Grand Ball Room A-B, New Orleans Hilton Riverside

1 **FIRST- AND SECOND-TRIMESTER EVALUATION OF RISK (FASTER) TRIAL: PRINCIPAL RESULTS OF THE NICHD MULTICENTER DOWN SYNDROME SCREENING STUDY** FERGAL D. MALONE[1], NICHOLAS J. WALD[2], JACOB A. CANICK[3], ROBERT H. BALL[4], DAVID A. NYBERG[5], CHRISTINE H. COMSTOCK[6], RADEK BUKOWSKI[7], RICHARD L. BERKOWITZ[8], SUSAN J. GROSS[9], LORRAINE DUGOFF[10], SABRINA D. CRAIGO[11], ILAN E. TIMOR[12], STEPHEN R. CARR[3], HONOR M. WOLFE[13], KIMBERLY A. DUKES[14], DIANA W. BIANCHI[11], ALICJA RUDNICKA[2], ALLAN HACKSHAW[2], GERALYN LAMBERT-MESSERLIAN[3], MARY E. D'ALTON[1], [1]Columbia University, New York, NY [2]Wolfson Institute of Preventive Medicine, London, United Kingdom [3]Brown University, Providence, RI [4]University of Utah, Salt Lake City, UT [5]Swedish Medical Center, Seattle, WA [6]William Beaumont Medical Center, Royal Oak, MI [7]University of Texas Medical Branch, Galveston, TX [8]Mount Sinai Medical Center, New York, NY [9]Albert Einstein College of Medicine, New York, NY [10]University of Colorado Health Sciences Center, Denver, CO [11]Tufts University, Boston, MA [12]New York University, New York, NY [13]UNC Medical Center, Chapel Hill, NC [14]DMSTAT, Boston, MA

OBJECTIVE: To compare performance of first- and second-trimester screening methods for the prenatal detection of Down syndrome.

STUDY DESIGN: Unselected patients with singleton pregnancies at 10 3/7 to 13 6/7 weeks were recruited at 15 U.S. centers. All patients had a first-trimester Combined test (1:150 cut-off), and returned at 15-18 weeks for a second-trimester Quad test (1:300 cut-off). Patients with septated cystic hygroma were followed separately. All results were reported at 16-18 weeks.

RESULTS: Results are based on 33,557 pregnancies (84 with Down syndrome) with complete first- and second-trimester data. With the Combined test the detection rate (DR) was 76% for a 3.2% false-positive rate (FPR), with the Quad test the DR was 84% for an 8.4% FPR, and with either or both positive the DR was 94% for a 10.8% FPR. Comparisons of first- and second-trimester, and integrated, tests are given below. These data are based on counting unaffected pregnancies above the risk cut-offs defined by the detection rates.

CONCLUSION: First-trimester Combined screening and second-trimester Quad screening are similarly effective. Integrated screening has the lowest false-positive rate at each detection rate.

	FPR (%) for DR of		
(all include maternal age)	80%	85%	90%
FIRST TRIMESTER:			
Nuchal Translucency (NT) alone	14	17	22
Combined (NT, PAPP-A, fbhCG)	3.4	7.6	14
SECOND TRIMESTER:			
Triple (AFP, hCG, uE3)	8.0	12	26
Quad (triple + inhibin-A)	5.0	10	18
BOTH TRIMESTERS:			
Serum integrated (PAPP-a/quad)	3.4	6.8	12
Fully integrated (NT/PAPP-a/quad)	1.4	2.8	5.4

2 **A RANDOMIZED TRIAL OF SINGLE VS WEEKLY COURSES OF CORTICOSTEROIDS** RONALD J. WAPNER[1], [1]for the NICHD MFMU Network, Rockville, MD

OBJECTIVE: To determine the efficacy and safety of repetitive courses of corticosteroids.

STUDY DESIGN: Randomized, placebo-controlled, clinical trial at nineteen centers. Women < 32 wks gestation at risk for spontaneous preterm delivery with intact membranes and pregnant one week after an initial course of corticosteroids were randomized to weekly courses of betamethasone or placebo; limited to 4 courses after the first 67 patients. The primary outcome was a composite of stillbirth/neonatal death, severe RDS, grade III-IV IVH, periventricular leukomalacia or chronic lung disease.

RESULTS: The initial sample size was 2200 but the Data/Safety Committee recommended termination at interim analysis. Of 495 randomized women, 492 (591 infants) were available for analysis; 252 received repetitive steroids. We found no difference in the primary outcome between multiple courses and placebo (7.7% vs 9.2%, $P = 0.67$). However, for those delivering < 32 weeks, we found a trend towards reduction in the primary outcome after repeat steroids (21.3 vs 38.5%, $P = 0.083$). In the entire cohort, trends towards improvement were seen in the repeat group for each component of the primary outcome and for secondary outcomes related to lung function: use of surfactant (12.5% vs 18.4%, $P = 0.02$), mechanical ventilation (15.5% vs 23.5% $P = 0.005$), treatment for hypotension (5.7% vs 11.2%, $P = .02$). Multiple courses were associated with insignificant trends towards reduced infant weight (2194 vs 2289 gm, $P = .09$) and length (44.2 vs 44.7 cm, $P = .09$). Infants exposed to ≥4 courses had a significant decrease in birth weight (2396 vs 2561 gm, $P = 0.01$). There was no difference in head circumference overall, nor in those exposed to ≥4 courses.

CONCLUSION: Four or more weekly courses of antenatal steroids significantly reduce birth weight. However, repeated courses may reduce infant morbidity, especially when delivery occurs before 32 weeks. Further investigation of limited repeated steroid administration to women at high risk for early preterm birth is warranted.

3 **IMMUNOMODULATORS PLUS ANTIBIOTICS TO PREVENT PRETERM DELIVERY IN EXPERIMENTAL INTRA-AMNIOTIC INFECTION (IAI)** M. GRAVETT[1], D. SADOWSKY[1], S. WITKIN[2], M. NOVY[1], [1]Oregon Hlth Sci U, Portland, OR [2]Weill Med College, New York, NY

OBJECTIVE: IAI is a major cause of extreme prematurity and is associated with elevated amniotic fluid (AF) cytokines and prostaglandins (PG). Antibiotic treatment alone does not prevent preterm birth in this setting. We utilized non-human primates to test the hypothesis that down-regulation of the inflammatory cascade given with antibiotics would delay preterm birth after experimental IAI.

STUDY DESIGN: 13 chronically instrumented rhesus monkeys at 135 (range 126-141) days' gestation (term, 167 days) received 1 of 3 treatments after the onset of uterine contractions following intra-amniotic inoculation of 10^6 cfu of group B streptococci (GBS): 1. No treatment (controls), n = 6; 2. Ampicillin (15 mg/kg maternal IV q6h), n = 4; 3. Ampicillin + dexamethasone (DEX, 1 mg/kg maternal IV q6h) + indomethacin (INDO, 50 mg orally q12h), n = 3. AF cytokines, prostaglandins, matrix metalloproteinases (MMPs), and uterine contractility (hourly contraction area, or HCA) were serially measured.

RESULTS: The mean inoculation-to-delivery intervals for the 3 groups were: 1. Control, 37 hours; 2. Ampicillin alone, 81 hours ($P = 0.2$ vs control); and 3. Ampicillin + DEX + INDO, 257 hours ($P = 0.01$ vs ampicillin alone). Despite eradication of GBS from AF by ampicillin alone, there were persistent elevations in AF cytokines, PGs, HCA, and MMPs until preterm delivery. In contrast, treatment with ampicillin + DEX + INDO suppressed initial increases in cytokines, PGs, to pre-inoculation levels, but did not alter elevations in MMPs.

CONCLUSION: Antibiotics given alone after the onset of IAI-induced contractions did not inhibit preterm labor & delivery. Antibiotics given together with DEX + INDO suppressed the inflammatory response and prolonged gestation. These data support the role of the inflammatory response in infection-induced prematurity and suggest the utility of immunomodulators with antibiotics in the treatment of infection-induced preterm labor and the prevention of prematurity.

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4 **FETOSCOPIC LASER SURGERY VERSUS SERIAL AMNIODRAINAGE IN THE MANAGEMENT OF SEVERE TWIN-TO-TWIN TRANSFUSION SYNDROME AT MIDGESTATION. A RANDOMIZED CONTROLLED TRIAL** MARIE-VICTOIRE SENAT[1], JAN DEPREST[2], MICHEL BOULVAIN[3], YVES VILLE[1], [1]Université Paris Ouest, Obstetrics/Gynecology, Poissy, France [2]Leuven University, Obstetrics/Gynecology, Leuven, Belgium [3]University of Geneva, Obstetrics/Gynecology, Geneva, Switzerland

OBJECTIVE: Monochorionic twin pregnancies complicated by severe twin-to-twin transfusion syndrome at midgestation can be treated by either serial amniocentesis amniodrainage with removal of large volumes of amniotic fluid or by selective endoscopic fetoscopic laser coagulation of the communicating vessels on the chorionic plate. We conducted a randomized controlled trial to compare the efficacy of these two methods of treatment.

STUDY DESIGN: Severe twin-to-twin transfusion syndrome before 26 weeks of gestation. Random allocation to Laser or Amniodrainage was performed using an Internet system. Amniodrainages were performed in 32 fetal medicine units and fetoscopies in 3 centers (Poissy, Leuven, and Providence). Primary outcome measures were survival of at least one fetus and neurological morbidity at 7-12 months. An interim analysis was planned to be performed after 144 inclusions.

RESULTS: A total of 142 women were included, 72 in the Laser group and 70 in the Amniodrainage group. The interim analysis showed a statistically significant benefit in the Laser group for the survival of at least one fetus (76.4% vs 51.4% in the Amniodrainage group) (RR = 1.49 [95% CI: 1.14-1.93], $P = 0.002$) and the decision to stop the recruitment was made. A higher median gestational age at delivery and mean birthweight were observed in the Laser group (33.3 vs 29.0 weeks'; $P = 0.004$ and 1757 g vs 1359 g; $P = 0.0004$, respectively). The incidence of periventricular leukomalacia was significantly lower in the Laser group (5.6% vs 14.5%; RR = 0.39 [95% CI: 0.18-0.86], $P = 0.02$) and survival without major neurological morbidity at 6 months was significantly higher in the Laser group (50.0% vs 29.8%; RR = 1.68 [95% CI: 1.16-2.41]; $P = 0.004$).

CONCLUSION: Endoscopic laser coagulation of chorionic plate vascular anastomoses is a more effective first-line treatment of severe twin-to-twin transfusion syndrome before 26 weeks' than serial amniodrainage.