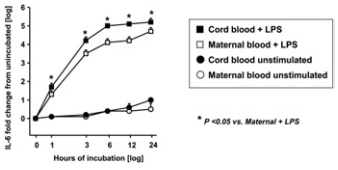
102 THE IMMEDIATE POSTNATAL PERIOD IS CHARACTERIZED BY AN INCREASED SENSITIVITY OF THE NEONATE TO E. COLI ENDOTOXIN SONYA S. ABDEL-RAZEQ[1], CATALIN S. BUHIMSCHI[1], ANTONETTE T. DULAY[1], GUOMAO ZHAO[1], MERT BAHTIYAR[1], IRFAN A. WARSY[2], IRINA A. BUHIMSCHI[1], [1]Yale University, Ob/Gyn & Reprod Sci, New Haven, Connecticut, [2]Yale University, Pediatrics, New Haven, Connecticut

OBJECTIVE: Neonatal inflammation represents a highly orchestrated process designed to combat infection and tissue injury. Although pro-inflammatory cytokines are essential for neonatal defense against Gram (-) infection, exaggerated cytokine production has deleterious effects. The present study addressed the question whether in comparison to the adult, the immediate postnatal period represents a life phase characterized by deficiency in the adaptive immune response to infection.

STUDY DESIGN: Paired, time-matched whole blood maternal-cord blood samples were obtained from 33 normal full-term pregnant women who had a clinically indicated Cesarean delivery in the absence of labor. Maternal and cord blood was collected under sterile conditions and incubated ***ex vivo*** with 1 μg/ml ***E. coli*** LPS (LPS) in a CO_2 thermostat at 37C for 1,3,6,12&24h. In addition, we studied the immune response of maternal and cord blood in response to rsLPS (LPS competitive antagonist). Interleukin-6 (activator of acute phase responses) was measured by ELISA.

RESULTS: **1**) There were significant differences in the response of the maternal vs. neonatal cord blood to LPS despite lack of differences in cytokine levels in unstimulated conditions; **2**) LPS elicited a significant IL-6 response at 1h of incubation in both maternal and neonatal blood; **3**) Both maternal and neonatal blood continued to respond to LPS challenge up to 6 hours and plateaued thereafter; **4**) At all times, the neonatal blood responded more robustly to LPS compared to maternal blood ($P<0.001$); **5**) rsLPS elicited an inhibitory response (antagonist) in maternal blood, but a stimulatory effect (agonist) in neonatal compartment.

CONCLUSION: We provide evidence that the neonate has a heightened sensitivity to endotoxin in the immediate postnatal period. The divergent effect of rsLPS suggests that the maternal and neonatal LPS recognition components (TLR4, CD14, MD2) may be functionally different.



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103 IS THE RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS (RAGE) INVOLVED IN PRETERM BIRTH? JUAN GONZALEZ[1], BRIANNA LYTTLE[1], HUA XU[1], ELLA OFORI[1], MICHAL ELOVITZ[1], [1]University of Pennsylvania, OBGYN; Maternal and Child Health Research Program, Philadelphia, Pennsylvania

OBJECTIVE: RAGE is the receptor for pro-inflammatory molecules and causes an amplification of the inflammatory response. S100A12, a ligand for RAGE, was recently found to be increased in the amniotic fluid of women with intra-amniotic infection. We determined the expression of the receptor through gestation in cervix (CX) and uterus (UT) and then used an in vivo model to assess if the activation of RAGE by its ligand (HMGB1) causes preterm birth (PTB).

STUDY DESIGN: 3 sets of experiments were performed: 1) CX and UT tissue were harvested from CD-1 pregnant mice on E15, E17, E19 (n=3-6 mice/group) 2) CD-1 mice were randomized to intrauterine LPS or saline. For these studies, CX and UT were harvested 6 hrs later to assess RAGE and HMGB1 (a ligand to RAGE) expression by QPCR. 3) Recombinant HMGB1 was injected intrauterine (IU) on E15 and mice were monitored for preterm birth (low dose = 5ug/dam, n=6/group; high dose = 20ug/dam, n=5/group).

RESULTS: RAGE mRNA was 2.5 fold increased in the UT($p=<0.05$) and 1.4 fold in CX ($p=0.03$) commpared to NP. Endogenous HMGB1 was up-regulated 1.6 fold ($p=0.04$) in the UT in intrauterine inflammation. Recombinant HMGB1 did not cause PTB or fetal loss.

CONCLUSION: RAGE and its ligand are differentially regulated in reproductive tissues during pregnancy. HMGB1, at 4-times the dose sufficient to cause a profound inflammatory response in other models, is insufficient to cause PTB. RAGE or its ligands may be biomarkers of PTB but are unlikely to be a critical mechanism in the pathogenesis of PTB.

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104 THE ASSOCIATION BETWEEN BACTERIAL VAGINOSIS AND SPONTANEOUS PRETERM BIRTH IS MODIFIED BY HISTORY OF PPROM DAVID STAMILIO[1], BONNIE CLOTHIER[2], ALISON CAHILL[1], ANTHONY ODIBO[1], SAMUEL PARRY[2], DEBORAH NELSON[3], GEORGE MACONES[1], [1]Washington University in St. Louis, St. Louis, Missouri, [2]University of Pennsylvania, Philadelphia, Pennsylvania, [3]Temple University, Philadelphia, Pennsylvania

OBJECTIVE: To estimate if the risk of spontaneous preterm birth (SPTB) associated with bacterial vaginosis (BV) is modified by three specific components of pregnancy history.

STUDY DESIGN: We performed a 4-year prospective cohort study of urban pregnant subjects who were universally screened for BV at <13 weeks with vaginal Gram stain and the Nugent criteria interpreted by a trained technician. The primary outcome was spontaneous preterm delivery (<37 weeks). Providers and investigators were blinded to the BV screen results. Data on multiple obstetric, medical and demographic variables were collected using a questionnaire, mid-pregnancy interview and postpartum chart review. Bivariable and multivariable statistical methods were used to assess the exposure-outcome association and pertinent interactions identified a priori: preterm premature rupture of membranes (PPROM), symptomatology, and antibiotic therapy.

RESULTS: Among 1826 enrolled patients, 1452 progressed beyond 22 weeks and had complete data. The prevalence of BV was 37% (n=537): 13% symptomatic and 24% asymptomatic. The prevalences of spontaneous and any preterm birth were 7.3% (n=106) & 11.4% (n=153), respectively. BV was not significantly associated with spontaneous preterm birth in the overall population in the unadjusted or multivariable analysis (Adjusted OR 0.8, 95%CI 0.5-1.2). However, the association between BV and SPTB was modified by pregnancy history, such that women with prior PPROM and current BV had a markedly increased odds of preterm birth compared to women with BV without prior PPROM (Interaction adjusted OR 8.3, 95%CI 1.5-47.6). The BV-SPTB association was not modified by symptomatology or prenatal antibiotic treatment.

CONCLUSION: In this general obstetric population, BV conveyed increased risk for spontaneous preterm birth only if preceded by a history of PPROM in a prior pregnancy. This interaction could be the result of genetic variation or environmental factors that predispose the high-risk patient to a hyper-inflammatory response to BV.

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105 HISTOPATHOLOGICAL PLACENTAL FEATURES ASSOCIATED WITH DEVELOPMENT OF PERIVENTRICULAR LEUKOMALACIA IN PRETERM INFANTS ANYA BAILIS[1], ZAHRA MALEKI[2], FRED ASKIN[2], ERNEST GRAHAM[1], [1]Johns Hopkins University, Baltimore, Maryland, [2]Johns Hopkins University, Pathology, Maryland

OBJECTIVE: Periventricular leukomalacia (PVL) is a complication of preterm delivery often leading to cerebral palsy. We seek to identify placental histopathological features that predict the development of PVL in premature infants.

STUDY DESIGN: Case-control study of neonates born from 23 to 34 weeks at a university hospital between 5/94 and 10/04 diagnosed with PVL by ultrasound 6 weeks after birth. Cases were matched by gestational age to controls without PVL. A perinatal pathologist blinded to neonatal course reviewed the placentas. Data were analysed using t-tests and chi square ($p<0.05$ significant).

RESULTS: Cases (n=101) and controls (n=101) were matched by age (27.5±2.6, 27.6±2.5 weeks). Cases had lower birth weight (972±307, 1044±368 grams, $p=0.04$). There was no difference in cesarean delivery (51.5%, 48.5%), neonatal death (4.0%, 7.9%), umbilical artery pH (7.26±0.10, 7.27±0.12) or base deficit (3.1±4.0, 3.0±4.5 mM).

CONCLUSION: This study suggests an association between chronic placental inflammation and subsequent PVL in infants born prematurely and disagrees with previously reported associations between acute chorioamnionitis and PVL.

	PVL	Control	p value
Placental wt (g)	312±97	320±114	0.57
Placental wt/ birthwt	0.34±0.11	0.33±0.12	0.55
Acute chorioamnionitis	51 (50.5%)	51 (50.5%)	1.0
Chronic inflammation	26 (25.7%)	16 (15.8%)	0.04*
Maternal vascular obstruction	48 (47.5%)	56 (55.4%)	0.26
Fetal vascular obstruction	28 (27.7%)	25 (24.8%)	0.59
Fetal vascular disturbance of integrity	7 (6.9%)	5 (5.0%)	0.77
Perivillous fibrin depositition	3 (3.0%)	1 (1.0%)	0.63
Increased nucleated RBCs	12 (11.9%)	8 (7.9%)	0.42
Meconium change	4 (4.0%)	2 (2.0%)	0.69

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