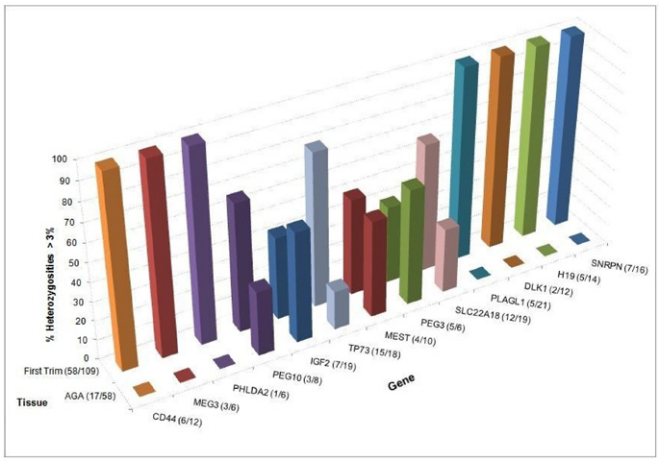

Loss of Imprinting in First Trimester Placentas

CONCLUSION: Our results show that LOI is more common in 1st trimester placentas than in term human placentas. This is the first biological observation suggesting that genetic imprinting is not completely established and occurs beyond the 1st trimester of pregnancy. Genes like CD44, MEG3, PLAGL1, DLK1, H19 and SNRPN show appreciable rates of LOI in the1st trimester placentas, but become totally imprinted by the 3d trimester of human gestation. Our findings also suggest that many mechanisms, rather then methylation alone, might be responsible for imprinting in the placenta.

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39 Cervical funneling: effect on gestational length and ultrasound-indicated cerclage in high-risk women

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OBJECTIVE: To assess the relationship between the type of cervical funneling and birth gestational age (GA) in women with prior spontaneous preterm birth (SPTB) and cervical length (CL) < 25 mm enrolled in a randomized intervention trial of ultrasound-indicated cerclage.

STUDY DESIGN: This is a planned secondary analysis of the NICHD-sponsored cerclage trial. Women with prior SPTB at 17 – 33 6/7 weeks underwent serial vaginal scans between 16 and 22 6/7 weeks. 301 women whose CL was < 25 mm were randomized to receive cerclage or no cerclage. At the qualifying scan for randomization, the presence and type of funnel (U or V-shaped) were recorded.

RESULTS: 147 of 301 (49%) had a funnel: 99 were V-shaped (V-F) and 48 were U-shaped (U-F). In univariate analyses, the presence of U-F, but not V-F, was associated with an increased risk of preterm birth < 24 weeks (p= 0.0092), < 28 weeks (p=0.0002), < 35 weeks (p=0.0005), and < 37 weeks (p=0.002). In a multivariable regression model of GA as the dependent variable, U-F (but not V-F) remained significant (p=0.003) after controlling for baseline CL and cerclage group, demonstrating a mean 3 week earlier birth. We also considered the possibility of an interaction between U-F and cerclage. The interaction term (p=0.06) suggested that women with U-F have a disproportionate benefit from cerclage: women with U-F were delivered a mean 4.9 weeks later in gestation with cerclage than without cerclage.

CONCLUSION: The finding of a U-F, but not a V-F, in women with shortened midtrimester CL is associated with a earlier birth GA. The pathophysiologic mechanisms of a U-F appear to be more amenable to cerclage therapy in women with prior SPTB and shortened CL < 25 mm.

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40 Preterm severe preeclampsia is associated with decreased decidual T regulatory cells

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OBJECTIVE: Immunologic mechanisms play a pivotal role in the pathophysiology of preeclampsia (PE). Specifically, immunosuppressive T regulatory (Treg, FoxP3+, CD4+, CD25bright) cells control the cytotoxic T cell (CD8+) response and tolerance to the fetus. In maternal peripheral blood Tregs are elevated in pregnancy, decrease across gestation, and are decreased in pregnancies with PE. To determine the role of these cells at the implantation site, we characterized the proportion of decidual Treg and cytotoxic T cells in normal and preeclamptic pregnancies.

STUDY DESIGN: Decidua from first trimester terminations (n=5) and fetal chorioamniotic membranes, containing decidua, from term deliveries (n=14), early onset (<=34 weeks) severe PE (n=7), and late onset (>34 weeks) severe PE (n=7) were evaluated. Immunohistochemistry for CD3, CD8, and FoxP3 was performed. Cells were counted in three 5x fields; CD8+ and FoxP3+ cells were calculated as a percentage of CD3+ cells (total T cells) and analyzed non-parametrically.

RESULTS: The median percentage of decidual Tregs decreases with advancing gestational age (59.67% first trimester, 5.21% third trimester; p=0.001). The median proportion of decidual Treg cells is significantly lower in pregnancies complicated by early onset severe PE (0.65%) compared to uncomplicated term pregnancies (5.21%; p=0.004), and to pregnancies complicated by late onset severe PE (3.67%; p=0.003). The latter two categories were not significantly different (p=0.628). The proportion of CD8+ cells was significantly higher in pregnancies complicated by severe PE compared to gestational age-matched controls (p=0.018).

CONCLUSION: In normal pregnancy, decidual Tregs decrease with advancing gestational age. Early onset severe PE showed a significantly lower percentage of Tregs compared to estimates of gestational age-matched controls. Taken together with increased cytotoxic T cells in PE, our data suggest that early onset severe preeclampsia has a unique pathophysiology involving defective immuno-regulatory pathways at the implantation site.

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41 Labor induction with a foley balloon trial (LIFT) – a randomized controlled trial of 30mL versus 60mL Foley balloon inflation

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OBJECTIVE: To compare 30mL and 60mL Foley balloon inflation in labor induction and the effect on length of labor and mode of delivery.

STUDY DESIGN: 192 women with term, vertex, singleton pregnancies & Bishop score <5 were randomized to receive a 30mL or 60mL Foley balloon (FB). Exclusion criteria were regular contractions on admission, ruptured membranes, low-lying placenta or prior hysterotomy. Randomization was stratified by parity and providers were blinded to FB size. Outcomes included delivery times, time to FB expulsion, cervical dilation after FB expulsion, maximum oxytocin dose, method of delivery, chorioamnionitis, meconium, cervical laceration, abruption, 5-minute Apgar and umbilical cord artery gas.

RESULTS: FB inflation to 60mL produced a higher rate of delivery within 12 hours compared to 30mL. Stratified by parity, delivery within 12 hours remained significant for nulliparous women. Inflation to 60mL produced a larger cervical dilation after FB expulsion. There was no difference in median delivery time, cesarean delivery rate or neonatal outcomes.

	30mL FB (n=94)	60mL FB (n=98)	p
Dilation after FB expulsion (cm)*	3 (3-4)	4 (3-4)	0.003
Delivery within 12 hours	13 (14%)	25 (26%)	0.04
Nulliparous	4 (6%)	12 (16%)	0.045
Multiparous	9 (39%)	13 (54%)	0.3
Time to delivery (hrs)*	20.0 (13.9–30.0)	18.8 (12.0–27.1)	0.37
Cesarean delivery	20 (21%)	23 (23%)	0.71
Chorioamnionitis	14 (15%)	19 (19%)	0.41
Meconium	20 (21%)	20 (20%)	0.88
5-minute Apgar**	8.5 ± 1.0	8.6 ± 0.9	0.78
5-minute Apgar <7	5 (5%)	4 (4%)	0.69
CUA pH**	7.27 ± 0.07	7.27 ± 0.07	0.64

* median (IQR)
** mean ± SD

CONCLUSION: Transcervical Foley balloons inflated to 60mL for labor induction produce higher rates of delivery within 12 hours as compared to 30mL inflation, particularly for nulliparous women. There are no differences in cesarean delivery, labor complications or neonatal outcomes.

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42 Placental cytokine response to lipopolysaccharide: mechanism for enhanced inflammation susceptibility of the preterm fetus

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OBJECTIVE: Recent studies have demonstrated that fetal and/or intra-amniotic infection may be associated with the induction of fetal cytokines and the development of neurologic injury. Whereas clinically significant fetal infection is uncommon, maternal infections (eg, pyelonephritis) occur both antepartum and intrapartum. Maternal inflammatory agents may activate placental cytokine production and with secretion into the fetal compartment. To explore the characteristics of maternal infection required to produce a fetal inflammatory response, we examined rat placental cytokine production in response to lipopolysaccharide (LPS) exposure at preterm and nearterm gestational ages.

STUDY DESIGN: Pregnant rats were sacrificed on gestational day E16 and E18 (term = 21 d) and each placenta was dissected into 2 explant sections. The explants were incubated in untreated culture media in 12-well plate transwells for 12h and then treated with LPS (1 or 10g/ml) for further 6 or 12h. Culture supernatant was analyzed for IL-6 cytokine release (ELISA). Viability of explants was assessed by release of lactate dehydrogenase.

RESULTS: At E16 placental explants exposed to 1g/ml LPS for 6h demonstrated a significant increase in IL-6 (5072±624 vs. 2062±587 pg/ml/g tissue, $p < 0.01$) with further increase after 12h (9290±467 vs. 2313±268 pg/ml/g tissue, $p < 0.01$) as compared to untreated placentas. Furthermore, placental explants at E16 showed a significantly higher IL-6 cytokine response (2-fold) to 12h exposure of 1g/ml LPS as compared to E18 explants.

CONCLUSION: LPS stimulates placental IL-6 cytokine responses with a greater effect at gestational age E16 as compared to E18. These findings suggest that the preterm placenta may be more susceptible to maternal infection-induced placental cytokine response resulting in fetal inflammation.

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43 Sonographic cervical length and hemorrhage in women with placenta previa

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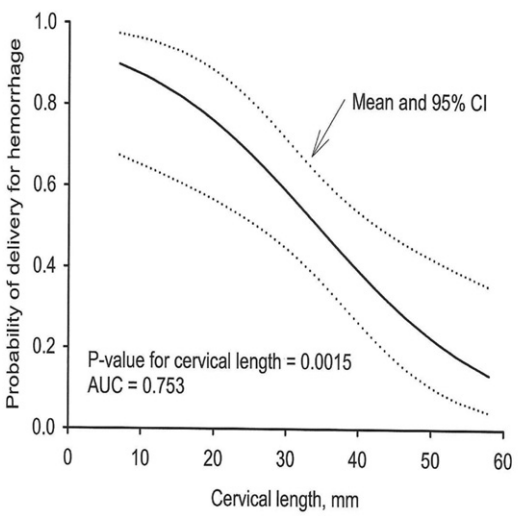
OBJECTIVE: To determine if there was an association between sonographic cervical length and hemorrhage leading to preterm delivery in women with placenta previa.

STUDY DESIGN: Between October 2007 and May 2009, transvaginal cervical length measurements were prospectively measured in all women with singleton pregnancies and placenta previa identified during ultrasound examination 24 weeks. Only women who delivered liveborn or stillborn infants at our hospital and who had previa confirmed at delivery were included. A cervical length 30 mm was considered short and clinicians were blinded to cervical measurements. Chi-square and logistic regression were used for analysis.

RESULTS: Of 105 identified women, 68 had confirmed placenta previa at delivery: 29 (42%) had cervical length 30mm and the remaining were > 30 mm. Gestational age at cervical length measurement was 32.2 +/−4 and 32.9+/−2 weeks respectively, P = 0.44. Women with previa and short cervix were more likely to require delivery for hemorrhage (79% v. 28%, P <0.001) and to deliver preterm (69% v. 21%, P < 0.001). Reports of uterine contractions as well as contractions during tocodynamometry were significantly more common in women with a short cervix (55% v. 13% and 69% v. 21%, respectively, P <0.001). Conversely, 72% of women with cervical length > 30 mm had no bleeding episodes and underwent elective cesarean delivery for placenta previa at term.

CONCLUSION: Sonographic short cervical length was associated with hemorrhage, uterine contractions, and preterm birth in women with placenta previa.

Figure 1. Probability of delivery for hemorrhage according to cervical length in women with placenta previa



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