

1753

BRONCHOPULMONARY DYSPLASIA - WHO GETS IT? PERTINENT FACTORS. K. Desmond, P. Van Reempts, R. Pye, A.L. Coates, A. Papageorgiou. McGill University, The SMD

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Many factors have been implicated in the development of BPD with  $O_2$  and IPPV being the most important. However, not all ventilated infants develop BPD. In order to determine which factors associated with IPPV therapy contribute to the development of BPD, 145 successively ventilated infants were studied. All were inborn. The 75 infants who were ventilated for >3 days and survived >10 days were analyzed. Of these, 41 developed clinical and radiological BPD and 33 did not. The two groups were similar (BPD vs non BPD) for GA ( $28.0 \pm 3.0$  vs  $28.9 \pm 3.4$  weeks), BW ( $1167 \pm 561$  vs  $1207 \pm 534$ gms), sex, temperature on arrival at the NICU, appropriateness for GA, indication for ventilation, incidence of pneumothoraces (8/41 vs 6/33) and PDA (16/41 vs 14/33). Statistically significant differences were found in  $O_2$  exposure, peak pressures ( $28.6 \pm 10$  vs  $21.5 \pm 7.4$  cm H $_2$ O,  $p = 0.001$ ), length of time on pressure >20 cm H $_2$ O ( $13.0 \pm 20.0$  vs  $3.6 \pm 5$  days  $p = 0.01$ ) and duration of ventilation ( $27.7 \pm 25.1$  vs  $10.8 \pm 8$  days  $p = 0.001$ ). Our data support the concept that  $O_2$ , pressures and time spent on IPPV are strongly associated with BPD. However, contrary to what has been previously reported, we found that the presence of pneumothoraces or PDA were not significant associated factors in the development of BPD.

1754

THE EFFECT OF DIABETIC PREGNANCY ON LECTIN BINDING OF THE ALVEOLAR EPITHELIUM. Maria Teresa Dixon and Ralph A. Jersild, Jr., Indiana University, School of Medicine, Anatomy Dept., Indianapolis, Indiana. (Spon. by W. H. Tooley)

Maternal hyperglycemia, secondary to diabetes, has been associated with an increased incidence of respiratory distress syndrome (N. Engl. J. Med. 294, 1976). We have previously reported (Am. J. Pathol. 113, 1983) that diabetic pregnancy in the rat increases ConA binding to the luminal surface of the alveolar epithelium of the fetus and newborn. The present study shows that the increase in ConA binding reverses to normal within 7-9 days post-partum; there is also an increase in RCA-I binding to the cell surface of alveolar epithelial cells without significant differences in WGA binding. Lungs from normal and diabetic pregnancy neonates were studied at intervals from 1-21 days post-partum. Portions of lavaged and fixed tissue were incubated in either ferritin conjugated ConA, WGA, RCA-I or in control media and prepared for EM. The density of cell surface binding sites was measured. A significant increase in lectin binding was shown in diabetic pregnancy neonates for ConA and RCA-I. WGA binding was not significantly different from controls, but was 2-fold greater than the adult lung. In contrast to the control, in the lung of the neonate of diabetic pregnancy, some of the WGA binding was neuraminidase insensitive. The results show that maternal diabetes leads to alterations in glycosylation of membrane glycoconjugates in the newborn that might influence differentiation or function.

1755

WHAT IS THE OBJECTIVE OF FUROSEMIDE THERAPY IN INFANTS WITH CHRONIC LUNG DISEASE? Barbara Engelhardt and Thomas A. Hazinski. Vanderbilt School of Medicine, Department of Pediatrics, Nashville, TN. (Sponsored by Robert B. Cotton)

Although furosemide (F) improves lung mechanics in infants with chronic lung disease (CLD), this effect may not be important unless gas exchange also improves. To determine the relationship between improvement in mechanics and improvement in gas exchange, we studied the acute and chronic effects of F therapy in 10 infants with CLD aged 4-24 weeks who were both oxygen dependent and hypercarbic. Each infant was studied 3 times: before F therapy, 1 h after the first dose of F (2 mg/Kg IV), and after a 6-10 day course (2 mg/Kg/day IV or 4 mg/Kg/day po). We measured skin surface (s)  $pO_2$  and  $pCO_2$ , esophageal pressure, airflow and tidal volume; and we calculated pulmonary resistance (R), lung compliance (C) and the alveolar to skin (A-s)  $pO_2$  gradient. Criteria for improvement were a fall in  $PsCO_2 > 2$  torr, a fall in the A-s gradient >10 torr, and a > 15% rise in C or fall in R. For the latter 4 variables we compared the acute effect of F with its chronic effect. We found that after both acute and chronic F, compliance, resistance and  $PsCO_2$  improved significantly from baseline values, but A-s  $pO_2$  gradient did not. Overall, mechanics improved in 9 patients, but gas exchange improved in only 6. In individual patients, improvement in R or C was unrelated to improvement in either gas exchange variable. However, the infants whose gas exchange chronically improved could be predicted by the acute change in  $PsCO_2$  or in  $pO_2$  gradient. We conclude that 1) F improves lung mechanics but may have little effect on gas exchange and 2) skin surface monitoring of the first dose of F can accurately identify those who will respond to chronic F therapy.

1756

FETAL LUNG DYNAMICS. E. E. Farrell, M.D., Dept. of Pediatrics, Evanston Hospital, Northwestern Medical School and J. C. Birnholz, M.D., Dept. of Radiology, Rush Medical College, Chicago, IL. (Spon. by Dr. C.E. Hunt)

The fetal lung may be visualized ultrasonically. Lung hypoplasia can be recognized antenatally from relative measurements of the lung, heart, and upper abdomen.

We have studied the changing dynamic behavior of the lung by grading lingular or right middle lobe movements during diastole with a large aperture, magnification imaging system. The lungs appear to be "stiff" initially (en block movement) and become "compressible" abruptly in the majority of cases around 36 weeks (cross sectional survey of 250 cases of known gestational age,  $p < .001$ ). "Compressibility" can occur earlier in the third trimester. A group of 21 cases with "compressibility," normal lung volume, and premature delivery within 36 hours of the ultrasound examination were without respiratory distress syndrome, independent of gestational age or amniotic fluid L/S values. Conversely, four fetuses with "stiff" lungs were delivered prematurely for maternal reasons and all developed respiratory distress syndrome.

We believe these ultrasonically observable features of lung mechanics can be correlated with the thickness of the interstitium and may be an indicator of fetal lung maturation.

1757

NO CARDIAC ARRHYTHMIAS WITH COMBINED BRONCHODILATOR THERAPY IN CHILDREN WITH ASTHMA. Charles Feldman, Allan Hordof, Bernard Feldman, Robert Garofano, William Davis. St. Mary's Hospital for Children, Bayside, New York and Columbia University College of Physicians and Surgeons, Department of Pediatrics, New York.

Theophylline (T) and beta adrenergic agonists are commonly used in combination therapy for the control of asthma. Previous animal studies have suggested that this may result in the induction of significant cardiac arrhythmias (CA). This study examined the effects of combined bronchodilator therapy in 7 children with chronic asthma (ages 9-14 years) and used 24 hour Holter monitoring (HM) to document the drug effects on cardiac rhythm. Three drug regimens were administered in random order for 24 hour periods: sustained release (SR) T alone; inhaled albuterol (A) alone; and combined SR T plus A. HM was carried out during each 24 hour drug period. During T alone and T plus A, mean trough T levels were  $12.8 \pm 3.1$  and  $13.4 \pm 3.3$  ug/ml ( $M \pm SD$ ). For A alone, T had been withheld for 24 hours, with trough T level of  $1.6 \pm 1.7$ . Sequential pulmonary function testing performed for 8 hours for each drug regimen showed comparable improvement of FEV $_1$ , PEFR and FEF $_{25-75}$  above baseline levels. Peak heart rate during a dosing interval was increased to a comparable degree by all treatment regimens: T= $18.9 \pm 17.5$  beats/min; A= $12 \pm 7.6$ ; T plus A= $18.3 \pm 11.5$ . Only 1/7 patients had ventricular ectopy, uniform single ventricular premature depolarizations (VPD), with the mean hourly frequency identical for all treatment regimens ( $2.4 \pm 2.6$  VPD/hour). We conclude that the combination of SR T plus A does not significantly increase heart rate more than T or A alone and does not induce significant CA.

1758

IDENTIFICATION OF POPULATIONS OF CELLS FROM FETAL RABBIT LUNG USING MONOCLONAL ANTIBODIES AGAINST ADULT TYPE II PNEUMOCYTES. Jacob N. Finkelstein, James F. Leary, Robert H. Notter, Donald L. Shapiro. University of Rochester School of Medicine, Strong Memorial Hospital, Department of Pediatrics, Rochester, NY 14642.

A panel of monoclonal antibodies (McAb) prepared against surface antigens of freshly isolated adult rabbit type II pneumocytes was used to investigate the appearance of type II pneumocyte specific populations in fetal rabbit lung. Antibody binding to cells was assessed both by immunoperoxidase assay as well as indirect immunofluorescence detection with avidin conjugated phycoerythrin (PE). Fluorescent cells were analyzed by laser flow cytometry to identify specific cellular populations at various fetal ages. Polyacrylamide gel electrophoresis and immunoblot analysis were used to identify specific antigenic species on the cells. In adult lung cell populations a McAb (API63) exhibited prominent staining of lamellar body (LB) containing cells. API63 also showed high staining of LB-containing cells from fetuses at 27 day and 28 day gestation. Moreover, API63 exhibited a distinct antibody positive subpopulation in cells from 24 day fetuses, where LB containing cells are negligible. Two additional McAbs, API117 and API125 were also positive for LB containing cells in adults but showed progressive decline with decreasing gestational age. These results suggest that different patterns of expression of cell surface antigens are present in the developing lung. Combinations of McAb bound to specific antigens may be useful in isolation of undifferentiated precursors of type II pneumocytes. (Supported by NSF Grant PCM8215152 and NIH Grant HL 29915)