**1499** SEVERITY OF PLATELET DYSFUNCTION INDUCED BY PROPHYLACTIC INDOMETHACIN IN THE PREMATURE. Emmalee S. Setzer, Meindert Smith, Patricia J. Goulding, and Ted E. Bandstra, (Spon. by Eduardo Bancalari), University of Miami, Jackson Memorial Hosp., Department of Pediatrics, Miami, FL.

The effect of indomethacin [I] upon platelet dysfunction in the very-low-birth-weight infant was assessed during an investigator-blind trial of [I] prophylaxis for patent ductus arteriosus.

Sixty-one inborn infants were randomized by birth weight (Group A: <900 gm; Group B: 900-1300 gm) to receive either placebo [P] or [I]. The first dose (0.2 mg/kg), given within 12 hours after birth, was followed by two q 12 hourly doses (0.1 mg/kg each). Platelet count (PC) and bleeding time (BT) were obtained prior to Dose # 1, twice within 1-72 hours following dose # 3, and at 1 week postnatal age.

| Group | | PC ($1 \times 10^3$/mm$^3$; $\bar{x}$±SD) Pre-Dose#1 | Post-Dose#3 | p | BT (min.; $\bar{x}$±SD) Pre-Dose#1 | Post-Dose#3 | p |
|---|---|---|---|---|---|---|---|
| A: | P (n=10) | 191±48 | 82±54 | <0.001 | 5±3 | 9.1±5 | <0.05 |
| | I (n=10) | 216±71 | 152±45 | <0.01 | 4.4±1 | 12.3±3 | <0.001 |
| B: | P (n=20) | 202_62 | 145±60 | <0.002 | 5.0±3 | 5.6±3 | NS |
| | I (n=19) | 196±51 | 116±45 | <0.002 | 4.6±2 | 12.7±3 | <0.001 |

Pre-dose #1, mean PC and BT were normal in all groups. PC declined significantly during the first postnatal week in all groups. Maximum BT ≥10 min. post-dose # 3 was noted in 6/10 [P] and 9/10 [I] infants in Group A and 3/20 [P] and 17/19 [I] infants in Group B; p<0.001. In Group A, severely abnormal PC (<75,000/mm$^3$) rather than platelet dysfunction may have affected BT in 5 [P] infants, whereas only 1 [I] infant had PC <75,000/mm$^3$. By one week postnatal age, BT had returned to normal(<6 min) in the majority of [I] infants in both groups A and B.

**†1500** CARDIOPULMONARY EFFECTS OF PROPHYLACTIC INDOMETHACIN IN THE VERY-LOW-BIRTH-WEIGHT INFANT. ES Setzer, E Torres-Arraut, M Gomez-del-Rio, ML Young, I Pacheco, PL Ferrer, RF Scherf, E Bancalari. University of Miami, Jackson Memorial Hospital, Department of Pediatrics, Miami, FL.

To assess the efficacy of prophylactic indomethacin [I] in preventing clinically significant patent ductus arteriosus (PDA), 61 infants were prospectively randomized by birth weight (Group A: <900 g; Group B: 900-1300 g) to receive either placebo [P] or [I] intravenously. The first dose (0.2 mg/kg), given within 12 hours of birth, was followed by two q12 hourly doses (0.1 mg/kg). Investigators were unaware of the study drug given. PDA was considered clinically significant if a murmur and/or positive 2-D Doppler was associated with two of four additional findings: bounding pulses, hyperdynamic precordium, pulmonary plethora, or failure to wean from mechanical ventilation within 48 hours. After the initial course of prophylactic [I] or [P], therapeutic [I] was prescribed for clinically significant PDA unless contraindicated.

| Initial Course | | Significant PDA Yes | No | Neonatal Survival Yes | No |
|---|---|---|---|---|---|
| Group A: | Placebo | 7 | 3 | 8 | 2 |
| | Indomethacin | 1 | 9 | 10 | 0 |
| | | P <0.025 | | P =NS | |
| Group B: | Placebo | 3 | 19 | 21 | 1 |
| | Indomethacin | 1 | 18 | 18 | 1 |
| | | P=NS | | P=NS | |

Prophylactic [I] appeared efficacious in preventing significant PDA in premature infants < 900 grams; however, [I] resulted in no significant impact upon intensity or duration of oxygen requirements or survival.

**1501** ANTENATAL PHENOBARBITAL FOR PREVENTION OF NEONATAL INTRAVENTRICULAR HEMORRHAGE:PRELIMINARY OBSERVATIONS. Seetha Shankaran,Nestor Ilagan,Eugene Cepeda,Federico Mariona,Mary P. Bedard,Ronald L. Poland,Enrique M.Ostrea. Depts. of Pediatrics,Obstetrics & Gynecology,Wayne State Univ.,Childrens Hospital of Mich. & Hutzel Hospital, Detroit.

Eighteen mothers in premature labor <35 week gestation were enrolled in a study to evaluate the effect of antenatal phenobarbital(PB) in preventing neonatal intraventricular hemorrhage.Mothers were randomly assigned to treatment or control groups; the treatment group received 500 mg PB administered intravenously.Maternal and cord blood PB levels were measured at delivery. Echoencephalograms were performed on days 3 and 14 and hemorrhage graded as mild, moderate and severe.

Nine mothers(including one multiple pregnancy) received antenatal PB. Mean time between administration of PB and delivery was 2.9±2.7 hours. Maternal PB levels at delivery were 9.2±2.3 µg/ml. Cord blood PB levels were 9.8±2.1 µg/ml. The PB and control groups were comparable regarding maternal age,duration of rupture of membranes, route of delivery, presentation, birth weight,gestational age,Apgar scores and incidence of pneumothoraces, hypotension,acidosis, hypoxemia,hypercarbia or amount of fluid intake or bicarbonate therapy during the first 3 days. Seven of 10 infants in the PB group had no hemorrhage while 1 had a mild and 2 had severe hemorrhages.Five of 9 infants in the control group had no hemorrhage while 2 had moderate and 2 had severe hemorrhages. When comparing mild or no hemorrhage vs moderate and severe hemorrhage in the 2 groups no significant difference has been found thus far (p = .21).

**●1502** INSULIN RECEPTORS AND EFFECTS ON TYPE II PNEUMOCYTES-AN HYPOTHESIS FOR THE ETIOLOGY OF DECREASED SURFACTANT SYNTHESIS IN INFANTS OF DIABETIC MOTHERS, Donald L. Shapiro, J. N. Livingston, William M. Maniscalco, and Jacob N. Finkelstein, University of Rochester School of Medicine, Department of Pediatrics, Rochester, NY 14642

We analyzed type II pneumocytes, isolated to purity from adult rabbits, for the presence of insulin receptors. Assays were performed on cells cultured for 24 hours in Eagles minimal essential medium. Insulin binding to cells in culture approached a steady-state level by 180 minutes and remained constant for at least one hour. Competition experiments using native insulin, proinsulin, and desoctateptide established specificity of binding. Scatchard analysis of binding revealed a class of high affinity receptors (Kd = $1.5 \times 10^{-10}$ M) and a low affinity component (Kd - $4 \times 10^{-9}$M). The number of receptors was estimated at 2,000 - 4,000/cell. Insulin added to cultures at physiologic concentrations produced a 60% increase in incorporation of labelled glucose into cellular fatty acid and in incorporation of choline into phosphatidylcholine. A dose response relationship was demonstrated. The presence of insulin receptors on type II pneumocytes and the effect of insulin on phospholipid synthesis suggest a mechanism for the disorder of surfactant synthesis in infants of diabetic mothers: chronic hyperglycemia & hyperinsulinemia leads to diminished reactivity ("down-regulation") of insulin receptors during fetal life; in late gestation and after birth the hyporeactive insulin receptors do not allow sufficient substrate into cells for surfactant synthesis.

**1503** RELIABILITY OF ROUTINE TRANSCUTANEOUS OXYGEN MONITORING IN NEWBORN INTENSIVE CARE. Richard J. Sheridan and Sheldon B. Korones, Univ. of Tenn. CHS, Depts. of Pediatrics and OB-GYN, Memphis, TN. (Spon. by Henrietta Bada)

Questions have been raised regarding the reliability of routine transcutaneous oxygen ($TcPO_2$) monitoring in newborn care. We carried out a prospective study to determine whether the problems with $TcPO_2$ monitoring were related to the instrumentation itself or to personnel operation. In our nursery, $TcPO_2$ monitors are maintained, calibrated and electrodes applied on the infants by their nurses. 51 paired $TcPO_2$-$PaO_2$ readings obtained under these routine conditions correlated significantly, r = 0.48, p <.001. A second series of observations were then made with one individual responsible for all the monitoring. 56 $TcPO_2$-$PaO_2$ determinations also correlated, r = 0.93, p <.001. While in both sets of data, $TcPO_2$ correlated significantly with $PaO_2$, a better correlation was obtained under restricted conditions (p <.03). The table summarizes the frequency of failure and error in detection of hypoxia and hyperoxia.

| | Routine Use | Restricted Use |
|---|---|---|
| Hypoxia undetected | 3/7 (43%) | 1/10 (10%) |
| Hyperoxia undetected | 9/11 (82%) | 5/12 (42%) |
| Erroneous hypoxia | 7/33 (21%) | 3/34 ( 9%) |
| Erroneous hyperoxia | 2/33 ( 6%) | 0/34 ( 0%) |

Higher frequencies of errors were observed with routine use, 21/51 (42%) compared to the restricted use, 9/56 (16%), $X^2$ = 8.34, df = 1, p <.005. This study demonstrates the reliability and accuracy of routine $TcPO_2$ monitoring is significantly affected by personnel operation.

**1504** MACACA MULATTA AS AN HOMOLOGOUS MODEL FOR CHRONIC PROBLEMS OF PREMATURITY. Craig T. Shoemaker, Boyd W. Goetzman, and John Anderson. Department of Pediatrics and California Primate Research Center, University of California, Davis.

Some investigators do not consider smaller primates a reasonable model for chronic problems of VLBW infants by because of mechanical difficulties in life support. We evaluated the premature rhesus monkey as a feasible model of long term complications of prematurity.

We delivered, by hysterotomy, three M. Mulatta primates at 74-87% of gestation. Weights ranged from 313-467 gms. Two infants had radiograpahic evidence of HMD. All animals had tracheal intubation immediately after delivery and required continuous medical support until resolution of their lung disease, which had occured in 2 animals by day 5. The infants were ventilated with a Baby Bird ventilator, and temperature was maintained under a radiant warmer. Periodic sampling was done through an umbilical artery catheter for blood gas, hematology, and chemistry values. Blood was replaced from an adult rhesus donor. Infant monkeys required similar ventilator management to VLBW human infants. Except for increased glucose requirements, metabolic needs appeared similar to those of human infants, as were hematologic and serum chemical values. During the first four days of management, we successfully assessed auditory evoked potentials during bilirubin infusion, pulmonary macrophage function, and cord blood neutrophil function. Thus, the premature rhesus monkey appears to be a feasible and useful homologue for a variety of postnatal problems of VLBW infants.