

**9 DIFFUSE DECIDUAL LEUKOCYTOCLASTIC NECROSIS (DDLN) OF THE DECIDUA BASALIS IS ASSOCIATED WITH DIMINISHED IQ AT AGE 6 YEARS** WILLIAM ANDREWS<sup>1</sup>, ROBERT GOLDENBERG<sup>2</sup>, ONA FAYE-PETERSEN<sup>3</sup>, SUZANNE P. CLIVER<sup>1</sup>, FRED BIASINI<sup>4</sup>, MYRIAM PERALTA-CARCELLEN<sup>5</sup>, JOHN HAUTH<sup>1</sup>, <sup>1</sup>University of Alabama at Birmingham, Obstetrics & Gynecology, Birmingham, Alabama, <sup>2</sup>Drexel University College of Medicine, Obstetrics & Gynecology, Philadelphia, Pennsylvania, <sup>3</sup>University of Alabama at Birmingham, Pathology, Birmingham, Alabama, <sup>4</sup>University of Alabama at Birmingham, Psychology, Birmingham, Alabama, <sup>5</sup>University of Alabama at Birmingham, Pediatrics, Birmingham, Alabama

**OBJECTIVE:** DDLN at the chorionic interface is a possible marker of placental hypoxia and vascular compromise. We assessed the association of DDLN and chronic placental inflammation (CPI) with cerebral palsy (CP) and IQ at age 6 years.

**STUDY DESIGN:** A cohort of 261 infants delivered between 23 and 32 weeks gestation were evaluated for CP and IQ at age 6.8±0.7 years (using the Weschler Intelligence Scale for Children-III). Placental histology was performed by a single pathologist.

**RESULTS:** DDLN was present in 75 (30%) placentas and was associated with preeclampsia (Pre-E; 57.3% vs. 23.1%, p<.0001), indicated preterm birth (IPTB; 65.3% vs. 24.9%, p<.0001) and CPI (20% vs. 11%, p=.058). CPI was associated with IPTB (52.8% vs. 35.3%, p=.045) but less so with Pre-E (47.2% vs. 31.7%, p=.067). No difference was observed among cases with and without DDLN or CPI regarding race, income, smoking, marital status, or infant gender (all p≥.01). Those with CPI were less likely to have <12 years of maternal education (27.8% vs. 45.4%, p=.048) and zero parity (33.3% vs. 52.1%, p=.037). DDLN was associated with an increased risk of an SGA baby (21.3% vs. 1.7%, p<.0001). The frequency of CPI decreased with increasing delivery GA (21.7% at 23-26 wks' to 7.6% at 31-32 wks', M-H p=.051). DDLN was unrelated to delivery GA (31.0% at 23-26 wks' to 32.7% at 31-32 wks', M-H p=.943). An IQ<70 occurred in 41 (15.8%) children and was more common in cases with CPI (30.6% vs. 13.9%, p=.012) and DDLN (21.3% vs. 14.0%) but not significantly so (p=.153). However, in a regression model controlling for delivery GA and other factors associated with childhood IQ (including maternal IQ), DDLN (p=.043), but not CPI (p=.437), was significantly associated with childhood IQ accounting for a 4-point reduction in IQ score. DDLN was not significantly associated with CP (n=11;RR 1.91,95%CI .6-6.1).

**CONCLUSION:** DDLN, a possible marker of placental hypoxia and vascular compromise, is not associated with delivery GA between 23 and 32 wks' but is associated with Pre-E, IPTB, SGA and significantly lower IQ at age 6 years.

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**10 MAINTENANCE NIFEDIPINE VS. PLACEBO: A PROSPECTIVE, DOUBLE BLIND TRIAL** DEIRDRE LYLE<sup>1</sup>, KRISTIN PULLEN<sup>1</sup>, JANA MANNAN<sup>2</sup>, USHA CHITKARA<sup>1</sup>, MAURICE L. DRUZIN<sup>1</sup>, AARON CAUGHEY<sup>2</sup>, YASSER EL-SAYED<sup>1</sup>, <sup>1</sup>Stanford University, Obstetrics and Gynecology, Stanford, California, <sup>2</sup>Santa Clara Valley Medical Center, Obstetrics and Gynecology, San Jose, California, <sup>3</sup>University of California, San Francisco, Obstetrics and Gynecology, San Francisco, California

**OBJECTIVE:** To test whether treatment with nifedipine after arrested preterm labor prolongs pregnancy and improves neonatal outcomes.

**STUDY DESIGN:** A prospective, randomized, double-blind, multi-center study was conducted. After successful tocolysis of preterm labor patients were randomized to 20 mg nifedipine or an identical-appearing placebo every 4-6 hours, and treatment was continued until 37 weeks. The primary outcome was attainment of 37 weeks gestation. Patients were included between 24 and 34 weeks if they had 6 or fewer contractions per hour, intact membranes, and <4 cm cervical dilation. Exclusion criteria included placental abruption or previa, fetal anomaly incompatible with life, or maternal medical contraindication to tocolysis. In order to have an 80% power to detect a 50% reduction in birth prior to 37 weeks, with an alpha of .05 and a beta of .2, 66 patients were required. Statistical comparisons were made using 2-sided Fisher's Exact tests, Student t-tests, and Mann-Whitney tests.

**RESULTS:** 71 patients were randomized, 2 were excluded after randomization, and 1 was lost to follow up. 35 patient received placebo and 33 received nifedipine. There were no maternal demographic differences between groups. Results are shown in the table.

**CONCLUSION:** Prolonged tocolysis following an episode of arrested preterm labor did not significantly prolong pregnancy or improve neonatal outcomes.

Nifedipine vs. placebo outcomes			
	Nifedipine	Placebo	p-value
Achieved 37 weeks	13 (39%)	13 (37%)	1.00
Delivery delay (days)	31	30	0.81
Mean GA delivery	35.0	35.2	0.82
Delivery delay >48 hours	33 (100%)	33 (94%)	0.49
>1 week	31 (94%)	31 (89%)	0.67
>2 weeks	28 (85%)	27 (77%)	0.54
>3 weeks	24 (73%)	24 (69%)	0.54
>4 weeks	22 (67)	19 (54%)	0.33
BW (grams)	2453	2531	0.69
Composite neonatal morbidity	10 (30%)	7 (20%)	0.41

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**11 PROGESTERONE (P4), BUT NOT 17ALPHA HYDROXYPROGESTERONE CAPROATE (17P), INHIBITS HUMAN MYOMETRIAL CONTRACTIONS** NICOLE RUDDOCK<sup>1</sup>, SHAO-QING SHI<sup>1</sup>, SANGEETA JAIN<sup>1</sup>, GRADIE MOORE<sup>1</sup>, GARY D.V. HANKINS<sup>1</sup>, ROBERTO ROMERO<sup>2</sup>, ROBERT GARFIELD<sup>1</sup>, <sup>1</sup>University of Texas Medical Branch at Galveston, Galveston, Texas, <sup>2</sup>Wayne State University, Detroit, Michigan

**OBJECTIVE:** Recent evidence supports a role for progestins in the prevention of preterm labor and delivery. The aim was to determine whether P4 or 17P directly inhibit human uterine contractility in vitro and thereby clarify their mechanisms of action.

**STUDY DESIGN:** Myometrial tissues were obtained from the lower uterine segment of women (n=80) at term undergoing cesarean section. Tissue strips (8/patient) were suspended in organ chambers and exposed for 2 to 12 hours to varying concentrations of P4 or 17P dissolved in ethanol. Solvent time-controls were run in parallel. Contractile activity was registered, stored and analyzed. Contractility was compared before and after addition of each agent and following a high KCl concentration. Dose response curves were then generated for P4 or 17P at various times. Data were analyzed by ANOVA for statistical differences (P<0.05).

**RESULTS:** 1) P4 significantly inhibited spontaneous contractility dose dependently after 1 hour with an ED<sub>50</sub> of less than 10<sup>-7</sup>M (10µM). The inhibition was not blocked by RU486 but was reversible after washing. 2) The responses to KCl were also significantly lower following P4. 3) Surprisingly 17P dose dependently stimulated contractility. 4) HPLC and GC-MS methods were used to determine the detectable concentrations of progestins in the baths. The concentrations of 17P but not P4 were significantly lower than expected.

**CONCLUSION:** P4, at concentrations equivalent to those present in the placenta and uterus, inhibits spontaneous myometrial contractility in vitro probably by nongenomic mechanisms and repression of Ca influx, since KCl-induced responses are also reduced. This study supports the concept that P4 directly suppresses myometrial contractility and thus its use in the prevention of preterm labor and delivery. The effects of 17P are difficult to assess because a large proportion is lost inexplicably during incubation, but 17P stimulated contractions. This study model might be used to further examine the mechanisms of progestin action on the myometrium.

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**12 PREVENTING CERVICAL RIPENING: THE PRIMARY MECHANISM BY WHICH PROGESTATIONAL AGENTS PREVENT PRETERM BIRTH?** HUA XU<sup>1</sup>, JUAN GONZALEZ<sup>1</sup>, ELLA OFORI<sup>2</sup>, MICHAEL ELOVITZ<sup>1</sup>, <sup>1</sup>University of Pennsylvania, Philadelphia, Pennsylvania, <sup>2</sup>University of Pennsylvania, Pennsylvania

**OBJECTIVE:** Two recent randomized trials demonstrated that progestational agents (PAs) prevent preterm birth (PTB). More recent clinical data suggests that these agents may delay PTB in patients with advanced cervical ripening (AJOG 2007). These studies sought to assess whether PAs may prevent PTB through modulation of known and unknown pathways involved in cervical ripening.

**STUDY DESIGN:** In experiment #1, E15 dams were injected with MPA( 1mg/dam) or vehicle on E15 and cervical tissues were collected 48 hours later. RNA was extracted and used for microarray analysis using Affymetrix Gene Chip. Data and cluster analyses were performed using SAM. Pathway analysis was performed using DAVID. In experiment #2, E15 dams were treated with MPA (1mg/dam, n=6), Progesterone (P) (2mg/dam, n=6), dexamethasone (DEX, n=6) or vehicle (n=3). Cervices were collected 24 hrs later. QPCR was performed on cervical tissues from time points.

**RESULTS:** 94 genes in the cervix were differentially regulated 2 fold 48 hours after treatment of MPA. Based on significance and pathway analysis, select target genes were assessed by QPCR. The HAS-2 and Claudin-2 mRNA expression were significantly differentially regulated by PAs (TABLE).

**CONCLUSION:** HAS-2, already implicated in cervical ripening, is significantly inhibited by PAs. The up-regulation of Claudin-2 by PAs would serve to increase tight cell junctions and may represent a novel target for PA action. These molecular studies suggest that PAs, used clinically in humans, may serve to modulate genes involved in cervical ripening thus prevent cervical change and inhibit PTB.

Fold change in mRNA expression by PA

Treatment Groups	HAS-2	P value (compared to control)	Claudin-2	P value (compared to vehicle)
MPA/vehicle-48hr	-3.3	0.04	2	0.04
MPA/vehicle-24hr	-1.9	0.025	7.8	0.004
P/vehicle-24 hr	1.6	NS	4.9	0.05
DEX/vehicle-24 hr	2.5	0.01	1.9	0.19

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