1270 DEVELOPMENT OF PULMONARY METABOLISM OF PROSTAGLANDIN E_2 Ronald I. Clyman, Michael A. Heymann, Univ. of Calif. CVRI and Dept. Peds, Mt. Zion Med. Center, SF

The preterm newborn lamb has high concentrations of circulating prostaglandin E_2 (PGE_2) that may play a role in maintaining the patency of the ductus arteriosus. PGE_2 is removed rapidly from the venous circulation by the lung and is metabolized to its 15-keto metabolites by the intracellular enzyme, 15-OH prostaglandin dehydrogenase (15-OHPD). We studied the ability of the isolated, perfused lung from 100 days gestation (n=8) and near term (term is 150 days) lamb fetuses (n=10) to metabolize PGE_2. After an intraaterial infusion of ^3H-PGE_2 and ^{14}C-inulin (to act as a marker of extracellular space), the majority of ^3H activity was cleared through the lung after the ^{14}C activity had fallen to negligible values. The ^3H activity that was retained longer in the lung was primarily associated with the 15-keto metabolites of PGE_2. Lungs from immature fetal lambs metabolized 25% less PGE_2 than did lungs from animals near term. 15-OHPD activity in homogenates of lamb lung is not higher near term than at 100 days. This suggests that transport processes that regulate the uptake of PGE_2 into the intracellular compartment, and not 15-OHPD, may represent the limiting step in the pulmonary clearance of PGE_2 in the developing lamb lung. This is consistent with our prior observation that premature lambs have decreased plasma clearance rates (in vivo) and elevated circulating concentrations of PGE_2 when compared with term newborn lambs.

1271 PDA WITH SURFACTANT REPLACEMENT THERAPY Ronald I. Clyman, Alan Jobe, Michael A. Heymann, and Machiko Ikegami Univ. CA, CVRI, and Dept. Peds, Mt. Zion Med. Ctr., SF and Harbor-UCLA, Torrance

Surfactant instillation into the trachea of preterm infants with RDS is associated with a 90% incidence of PDA. We studied the effects of surfactant therapy on the ductus arteriosus (DA) in 12 preterm lambs (.89 gestation). Flow (Q) across the DA and systemic blood flow were calculated from microsphere injections. All 12 lambs were paralyzed and ventilated with 100% O_2. All developed respiratory failure (pH<7.1, PCO>60) by 30 min after birth. Between 30-60 mins after birth, 6 lambs were treated with tracheal instillation of 50 mg/kg surfactant lipid (purified from alveolar washes from adult sheep). There were no significant differences between control and treated animals prior to surfactant instillation for PCO_2, pH, prostaglandin (PG) E_2 concentrations, the ratio of L→R shunt through the DA vs systemic flow (Q shunt/Q syst), DA resistance, or the ratio of pulmonary to systemic vascular resistance (RP/RS). By 2 hr after birth treated lambs differed significantly from controls in pH (7.27±.02 vs 6.97±.08) and PCO_2 (43.3±4.1 vs 85±15). There were no differences in PO_2 (146±50 vs 84±44), PGE_2 concentrations or DA resistance. However, there was a significantly larger shunt through the DA in treated lambs (Q shunt/syst=.70±.14 vs .25±10). This increased DA shunt was due to the significant drop in pulmonary vascular resistance (RP/RS=.47±.08 vs .76±.08) and not to a change in patency of the DA. Surfactant replacement may require interventions directed at the PDA to adequately treated sick preterm infants.

1272 RELATIONSHIP OF THE PULMONARY EXCRETION RATE OF CO (Ve_{CO}) AND THE BLOOD CARBOXYHEMOGLOBIN LEVEL (COHb) IN PREMATURES AND TERMS. Ronald S. Cohen, Andrew O. Hopper, Barrett E. Cowan, Clinton R. Ostrander and David K. Stevenson (Spon. by Philip Sunshine), Dept. of Pediatrics, Stanford Univ. School of Medicine, Stanford, California.

Using a flow-through collection system and a reduction gas detector (res.= 1 ppb CO/2.5 ml sample), we made paired measurements of Ve_{CO} and COHb in 32 terms (38-42 wks) and 24 prematures (28-36 wks) breathing room air in the first week of life. The terms included babies with a wide range of endogenous CO production rates (V_{CO}). For an individual baby, Ve_{CO} was repeatable with an error of ± 8% of the mean Ve_{CO} over 3-4 hrs despite changes in room air CO (RA_{CO}). Based on the line (COHb=.16 RA_{CO}+ .53; r=.59; n=56; p < .0005), we corrected COHb for each baby ($COHb_c$=COHb-.16 RA_{CO}). Using $COHb_c$, we found that $COHb_c$=.021 Ve_{CO}+.19 (r=.71; n=56; p < .0005). When prematures were analyzed alone, the line ($COHb_c$=.017 Ve_{CO}+.30) was less significant (r= .43; p < .05) compared to that ($COHb_c$=.024 Ve_{CO}+.13; r=.75; p < .0005) of terms. A correction for terms alone (.17) did not alter their line; for prematures alone (.097), a 40% increase in the intercept resulted from babies with a high COHb and a low Ve_{CO}. These data suggest that in the steady state 1a) Ve_{CO} reflects V_{CO} and is not affected by RA_{CO}, 1b) COHb reflects both V_{CO} and RA_{CO} and requires correction for RA_{CO}, 2) Ve_{CO} and $COHb_c$ are correlated over a wide range of V_{CO} in prematures and terms, and 3) a paired high COHb and low Ve_{CO} may reflect problems of ventilation and perfusion or shunt which occur in prematures.

1273 THE PULMONARY EXCRETION RATE OF CARBON MONOXIDE (Ve_{CO}) AND THE BLOOD CARBOXYHEMOGLOBIN LEVEL (COHb) IN PREMATURES AND NORMAL TERMS. Ronald S. Cohen, Andrew O. Hopper, Gloria B. Stevens, Clinton R. Ostrander, and David K. Stevenson (Spon. by Philip Sunshine), Dept. of Pediatrics, Stanford Univ. School of Medicine, Stanford, California.

Using a flow-through collection system and a highly sensitive (1 ppb CO per 2.5 ml sample) reduction gas detector, we measured Ve_{CO} and COHb (1-2 λ whole blood) in 20 normal terms (38-42 wks) and 23 prematures (28-36 wks) breathing room air in the first week of life. The mean Ve_{CO} (16.7±5.0 µl/kg/hr) of the prematures was greater than that (13.9±3.5 µl/kg/hr) of the normal terms (p < .05). Ve_{CO} varied among the prematures (range 5.6 to 28.1 µl/kg/hr) and was not related simply to gestational age. Based on a linear relationship between room air CO (RA_{CO}) and COHb (p < .0005), each infant's COHb was corrected ($COHb_c$) for RA_{CO} (.36 - 3.10 ppm). The mean $COHb_c$ (.58±.18% sat.) of prematures (range .29-1.19%) was greater than that (.45±.11% sat.; n=15) of normal terms (p < .025). The 8 prematures who required phototherapy had higher Ve_{CO} (19.5±5.5 vs 15.1±4.1 µl/kg/hr; p < .05) and higher $COHb_c$ (.71±.21 vs.51±.12% sat.; p < .01) means compared to those of the prematures who did not. These data suggest that 1) prematures have a wide range of CO production rates, 2) this range is not the result of known hemolytic disease or related simply to gestational age, and 3) other factors associated with prematurity but variable among individual prematures may be contributing to increased CO production rates in certain infants.

1274 OUTCOME OF VERY LOW BIRTH WEIGHT (VLBW) INFANTS. Ronald S. Cohen, David K. Stevenson, Natalie Malachowski, Andrew O. Hopper, Keith J. Kimble, Ronald L. Ariagno, John D. Johnson and Philip Sunshine, Dept. of Pediatrics, Stanford Univ. School of Medicine, Stanford, Calif.

From 1961-76, 229 VLBW infants (750-1000 gm) were admitted to the Stanford Intensive Care Nursery. Of these, 144 (63%) died at < 28 days of age; there were 11 late deaths, including 4 post-discharge. The overall mortality was 68%. Of 74 survivors, 60 with a mean BW of 928±67 (S.D.) gm were followed for 3 years. Thirty-eight % of those followed had a history of mechanical ventilation; none requiring this prior to 1967 survived. Psychometric testing of 48 children at 3 years of age resulted in a mean IQ of 92±20 (S.D.); using matched-pair analysis, the mean IQ 90±20 (S.D.), of 28 children was not different from that, 96±18 (S.D.), of their siblings. Seventy-two % of all survivors followed were completely normal at 3 years of age. Of 17 with late morbidity, 10 have moderate handicaps (IQ 60-80, neuromuscular disability requiring physical or orthopedic therapy but not compromising functional independence, or remediable visual or hearing deficits), and 7 have severe handicaps (IQ < 60, neuromuscular disability compromising functional independence, blindness, or deafness). From 1977-79, the mean yearly admission rate of VLBW infants was > 2-fold that from 1961-76; this fact was associated with a 76% (75/99) overall survival which was > that, 32% (74/229), prior to 1977 (p < .001). Our improved survival rate for more infants yearly and our low incidence of severe late morbidity (12%) are encouraging results of intensive care for VLBW infants.

1275 EPIDEMIOLOGY OF ADVERSE REACTIONS TO TOTAL PARENTERAL NUTRITION (TPN) Judith M.Collinge, Patrick Seliske, Jacob V. Aranda, Depts of Pediatrics, Pharmacology & Therapeutics, McGill Univ-Montreal Children's Hospital, Montreal, Quebec, Canada.

To determine the magnitude of the risks in TPN delivered via peripheral vein, the incidence of adverse reactions to TPN was evaluated as a part of on-going prospective study on neonatal adverse drug reactions. Data on 456 neonates admitted to the Neonatal Intensive Care Unit were analyzed. Of these, 105 babies (23%) had TPN(glucose, amigen, intralipid) for 3024 days with a mean TPN duration of 28.3 days per patient (range 1-174 d). TPN was started at age 5.1 d (range 1-48) for GI abnormalities (33.3%,e.g. necrotizing enterocolitis omphalocoele), severe prematurity (13.3%) and respiratory disorders (39.0%). 96 neonates survived (91.4%). 7 had a total of 9 central venous lines. The average weight gain per day was 8.36 g (range- 35 to 30.5 g). Hyperglycemia (>150 mg/dl, peak 695 mg/dl) occurred in 28 babies (26.7%), glycosuria in 19.0% and significant lipidemia in 18.1%. Abnormal liver function tests and liver disease were noted in 20 babies (19.0%); due to cytomegalovirus in one with no definitive cause in the others. 324 skin necrosis or sloughs (>0.5 cm) occurred in 71 babies (67.6%) while on TPN. 2 neonates developed severe trace metal deficiency, 1 died. Data underscore need for close surveillance and improvement of TPN techniques in the neonate.