61 THERAPEUTIC POTENTIAL OF ANTIBIOTICS IN METHYLMALONIC ACIDAEMIA.

M. Bain, S.P. Borriello, P.J. Reed, M. Jones, R.A. Chalmers, B.M. Tracey, T.E. Stacey. Perinatal and Child Health, Division of Communicable Diseases, MRC Clinical Research Centre, Harrow, Middx. UK

The chance observation that a patient with methylmalonic acidaemia (MMA) improved clinically and biochemically with amoxycillin given for a chest infection led to speculation about the contributory role of volatile fatty acids (VFA) produced by faecal bacteria. Response to amoxycillin was not sustained, and metronidazole was selected for further study, being active against anaerobes, which are the major producers of VFA's. Urinary methylmalonic acid (MM) and stool propionate, a precursor of MM were estimated over a period of 40 days before and 90 days during metronidazole treatment (11 mg/kg). Urinary MM fell from 12.8 mole/mole creatinine (SD 4.21 n=17) to 3.5 (SD 1.5 n=15), $p < 0.001$. Stool propionate fell from 101 µmole/ml stool (SD 5.3 n =13), to 2.1 (SD 6.8 n=23), $p < 0.001$. Neomycin had previously been shown to improve metabolic control in MMA. This is the first study correlating stool propionate and urine methylmalonate excretion in response to antibiotics in MMA. The faecal flora may contribute up to 70% of the substrate for propionate metabolism. This suggests a previously largely unexplored metabolic role for the intestinal flora and a novel avenue of therapy for MMA.

62 OBSERVATIONS ON LIPOSOME SUBSTITUTION IN PRETERM INFANTS WITH RESPIRATORY DISTRESS SYNDROME (RDS)

M. Obladen, M. Flörecke, B. Kaminski, P. Stevens. University Children's Hospital, 4630 Bochum, F.R.G.

Surface active large unilamellar vesicles containing 80% dipalmitoylphosphatidylcholine and 20% phosphatidylglycerol were injected into the tracheal tube of 6 preterm infants (birth weight 820-1230 g) with severe RDS and poor prognosis. Entry criteria for the pilot study were: Respiratory failure, X ray grade >2, gestational age <30 weeks, weight <1500 g, age <6 hours, parental informed consent. The phospholipid lung profile was studied in tracheal aspirates, tidal volume was measured by pneumotachography. - Neonatal courses were highly variable, probably due to different age and degree of RDS at the time of substitution. No infant showed complete and continuing recovery immediately after phospholipid application. 4 newborns survived. No patent ductus, but 2 pneumothoraces were observed. After a short initial decrease, tidal volume increased from 4 to 8 ml/kg and compliance from 0.3 to 0.6 ml/cm H_2O/kg in 3 infants within 6 hours after treatment. In two of them, FiO_2 could be reduced from 1.0 to .25 within few hours, in one of them respiratory failure returned after 24 hours. The other showed a dramatic improvement of compliance and oxygenation, but died at the age of 46 hours from intraventricular hemorrhage. One infant did not respond to substitution and died at 16 hours from hypoxia. In two infants treated at 3-5 hours of age, an increase of tidal volume and oxygenation did not occur until 6-24 hours after substitution. Phosphatidylglycerol was detectable in tracheal aspirates 24 hours to 4 days after liposome application.

63 "SURFACTANT REPLACEMENT THERAPY" IN SURFACTANT DEPLETED RABBITS: LUNGFUNCTION, SURVIVAL AND BIOCHEMICAL ASPECTS.

S. Bambang Oetomo, D.J. Reyngoud, Ch.R.H. Wildevuur, A. Okken. Depts. Pediat. and Exp. Surgery State University Groningen The Netherlands.

To study the effects of surfactant replacement therapy in Respiratory Distress Syndrome we induced surfactant deficiency in adult artificially ventilated (F_iO_2 1.0) rabbits by lung lavage. 19 Animals received natural sheep surfactant intratracheal, 6 served as controls.
Results: In all surfactant treated animals PaO_2 rose instantaneously from 11.31±5.00 to 37.78±13.40 kPa (mean±S.D.) ($p<0.01$). $PaCO_2$ did not change significantly neither did dynamic lungcompliance. 9 Of the 19 surfactant treated animals were succesfully weaned off the ventilator. Static lung compliance was 1.07±0.30 in surviving, 0.71±0.08 in non-surviving ($p<0.05$) and 0.33±0.09 ml/cm H_2O/kg bodyweight in controls ($p<0.01$). Phospholipid content of the lamellar body fraction, isolated from lung tissue increased from 0.97±0.33 to 2.50±0.10 µmol/g wet weight in the surfactant treated animals.
Conclusion: Surfactant replacement results in an instantaneous rise in PaO_2. This rise is not associated with a change in dynamic lung compliance, however static lung compliance is improved after surfactant replacement. Phospholipid analysis of the lamellar body fraction indicates that the administered surfactant phospholipids seem to be incorporated by the lamellar bodies of the type II alveolar cells.

64 UNDERESTIMATION OF PaO_2 BY $tcPO_2$ WITH INCREASING POSTNATAL AGE.

PA Hamilton, MD Whitehead, EOR Reynolds. Dept. of Paediatrics, University College London, London WC1E 6JJ, England.

This study was performed to find out whether the relation between transcutaneous oxygen tension ($tcPO_2$) and arterial oxygen tension (PaO_2) changed with increasing gestational and postnatal age.
160 simultaneous measurements of $tcPO_2$ and PaO_2 were made at weekly intervals on 42 babies born at 24-41 weeks of gestation and aged 0-32 weeks from birth. $tcPO_2$ was measured using a Dräger Transoxode $tcPO_2$ electrode set at 44°C and connected to a chart recorder. Arterial blood samples were obtained with minimal disturbance of the baby as judged by the stability of the $tcPO_2$ record. PaO_2 was measured using an IL 1303 blood gas analyser.
At 0-1 week of postnatal age, mean $tcPO_2/PaO_2$ in 15 babies born at <30 weeks of gestation was 1.11 ± SD 0.11, n=19, and in 11 babies of >30 weeks of gestation it was 1.02 ± 0.09, n=13 (n.s.). The tendency towards higher values for $tcPO_2/PaO_2$ in less mature babies persisted during the succeeding weeks but was not statistically significant. Irrespective of gestation, a progressive underestimate of PaO_2 by $tcPO_2$ with increasing postnatal age was found. For example, mean $tcPO_2/PaO_2$ from observations on 16 babies >8 weeks old was 0.83 ± 0.15, n=72, significantly lower than in 36 babies <8 weeks old, 1.00 ± 0.13, n=88 ($p<0.001$).
We conclude that (1) $tcPO_2$ underestimated PaO_2 with increasing postnatal age and (2) this underestimate could lead to older babies being nursed in an inappropriately high ambient oxygen concentration.

65 REDUCTION OF RESPIRATORY WORK DURING HELIUM-OXYGEN BREATHING IN BRONCHOPULMONARY DYSPLASIA.

M.R. Wolfson, V.K. Bhutani, F.W. Bowen Jr., and T.H. Shaffer. Temple Univ. Sch. of Med., Dept. of Physiol., Univ. of Pennsylvania, Sec. on Newborn Pediatrics, Pennsylvania Hospital, Phila., Pa., U.S.A.

Pulmonary functions were evaluated in 12 preterm neonates with Bronchopulmonary Dysplasia (BPD) before and during administration of Heliox in order to study the effect of reduced turbulence associated with a low density gas mixture. Mean gestational age and birth weight were 28.5±.60 SEM weeks and 970±80 SEM grams, respectively. The infants were studied at a mean age of 57.3±10 SEM days, weight of 1980±220 SEM grams, and the inspired oxygen concentration ranged from 21-33%. All neonates were spontaneously breathing and symptomatic of BPD characterized by tachypnea, retractions, radiographic alterations and the need for supplemental oxygen. Control (mean ± SEM) pulmonary function data were: frequency (f)=60.5±3.3 bth/M; tidal volume (V_T)=8.4±1.0ml/kg; pulmonary resistance (R_L)=3.49±.33cmH_2O/L/M; minute ventilation (MV)=504.6±68ml/M/kg; resistive work of breathing (WOB)=.102±.02kg/cm/kg; and mechanical power of breathing (POB)=5.39±.65kg cm/kg/M. During Heliox breathing, there was a significant decrease in R_L (Δ30%; $p<.0025$), WOB (Δ53%; $p<.025$), and POB (Δ40%; $p<.0025$) while f, V_T, MV, and C_L remained unchanged. Utilizing this data it was predicted that the oxygen cost of breathing decreased by .26±.05 SEM ml/M/kg resulting in a caloric savings of 1.87±.36 SEM kcal/kg/day while breathing Heliox. These data indicate that in this population, ventilation is maintained while demands on respiratory muscles are decreased during Heliox breathing. Consequently, this modality may reduce respiratory muscle fatigue and caloric requirements for breathing, thus provide additional calories for growth and recovery. (Supported by NIH Grant HL/HD 32031).

66 RELIABILITY AND SAFETY OF TRANSCUTANEOUS CARBON DIOXIDE TENSION ($tcPCO_2$): MONITORING AT 42°C SENSOR TEMPERATURE DURING 24 HRS WITHOUT REPLACEMENT

HU Bucher, S Fanconi, G Duc: Depts of Pediatrics, Obstetrics and Gynecology, University of Zurich, Switzerland

$TcPCO_2$ monitoring is widely used in the neonatal ICU. Reliability and safety of this indirect method to measure arterial PCO_2 ($PaCO_2$) have been questioned, particularly when the sensor remains in place for more than 4 hours. Goal of this study was to assess correlation between $tcPCO_2$ and $PaCO_2$ and skin alterations during 24 hours monitoring without replacement. Patients: 51 critically ill newborns who required an arterial catheter for the clinical management. Weights 680-4170 g, Gestational ages 27-41 weeks. Method: An iridium oxide electrode (Transcapnode Hellige) heated at 42°C was chosen because of better stability than conventional glass electrodes. The sensor was calibrated with 5 and 10% CO_2 and attached to the trunc or to the thigh. $TcPCO_2$ was recorded continuously. Arterial blood samples were drawn systematically at 30' and at 24 hours and on clinical indications. $PaCO_2$ was measured with an IL 313 or an AVL 945 gas analyser. Results: After removal of the sensor no visible change of the skin was noted in 44 infants and a discrete erythema in 7. A blister developed in one patient 24 hours later which disappeared without scar. The correlation of $tcPCO_2$ (y;Torr) vs. $PaCO_2$ (x; Torr) was calculated for 504 paired values: $y = 5.4 + 1.4x$; $r=.89$; $s_{y.x}=6.0$ Torr. There was no systematic difference between the paired values at 30' and those at 24 hours. The transcutaneous sensor detected 61% of hypocapnia ($PaCO_2$<30 Torr, n=38) and 88% of hypercapnia $PaCO_2$>50 Torr, n=73). Conclusion: The correlation between $tcPCO_2$ (42°C) and $PaCO_2$ is acceptabel for clinical use and not influenced by the duration of fixation of the sensor up to 24 hours.