONIDAZOLE AND AZITHROMYCIN DID NOT PREVENT PRETERM BIRTH IN WOMEN AT INCREASED RISK: A DOUBLE-BLIND TRIAL JC HAUTH¹, S CLIVER¹, P HODGKINS¹, WW ANDREWS¹, JR SCHWEBKE¹, EW HOOK¹, RL GOLDENBERG¹; ¹University of Alabama at Birmingham, OB/GYN, Birmingham, AL

OBJECTIVE: To reduce preterm birth (PTB) with mid-trimester antimicrobial treatment in women at increased risk.

STUDY DESIGN: Women at increased risk for PTB were identified between 21 and 25 weeks' gestation (GA). Randomization occurred in 235 women with a cervical/vaginal fetal fibronectin level of ≥ 50 ng/ml, in 60 women with bacterial vaginosis (BV) and a prior PTB and in 75 with BV and whose prepregnancy weight was ≤ 50 kg. Diagnosis of BV was by Gram stain using the Nugent criteria. Treatment was either metronidazole SR (M) 750 mg qd $\times 7$ and azithromycin (A) 1 gm repeated in 4 days or identically appearing placebos. The primary outcome was birth prior to 37 weeks' gestation. A sample size of 368 was needed to document a significant 1/3 reduction in birth prior to 37 weeks GA.

RESULTS: Of 4056 women screened for eligibility, 370 were randomized. Follow-up to outcomes occurred in 366 (99%). Distribution between the antimicrobial and placebo groups was similar in these three risk groups as was race and marital status. Women randomized to antimicrobial treatment had a similar rate of PTB at <32, <35, and at <37 weeks GA as women receiving placebo (Table). Spontaneous PTB was also similar in these groups. In women with FFN as the risk factor, 12.6% assigned to placebo had a PTB <37 weeks and in 21.7% to M+A ($P = .06$). In the combined FFN and BV with prior PTB risk groups (#291), delivery at <37 weeks gestation occurred in 13.8% assigned to placebo and in 24% to M+A ($P = .027$). However, in these subgroups PTB <35 and <32 weeks was nearly identical.

CONCLUSION: Mid-trimester treatment with metronidazole and azithromycin did not decrease PTB. In 2 of the 3 risk groups, PTB at 35-36 weeks GA was significantly increased in women assigned to M+A.

Table
Preterm birth in relation to treatment

TREATMENT	<32 WEEKS GA	<35 WEEKS GA	<37 WEEKS GA
Placebo	7/182 (3.9%)	16/182 (8.8%)	29/182 (15.9%)
M+A	6/184 (3.3%)	16/184 (8.7%)	41/184 (22.3%)

38 THE RELATIONSHIP BETWEEN TUMOR NECROSIS FACTOR ALPHA GENOTYPE AND SUCCESS OF EMERGENT CERCLAGE LORAINÉ ENDRES¹, EILEEN WANG¹; ¹Northwestern University, Obstetrics and Gynecology, Chicago, IL

OBJECTIVE: The guanine (G) to adenosine (A) substitution at the -308 position in the tumor necrosis factor alpha (TNF-alpha) gene promoter region results in a 6-fold greater cytokine response to an inciting event and has been implicated in the pathogenesis of preterm labor. We investigated whether this polymorphism is associated with adverse pregnancy outcome after emergent cerclage (EC).

STUDY DESIGN: Women with a diagnosis of incompetent cervix requiring an EC between 15 and 24 completed weeks' gestation were enrolled. Women of the same gestational age (GA) range without pregnancy complications were recruited as controls. DNA was extracted from peripheral blood samples and PCR amplification of a 144 base pair segment of the TNF-alpha gene was performed with subsequent sequencing. Clinical factors were also recorded and subjects followed prospectively. Delivery after 28 completed weeks' gestation was defined as a successful outcome. Chi-square and Mann-Whitney tests were used for statistical analysis.

RESULTS: 23 women underwent EC and participated in the study, 13 (57%) of whom delivered after 28 weeks' gestation. 23 women served as controls. The TNF-alpha genotype was determined in 43 of 46 subjects (93.5%). The frequencies of heterozygosity and homozygosity for the TNF-alpha polymorphism were not significantly different across the EC success, EC failure, and control groups (Table). The median GA at the time of the EC was significantly different between the success and failure groups (22 weeks vs. 20.5 weeks, $P < .01$) as was the incidence of prolapsing membranes (46% vs. 100%, $P < .05$). Neither median cervical dilation (2cm vs. 3cm, $P = NS$) nor cervical length (2cm vs. 1cm, $P = NS$) was associated with pregnancy outcome.

CONCLUSION: The TNF-alpha genotype was not associated with delivery prior to 28 weeks' gestation in women who had received an emergent cerclage.

Table
Frequencies of the TNF-alpha genotype

	G/G	G/A	A/A
Success (n = 10)	7	3	0
Failure (n = 10)	9	1	0
Control (n = 23)	17	5	1