DOES FIRST-TRIMESTER ULTRASOUND PREDICT OBSTETRICAL AND NEONATAL OUTCOMES IN MONOCHORIONIC DIAMNIOTIC TWIN PREGNANCIES?

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OBJECTIVE: To determine the associations of discordant nuchal translucency (NT) or crown-rump length (CRL) measurements at the time of aneuploidy screening with adverse obstetrical and neonatal outcomes.
STUDY DESIGN: A multicenter, retrospective cohort study in 6 regional perinatal centers in the Northeastern United States from 01/2006 to 06/2010. All monochorionic-diamniotic (MCDA) twin pregnancies with two live fetuses at the 11–14 week ultrasound examination and serial follow-up ultrasonography until delivery were included. Pregnancies with known chromosomal abnormalities or major malformations were excluded. The NT and CRL discordances were calculated as the difference between the two fetuses expressed as a percentage of the larger measurement. Composite obstetrical outcomes included any of the following: IUFD, twin-to-twin transfusion syndrome (TTTS), intrauterine fetal growth restriction (IUGR) or preterm birth ≤ 32 weeks. Composite neonatal outcomes included any of the following: Apgar score < 7 at 5 minutes, respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, early onset sepsis, or neonatal demise. We defined NT discordance as ≥ 20% and CRL discordance as ≥ 15. We also developed our receiver operating characteristic (ROC) curves of NT and CRL discordance cut-offs for the prediction of composite obstetrical and neonatal outcomes.

RESULTS: A total of 166 twin pregnancies met inclusion criteria. Mean first-trimester gestational age was 12.4±0.6 weeks. A 20.5% (n=34) twin pregnancies had NT discordance and 16.2% (n=27) had CRL discordance. Mean (±SD) gestational age at delivery was 34±4.3 weeks. A total of 42 (25.3%) pregnancies were found to have adverse composite obstetrical outcome. Pregnancies with adverse obstetrical outcomes were: TTTS in 12 (7.2%) pregnancies, IUGR in 12 (7.2%) pregnancies, IUFD in 10 (6%) pregnancies and 23 (13.8%) pregnancies with preterm birth ≤ 32 weeks. There was no significant difference in the adverse composite obstetrical outcomes between twins with and without NT discordance (26.1% vs 19.1%; p=0.34) likewise between twins with and without CRL discordance (16.6% vs 16.2%; p= 0.95). Neither ROC curve was discriminating between NT or CRL discordance and the prediction of adverse composite obstetrical or neonatal outcomes.

CONCLUSION: In our population, NT or CRL discordance in monochorionic-diamniotic twin pregnancies was not associated with increase in adverse composite obstetrical or neonatal outcomes.

PREDICTORS OF NEONATAL GROWTH VELOCITY IN EXTREMELY LOW GESTATIONAL AGE NEWBORNS. THE ELGAN STUDY.

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Objectives: We sought to identify maternal and infant characteristics associated with reduced neonatal growth velocity while controlling for confounders in a large cohort of extremely low gestational age newborns.

Methods: The sample included 1187 infants born between 23 and 27 weeks of gestation, at 14 institutions during the years 2002-2004 who survived until day 28 and for whom nutritional information was available for days 7 to 28. Growth velocity (GV), expressed as grams per kilogram per day, was calculated for the interval between days 7 and 28. Caloric intake was defined as mean intake in kcal per kilogram per day on days 7, 14, 21 and 28. We evaluated the likelihood of children being in the lowest quartile for growth velocity and caloric intake in light of maternal and infant characteristics, including neonatal morbidities and treatments.

Results: During the first 28 days of life, newborns with low gestational age, low birth weight, intrauterine growth restriction, and high SNAP-II scores received relatively fewer calories than their peers without these risk factors, but they were not at increased risk of being in the lowest growth velocity quartile. Neither abnormal placenta histologic characteristics nor other pregnancy/maternal characteristics were associated with caloric intake or growth velocity. Newborns with bacteremia, a patent ductus arteriosus, retinopathy of prematurity stage 3-5, and pulmonary illness received fewer calories, as did those who received surfactant, postnatal steroids, analgesics, sedatives, and blood transfusions. In univariable analyses, children with low caloric intake tended to have low growth velocity, when caloric intake and growth velocity were categorized as quartiles and in correlation analysis of continuous variables (both $p<0.0005$). However, in a multivariable model adjusting for confounders, only ventilator-dependence on postnatal day 7 (Odds ratio 2.0, 95% CI 1.3-2.9), early persistent pulmonary dysfunction (1.7, 1.2-2.4), and exposure to dexamethasone (2.6, 1.1-6.5) were associated with an increased risk of being in the lowest GV quartile. In this model, low caloric intake during the first 28 days of life was not associated with low GV (1.3, 0.9-1.9).

Conclusion: Variables associated with severe pulmonary disease, but not caloric intake, appear to be associated with reduced GV during the first 28 days of life.

BODY MASS INDEX-SPECIFIC WEIGHT GAIN IN TWIN PREGNANCIES AND ADVERSE OUTCOMES. Rachel A Billstrom[1*], James Egan[1], Navid Hussain[2], Winston Campbell[1], Alireza A. Shamshirsaz[1]. [1]Department of Obstetrics & Gynecology, UConn, [2]Department of Pediatrics, UConn

OBJECTIVE: The 2009 Institute of Medicine (IOM) "provisional" guidelines recommend BMI-specific weight gain in twin pregnancies. Our objective was to establish new weight gain recommendations for twin pregnancies and association with improved perinatal outcomes. **METHODS:** We performed a retrospective study of twins we delivered from 01/1991-01/2011. We excluded infants with major malformations, monochorionic-monoamniotic twins, monochorionic-diamniotic twins with twin to twin transfusion syndrome, alloimmunization, and fetal demise. We calculated Weight gain rate/week (WGR) by dividing total weight gain in pregnancy by age of gestation (AOG) at delivery. We analyzed pregnancy outcomes [Mean (AOG) at delivery; Preterm delivery <34 and <32 wks, Mean Birth Weight (MBW) and Low Birth Weight (LBW) < 1500 G] by WGR category for BMI groups :(I<18.5: II >18.5<25; III >25<30; and IV>30). We used 25th and 75th percentiles of WGR as the cut off values and divided the study subjects into three categories, ie < 25^{th}, 25^{th}-75^{th}, and > 75^{th}. ANOVA and X^2 analysis was used. **RESULTS:** A total of 452 twin pregnancies (904 infants) were included. Using the prepregnancy BMI, we found 22 (4.9%) who were underweight (Group I), 239 (52.9%) normal weight (Group II), 111 (24.5%) overweight (Group III), and 80 (17.7%) obese women (Group IV). In Group II and III women whose WGR is between 25^{th}-75^{th} had significantly improved outcomes compared with patients who gain weight < 25th percentile (Table 1,2). No differences were noted in Groups I and IV. **CONCLUSIONS:** Twin pregnancies with normal or overweight starting BMIs, whose WGR is between 25^{th}-75^{th} percentiles have better outcomes, including a decreased risk of prematurity and larger birth weights. We propose new weight gain recommendations for twin pregnancies based on percentiles which must be prospectively tested.

	BMI (18.5-24.9 kg/m²) (n=478 infants) Weight change per week (Kg)					
	A	B	C	P-values		
	<=0.38 (n=120)	0.38-0.64 (n=238)	<0.64 (n=120)	AB	AC	BC
Mean Gestational age at delivery in weeks (95% CI)	32.0(31.4-32.7)	34.1(33.6-34.5)	33.4(32.7-34.0)	<.0001	0.0119	0.1559
Preterm delivery <34 w (%)	79(66)	97(41)	57(48)	<.0001	0.011	0.4794
Preterm delivery <32 w (%)	55(46)	55(23)	27(23)	<.0001	0.0004	0.9916
Mean Birth Weight in grams (95% CI)	1659(1543-1775)	2071(1988-2153)	2073(1957-2188)	<.0001	<.0001	0.9997
Low Birth Weight < 1500 G (%)	45(38)	50(21)	24(20)	0.0051	0.0083	0.9753

	BMI (25-29.9 kg/m²)(n=222 infants) Weight change per week (Kg)					
	A	B	C	P-values		
	<=0.32 (n=54)	0.32-0.62 (n=114)	> 0.62 (n=54)	AB	AC	BC
Mean Gestational age at delivery in weeks (95% CI)	31.8(30.9-32.7)	33.5(32.8-34.1)	33.4(32.5-34.3)	0.008	0.035	0.9921
Preterm delivery <34 w (%)	33(61)	60(53)	31(56)	0.5794	0.8807	0.9007
Preterm delivery <32 w (%)	29(54)	32(28)	19(35)	0.0058	0.1218	0.7002
Mean Birth Weight in grams (95% CI)	1619(1434-1803)	2059(1932-2186)	2088(1903-2272)	0.0004	0.0014	0.9643
Low Birth Weight < 1500 G (%)	30(56)	24(21)	13(24)	<0.0001	0.0015	0.932

EARLY NEONATAL WEIGHT LOSS DIFFERS BY MODE OF DELIVERY IN HEALTHY TERM AND LATE PRETERM NEONATES. * Richard M Burwick, MD, MPH[1] and Thomas D Shipp, MD[1]. [1]Obstetrics and Gynecology, Division of Maternal Fetal Medicine, Brigham and Women's Hospital, Harvard Medical School, MA, United States, 02115.

Aims: To determine if early neonatal weight loss is influenced by mode of delivery in healthy neonates born after 36 weeks gestation.

Methods: Through an electronic database we generated a random sampling of 71 women with non-anomalous, singleton gestations, who received prenatal care and delivered at Brigham and Women's Hospital between 1/1/09 to 1/1/10. Neonates were excluded if they were admitted to the neonatal intensive care unit (NICU), delivered prior to 36 weeks gestation, or if they required greater than 3-day stay after vaginal delivery or greater than 5-day stay after cesarean section. Neonatal weight loss was compared by mode of delivery categories including vaginal delivery, cesarean section with preceding trial of labor, and cesarean section without labor. Multivariate regression models were utilized to adjust for confounding factors, including gestational age at delivery, parity, race and neonatal feeding method (exclusive breast vs. any bottle).

Results: Mean (±SD) maternal age was 30.8±6.5yrs, with gestational age at delivery of 39.1±1.2wks and birthweight 3194±435g. At hospital discharge, 41.4% of women were exclusively breastfeeding. Mean neonatal weight loss (percent birthweight/day) was significantly greater after vaginal delivery compared to cesarean section (2.06±1.1%/d vs. 1.42±0.88%/d, p=0.008). However, neonatal weight loss was greater in women who had an elective cesarean section compared to women who had cesarean section following a trial of labor (1.78±0.84%/d vs. 0.88±0.69%/d, p=0.003). Furthermore, 80% of neonates born after elective cesarean section lost ≥5% of their birthweight by the time of discharge compared to only 38.5% of neonates born after cesarean section with preceding labor (p=0.020). In multivariate regression models, this association remained significant even after adjustment for gestational age at delivery, parity, race, and neonatal feeding method (p=0.033).

Conclusions: Among healthy term and late preterm neonates, mode of delivery significantly influences early neonatal weight loss. Neonates born after elective cesarean section lose significantly more weight than those born after a cesarean section with a preceding trial of labor. Further research is warranted to determine if any long-term health benefits or consequences exist.

EARLY VERSUS LATE-ONSET PREECLAMPSIA IN SINGLETON PREGNANCIES: EVALUATION OF MATERNAL CHARACTERISTICS AND ANGIOGENIC MARKERS

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Aims: To evaluate the differences in maternal characteristics and angiogenic markers in women who develop early compared to late-onset preeclampsia.

Methods: We enrolled subjects prospectively from October 2007 to June 2009 at three centers: Brigham and Women's Hospital, Beth Israel Hospital, and Hospital of the University of Pennsylvania. Women were at least 18 years of age, presented for routine prenatal care prior to 15 weeks, and planned to deliver at the enrolling institution. Women with higher-order multiple gestations (triplets or greater) were excluded. The primary outcome of this study was the occurrence of preeclampsia. Preeclampsia was defined according to ACOG criteria. Maternal blood and urine samples were obtained at four visits during the pregnancy: median 10, 17, 24, and 35 weeks gestation. sFlt-1 and PlGF were measured using prototype ARCHITECT immunoassays (Abbott Laboratories, Abbott Park, IL). The PlGF immunoassay measured the free form of PlGF1. Maternal characteristics were compared with the t-test, Chi-square or Fisher's exact test, and with the Wilcoxon Rank Sum test for non-parametric measures.

Results: A total of 2,489 subjects with singleton gestations delivered at 24 weeks or later. 2,048 women did not develop gestational hypertension or preeclampsia. Twenty women developed early-onset preeclampsia (≤34 weeks), and 182 developed late-onset preeclampsia (>34 weeks). Chronic hypertension was the most significant maternal risk factor associated with early-onset compared to late-onset preeclampsia (50% vs 19.8%, p=0.002). Women of advanced maternal age (≥35 years) tended to develop late-onset vs. early onset preeclampsia. Obesity was associated with both early and late-onset preeclampsia (45% vs 46.7%), but this did not reach statistical significance (p=0.88). Tobacco use, race/ethnicity, and assisted reproduction were not associated with early-onset preeclampsia. In regards to serologic markers, women with early-onset preeclampsia had decreased PlGF levels compared to late-onset preeclampsia that were persistent throughout gestation. sFlt-1 increased by 24 weeks gestation (median) in early-onset preeclampsia but not late-onset preeclampsia or non-hypertensive controls.

Conclusions: Our study suggests that women who develop early-onset preeclampsia are no different than women with late-onset preeclampsia in regards to race/ethnicity, BMI, assisted reproduction, and tobacco use. Chronic hypertension was the primary maternal characteristic associated with early-onset preeclampsia. Levels of the angiogenic marker PlGF were significantly lower throughout gestation in early-onset disease, while sFlt-1 levels increased sooner in early vs late-onset preeclampsia. To date, epidemiological studies investigating preeclampsia have not differentiated disease onset by gestational age, but given the major morbidities associated with early-onset preeclampsia, further research is warranted to determine if distinct risk factors exist.

AFRICAN-AMERICAN MULTIPLES AND RETINOPATHY OF PREMATURITY

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Background: Retinopathy of prematurity (ROP) is a potentially blinding disorder and risk factors need to be thoroughly explored. In a previous study, we had found an increased risk for African-American multiple birth infants to develop ROP (crude OR of 3.0, 1.0-8.7).

Objective: The purpose of this study was to find an explanation for this observation.

Methods: From an institutional cohort of 2049 preterm infants with a gestational age <30 weeks or birth weight < 1500 grams, newborns who met criteria for a ROP screening (N=752) were selected for the study population. We explored variables that could be confounders, such as low gestational age, respiratory distress syndrome, and sepsis. We also hypothesized that a shared genetic background might contribute to the increased risk for multiples and simulated the implications of a small African-American sample size.

Results: We were not able to find individual or groups of variables that could explain the increased risk. However, one explanation might simply be the small size of the subgroup of African-American multiples. Gestational age appears to be an effect modifier in that African-American multiples < 26 weeks old did not have an increased ROP risk while those ≥ 26 weeks did. This might be due to a differential mortality rate among African-American multiples (41%) and other populations.

Conclusions: For the time being, we have not yet been able to "fully explain away" the increased ROP risk for African-American multiples.

WEIGHT GAIN IN TERM TWIN PREGNANCIES: *EXAMINING THE 2009 INSTITUTE OF MEDICINE (IOM) GUIDELINES*

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OBJECTIVE: Institute of Medicine (IOM) 2009"provisional" guidelines (IOMG) recommend BMI-specific maternal weight gain in twins. The objective of this study was to estimate whether the weight gain recommendations for term twin pregnancies with normal prepregnancy BMI (18.5–24.9 kg/ m^2) in the 2009 IOM guidelines (17–25 kg for term pregnancy) are associated with improved neonatal weight.

METHODS: We performed a retrospective study at our University Hospital from 1/1/1991 to 1/12011. We excluded infants with major malformations, monochorionic-monoamniotic twins, monochorionic-diamniotic twins with twin to twin transfusion syndrome, alloimmunization, and fetal demise. Neonatal weights were compared between patients whose weight gain less the IOM recommendations and patients who equaled or exceeded the IOM recommendations. We defined the study population as mother-infant pairs. ANOVA and X^2 analysis was used.

RESULTS: A total of 41 twin pregnancies (82 infants) met the inclusion criteria. Patients with normal prepregnancy BMIs whose weight gain met or exceeded IOM recommendations had significantly higher mean birth weight and fewer low birth weight <2500 G compared with patients who gained less weight than the IOM recommendations (Table-1). These were significant even after adjustment for; chronic hypertension; pregestational diabetes; smoking; previous history of preterm labor; type of twin and maternal age.

CONCLUSION: In women with term twins and normal starting BMIs, IOM recommended weight gain, or more, during pregnancy is associated with higher birth weights.

Table 1. Birth weight in term twins with normal prepregnancy BMIs.

	BMI (18.5-24.9) (n=82 infants)		
	Total weight gain (Kg)		P-values
	<17 Kg (n=26)	>=17 Kg (n=56)	
Mean Birth Weight in grams (±SD)	2600(±378)	2777(±328)	0.0327
Low Birth Weight < 2500 G (%)	12(44)	12(21)	0.0267

ABNORMAL ANALYTE PREECLAMPSIA": DO SECOND-TRIMESTER MATERNAL SERUM ANALYTE DIFFERENCES IDENTIFY PREECLAMPTIC PREGNANCIES CHARACTERIZED BY SMALL-FOR-GESTATIONAL-AGE NEWBORNS AND MATERNAL END-ORGAN INJURY?

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Objective: Abnormalities in maternal serum screen analytes have been associated with later development of preeclampsia. As preeclampsia is a clinically heterogeneous disorder, our objective was to determine whether, in women with established preeclampsia, abnormalities in 2nd trimester serum screen analytes can identify pregnancies at risk for small-for-gestational-age (SGA) newborns and maternal end-organ injury.

Study Design: We performed a retrospective cohort study of 102 preeclamptic women (singletons, 2008 - 2011) with available 2nd trimester serum screens. Maternal demographic data, serum analytes (Inhibin-A, MSAFP, hCG & estradiol), pre-delivery laboratory values and newborn data were collected. Pearson and Spearman correlation coefficients and Relative Risks were estimated to measure associations between analytes and clinical outcomes. Chi Square, Fishers Exact Test and Cochran-Armitage Trend Tests were performed as appropriate.

Results: Significant negative correlations were noted between both 2nd trimester Inhibin-A and MSAFP and newborn birth weight %ile ($r = -0.27$, $p=0.006$; $r = -0.22$, $p=0.03$), as well as positive correlations between maternal pre-delivery AST ($r = 0.22$, $p=0.03$; $r = 0.21$, $p=0.04$) and LDH ($r = 0.33$, $p=0.0007$; $r = 0.29$, $p=0.004$). HCG and estradiol were not associated with these outcomes. Patients with 2nd trimester Inhibin-A levels ≥ 2MoM had an increased risk of an SGA newborn (RR 2.0, 95% CI 1.4 – 2.8, $p = 0.0004$). A significant association was noted between an increasing number of abnormal serum analytes and the percentage of patients with an SGA newborn ($p= 0.007$).

Conclusions: Preeclamptic patients with abnormal second trimester Inhibin-A and MSAFP are more likely to have an SGA newborn and evidence of maternal end-organ injury compared to those with normal analyte values. This suggests that "abnormal analyte preeclampsia" likely represents a unique subset of preeclampsia. We hypothesize that such patients have abnormal placentation that manifests as abnormal serum analytes in the second-trimester and later as preeclampsia with poor fetal growth and maternal end-organ injury.

PERMEABILITY PROPERTIES OF CERVICAL MUCUS IN WOMEN AT HIGH RISK FOR PRETERM BIRTH

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Objective: Cervical mucus is an important defensive barrier to ascending infection during pregnancy. Our objective was to study permeability properties of cervical mucus from women at high risk of preterm birth.

Study Design: Cervical mucus samples were aspirated from the external cervical os and flash frozen or used fresh (within 4 hours). Two assays were performed: bead permeability and bioinfectivity. For bead permeability, mucus samples were applied to streptavidin coated glass slides. Biotin-labeled, fluorescent polystyrene microbeads (0.2 micron Fluorospheres, 25,000 beads/well) were applied to the mucus samples. After two hours, beads passing through the mucus and bound to the bottom of the slide were visualized with fluorescence microscopy (10x). Controls included mucus samples from women at low risk for preterm birth. For bioinfectivity, mucus samples (50 µL) were applied to 96 well plates pre-plated with HeLa cells. Human Papilloma Virus (HPV) particles containing green fluorescent protein (GFP) reporter vectors were applied the mucus samples. Virus particles passing through the mucus samples infected the HeLa cells. Infected cells expressed GFP which was detected with flow cytometry.

Results: Mucus samples were collected from 25 women with singleton pregnancies (20 – 34 wks) at high risk (n=11) and low risk (n=14) for preterm birth. Mean volume of cervical mucus obtained was 220 µL. Cervical mucus from high risk subjects showed increased permeability to microbeads compared to low risk subjects (5.8 beads/field vs 2.2 beads/field, $p = 0.03$). The bioinfectivity assay showed no significant difference in GFP expression in HeLa cells exposed to frozen vs fresh cervical mucus (5.3% vs 4.2%, $p=0.3$). Significantly fewer HeLa cells expressed GFP when exposed to mucus compared to buffer (4.6% vs 73.3%, $p = 0.001$).

Conclusions: Our results suggest increased permeability of cervical mucus from women at high risk for preterm birth compared to low risk women. Investigation of cervical mucus permeability properties could improve our understanding of cervical barrier function during pregnancy.

PLACENTAL PATHOLOGIC FINDINGS IN NEWBORNS WITH PERIVENTRICULAR LEUKOMALACIA.

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OBJECTIVE: To determine if there are placental histopathologic abnormalities associated with neonatal periventricular leukomalacia (PVL), a major precursor of cerebral palsy.

METHODS: We reviewed our tertiary neonatal intensive care unit [NICU] database from 1990 to 2010 for neonates with PVL and/or ventriculomegaly (VM). We excluded newborns with major congenital anomalies. Cases were selected from neonates admitted to our NICU between 23-32 weeks and were diagnosed with PVL by head ultrasonography within six weeks of delivery and had a placental pathologic exam by our perinatal pathologist who was blinded to neonatal outcome. Two controls per case were matched by gestational, no neurologic morbidity and had a placental pathologic exam [PPE]. We used Chi square and student "t" test for statistical analysis.

RESULTS: There were 3520 neonates admitted to our NICU. Of these 93 had PVL and 66 [71%] had a PPE. Patient demographics were comparable between the two groups with no significant differences in maternal age, gestational age, race, parity, mode of delivery and neonatal weight percentiles. Placenta pathology findings are shown in Table 1.

CONCLUSION: Periventricular leukomalacia was significantly associated with abruption and maternal vascular lesion- obstructive. We found no association with chronic or acute inflammation. These results suggest those placental maternal circulatory disturbances are associated with the development of PVL in some cases.

Placental findings	PVL Group (n=66)	Control Group (n=132)	P-Value
Placenta weight (g)	362 ± 92	384 ± 62	0.56
Acute maternal inflammation response, n (%)	35 (53.0%)	76 (57.6%)	0.42
Acute fetal inflammation response, n (%)	16 (24.2%)	38 (28.8%)	0.38
Chronic Deciduitis, n (%)	4 (6.1%)	5 (3.6%)	0.058
Fetal circulatory abnormalities, n (%)	5 (7.7%)	9 (6.8%)	0.52
Chronic and acute abruption, n (%)	8 (12.0%)	5 (3.6%)	0.02
Maternal vascular lesion- obstructive, n (%)	44 (66.6%)	64 (48.4%)	0.01

NEONATAL OUTCOMES IN TWIN PREGNANCIES DELIVERED MODERATELY PRETERM, LATE PRETERM, AND AT TERM.

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Objective: To determine neonatal outcomes in twin pregnancies following moderately preterm birth (MPTB), late preterm birth (LPTB), and term birth (TB).

Method and Materials: We retrospectively developed the Twin Pregnancies Perinatal Database (TPPD) in our University hospital for deliveries between January 1, 1991 and January 1, 2011. MPTB was defined as delivery between $32^0/_7$ and $33^6/_7$ weeks, LPTB between $34^0/_7$ and $36^6/_7$ weeks and TB $\geq$ $37^0/_7$. Maternal demographic and pregnancy risk factors were recorded. The short term neonatal outcomes were; respiratory distress syndrome (RDS), early onset sepsis, necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), severe retinopathy of prematurity (ROP), intraventricular hemorrhage (IVH), 5-minutes APGAR score, use of continuous positive airway pressure (CPAP) and mechanical ventilation (MV). Infants with major malformations, monochorionic-monoamniotic twins, monochorionic-diamniotic (Mono-Di) twins with twin to twin transfusion syndrome, alloimmunization, and fetal demise were excluded. Analysis of variance and test for linear trend was used for comparing parametric continuous variables. Nonparametric continuous variables were compared using the Kruskal-Wallis test. **Results:** Of the 747 twin pregnancies in TPPD, 106 (14.1%) were excluded and 188 (25.1%) were less than $32^0/_7$ weeks. Of the 641 twins pregnancies which meet our criteria, 145 (22.6%) were MPTB, 206 (37.1%) were LPTB and 102 (20.9%) were at term. Mean gestational age (±SD) for MPTB, LPTB and TB was 32.9 (±0.2), 35.2 (±0.5) and 37.7 (±0.2) weeks respectively. Maternal age, race, ethnicity, nulliparity, pre-gestational BMI, ending BMI at the time of delivery, percentage of Mono-Di twins, chronic hypertension and diabetes were similar in all three groups. All the short term neonatal outcomes are shown in Table 1. **Conclusions:** Twin pregnancies born moderately and late preterm encounter higher rates of neonatal morbidities compared with twins born at term.

		MPTB (n=290)	LPTB (n=412)	TB (n=204)	p-value
RDS, n (%)		50 (17.2)	33 (8.0)	1 (0.5)	<0.0001
Early Sepsis, n (%)		22 (7.5)	13 (3.1)	1 (0.5)	0.0001
NEC, n (%)		2 (0.6)	3 (0.7)	0 (0)	0.6190
BPD, n (%)		7 (2.4)	5 (1.2)	0 (0)	0.0545
ROP, n (%)		3 (1.0)	0 (0)	0 (0)	0.0439
IVH, n (%)	I&II	3 (1.0)	0 (0)	0 (0)	
	III &IV	1(0.3)	0 (0)	1(0.5)	0.0303
APGAR 5-minutes <7, n (%)		8 (2.7)	7 (1.7)	1 (0.5)	0.1764
MV, n (%)		55 (18.9)	31 (7.5)	2 (1.0)	<0.0001
CPAP, n (%)		109 (37.6)	81 (19.6)	5 (2.4)	<0.0001
NICU admission, n (%)		290 (100.0)	262 (63.6)	17 (8.3)	<0.0001
Median Length of NICU, (range)		20 (4-101)	13 (1-56)	5(2-113)	<0.0001
PVL		0(0)	0 (0)	0 (0)	NA

CHARACTERIZATION OF CORD BLOOD BASOPHILS AND PLASMACYTOID DENDRITIC CELLS IN INFANTS BORN TO ALLERGIC AND NON-ALLERGIC WOMEN

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Background: Maternal allergy is a risk factor for developing allergic disease in children. The cell type(s) mediating this maternal influence remains unclear.

Objective: We sought to determine the influence of maternal allergic status on the relative frequencies of cord blood (CB) basophils and plasmacytoid dendritic cells (pDCs), and to characterize the expression of IgE and FcεRI on these cell types.

Methods: A total of 96 mother/infant dyads were recruited prenatally. Maternal allergic status was determined by questionnaire. Maternal blood was collected prior to delivery and CB was collected immediately after birth. Flow cytometry was used to identify cryopreserved CB basophils and pDCs, and to determine IgE and FcεRI expression. For frequency calculations, CB samples containing a minimum of 100,000 total leukocytes were analyzed. For IgE and FcεRI expression, CB samples containing a minimum of 200 total basophils or pDCs were analyzed. Maternal and CB total IgE levels were determined by Phadia (Thermo Fisher Scientific) ImmunoCap. IgA was measured to detect maternal blood contamination of CB specimens. **Results:** CB basophils and pDCs were enumerated in 24 infants of allergic mothers and 65 infants of non-allergic mothers. There was no difference in the total number or relative frequencies of CB basophils or pDCs based on maternal history of allergic disease. Cellular IgE and FcεRI expression was determined in 14 infants of allergic mothers and 37 infants of non-allergic mothers. CB basophil IgE expression was significantly greater in infants of allergic mothers compared to infants of non-allergic mothers ($p<0.05$). In addition, CB basophil IgE expression correlated strongly with CB IgE levels (rho=0.72, $p<0.001$), and weakly with maternal serum IgE levels (rho=0.37, $p<0.01$). CB pDCs expressed low levels of IgE, which was not influenced by maternal allergic status. FcεRI was expressed by CB basophils and pDCs, however expression was not significantly correlated with CB or maternal serum IgE levels, and was not influenced by maternal allergic status.

Conclusions: The relative frequencies of CB basophils and pDCs are not influenced by maternal allergic status. CB basophils and pDCs express IgE and FcεRI, however only basophil IgE expression appears influenced by maternal allergic status.

ABSENT FETAL NASAL BONE: WHAT DOES IT MEAN FOR THE EUPLOID FETUS?

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Absent nasal bone on prenatal ultrasound (US) is associated with aneuploidy and has been extensively studied. Less information is available on the significance of this US finding once aneuploidy is excluded. Our objective was to review the outcomes of pregnancies where absent nasal bone was noted on 1st or 2nd trimester (TM) US and aneuploidy was not present.

We identified all singleton pregnancies with absent fetal nasal bone at our center from 2005-2011. Absent nasal bone was reported when no calcification was seen below the skin of the nasal bridge in a magnified mid-sagittal view of the fetal head. We excluded cases with aneuploidy. Subsequent US reports were reviewed for anomalies, growth, and amniotic fluid volume. Newborn records were reviewed for physical exams, complications, and radiologic or genetic tests.

We identified 72 fetuses with US appearance of absent nasal bone (25 1st trimester (TM), 47 2nd TM). Of these, we excluded 37 with aneuploidy, 1 with 1st TM fetal demise and 5 were lost to follow up. Of the remaining 29 patients, 21% were African American. In this series, 2/29 euploid fetuses with absent nasal bone on US had an adverse outcome: (1) 17q21.31 microdeletion syndrome, with US findings of abdominal calcifications and short femur, and postnatal exam with a VSD, hypospadius, undescended testes, and a sacral dimple; (2) with multiple malformations on a 2nd TM US resulting in pregnancy termination. The remainder of the fetuses were without anomalies on 2nd TM US or on newborn exam, although echogenic intracardiac focus (N=4), hydronephrosis (N=2) and postaxial polydactyly (N=1) were seen. Fifteen fetuses had normal karyotypes. Fourteen patients declined karyotype but newborn exams were not suggestive of trisomy.

This data provides some reassurance to women with a euploid fetus with an absent nasal bone on US that they can expect a normal physical exam at birth. However, longer follow-up is needed to assess if absent nasal bone is significant or is a marker of developmental delay or subtle syndromes or is a normal variant in the absence of aneuploidy.

FETAL BISPHENOL A EXPOSURE: CONCENTRATIONS OF CONJUGATED AND UNCONJUGATED BPA IN SECOND TRIMESTER AMNIOTIC FLUID

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BACKGROUND/OBJECTIVE: Bisphenol A (BPA) is an estrogenic compound widely used in polycarbonate plastics and many common household products. The placental enzyme B-glucuronidase may deconjugate BPA into its unconjugated or “free” active form, which has estrogenic, endocrine-disrupting properties. There are few data regarding BPA levels in the fetal compartment, and even sparser data regarding conjugated versus free BPA fractions in the fetal compartment. The effects of prolonged exposure of the fetus to the active form of BPA are unknown. Thus, we sought to quantify levels of conjugated and free BPA in second trimester amniotic fluid (AF) specimens to better define the role of the placenta in fetal exposure.

METHODS: Liquid chromatography coupled with mass spectrometry was used to measure BPA concentrations in 20 prospectively-collected second trimester amniotic fluid specimens. Concentrations were quantified using stable-isotope BPA. Free BPA was measured by direct analysis of specimen samples without overnight enzymatic hydrolysis, total BPA was measured after overnight enzymatic hydrolysis. Conjugated BPA concentrations were obtained by subtracting free BPA levels from the total BPA measurements.

RESULTS: Total BPA was detected in 17/20 samples, with levels ranging from non-detectable to 0.75 ng/mL, median concentration 0.45 µg/L. Three samples contained no BPA, 7 samples contained only conjugated BPA. Free BPA was detected in 10/20 samples, and levels ranged from 0.26 to 0.43 µg/L, median concentration of 0.38 ng/mL. When detected, free BPA represented an average of 81% of total BPA measured.

DISCUSSION: Free BPA was detected in the fetal compartment in 50% of second trimester amniotic fluid specimens collected. When free BPA was detected in second trimester amniotic fluid, it comprised 81% of total BPA. Because BPA is quickly conjugated in the adult liver once absorbed, our data suggest that BPA may be deconjugated in the placenta by B-glucuronidase, increasing potential fetal exposure to the active form.

ERBB4-MEDIATED STIMULATION OF SURFACTANT PROTEIN C PRODUCTION IS GAMMA SECRETASE-DEPENDENT

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Background: ErbB4 signaling is important for type II cell surfactant synthesis. ErbB4 may mediate gene expression via canonical signal transduction pathways such as PI3Kinase or through a novel mechanism of receptor cleavage by gamma secretase followed by transport of the intracellular domain to the nucleus where it participates in gene regulation. The active component of gamma secretase is the enzyme Presenilin-1 (PSEN-1). The role of PSEN-1 in regulating SP-C protein production is unknown.
Objective: We hypothesized that knockdown of PSEN-1 in type II cells alters ErbB4-regulated SP-C production.
Design/Methods: We used pre-designed siRNAs (Applied Biosystems) targeting three separate regions of the PSEN-1 mRNA. We investigated changes in SP-C protein production as a function of PSEN-1 knockdown using MLE-12 cells. MLE-12 cells were transfected with different concentrations of a cocktail containing equimolar amounts of the three siRNA sequences targeting PSEN-1 using DharmaFECT 2 (Thermo Scientific) as transfection reagent. Experiments showed an average PSEN-1 mRNA knockdown to 20% of scrambled siRNA controls at 48 hrs at a concentration of 5 nmoles of each siRNA. We then used Western blot analysis to measure SP-C protein following PSEN-1 knockdown. Results were quantified using densitometry, normalized to beta actin as an internal standard, and expressed as % of scrambled siRNA results.
Results: We examined SP-C protein production as a function of the level of PSEN-1 knockdown. An intermediate knockdown of PSEN-1 (to 60% of scrambled control) did not affect the level of SP-C protein. However, when PSEN-1 protein was reduced to $\leq$20% of the scrambled control the level of SP-C protein was reduced to 40% of the scrambled control. The specificity of SP-C effects was checked by assay of GAPDH protein, which showed no significant decrease at the highest level of PSEN-1 knockdown.
Conclusions: Our data support the hypothesis that PSEN-1 activity is a crucial component of ErbB-4 signaling for regulation of SP-C protein production in MLE-12 type II cells. Moderate reductions of PSEN-1 protein are not adequate to produce this effect, suggesting that PSEN-1 cleavage of ErbB4 is a highly active process. We propose a model of ErbB-4 signal transduction involving receptor cleavage followed by nuclear transport of the intracellular ErbB-4 fragment in regulation of surfactant protein synthesis. Supported by NIH HL085648.

ANTENATAL STEROID ADMINISTRATION FOR PRETERM DELIVERIES

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Objective: The Joint Commission has included the administration of antenatal steroids in preterm births as an obstetrical core measure of quality of care. However, little baseline information is available. We evaluated administration of antenatal steroids for patients delivering before 34 weeks at our tertiary care institution.

Methods: From January 2009 to June 2010, there were 178 patients that delivered between 23-34 weeks gestational age (GA). Their charts were reviewed and data collected included parity, race, delivery type, indication for delivery, and steroid administration.

Results: Of the 178 charts reviewed, 102 patients (57.3%) received 48 hours of steroid treatment. Any steroid administration of any duration was noted in 143 patients (80%). When results were separated into weeks GA, the lowest rate of administration was in the 23 week GA group, with only 20% receiving 48 hours of treatment. The highest rate was in the 34 week group, with 88% receiving 48 hours of treatment. Steroid administration of any duration was more evenly distributed with the highest percentage (91%) at 24 weeks GA.

Conclusions: At our facility a significant percentage (19.7 %) of preterm deliveries did not receive antenatal steroids. An even larger percentage (42.7%) of patients did not receive a full 48 hour course of antenatal steroids prior to delivery. Further research in needed to evaluate the reasons eligible patients did not receive antepartum steroids if this is to be a core measure of the quality of obstetrical care.

A COMPARISON OF THE QUALITY OF END-OF-LIFE CARE BEFORE AND AFTER INITIATION OF A NEONATAL PALLIATIVE CARE PROGRAM

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Background: High quality palliative care should be available to newborn infants at the end of life. The American Academy of Pediatrics (AAP) recommends that decisions about the non-initiation or withdrawal of intensive care for neonates be guided by a partnership between the health care team and the parents, and that such decisions be made in the best interest of the infant. The AAP also recommends that pediatric palliative care services be developed and made broadly available, to provide intensive symptom management and promote the welfare of children. Despite published guidelines for the provision of palliative care, little is known about how attempts to put them into practice are perceived by health care providers. **Objective:** The purpose of this study was to evaluate the end-of-life care, specifically symptom management and communication, provided in a neonatal intensive care unit (NICU) before and after initiation of a palliative care program. **Design/Methods:** Of 33 deaths during the study period, 20 deaths occurred before and 13 occurred after program implementation. We administered questionnaires to 208 health care providers (nurses, nurse practitioners and physicians) who cared for these infants during the 72 hours prior to the infant's death. Of the 208 surveys, 152 were returned and 8 were excluded for insufficient data, leaving 144 provider surveys for analysis. **Results:** Shortness of breath was reported more frequently before implementation of the palliative care program than after (37.6% vs 17%; p=0.014). Nurses reported overall poorer parental understanding of discussions post- program implementation (6.7% vs 14.3%; p=0.023). There was no difference in the reporting of pain, agitation or level of symptom management before and after program implementation. The level of agreement among providers caring for the same infant was not different in the pre- and post-program time periods for all questions analyzed. **Conclusions:** The implementation of a palliative care program resulted in minimal differences in staff perceptions of end-of-life care for infants and families in the NICU. Further research should attempt to determine whether this minimal effect arises from the high quality of palliative care present at baseline, an inadequate length of time between program implementation and assessment, or inadequacies in the program itself.

A SILK-BASED INJECTABLE BIOMATERIAL AS AN ALTERNATIVE TO CERVICAL CERCLAGE: AN IN-VITRO STUDY

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Objective: To develop an injectable biomaterial as an alternative to cervical cerclage.

Study Design: Human cervical tissue specimens were obtained from premenopausal gynecological hysterectomies for benign indications. A three part biomaterial was formulated, which consisted of purified silk protein solution (10% w/v) blended with a two part polyethylene glycol (PEG) gelation system. The chemically active PEG gelation system consisted of 4-arm PEG maleimide (10 kDa) and 4-arm PEG thiol (10 kDa). Solution A was PEG maleimide (10% w/v) in silk solution. Solution B was PEG thiol (10% w/v) in silk solution. The two solutions were injected into cervical tissue using a double barrel syringe with a mixing tip and a 20 gauge needle. After injection, the tissue was placed in absolute alcohol for 10 minutes to accelerate beta sheet formation in the silk. The injected tissue was evaluated for mechanical properties and swelling using standardized and validated test protocols performed in triplicate. Controls included uninjected tissues and tissues injected with PEG only. Cytocompatibility was tested with primary human cervical fibroblasts.

Results: Initial gelation of the silk/PEG biomaterial occurred 5 seconds after injection due to cross-link formations between thiol and maleimide functional groups. Further stiffening occurred with silk beta sheet formation. The mean $\pm$ SD increase in tissue wet weight after injection was 17.0 $\pm$ 6.7%. We found the increase of tissue stiffness after injection more than doubled (mean ± S.D. increase in peak force of treated/untreated was 2.6 ±1.4; p=.02, paired Student's t-test). Swelling properties of injected tissue were no different than native tissue controls. However, swelling was significantly increased ($p<0.001$) if silk was not used (PEG only). Cervical cells remained viable for 48 hours when cultured on the biomaterial.

Conclusions: We report a silk-based, biocompatible, injectable biomaterial for potential treatment of cervical insufficiency. Injected cervical tissue was more stiff compared to uninjected controls. Animal studies are needed to assess this biomaterial in-vivo.

IMPROVING CARE DELIVERY TO FAMILIES IN A PERINATAL HOSPICE PROGRAM

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Background: Fetal and Perinatal Palliative Care is an emerging field in Maternal-Fetal Medicine and Neonatology. Although prenatal diagnosis of lethal or life-limiting fetal birth defects has led to an increase in number of elective terminations, there are families who choose to continue the pregnancy. Significant efforts have been made to develop guidelines for providing care to families and infants in these difficult circumstances, with the concept of Perinatal Hospice gaining recognition.

Objectives: (1) To establish a multi-disciplinary Perinatal Hospice Program, with a goal of ensuring consistent, compassionate, and family-oriented care (2) To create a Quality Improvement model to assess process and outcomes

Design/Methods: A Center for Compassionate Care and Perinatal Hospice Program was created in a collaborative manner. A dedicated pool of providers from Maternal-Fetal Medicine, Neonatology, Genetics, Social Work, and Pastoral Care made a pledge to adhere to Program goals, with the aim of providing medical, spiritual, and emotional support to families and infants in Perinatal Hospice Program.

Simultaneously a Quality Improvement study to assess providers' and families' attitudes regarding care and services offered by the Perinatal Hospice Program was undertaken. The quality improvement cycle followed a well-established Plan-Do-Study-Act model (PDSA). A providers' survey and a parental survey were created, with an aim of identifying possible gaps in communication, expectations of care, documentation, referral and admission policies, and assessing the degree of satisfaction with the multitude of services provided within a Program. To our knowledge, this is a first Quality Improvement study in this particular discipline.

Results: We successfully established a Perinatal Hospice Program at Tufts Medical Center. Our multi-disciplinary group developed Perinatal Hospice referral guidelines, communication and documentation templates, delivery protocols, and newborn admission guidelines. Within the PDSA quality improvement model, we established specific goals to be put into action as a result of the project, and developed and pilot-tested both surveys. We are now in the phase of data collection and analysis. The data obtained will guide further improvements within our care delivery model.

Conclusions: The Center for Compassionate Care and Perinatal Hospice Program at Tufts Medical Center has been successfully launched. Quality improvement initiatives are necessary to assess the process and outcomes within the Program, and to develop new standards that might be used as benchmarks in the field of Fetal and Perinatal Palliative Care.

HELPING BABIES BREATHE TRAINING INCREASES NEONATAL RESUSCITATION KNOWLEDGE AMONG MASTER TRAINER CANDIDATES IN ETHIOPIA

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Background: Helping Babies Breathe (HBB) is an evidence-based neonatal resuscitation education curriculum designed for low resource settings. Insufficient data currently exist describing the impact of HBB on transfer of knowledge and skills in high priority areas

Objective: We hypothesized that a national-level training program in Ethiopia would improve knowledge of key concepts and practices. We also wanted to identify other factors associated with successful training in this setting.

Design/Methods: Data were collected from 4 training sites across Ethiopia in September 2010. National HBB master trainer candidates completed a 10-question multiple choice questionnaire (MCQ) before and after a 2 day HBB course. After training, learners were assessed on bag-mask ventilation (BMV) skills using a validated checklist and completed a questionnaire describing their professional background. Mean pre and post-test scores were determined for each site and compared with Wilcoxon signed rank sum testing. ANOVA was used to determine if results varied by profession or by trainer:trainee ratio.

Results: Data were available for 69 participants. Significant improvement in newborn resuscitation knowledge was found, with an increase in mean pre- vs. post-training MCQ scores from 8.7/10 (SD 1.4) to 9.4/10 (SD 1.1; p=0.003). There were significant differences between physicians, nurses, and health officers in pre-test scoring (p=0.003), with physicians scoring highest. Knowledge differences disappeared post-training (p=0.21). Post-testing MCQ scores indicated differences between sites with scores increasing as trainer:trainee ratio decreased (p=0.004). The mean post-HBB BMV score for trainees was 5.7/7 (SD 1.6). Trainer:trainee ratio did not significantly impact BMV score. Over 1/3 of participants missed 2 BMV skills related to improving ventilation if poor chest rise - clearing secretions and squeezing the bag harder. Nearly all participants (90%) adequately demonstrated a facial seal with the mask, ventilation at an appropriate rate, and checking for chest rise.

Conclusions: A two-day HBB national training session led to improved knowledge of neonatal resuscitation among Ethiopian master trainer candidates. Lower trainer:trainee ratio was associated with increased post-course MCQ scores. HBB appears to eliminate baseline differences in neonatal resuscitation knowledge in different health care worker cadres.

SELECTIVE ARTERIAL EMBOLIZATION AS AN ADJUNCT TO BALLOON TAMPONADE FOR POST-PARTUM HEMORRHAGE

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Objective: We sought to evaluate the benefits & morbidity of selective arterial embolization (SAE) at time of balloon tamponade for postpartum hemorrhage (PPH).

Methods: This was a retrospective cohort study of 81 women who had a postpartum hemorrhage controlled with balloon tamponade between 1/2007 and 12/2010 at a single tertiary care center. 28 women who underwent immediate SAE were compared to the 53 who were expectantly managed. Our primary outcome was febrile or major non-febrile morbidity. Secondary outcomes included recurrent hemorrhage, ICU admission, or prolonged hospitalization.

Results: Women who did or did not undergo immediate SAE were similar in terms of demographics, mode of delivery, and cause of hemorrhage. Thirty percent of SAE patients had evidence of arterial extravasation on angiogram, but all underwent embolization. Those having SAE were more likely to be coagulopathic (89.3% vs. 54.7%, p=<0.01) and received more blood products (12 units vs. 5, p = <0.01). Women who underwent SAE experienced increased morbidity; 44% vs. 25% of patients had a fever (RR=1.78, 95% CI=0.84-3.74) and 28% vs. 4% had a non-febrile complication (RR=7.57, 95% CI=1.72-33.27). These results did not change after controlling for number of transfused units, coagulopathy, or mode of delivery. There were no differences in recurrent hemorrhage (7% vs. 5.6%, p=0.99).

Conclusion: Use of arterial embolization in addition to the balloon did not improve success in prevention of further hemorrhage and was associated with increased morbidity. We recommend early and active transfusion at initial presentation of major hemorrhage, and judicious use of concomitant SAE.

CUE BASED FEEDING: A LOOK AT ATTAINMENT OF FULL ORAL FEEDING FOR THE VERY LOW BIRTH WEIGHT INFANT. Carol M. Ilzarbe, M.D.*,[1] Nicole Grady, M.D.*, [1] and Elisabeth McGowan, M.D. [1]
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OBJECTIVE: Cue Based Feeding (CBF) is a clinical pathway for determining oral feeding readiness based on the infant's ability to organize autonomic, motor and behavioral state systems as assessed by a bedside nurse. We hypothesize that very low birth weight infants (VLBW, birth weight less than 1500 grams) fed according to this more neurodevelopmentally, infant-driven CBF approach, reach full oral feeds sooner compared to VLBW infants fed via a traditional, physician driven feeding regimen.

METHODS: This is a retrospective cohort study of VLBW CBF infants vs. historic controls (traditionally fed infants). CBF infants were eligible for study after the completion of NICU-wide CBF nurse training followed by a 4 month "start-up" period. The primary outcome was the time to attain full oral feeds, defined as when the nasogastric feeding tube was successfully removed. Excluded were infants with congenital anomalies, craniofacial abnormalities or genetic disorder that would affect oral feeding skills, g-tube fed infants and those transferred to Level 2 nurseries before full oral feeds were obtained. Charts were reviewed for all clinical data. IRB exemption was obtained.

RESULTS: Thirty-nine infants (n= 27/132 control and n=12/93 CBF infants) were studied. Gender, birth weight and gestational age were not different between groups. Controls spent more days on the ventilator and had more late onset sepsis than CBF infants (median 3.0d vs 1.5d, p=0.03 and 48% vs. 1%, p=0.03). CBF infants attempted their first PO feed at an earlier postmenstrual age (PMA) and successfully reached full PO feeds at an earlier PMA than traditionally fed infants (mean 34 2/7 weeks vs. 35 3/7 weeks, p=0.11 and mean 37 weeks vs. 38 3/7 weeks, p=0.39), however, it took longer for the CBF group to attain this goal (19 days vs. 15 days, p=0.11).

CONCLUSIONS: The above results show trends of CBF starting and attaining full feeds at an earlier PMA, but only a small number of CBF infants have been enrolled to date. Therefore these results must be interpreted with caution. Further study with larger numbers of infants are needed.

DETECTION OF C-REACTIVE PROTEIN IN NEONATAL SALIVA AND ITS CORRELATION TO SERUM LEVELS

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Background: Noninvasive measurement of C-Reactive Protein (CRP) levels could significantly improve neonatal care. To date, there are no published data regarding the presence of CRP in neonatal saliva or its relationship to serum concentration levels.

Objective: To determine if CRP is detectable in neonatal saliva and, if so, is representative of serum concentrations.

Design/Methods: Neonatal salivary samples (n=18; post-conceptual ages: 32 - 50 weeks; weight: 1.0 - 4.7 kg) were collected at the time of clinically indicated blood sampling for the measurement of serum CRP levels. Saliva samples were stabilized in a protease inhibitor (SigmaFAST™) and RNAprotect saliva (QIAGEN™) solution and stored at – 80°C pending further analysis. Salivary CRP levels were determined with the MesoScale Discovery™ CRP electrochemiluminescence immunoassay and normalized based upon total protein levels in each sample. Serum CRP levels were determined by hospital laboratory protocol. Pearson correlation analysis calculated the relationship between salivary and serum CRP concentrations.

Results: Salivary volumes ranged from 5 to 10 uL with total protein concentrations ranging from 0.53 to 6.32 mg/mL. CRP was detected in 17/18 (94%) of salivary samples. Mean CRP concentration levels for normalized saliva and serum were 0.14 mg/L and 103 mg/L, respectively. The correlation coefficient between serum and salivary CRP concentrations was 0.44 ($p = 0.065$).

Conclusions: CRP is detectable in small volumes of neonatal saliva via a noninvasive method and can be correlated to serum CRP levels. Using saliva as an alternative to serum sampling warrants further study.

NEONATAL OUTCOMES IN MONOAMNIOTIC-DICHORIONIC TWINS WITH COMPARISON OF AMNIOTIC FLUID ASSESSMENT TECHNIQUES

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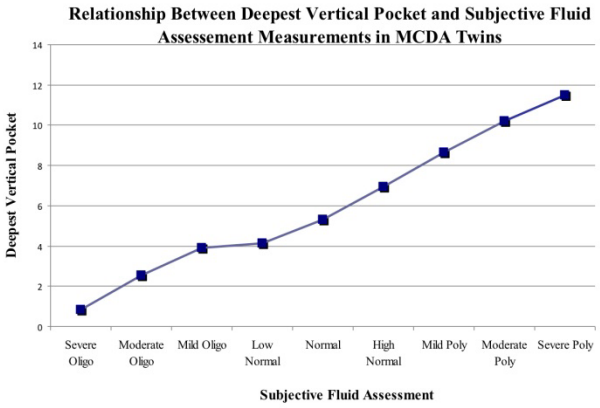
OBJECTIVE: Assessment of amniotic fluid volume in monochorionic diamniotic (MCDA) twins is a key element of antepartum surveillance. Multiple techniques exist, but it is unknown which, if any, best correlates with neonatal outcomes. Over diagnosis of fluid abnormalities can result in unnecessary monitoring, while under diagnosis may result in adverse outcomes. We compared deepest vertical pocket (DVP) to subjective fluid assessment (SFA) to determine which is superior in identifying pregnancies at risk of poor outcome.
STUDY DESIGN: We reviewed all MCDA pregnancies at a single institution from 1/2009 - 4/2011. 89 non-anomalous pregnancies with 2 live fetuses at 16 weeks were identified, with a total of 740 scans. ANOVA analyses were performed to confirm correlation between DVP and SFA. Neonatal outcomes including demise, GA at delivery, birth weight, APGAR <5, need for fetal intervention, and growth discordance were evaluated in relation to oligo- or polyhydramnios diagnosis by either technique at three time points (18-22 wks, 24-26 wks, and last scan prior to delivery), using Wilcoxon rank-sum and Fisher exact tests. Not all patients had both measurements at all time points.

RESULTS: ANOVA analysis demonstrated that SFA was able to detect subtle variance in DVP ($p<0.001$) [Fig. I]. There was a trend towards more oligo diagnoses with SFA. When oligo was diagnosed by SFA but not DVP at 18-22 wks, median GA at delivery and birth weight were higher (34.6 vs 24.8 wks, $p=0.012$, and 1913 vs 928 gms, $p=0.023$). Rates of growth discordance throughout gestation were not significantly higher with SFA diagnosis of oligo compared to DVP alone. [Table I] Outcomes of pregnancies with polyhydramnios by SFA or DVP were similar.

Neonatal outcomes when oligohydramnios is diagnosed by subjective or objective criteria

	GA 18-22 WEEKS (N = 57)			GA 24-26 WEEKS (N = 52)			LAST US PRIOR TO DELIVERY (N = 53)		
Outcome	Subjective (N=12)	DVP (N=6)	p-value	Subjective (N=9)	DVP (N=4)	p-value	Subjective (N=8)	DVP (N = 3)	p-value
5 minute Apgar < 5	1	2	NS	0	1	NS	**0**	**0**	NS
Birthweight median/IQR	1913 (1644–2379)	928 (566–1219)	**0.0233**	1913 (1644– 2143)	1020 (758– 1219)	NS	1849 (1481– 2115)	1945 (1575– 2315)	NS
GA at delivery median/IQR	34.6 (31.9 – 36.3)	24.8 (19.0 – 30.7)	**0.0124**	33.7 (33.0 – 34.9)	28.5 (25.3 – 31.4)	NS	34.3 (32.7 – 35.5)	32.9 (32.7 – 33.1)	NS
Growth discord > 15%	5	1	NS	7	2	NS	5	1	NS
Growth discord > 25%	3	1	NS	5	2	NS	5	0	NS
Fetal intervention	4	4	NS	3	3	NS	1	0	NS
Demise	1	1	NS	0	0	NS	0	0	NS



CONCLUSIONS: SFA appears to increase diagnosis of oligohydramnios among MCDA twins as compared to DVP. DVP oligohydramnios was associated with worse neonatal outcomes when seen at 18-22 wks GA. SFA may better identify those fetuses at risk for growth discordance, but a larger cohort will be necessary to confirm this finding. These data add to our understanding of fluid assessment in MCDA twins.

EFFECTS OF PRENATAL MATERNAL EXPOSURE TO AMBIENT BLACK CARBON AND STRESS ON FETAL GROWTH IN AN URBAN COHORT

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Background: While studies link ambient air pollution and psychological stress exposures in pregnant women to adverse birth outcomes, the extent to which air pollution impacts fetal growth independent of stress is unknown.

Objective: To examine associations among black carbon (BC), a surrogate of traffic-related particles, prenatal stress and fetal growth.

Design/Methods: Analyses included 864 mother-infant pairs enrolled in the Asthma Coalition on Community, Environment and Social Stress (ACCESS) pregnancy cohort. BC levels were estimated using a validated spatial-temporal land-use regression model based on residence and averaged over pregnancy. Mothers completed the Crisis in Family Systems-Revised survey of life events across multiple domains (e.g., financial, violence, racism) reporting negative life events (NLE's) experienced during pregnancy. Domains of negative events were summed to create a NLE score (range 0-9); stress was categorized as low (NLE's 0-2) and high (NLE's ≥3). We determined birth weight for gestational age (BWGA) z-scores using US national reference data to index fetal growth. Outcomes were (1) the BWGA z-score and (2) small for gestational age (SGA) status defined as a z-score <10th percentile. Linear and logistic regression was used to examine independent effects of BC and NLEs entered concurrently in the models predicting fetal growth adjusting for gender, maternal education, race/ethnicity, and prenatal smoking.

Results: Median (interquartile range, IQR) birth weight was 3.3 kg (2.9-3.6); 52% of mothers were Hispanic and 33% were Black; 66% reported ≤12 years of education. Mean (SD) BC was 0.43 (0.33) μg/m3 and 41.6% reported high NLEs. In unadjusted analyses, both higher BC exposure (estimated for each IQR increase) (-0.14, 95% CI: -0.2, -0.08) and increased stress (-0.22, 95% CI: -0.39, -0.04) were associated with lower BWGA z-scores. In fully adjusted models, the change in BWGA z-score remained significant for each IQR increase in BC exposure (-0.13, 95% CI: -0.18, -0.06) but not for increased stress (-0.17, 95% CI: -0.39, 0.05). In the adjusted logistic model, mothers with BC levels above the mean had higher odds of delivering a SGA infant (OR 1.6, 95% CI: 1.13-2.12).

Conclusions: Higher level exposure to traffic-related air pollution during pregnancy was associated with poorer fetal growth, independent of prenatal stress and other important confounders.

PREGNANCY DISORDERS APPEAR TO MODIFY THE RISK FOR RETINOPATHY OF PREMATURITY ASSOCIATED WITH NEONATAL HYPEROXEMIA AND BACTEREMIA

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Background: The pregnancy disorders that lead to preterm delivery can be classified into two broad groups: inflammation-associated (preterm labor, prelabor premature rupture of membranes, placental abruption, and cervical insufficiency) and placental dysfunction (preeclampsia and fetal indication/intrauterine growth restriction). The complex relationships between these disorders and ROP have yet to be explored.

Objective: To explore (1) to what extent extremely low gestational age newborns exposed to inflammation-associated pregnancy disorders differ in their risk of retinopathy of prematurity (ROP) from their peers exposed to pregnancy disorders associated with placental dysfunction, and (2) to what extent exposure to either type of pregnancy disorder modifies the known risk for ROP associated with postnatal hyperoxemia and bacteremia.

Methods: The sample for this study consisted of 1,199 infants born during 2002-2004 before 28 completed weeks of gestation at one of 14 institutions in 11 U.S. cities, who were examined routinely for ROP beginning at 31-33 weeks post-conceptional age.

Results: In multivariable analysis, none of the pregnancy disorders was associated with an increased risk for ROP. However, preterm prelabor rupture of membranes and placental abruption were associated with a reduced risk of plus disease (Odds ratio = 0.4, 95% confidence interval: 0.2-0.8) and prethreshold/threshold ROP (0.5, 0.3-0.8), and for prethreshold/threshold (0.3, 0.1-0.7) and any ROP in zone I (0.2, 0.1-0.8), respectively. In stratified multivariable analyses, exposure to both neonatal hyperoxemia and bacteremia was associated with much higher risks for plus disease (17, 2.3 – 130), zone I ROP (11, 1.6-68), and prethreshold/threshold ROP (37, 4.5-299) among infants born after placental dysfunction than in the stratum of infants born after inflammation-associated pregnancy disorders.

Conclusion: Among ELGANs, pregnancy disorders modify the increased relative risk for ROP associated with postnatal hyperoxemia and bacteremia.

RETINOPATHY OF PREMATURITY IN THE DOMINICAN REPUBLIC: CHALLENGES TO SCREENING AND PREVENTION

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Background: Retinopathy of prematurity (ROP) is a common cause of blindness in preterm infants throughout the world. Of the 50,000 children worldwide who are blind from ROP, almost half of them live in Latin America and the Caribbean. Current screening criteria capture the vast majority of infants with ROP in industrialized countries, however a substantial number of high-risk infants could be missed if adopted in developing countries.

Objective: To determine the incidence of retinopathy of prematurity (ROP) in an intensive care nursery in the Dominican Republic, and to identify factors that impact ROP outcomes, screening, and treatment.

Study Design: A database analysis was performed. The database was prospectively created by the pediatric ophthalmologist in a major public maternity hospital in Santo Domingo, Dominican Republic during 2009. From January 2009 - December 2009, all infants (n=234) who met criteria for ROP screening and who received at least one ophthalmology examination were included.

Results: Overall, 22% were diagnosed with ROP and 4.3% had severe disease. Infants with ROP had a mean birth weight of 1452g and a mean gestational age of 31 weeks, with 35% having a gestational age >32 weeks. In multivariable regression, only gestational age remained significant (0.8, 0.68 - 0.95). Approximately 22% of infants diagnosed with ROP did not complete all screening procedures.

Conclusion: There are many challenges to preventing and treating ROP in the Dominican Republic as well as in other developing countries. Increased awareness of the detrimental effects of hyperoxia, broader screening criteria, and an improved screening program will help to reduce visual impairment from this disorder.

FOLLOW-UP TESTING OF FIRST TRIMESTER PATIENTS WHO SCREEN POSITIVE FOR TRISOMY 21

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Objective: To estimate the frequency of follow-up testing for patients whose first trimester [FT] aneuploidy screen for trisomy 21 [T-21] was positive.

STUDY DESIGN: We retrospectively developed the Central Connecticut Perinatal Database (CCPD) of all singleton pregnancies seen in our ultrasound units between 10/1/06-1/01/10 for first trimester aneuploidy screening [11-1/7 - 13-6/7 weeks]. FT aneuploiody risk was based on maternal age, NT, PAPP-A, and beta-hCG. FT screening risk was presented to the patient by a genetic counselor or obstetrician, and follow-up options were reviewed. Second- trimester risk assessment, was based on combination of FT screen plus second trimester serum markers [AFP, hCG, unconjugated estriol, and inhibin-A]. Second trimester genetic sonogram, was performed between15-0/7 and 22-6/7 weeks. First and second trimester ultrasound exams were performed by accredited sonographers and maternal fetal medicine physicians.

Results: A total of 12,218 women underwent FT screening in our ultrasound units of which 773 (6.3%) were screen positive for T-21. Of the 773 women who were FT screen-positive, 497 (64.3%) had both second trimester serum markers and genetic sonogram, 92 (11.9%) had only a genetic sonogram, 64 (8.3%) had only second trimester serum markers, 69 (8.9%) had invasive testing (CVS and amnio) and 51(6.6%) had no more testing. Of the women who chose to have second trimester serum markers and genetic sonogram (n=497), 334 women (67.2%) became screen-negative on their second trimester serum analyte test and 58 women (11.6%) underwent invasive testing and. The net number of women who had invasive testing (CVS and amnio) was 127 (16.4%).

Conclusions: The majority of women (64.3%) with a positive FT screen for trisomy 21 prefer to have non-invasive second trimester follow-up evaluation and fewer (16.4%) chose invasive tests. This data may be helpful to better counsel women who are screen-positive for T-21 from their first trimester aneuploidy screen.

THE EFFECT OF THE INFANT HEALTH AND DEVELOPMENT PROGRAM ON NEED FOR SPECIAL EDUCATION AND THERAPEUTIC SERVICES AT AGE 6.5 YEARS

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Objectives: The aim of this study is to evaluate the effect of participation in an intensive early intervention program for infants with low birth weight (LBW) on need for special education and physical and occupational therapy services at early school-age.

Methods: The Infant Health and Development Program included home visits, child development center attendance, and parent support groups for infants <2500 gram birth weight. A multi-site, randomized trial compared this intensive program to usual pediatric care. We fit logistic regression models to assess program impact on the need for special education, remedial math, remedial, physical therapy (PT), and occupational therapy (OT) at age 6.5 years. We also tested for effect modification by key covariates.

Results: Of the 985 infants in the original sample, 853 participated in 6.5 year follow-up. Fifteen percent (132) needed special education, 7% (63) remedial math, and 11% (98) remedial reading, while 4% (38) needed PT and 5% (41) OT. Compared to controls, the intervention group was half as likely to need remedial reading (OR 0.62, 95% CI 0.39, 0.99), while twice as likely to need PT (Or 2.11, 95% CI 1.08, 4.12) or OT (Or 1.91, 95% CI 0.99, 3.68). There was no evidence for effect modification by birth or demographic variables.

Conclusion: Our finding of decreased odds of needing remedial reading assistance is consistent with improved cognitive scores at 3 and 5 years in the intervention group. The increased need for therapeutic services at age 6.5 is surprising. This finding likely reflects the effects of the intervention on raising parental awareness of their child's risk for developmental delays and enhancing parental advocacy skills.

DOES OBTAINING AN ULTRASOUND ESTIMATED FETAL WEIGHT NEAR TERM INCREASE THE RISK OF CESAREAN DELIVERY?

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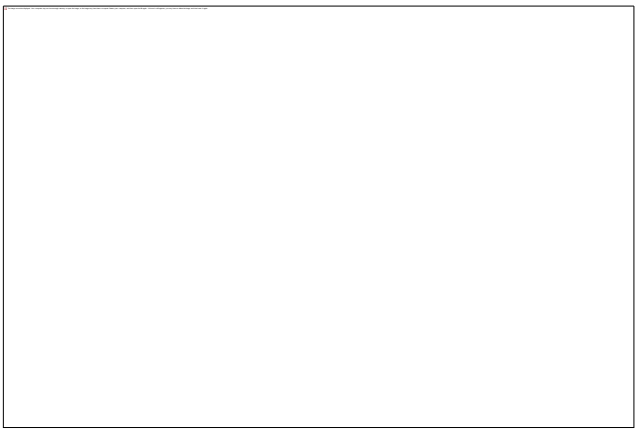
OBJECTIVE: As ultrasound becomes increasingly accessible, indications for obtaining a study become ever more broad. It is unknown what impact knowledge of estimated fetal weight (EFW) has on practice patterns. We hypothesized that having an EFW near term may lead to changes in provider and/or patient behavior that could result in a higher rate of cesarean section (CS).

STUDY DESIGN: We performed a retrospective cohort study of 2345 non-diabetic women undergoing a trial of labor at 39+ weeks who delivered at a single tertiary care center in 2009-2010. Wilcoxon, chi-square and logistic regression were used to evaluate whether EFW within 1 month of delivery was an independent risk factor for CS.

RESULTS: 49.8% of our cohort had an EFW within 1 month of delivery. The most common indications for ultrasound were growth assessment (32%), postdates (20%) and AMA (16%). Women with an EFW were significantly older (30 vs. 27), more likely to be delivered by an MD vs. CNM (65 vs. 44%), and more likely to be Caucasian (43 vs. 25%). There were no differences in gestational age (avg 40 wks), nulliparity (avg 49%), or birthweight (avg 3373g). EFW was more common in women with a CS (Figure) and women with an EFW were significantly more likely to have a CS or induction of labor (Table). In logistic regression, EFW was an independent risk factor for CS(OR 1.7; CI 1.3-2.1). When looking at only EFWs > 3500g this association was stronger (OR 2.9; CI 2.1 - 4.0). Even in a low risk subset (excluding those delivered for fetal or maternal indictions) this association remained significant (OR 1.6; CI 1.2-2.2).

CONCLUSION: In our population, ultrasound EFW within 1 month of delivery significantly increased the risk of cesarean section independent of age, race, parity, provider group or birthweight. This elevated risk held true in a low risk subset of women and was even stronger if the EFW was > 3500 grams. Avoiding unindicated ultrasound assessments of EFW at term may contribute to lowering the cesarean delivery rate.



CESAREAN DELIVERY BEFORE 35 WEEKS: DOES TYPE OF UTERINE INCISION AFFECT OUTCOME?

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Objective: The primary purpose of this study was to determine neonatal and maternal outcomes by cesarean section incision type in early preterm deliveries. As part of these outcomes we also elected to determine length of time from incision to birth based on incision type.

Materials and Methods: This retrospective chart review was based on a cohort of preterm singleton gestations between 23 and 34 weeks, delivered by cesarean at our institution from 2001-2009. We evaluated uterine incisions as four types: low transverse, low vertical, classical, and J or T incision. The distribution of various maternal and neonatal outcomes was stratified by type of uterine incision as well as difficulty of cesarean extraction. Multivariable logistic regression assessed the effect of type of incision on various maternal and neonatal outcomes.

Results: Out of the 773 singleton cesarean deliveries, low transverse incision was the most common type of incision (75.8%) but 2.2% of these incisions required a cephalad extension of the original incision ('J' or 'T' type of incision). Classical incisions were required in 17.3% of cesarean deliveries. In a multivariate analysis, low vertical incision was associated with a higher risk of receiving a blood transfusion; all other maternal and neonatal outcomes were shown to be non-significant.

Conclusion: We found no significantly increased risk for immediate maternal morbidity related to classical cesarean section, but we also could not demonstrate a clear neonatal advantage. Since there remains the risk for uterine rupture in future pregnancies we believe strategies need to be developed through prospective studies, to assess the safety of decreasing the incidence of classical cesarean section.

EFFECT OF SYSTEMIC INFLAMMATION ON HIPPOCAMPAL VOLUME IN NEWBORN MICE: AN MRI-BASED STUDY.

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Background: Perinatal infection and inflammation are important in the pathogenesis of preterm delivery and brain damage. The inflammatory process can continue postnatally and further contribute to brain injury. Premature infants have grey and white matter damage and reduced hippocampal volumes which correlate with deficits in working memory later in life. The hippocampus plays a role in recovery after brain injury. Intraperitoneal (IP) lipopolysaccharide (LPS) administration to newborn mice has been used as a model for systemic inflammation. The effect of sustained systemic inflammation on the developing brain with a focus on the hippocampus has not been clearly defined.

Objective: Test the Hypothesis that daily IP administration of LPS between postnatal day 3 and 13 is associated with brain injury and reduced hippocampal volume in juvenile mice.

Methods: C57BL6/J mouse pups received daily IP injections of 0.3µg/gram LPS (E. coli 055:B5, Sigma; 5 litters) or saline (4 litters) between day 3-13. Brains were harvested on day 14 and fixed in 4% paraformaldehyde. Four random whole brain samples from each group were suspended in 2% agarose and non-enhanced coronal T2-MRI images with an in plane resolution of 27µm were obtained. Crysel Violet stained 30µm coronal tissue sections obtained at the level of the third ventricle from three samples in each group were also compared. The hippocampal region in each image was manually demarcated and its area measured using Image J software (rsb.info.nih.gov/ij). Brain weights, hippocampal volumes and areas were compared between the two groups by t-test.

Results: 18/22 pups in the control and 17/34 pups in the LPS group survived to day 14 ($P<0.05$). The average brain weight was reduced by 16%, and hippocampal volume by 20% in the LPS compared to the control group on day 14 ($P<0.01$). Microscopic analysis of the hippocampal region on matching tissue sections confirmed the reduction in hippocampal volume seen on MRI.

	Control	LPS	P-value
Brain weight* (g)	0.37 ± 0.01	0.31 ± 0.01	P<0.01
Hippocampal volume on MRI* (mm^3)	9.42 ± 0.17	7.53 ± 0.46	P<0.01
Hippocampal area in tissue sections* (mm^2)	8.33 ± 0.19	5.15 ± 0.39	P<0.01

*Mean ± SEM

Conclusions: Systemic inflammation sustained during the early postnatal period was associated with reduced brain weight and hippocampal volume in newborn mice. We speculate that injury to the hippocampus from perinatal inflammation will have important implications in newborn infants that contribute to neurodevelopmental impairment.

IMPACT OF APPLYING THE 2010 CDC PREVENTION OF PERINATAL GBS DISEASE GUIDELINES

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Background: Despite the use of intrapartum antibiotic prophylaxis (IAP) to prevent neonatal Group B Streptococcal (GBS) disease, GBS remains the most common cause of EOS among term infants. CDC issued guidelines for evaluation of newborns at risk for GBS EOS in 1996, 2002 and 2010. The 2010 revision refines criteria for evaluating infants born to GBS-colonized mothers with inadequate IAP.

Objective: To determine the frequency of EOS evaluations for inadequate IAP among asymptomatic infants born ≥ 36 weeks gestation; and to measure differences in costs, comparing time periods during which either the 2002 or the 2010 CDC GBS guidelines were followed.

Design/Methods: Retrospective study of asymptomatic infants born at ≥36 weeks evaluated for EOS. We compared evaluations during 5-month time periods in 2009 and 2011, before and after our local algorithm for EOS evaluation was revised based on the CDC 2010 guideline. A retrospective economic evaluation was performed to determine the cost difference between periods.

Results: During the study period, 6504 eligible infants were born; 662 infants were evaluated for EOS (102/1000). The incidence of EOS among the study population was 0.62/1000. The frequency of evaluation for inadequate IAP decreased from 33/1000 in 2009, to 3/1000 in 2011 ($p < 0.0001$.). The decrease in evaluations for inadequate IAP resulted in a decrease in overall EOS evaluation-associated costs ($27883.06 vs $2434.64).

Conclusions: Implementation of an EOS evaluation algorithm based on the CDC 2010 guideline significantly decreased resource utilization and costs. These findings may assist hospitals with anticipated staffing needs and resource allocation as they transition to the revised recommendations.

COMPARISON OF TWO PROTOCOLS FOR ULTRASOUND MARKERS IN DOWN SYNDROME SCREENING BY THE GENETIC SONOGRAM

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OBJECTIVE: To compare two protocols for ultrasound markers in Down syndrome (DS) risk modification by genetic sonogram.

METHODS: We retrospectively developed a Central Connecticut Perinatal Database (CCPD) of all singleton pregnancies seen in our ultrasound units between 03/1/05-1/01/2010 for first trimester screening [11-1/7 - 13-6/7 weeks], second trimester serum markers and follow-up genetic sonogram [15-0/7 - 22-6/7 weeks]. Midtrimester DS risks were estimated for stepwise sequential screening. We evaluated the performance of six minor markers (pyelectasis, increased nuchal fold, echogenic intracardiac focus, echogenic bowel, short femur and short humerus) and the presence of at least one major fetal structural malformation. Likelihood ratios from Aagaard-Tillery (Obstet Gynecol. 2009 Dec; 114(6): 1189-96) and Nyberg (Ultrasound Obstet Gynecol 1998; 12:8–14) were used to generate new risks. Detection rate (DR), false-positive rate (FPR), odds of affected fetus given a positive result (OAPR), positive predictive value (PPV) and receiver operating characteristic (ROC) curves were performed for each screening protocol before and after genetic sonogram risk modification.

RESULTS: There were 14,579 singleton pregnancies in the CCPD with first trimester screening of which 6,288 patients fulfilled our study criteria, including 17 with DS. The area under the ROC curve (AUC) of stepwise sequential with genetic sonogram for Aagaard-Tillery protocol was 0.952 and for the Nyberg protocol was 0.951. Comparison between two protocols for a DS risk $\geq$ 1:270 are shown in table 1.

CONCLUSION: Likelihood ratios for ultrasound markers in genetic sonography from the Aagaard-Tillery and Nyberg protocols yielded very similar results for the detection of Down syndrome. Centers using either protocol may expect comparable efficacy.

Table 1: Comparison of two protocols for likelihood ratios in genetic sonography at a DS risk $\geq$ 1:270.

Protocol	DR (n/N),SEN %	FPR (%)	PPV (%)	OAPR 1:X
Aagaard-Tillery	14/17, 82.4	4.2	5.0	18.8
Nyberg	14/17, 82.4	4.7	4.5	20.2

n= #DS detected, N= total # of DS, SEN= sensitivity (%)

ROLE OF THE SECOND-TRIMESTER GENETIC SONOGRAM AFTER FIRST TRIMESTER SCREENING

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OBJECTIVE: The FASTER trial revealed Down syndrome (DS) risks only after first and second trimester screening were completed. Most centers now reveal risks at each stage of screening. We determined the effectiveness of second-trimester genetic sonography (GenSono) in modifying DS screening risks after first trimester screening.

METHODS: We retrospectively developed a Central Conn. Perinatal Database (CCPD) of singletons seen between 03/1/05 to 1/01/2010 who had all of the following: first trimester screening [11-1/7 to 13-6/7 wks.], second trimester serum marker screening and a follow-up GenSono [15-0/7 to 22-6/7 wks.]. We excluded patients with a definitive diagnosis through invasive testing after first trimester screening alone. We evaluated six minor markers (pyelectasis, increased nuchal fold, echogenic intracardiac focus, echogenic bowel, short femur and short humerus) and the presence of at least one major fetal structural malformation. Likelihood ratios (Aagaard-Tillery Obstet Gynecol. 2009; 114(6): 1189-96) from the FASTER trial were used to generate the new risks. DS risks were calculated for patients receiving both first and second trimester screening. Detection rate (DR), false-positive rate (FPR), odds of an affected given a positive result (OAPR), positive predictive value (PPV) and receiver operating characteristic (ROC) curves were determined before and after GenSono risk modification.

RESULTS: Of the 14,579 singletons with first trimester screening, 6,287 fulfilled our criteria, including 17 with DS. Area under the ROC curve was: (0.944) for stepwise sequential and (0.954) for stepwise sequential with GenSono. Comparison between screening protocols for a second trimester DS risk of $\geq$ 1:270 are shown in Table 1.

CONCLUSION: Addition of the GenSono increased the OAPR for women who had received stepwise sequential screening, in a population which has already undergone first trimester screening.

Table 1: Comparison of screening protocols at a DS risk $\geq$ 1:270

Screening Protocol	DR (n/N), SENS%	FPR (%)	PPV (%)	OAPR 1:X
Stepwise sequential screening	**15/17, 88.2**	**6.2**	**3.7**	**25.9**
Stepwise sequential screening + genetic sonogram	**14/17, 82.4**	**4.2**	**5.0**	**18.8**

n= number of DS detected, N= total number of DS, SENS= sensitivity (%)

NUCHAL TRANSLUCENCY TO PREDICT MAJOR CONGENITAL HEART DISEASE IN EUPLOID SINGLETON NEWBORNS. Samadeh Ravangard[1]*, James Egan[1], Petter Benn[3], Adam Borgida[2], Winston Campbell[1], Alireza A. Shamshirsaz[1]

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OBJECTIVE: To determine if nuchal translucency (NT) assessment is a useful screen for major postnatal congenital heart disease (CHD) in euploid newborns. **METHODS:** We retrospectively developed a Central Connecticut Perinatal Database (CCPD) of all singleton pregnancies seen in our ultrasound units between 03/1/05-1/31/11 for an NT screen [11-1/7 - 13-6/7 weeks] and second trimester scan (2nd US) [17-0/7 - 22-6/7 weeks]. Cases with an abnormal karyotype (chorionic villous sampling, amniocentesis or diagnosed postnatally) were excluded. All the fetuses with abnormal cardiac findings (ACF) on 2nd US had a postnatal cardiac evaluation by pediatric cardiology. We determined the 95th and 99th percentile (%ile) NT MoMs for each center. We used student "t" test, Receiver operating characteristic curves (ROC) and odds of an affected given a positive result (OAPR) for analysis. **RESULTS:** Of 17,214 singleton pregnancies, 11,391 had both an NT screen and 2nd US. Fifty-five had an abnormal karyotype leaving 11,333 chromosomally normal cases. Of the 44 cases (3.9/1000) of ACF identified on 2nd US, 14 (31.8%) had normal subsequent ultrasound findings antenatally or postnatally, 6 (13.6%) were lost to follow up and 24 (54.5%) had postnatal major congenital heart confirmed postnatally giving an incidence of 2.1 per 1,000. The 24 major cardiac abnormalities were: 4 (16.6%) ventricular septal defects, 3 (12.6%) atrioventricular septal defects, 4 (16.6%) hypoplastic left ventricle, 2 (8.3%) Tetralogy of Fallot, 3 (12.6%) transposition of great vessels and 8 (33.3%) other. The mean (±SD) NT for normal's and CHD's were 1.61 (±0.45) mm and 2.17 (±1.06) mm, respectively (P <0.0001). The OAPR indicates that for every 69 patients with an NT MoM ≥ 95th percentile, there will be one major cardiac anomaly (Table 1).
CONCLUSION: Increased NT measurement was associated with a higher risk of CHD by fetal echocardiography in euploid fetuses. Using the 95%ile NT MoM was the most efficacious considering OAPR and the number of CHD detected. Patients with increased of NT should be referred for a fetal echocardiogram.

Table 1: Efficacy of NT to detect CHD in euploid fetuses.

NT (mm)	n	CHD n	CHD /1000	DR (%)	FPR (%)	OAPR
total	11,313	24	2.1			
<2	9308	13	1.4			
≥2	2005	11	5.5	45.8	17.7	181.7
≥ 2.5	400	6	15.0	25	3.5	65.9
≥ 3	138	3	21.8	12.5	1.2	45.2
≥ 4	33	1	30.3	4.2	0.2	33.9
≥ 5	13	1	75.9	4.2	0.1	11.3
≥ 95 %ile NT MoM	565	8	14.2	33.3	4.9	69.1
≥99 %ile NT MoM	424	7	16.5	29.2	3.7	59.7

FOLLOW-UP FREQUENCY OF TESTING IN PATIENTS AT VERY LOW RISK FOR TRISOMY 21 ON FIRST TRIMESTER SCREENING

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OBJECTIVE: Contingent screening protocols often use an upper first trimester Down syndrome risk of 1:1,500. We chose to determine the rate of utilization of second trimester serum screening among women who are at very low risk after the first trimester [1stT] aneuploidy screen risk for trisomy 21 [T-21].

STUDY DESIGN: We retrospectively developed the Central Connecticut Perinatal Database (CCPD) of all singleton pregnancies seen in our ultrasound units between 10/1/06-1/01/10 for first trimester aneuploidy screening [11-1/7 - 13-6/7 weeks]. FT aneuploidy risk was based on maternal age, NT, PAPP-A, and beta-hCG. 1stT screening risk was presented to the patient by a genetic counselor or obstetrician, and follow-up options were reviewed. Second- trimester risk assessment, was based on combination of 1stT screen plus second trimester serum markers [AFP, hCG, unconjugated estriol, and inhibin-A]. Second trimester ultrasound exam, was performed between 15-0/7 and 22-6/7 weeks. A very low T-21 risk was defined as <1:1500 in the 1stT and a screen-positive result as >1:270 in the second trimester. We excluded all the women with an increased trisomy 18 risk $\geq$ 1:100.

RESULTS: A total of 12,218 women underwent 1stT screening, 9,332 (76.4%) were classified as very low risk for a trisomy 21 fetus. Of these 9, 332 women, 3,329 (35.6%, group A) had both second trimester serum markers and ultrasound exam, 1,825 (19.5%, group B) had only ultrasound exam, 2,343 (25.1%, group C) had only second trimester serum testing and 1,835 (19.8%, group D) had no more screening. Of the women who had second trimester serum testing (group A and C) (n=5,672, 60.7%), 56 women (1.0%) were screen-positive after second trimester serum test. The net number of women who had invasive testing (amnio) was 50 (0.5%) of which 14 women had invasive testing (amnio) after becoming screen positive in the second trimester. Within the 5,672women (group A and C) who had second trimester serum testing there was one case of trisomy 21 that remained at screen-negative after the second trimester serum testing.

Conclusions: Women, who are at very low risk after the FT screening, are very unlikely to have a trisomy 21 affected pregnancy. The use of a full set of second trimester serum markers is not indicated for women who are at very low risk after 1stT screening and who have no other indications for further screening.

THE EFFECTS OF BUPRENORPHINE ON THE FETAL NONSTRESS TEST

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Objective : Opiate abuse in pregnancy carries significant risk to both the mother and fetus. In addition to methadone, buprenorphine is an alternative maintenance medication for opiate dependence. The objective of this study is to establish a baseline rate of non-reactivity in fetal nonstress tests (NSTs) in patients taking buprenorphine.

Study Design: This is a retrospective chart review of pregnant women at Boston Medical Center taking buprenorphine for opiate dependence. Patients were identified through the electronic medical record in our antenatal testing unit. We reviewed NSTs performed after 32 weeks gestation to determine the baseline rate of non-reactivity. This rate was compared to historical rates of non-reactivity in patients taking methadone.

Results: We identified 280 NSTs performed between January 2007 and May 2011 in patients taking buprenorphine for opiate dependence. 13 NSTs were excluded because they were performed on patients who had additional pregnancy complications. The overall rate of non-reactivity was 3.37% (95% CI = 1.78 -6.28)**.** The average maternal age at time of NST was 29 years old. The average number of NSTs for each pregnancy was 3.2.

Conclusion: To our knowledge, this is the first study to establish a baseline rate of non-reactivity in patients taking buprenorphine during pregnancy. Our findings suggest the rate of non-reactive NSTs is significantly lower in buprenorphine patients than that of published methadone rates, 19%-21%. This finding suggests that buprenorphine does not have a significant effect on the rate of non-reactivity. Lastly, given the recent findings suggesting buprenorphine is superior to methadone in neonatal abstinence syndrome outcomes, this study is yet another reason to offer buprenorphine to pregnant women with opiate dependence.

MATERNAL WEIGHT GAIN IN TWIN PREGNANCIES: EXAMINING THE 2009 INSTITUTE OF MEDICINE (IOM) GUIDELINES

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OBJECTIVE: The 2009 Institute of Medicine (IOM) "provisional" guidelines (IOMG) recommend BMI-specific maternal weight gain (MWG) in twins. We sought to assess if they improve perinatal outcomes.

METHODS: A retrospective study of twins we delivered from 01/1991-01/2011was done. We excluded infants with major malformations, monochorionic-monoamniotic twins, monochorionic-diamniotic twins with twin to twin transfusion syndrome, alloimmunization, and fetal demise. IOMG apply to deliveries >, =37 weeks. We adjusted MWG for gestational age (AOG) at delivery by dividing total MWG by AOG at last recorded visit(< 1 week to delivery) to yield MWG/week. Outcomes (mean delivery gestational age (MDGA); preterm birth <34, <32 wks, mean birth weight (MBW) and low birth weight (LBW) < 1500 G) were compared for patients whose weight gain met, exceeded or was less than IOMG. Maternal BMI defined: normal (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2) & obese (>30kg/m^2) groups. ANOVA and X^2 analysis was used.

RESULTS: 430 cases (860 infants) were identified. By prepregnancy BMI, there were 239 (55.6%) normal (Group I), 111 (25.8%) overweight (Group II), and 80 (18.6%) obese (Group III) patients. Group I patients who met IOMG had significantly improved outcomes (MDGA, MBW; fewer preterm births <34 wks,<32 wks and LBW infants) versus patients who gained less (Table 1). Group II patients who met IOMG had significantly better outcomes (higher MBW, fewer LBW infants) versus patients gaining less. In Group III patients who met IOMG there were no significant outcome differences.

CONCLUSION: In women with twin pregnancies and normal starting BMIs, weight gain during pregnancy is significantly associated with improved outcomes, including a decreased risk of prematurity and larger birth weights.

Table 1. Pregnancy outcomes in patients with normal prepregnancy BMIs.

	BMI (18.5-24.9) (n=478 infants) Weight change per week (Kg)					
	A	B (IOM recommendation rate)	C	P-values		
	<=0.45 (n=182)	0.45-0.66 (n=194)	>0.66 (n=102)	AB	AC	BC
Mean Gestational age at delivery in weeks (95% CI)	32.7(32.2-33.2)	34.2(33.7-34.7)	33.2(32.5-33.9)	0.0002	0.5289	0.05
Preterm delivery <34 w (%)	110(61)	72(37)	51(50)	<.0001	0.2143	0.1031
Preterm delivery <32 w (%)	74(41)	40(21)	23(23)	<.0001	0.004	0.9297
Mean Birth Weight in grams (95% CI)	1747(1653-1841)	2132(2040-2223)	2053(1928-2179)	<.0001	0.0004	0.584
Low Birth Weight < 1500 G (%)	61(34)	37(19)	21(21)	0.0051	0.0483	0.9532

TWIN CHORIONICITY AND THE RISK OF STILLBIRTH

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OBJECTIVE: To assess the impact of placental chorionicity on the risk of stillbirth in twins.

METHODS: We retrospectively developed the Twin Pregnancy Perinatal Database (TPPD) in a tertiary university hospital for deliveries between January 1, 1991 and January 1, 2011. We recorded maternal demographics, pregnancy complications and pregnancy outcomes. Pregnancies affected by major anomalies, twin-twin transfusion syndrome, multiple fetal reduction and alloimmunization were excluded. The risk of fetal death with advancing gestation was calculated for "apparently normal" monochorionic-diamniotic (Mono/Di) twins and for dichorionic-diamniotic (Di/Di) twins. Overall in utero survival was analyzed using a time-to-event (Kaplan-Meier) analysis using week of gestation as the time scale. Intrauterine fetal demise (IUFD) per pregnancy was defined as the event, and all other births were censored. Survival for Mono/Di vs. Di/Di twins, were compared by the log-rank test. Hazard ratios and 95% confidence intervals were estimated using a Cox proportional hazards model and adjusted for covariates that differed at baseline.

RESULTS: Of the 754 twin pregnancies in the TPPD, 106 (14.0%) were excluded, 121 (16.0%) were Mono/Di twins and 527 (70%) were Di/Di twins. Stillbirths occurred in 4 (3.3%) Mono/Di [25-1/7, 26-0/7, 28-6/7, 34-1/7 weeks] and 3 (0.6%) Di/Di twin pairs [27-0/7, 30-0/7, 34-2/7 weeks]. Mono/Di twins had a higher risk of stillbirth compared with Di/Di twins, (log-rank P=.007) (Figure A). After adjustment for maternal age at delivery, smoking, chronic hypertension and maternal DM, a Mono/Di twin pregnancy compared with a Di/Di twin pregnancy, is associated with 11.3 times higher risk of IUFD.

CONCLUSION: Monochorionicity has a negative effect on the in-utero survival of twins, even among apparently normal monochorionic-diamniotic twins. In the absence of a clinical indication for delivery, these data do not support elective late preterm [34-36 weeks] delivery for prevention of intrauterine fetal demise in "apparently normal" Mono/Di twins.

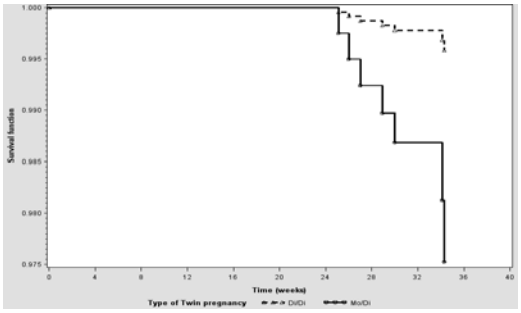

Figure A: Survival time for Di/Di vs. Mono/Di twin pregnancies

FIRST TRIMESTER TRISOMY 21 SCREEN POSITIVE PATIENTS:

COMPARING TYPE OF TESTING IN TWO CONSECUTIVE TIME PERIODS

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Objective: To compare the type and frequency of subsequent testing for patients whose first trimester [FT] aneuploidy screen for trisomy 21 [T-21] was positive in two consecutive time periods.

STUDY DESIGN: Our results for first time period (1st P) (09/01/2004 to 09/30/2006), have been published (AJOG 2007; 197: 312.e1-312.e5.). We also retrospectively developed the Central Connecticut Perinatal Database (CCPD) of all singleton pregnancies seen in our ultrasound units between 10/1/06-1/01/10 for first trimester aneuploidy screening [11-1/7 - 13-6/7 weeks] for second time period
(2nd P). FT aneuploiody risk was based on maternal age, NT, PAPP-A, and beta-hCG. FT screening risk was presented to the patient by a genetic counselor or obstetrician, who reviewed options for care. Second- trimester risk assessment, was based on a combination of FT screen plus second trimester serum markers [AFP, hCG, unconjugated estriol, and inhibin-A]. The ultrasound exams were performed by accredited sonographers and maternal fetal medicine physicians.

Results: A total of 1,528 women underwent FT screening in our ultrasound units in the 1st P while 12,218 were screened in 2nd P. A total of FT screen-positive for T-21 in 1st P was 133 (8.7%) and 2nd P was 773 (6.3%) (p=ns). In the 1st P, 30 women (22.6%) had invasive testing (CVS and amnio) after FT screen-positive for T-21 compared to 69 women (8.9%) in 2nd P (p< 0.001). In the 1st P, 88 women (66.1%) had second trimester serum markers compared to 561 women (72. 4%) in 2nd P (P=0.048). Of the women who had second trimester serum markers, in 1st P 7 women (7.9%) had amniocentesis compared to 58 women (11.6%) in 2nd P (p=ns). The net number of women who had invasive testing (CVS, amnio) in 1st P was 37 cases (27.8%) compared to 127 cases (16.4%) in 2nd P (p< 0.05).

Conclusions: Fewer FT positive women chose invasive diagnostic tests in the second time period of the study. The majority of women with a positive FT screen for trisomy 21 in 2nd P prefer to have non-invasive second trimester follow-up evaluation compare to 1st P. This data may be helpful to counsel women who are screen-positive for T-21 from their first trimester aneuploidy screen.

WHEN IS THE OPTIMAL TIME TO DELIVER MONOCHORIONIC AND DICHORIONIC TWINS?

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Objective: To determine the optimal timing of delivery for uncomplicated monchorionic and dichorionic twin gestations. **Study Design:** We created a decision analytic model to compare the outcomes of elective delivery at 34, 35, 36, 37, 38 or 39 weeks in two theoretical cohorts of uncomplicated twin pregnancies: monochorionic diamniotic and dichorionic diamniotic. Strategies involving expectant management until a later gestational age accounted for the probabilities of spontaneous delivery, indicated delivery, and IUFD during each successive gestational week, also accounting for the risk of co-twin death or disability following one IUFD in monochorionic gestations. Baseline probability assumptions were derived from the literature. Neonatal outcomes included minor learning disability, major morbidity, and neonatal death by gestational age. Total quality-adjusted life years (QALYs) were generated using both neonatal and maternal utilities, and sensitivity analyses were performed to examine the robustness of the findings. **Results:** Earlier gestational ages were associated with increased minor morbidity related to prematurity, while the rate of major morbidity nadired at 36 weeks for monochorionic and 39 weeks for dichorionic twins. Overall, the optimal delivery strategy was expectant management until 36 weeks for monochorionic twins and until 38 weeks for dichorionic twins, when total QALYs were maximized. Our results were most sensitive to the probability of IUFD and minor morbidity. For monochorionic twins, expectant management until 36 weeks was optimal when the probability of IUFD each week was less than 1.3 times our baseline, and for dichorionic twins, 38 weeks was optimal when the probability of IUFD each week was less than 1.77 times our baseline.

Table 1: Quality adjusted life years.

	Monochorionic twins	Dichorionic twins
Deliver at 34 wks	84.69	84.69
Expectant until 35 wks	84.77	84.85
Expectant until 36 wks	84.80	84.95
Expectant until 37 wks	84.74	84.95
Expectant until 38 wks	84.70	84.98
Expectant until 39 wks	84.65	84.96

Conclusion: Determining the optimal delivery strategy for monochorionic and dichorionic twins involves weighing the risks of IUFD against neonatal morbidity and mortality from iatrogenic prematurity, as well as accounting for unique risks associated with co-twin death. Taking these factors into consideration, we found that the optimal gestational age at which to deliver monochorionic diamniotic twins was 36 weeks, and for dichorionic diamniotic twins was 38 weeks.

VITAMIN D DEFICIENCY IS ASSOCIATED WITH INCREASED MEAN ARTERIAL PRESSURE AT TERM

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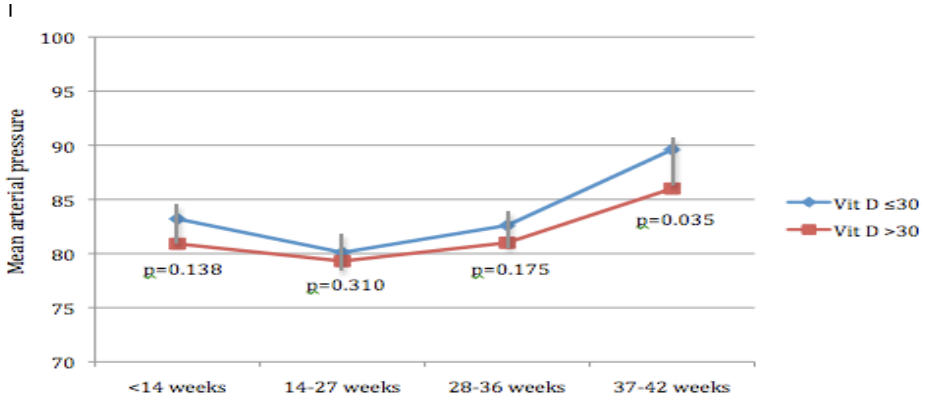
Background: Previous studies have suggested that low levels of 25(OH) Vitamin D and elevated mean arterial pressure (MAP) may be independent risk factors for preeclampsia. We hypothesize that the association between Vitamin D deficiency and preeclampsia may be mediated, in part, by an increase in MAP.

Methods: Retrospective review of records for 139 women with singleton pregnancies who received prenatal care at our institution between 2008 and 2010, and had 25(OH) Vitamin D measured within one month prior to conception or during pregnancy. Women with 25(OH) Vitamin D levels ≤30ng/ml were considered deficient and routinely received supplementation (800IU twice daily) in our practice. Blood pressure from prenatal visits in the first trimester (<14wks), second trimester (14-27wks), early third trimester (28-36wks) and term (37-42wks) were recorded, and the MAP calculated (2/3 diastolic pressure + 1/3 systolic pressure). The chi-square test was used to compare proportions, the Student's t-test compared mean values, and logistic regression was used to adjust for potential confounding factors.

Results: 67.6% of women were Vitamin D deficient. Those who were deficient demonstrated significantly higher MAP at term (see graph). Among Vitamin D deficient women, 70.9% had term MAP ≥85mmHg compared to 44.7% of women with normal Vitamin D levels (p=0.006). This effect persisted even after excluding women who developed preeclampsia, with 66.2% of Vitamin D deficient women having a term MAP ≥85mmHg compared to 44.7% with normal Vitamin D levels (p=0.032). Multivariate analyses showed an adjusted odds ratio of 3.52 (CI 1.40-8.85) for term MAP ≥85mmHg among Vitamin D deficient women after adjusting for race, maternal age, BMI, parity, chronic hypertension, and gestational age at 25(OH) Vitamin D measurement. No other factor was independently associated with term MAP ≥85mmHg.



Conclusion: Women with 25(OH) Vitamin D deficiency demonstrated higher MAP at term despite our institutional practice of routine supplementation. The association between Vitamin D deficiency and preeclampsia may be mediated by an independent effect of Vitamin D deficiency on MAP at term.

LATE PRETERM BIRTH: CAN IT BE REDUCED?

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Objective: Due to the evolving controversy regarding late preterm birth (AJOG. 2011; 20(6): 459-60), we evaluated the indications for late preterm twin birth (LPTB) (34 0/7-36 6/7 weeks).

Study Design: We retrospectively developed a Twin Pregnancy Perinatal Database (TPPD) at our University Hospital for deliveries between January 1, 1991 and January 1, 2011. Cases with major malformation, monoamniotic-monochorionic twins, monochorionic-diamniotic twins with twin to twin transfusion syndrome, alloimmunization, and fetal demise were excluded. We determined the rate of iatrogenic LPTB, as well as the rate of indicated LPTB supported by current recommendations endorsed by the American College of Obstetrics and Gynecology (ACOG) or published expert opinion (level III evidence). Spontaneous (ie, noniatrogenic) causes of preterm delivery were defined as those preterm births proceeded by either premature rupture of membranes (PPROM) or preterm labor with intact membranes. Delivery indications supported by ACOG guidelines and /or expert opinion were defined as evidence based (EB). Delivery indications not supported by either of these were labeled non-EB (NEB).

Results: There were a total of 747 twin pregnancies in TPPD, 206 (37.1%) were in LPTB. Indications for delivery in the LPTB were shown in Table. Spontaneous delivery of LPTB was 63.6% (n=131/206) and the rate of iatrogenic delivery in this late preterm cohort was 36.4% (n=75/206). The majority, 66.6% (n=50/75), of these iatrogenic deliveries were deemed non-evidence based, giving a total of 24.2% (50/206) NEB deliveries in LPTB group.

Conclusions: Over half of non-spontaneous late preterm births in our cohort were delivered for non-evidence based indications. There is a critical need to systematically evaluate indications for delivery in LPTB.

Indications	n (%)	Cause of LPTB
Spontaneous preterm labor	69 (33.6)	Spontaneous
Preterm premature rupture of membranes (PPROM)	41 (19.9)	Spontaneous
Spontaneous preterm labor/PPROM	21 (10.2)	Spontaneous
Severe preeclampsia/Eclampsia/HELLP syndrome	15 (7.2)	Iatrogenic EB
Non-reassuring fetal status	9 (4.4)	Iatrogenic EB
Mild preeclampsia/gestational hypertension	21 (10.2)	Iatrogenic NEB
Intrauterine growth restriction (IUGR) and/or oligohydraminos	13 (6.3)	Iatrogenic NEB
No clear indication (elective)	12 (5.8)	Iatrogenic NEB
Other indications†	5 (2.4)	Iatrogenic EB & NEB

PREVALENCE OF MATERNAL CELIAC DISEASE AMONG INTRAUTERINE GROWTH RESTRICTED INFANTS: A SINGLE CENTER PILOT STUDY

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Objective: Previous studies suggest that untreated maternal celiac disease (CD) is associated with intrauterine growth restriction (IUGR). However, recent epidemiological data show that approximately 90% of all CD is undiagnosed because many are asymptomatic. Hence, the proportion of IUGR that can be attributed to CD is truly unknown. The primary aim was to prospectively determine the prevalence of asymptomatic CD among women with IUGR infants.

Methods: All antenatal and postnatal women who had a diagnosis of IUGR were invited to participate. Serum IgA anti-TTG antibodies were obtained on all study subjects. Patients with elevated TTG levels had a small bowel biopsy done. Data was collected on history of substance abuse, smoking, and preeclampsia.

Results: A total of thirty-four women with a pregnancy diagnosis of IUGR were enrolled in the study. The prevalence of preeclampsia was 35%. The prevalence of substance abuse was 3%, while 15% were smokers. One patient was found to have celiac disease. The prevalence of unknown maternal Celiac disease among those with a diagnosis of IUGR was 3% (1:34), which is higher than the estimated national prevalence, 0.7% (1:133).

Conclusion: In this pilot single center study, women with a pregnancy diagnosis of IUGR may have occult celiac disease at an increased rate over the population as a whole. Larger and more comprehensive studies are warranted to confirm this trend. Implications include potential celiac disease testing in all pregnant woman, especially those with a past pregnancy outcome of IUGR. Future studies are also needed to determine if the treatment of a gluten free diet may prevent IUGR in future pregnancies.

PRECISION RENAL ULTRASOUND SCREENING FOR NEPHROCALCINOSIS IN VLBW INFANTS: A SINGLE CENTER STUDY (2005 – 2010)

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Objective: Preterm infants with nephrocalcinosis (NC) have potential risks of future renal dysfunction, hypercalciuria, kidney stones, decreased kidney growth, and hypertension. Currently, no universal recommended screening strategies exist. Therefore, screening practices vary greatly based on GA and BW. With elevated health care costs and need for precision screening, we sought to identify risk factors for selective renal ultrasonography in VLBW infants at risk for NC.

Methods: A case-control study nested within a review of retrospective review of the electronic medical records and renal ultrasounds on 632 premature infants <1500g (2005 to 2010) was performed at our institution. Collected data included gestational age (GA), birth weight (BW), gender, length of stay (LOS), nephrotoxic agents, serum calcium and phosphorus products and renal ultrasound findings.

Results: 632 infants <1500g, <37 weeks were admitted to our NICU from 2005 to 2010. Only 54% (N=344) had an abdominal/renal ultrasound of which 56% (n=193) had NC. Bilateral NC was seen in 84.2% (n=165). NC was significantly associated with GA <30 weeks ($p<0.001$) and BW <1250g ($p<0.001$). Unlike previous studies, TPN was not significantly associated with NC. No association was uncovered between NC and the serum calcium-phosphorous product when the value was set between 70-74 and 75-79. However, when serum calcium-phosphorus product value defined ≥80, an association was found with NC (OR = 1.8 [0.99-3.21]); adjusted for BW and exposure to TPN and furosemide (pWald=0.056).

Conclusion: Similar to other studies, there is an association with NC in VLBW infants of low GA, low BW, increasing LOS and exposure to furosemide. A new association was uncovered with NC and elevated serum calcium-phosphorous product value ≥80 when adjusting for BW and exposure to TPN and furosemide. With elevated health care costs and need for precision screening, we identified the group (<30 weeks, <1250 grams, and serum Ca-Phos product ≥80) who are most at risk for NC.

BRONCHIOALVEOLAR STEM CELLS INCREASE AFTER MESENCHYMAL STROMAL CELL TREATMENT IN A MOUSE MODEL OF BRONCHOPULMONARY DYSPLASIA

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Background: Bronchopulmonary dysplasia(BPD) remains a major complication of prematurity resulting in significant morbidity and mortality. The pathology of BPD is multifactorial and leads to alveolar simplification and distal lung injury. Previous work has shown a beneficial effect of treatment with bone marrow derived mesenchymal stromal cells (MSCs) leading to amelioration of lung parenchymal and vascular injury in the hyperoxia murine model of BPD. It is possible that this beneficial response is at least in part due to activation of endogenous lung epithelial stem cells. Bronchioalveolar stem cells (BASCs) are an adult lung stem cell population capable of self-renewal and differentiation in culture, and proliferation in response to bronchiolar and alveolar lung injury in vivo.

Objective: To investigate the role of BASCs in repair of neonatal lung disease and the effects of MSCs on endogenous lung stem cells.

Design/Methods: Neonatal mice were exposed to hyperoxia (75% O2) or room air on day 1 and treated systemically with MSCs or MSC-Conditioned Media (MSC-CM) on day 4. Immunofluorescence (IF) studies and BASC quantification was performed on day 14 lung tissue sections. In vitro co-culture experiments with FACS isolated BASCs in either MSC-CM or standard media were performed. Lineage tracing studies after bleomycin injury utilized a knock-in Cre recombinase modified estrogen receptor fusion mouse where CCSP-expressing cells including Clara cells, BASCs and their progeny are labeled with YFP signal. IF on 4 week post-injury lung tissue sections included quantification of YFP positive cells in the alveolar space.

Results: BASCs significantly increased in response to systemic MSC treatment by 1.4-fold and in response to MSC-CM by 2.1-fold compared to untreated controls. Treatment of BASCs with MSC-CM in culture showed a 1.8-fold increased growth efficiency, indicating a direct effect of MSCs on BASCs. Lineage tracing data showed that CCSP-expressing cells including BASCs are capable of contributing to alveolar repair after bleomycin lung injury.

Conclusions: MSCs and MSC-derived factors may stimulate BASCs to play a role in the repair of alveolar lung injury found in BPD and in the restoration of distal lung cell epithelia. This work highlights the potential important role of endogenous lung stem cells in the repair of chronic lung diseases.

SINGLE NUCLEOTIDE POLYMORPHISMS AND VARIABILITY IN SEVERITY OF NEONATAL ABSTINENCE SYNDROME.

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Background: There is significant variability in the incidence and severity of neonatal abstinence syndrome (NAS) from in-utero opioid exposure. Adult studies show that single nucleotide polymorphisms (SNPs) in the mu opioid receptor (OPRM1), multi-drug resistance (MDR1), and catechol-O- methyltransferase (COMT) genes affect opioid addiction risk, metabolism and dosing requirements. These SNPs may also affect infants with NAS.

Objective: To determine if SNPs in the ORPM1 (A118G), MDR1 (C3435T, G2677T, C1236T), and/or COMT (Val158Met) genes are associated with differences in the incidence and severity of NAS in infants exposed antenatally to methadone or buprenorphine. Outcome measures included length of hospital stay (LOS), maximum Finnegan score, and need for pharmacologic intervention.

Design/Methods: Full-term opioid-exposed newborns (n=28) were studied. A DNA sample was obtained and then genotyped for 5 SNPs. Infants were monitored for NAS and treated with replacement opiates according to institutional protocol. T-tests and chi square were used to evaluate for differences in NAS severity outcome measures.

Results: For the ORPM1 A118G SNP, infants with the AA genotype demonstrated a more severe phenotype compared to AG/GG infants; 65% vs 18% required treatment for NAS ($x^2=4.34$, $p<0.05$); LOS of 24.5 (95% CI 16.2, 32.8) vs 8.8 days (0.5, 17.2) ($p<0.01$); and daily dose of methadone of 1.1 vs 0.2mg ($p<0.05$). Infants with the COMT Val/Met or Met/Met genotype had decreased NAS severity as measured by LOS [34.3 (16.6, 52.1) vs 16.9 days (9.6, 24.1), $p<0.05$]; need for 2 NAS medications (68% vs 25%, $x= 3.54$, $p=0.05$); maximum Finnegan score [14 (9.7, 18.3) vs 11 (9.5, 12.5), $p=0.05$]; and daily dose of neonatal morphine (1.6 vs 0.5mg, $p=0.05$). There was no significant difference in NAS severity with the MDR1 SNPs.

Conclusions: These data suggest that SNPs in the OPRM1 and COMT genes affect NAS severity, with presence of the minor allele demonstrating a milder phenotype. This has important implications for the earlier identification and treatment of infants at highest risk for NAS.

STRETCH-INDUCED DIFFERENTIATION OF FETAL LUNG TYPE II CELLS IS MEDIATED VIA INTEGRIN-TACE SIGNALING PATHWAY

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BACKGROUND: Mechanical forces are essential for normal fetal lung development. However, the mechanisms by which strain promotes lung development are not well characterized. Previous studies from our laboratory showed that stretch-induced differentiation of fetal type II epithelial cells is mediated via release of the EGFR ligands HB-EGF and TGF-alpha.

OBJECTIVE: To investigate how stretch-induced release of ligands is regulated.

DESIGN/METHODS: Type II epithelial cells were isolated from wild-type and ADAM-17/TACE knockout mice on E17-18 of gestation and exposed them to mechanical stretch using the Flexcell Strain apparatus and magnetic force. TACE activation was investigated using a fluorescence FRET substrate. Release of ligands was analyzed by measuring alkaline phosphatase in the supernatant after cells were transfected by electroporation with plasmids encoding HB-EGF and TGF-alpha. Type II cell differentiation was assessed by SP-C mRNA expression

RESULTS: 2.5% continuous stretch and 5% intermittent stretch activated TACE on E17 cells. Stretch-induced release of HB-EGF and TGF-alpha or type II cell differentiation were inhibited in samples incubated with the TACE-specific inhibitor IC-3 or in cells isolated from TACE knockout mice. Cell adhesion assay showed that integrin alpha-3 and beta-1 bind to TACE. Blocking integrin binding on laminin-coated substrates or plating type II cells on integrin-coating substrates demonstrated that stretch-induced differentiation is mediated via alpha-6/beta-1 integrins. Furthermore, using magnetic beads coated with alpha-6 and beta-1 integrins, we found that force applied to these integrin receptors released HB-EGF and TGF-alpha into the supernatant.

CONCLUSION: Mechanical stretch activates TACE. Stretch-induced release of EGFR ligands and type II cell differentiation is mediated via TACE. Mechanical force applied to alpha-6 or beta-1 integrins release TACE and promotes type II cell differentiation. These studies provide novel mechanisms on how mechanical forces may promote lung development.