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EFFECTS OF MULTIPLE SMALL DOSES (MSD) OF EXOGENOUS SURFACTANT (S) VS. ONE BOLUS (B) IN SURFACTANT-DEFICIENT RABBITS

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After tracheal instillation of S, changes of blood pressure (BP) and of cerebral blood flow velocities have been observed.

Can such circulatory disturbances be avoided by instillation of MSD? Are oxygenation and pulmonary S distribution affected by this instillation method?

In 9 adult rabbits, respiratory distress was induced by repeated saline lung lavages (until PaO_2 was <80 mmHg with FiO_2 = 1.0). S (Curosurf) labelled with colored microspheres (CMS) was instilled either as B (1 x 200 mg/kg) or as MSD (5 x 50 mg/kg). Arterial blood gases and BP were monitored. To determine S distribution, the lungs of each animal were cut into 60-70 pieces to measure the number of CMS in each piece.

After B, PaO_2 increased to >300 mmHg within 2 min and remained stable. Mean BP dropped transiently from 89±2.1 to 62±6.0 mmHg (mean±SEM). Pulmonary S distribution was fairly homogeneous. After MSD, PaO_2 rose stepwise to >300 mmHg, but decreased again after 1 h. BP dropped from 91±2.1 to 75±10 mmHg. S distribution was very uneven.

With MSD of S instead of one bolus, BP changes cannot be avoided; an even S distribution was not achieved. In spite of a satisfactory initial increase of PaO_2, this beneficial effect of S was transient.

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THE INFLUENCE OF DEXAMETHASONE ON LYMPHOCYTE PROLIFERATION IN WHOLE BLOOD CULTURES OF NEONATES

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Lymphocyte proliferation (LYP) after stimulation with mitogens (phytohaemagglutinin (PHA), pokeweed mitogen (PWM), concanavalin A (CON A)) measured by ^{3}H-thymidine incorporation was performed in whole blood cultures of term (n=19) and preterm (n 13) neonates using minute amounts (100 µl) of cord blood. LYP increased 150 - 400 fold above baseline. Dexamethasone (DEX) (10^{-10} - 10^{-6} mol/l) suppressed stimulated LYP in a concentration dependent manner. In premature neonates treated with DEX for bronchopulmonary dysplasia serum levels of 0.2 - 0.8 x 10^{-8} mol/l were measured. At this concentration medians of only 15% (CON A), 54% (PHA) and 68% (PWM) of the unmedicated LYP were obtained. DEX, hydrocortisone, prednisolone and fludrocortisone in equipotent glucocorticoid concentrations suppressed LYP to the same extent. We conclude that DEX suppresses stimulated LYP in neonates considerably at concentrations applied during treatment for BPD which may well compromise immune function especially infection control.

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RANDOMISED TRIAL OF ROUTINE VERSUS SELECTIVE PARALYSIS DURING VENTILATION FOR NEONATAL RESPIRATORY DISTRESS SYNDROME (RDS).

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We aimed to compare the strategy of non-selective neuromuscular paralysis with that of synchronised (fast rate) ventilation and selective paralysis in infants receiving mechanical ventilation for RDS with chronic lung disease as the primary outcome measure.

One hundred and ninety-three infants under 24 hours of age were enrolled in the study and were allocated to receive either pancuronium during mechanical ventilation in the acute phase of RDS (non-selective group) or synchronised ventilation (initial ventilatory rate at or above that of the infant's) (selective group). Infants in the selective group received pancuronium if they were consistently expiring during the inspiratory phase of the ventilator.

There was no significant difference between the groups with respect to birth weight, gestation and sex distribution. There was no significant difference between the groups with respect to death (selective 19%; non-selective 16%), pneumothorax (selective 13%; non-selective 16%, CLD (selective 47%; non-selective 47%) and oxygen dependency at 36 weeks post conceptual age (selective 27%; non-selective 34%

Routine paralysis of ventilated infants has potential complications which may be avoided by using synchronised ventilation. As the latter is not associated with an increased incidence of long term respiratory complications we conclude that it is the optimal strategy of the two for ventilating infants with RDS.

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RELEASE OF XANTHINE OXIDASE (XO) TO THE SYSTEMIC CIRCULATION DURING RESUSCITATION AFTER SEVERE HYPOXEMIA

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XO may contribute to oxygen free radical production during reoxygenation after hypoxia, but in humans XO is present in substantial amounts only in liver and intestine and possibly to a smaller extent in vascular endothelium. We wanted to determine whether XO is released to the systemic circulation during reoxygenation after general hypoxia and thus possibly contributes to oxygen radical production in other organs also. Plasma levels of XO were determined in 19 newborn pigs resuscitated from severe hypoxemia (8% O_2 until systolic blood pressure had fallen to 20 mmHg). ^{14}C-xanthine was used as substrate, and the ^{14}C-uric acid product was isolated with an HPLC technique and counted Plasma XO was below 2.5 µU/ml in all piglets before hypoxemia and in 4 control piglets throughout the experiment. In 5 of 19 piglets plasma XO rose during reoxygenation to a mean value of 10 (range 4-18) µU/ml after 30 min. In these piglets plasma aspartate aminotransferase increased also (from 20 to 94 U/l), but not alanine aminotransferase (36 to 39 U/ml). We conclude that XO may be released to the systemic circulation after severe hypoxia although in the present experiment XO was only elevated in 5 out of 19 piglets.

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TOTAL PEROXYL RADICAL-TRAPPING CAPABILITY OF PLASMA IN PRETERM INFANTS

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Intensive care results in increased exposure to oxygen radicals and lipid peroxidation, while preterm infants may be unable to deal with such oxidative stress. We measured plasma total peroxyl radical-trapping capability (TRAP) and concentrations of various antioxidants in 21 preterm infants with a mean gestation of 30 wks (range 28-34). Arterial blood samples were taken at 3 and 10 days of age. All the infants needed supplementary oxygen, but none of the infants received vitamin supplementation. TRAP was measured with chemiluminescence, plasma concentrations of ascorbate and α-tocopherol with HPLC and those of urate, bilirubin and glutathione (GSH) with standard laboratory methods. Infants were divided into 2 groups: group I (n=9) with an unfavorable outcome (intracerebral hemorrhage (6) or death before the age of 10 d (3)), and group II (n=12) with a favorable short term outcome. The groups were similar in gestational age and birthweight. Group I needed more supplementary oxygen than group II at day 3 (59 vs 37 %), but not at day 10 (37 vs. 33%). Unexpectedly, group I had higher TRAP than group II at day 3 (2693 vs. 1103 µmol/l, p=0.001). By day 10 the TRAP values consistently decreased, but the difference between groups persisted (2046 vs. 870 µmol/l, p=0.02). TRAP and urate concentration had a significant positive correlation, and urate explained 43% of TRAP. Group I had also higher concentration of ascorbate at day 3 than group II (67 vs. 20 µmol/l, p =0.001). The groups did not differ in: α-tocopherol, bilirubin and GSH concentrations. In conclusion, the infants with a poor outcome had significantly higher TRAP and plasma urate values than the children with a good outcome. This may rather be a consequence of preceeding tissue damage than a cause for subsequent problems.

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ELECTRODERMAL ACTIVITY AND NEONATAL PAIN ASSESSMENT

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Endosomatic electrodermal activity is the electrical activity of the skin when no external current is applied. It is referred to as skin potential, and is measured by the application of surface electrodes. In general it is believed that skin potential gives a measure of arousal, and will change in response to autonomic nervous system activity. In order to assess the use of skin potential as an index of pain in the newborn, we have measured skin potentials in 29 healthy term and 11 healthy preterm neonates (median (range) GA 39 (37-42) and 34 (32-36) weeks respectively) and in 19 preterm neonates receiving intensive care (median GA 26 weeks, range 24-34).

Changes in background skin potential level (SPL) and the occurrence of skin potential responses (SPR) to both noxious stimulus (heel stab blood test) and non-noxious stimuli, such as touch have been assessed in 79 recordings.

SPRs were recorded in 22% sick preterm infants and 45% of healthy infants in response to noxious stimuli. Infants were more likely to show SPR to a non-noxious stimuli than to a noxious stimulus. Spontaneous SPRs were also seen in a number of infants.

Endosomatic electrodermal activity is not a suitable means of pain assessment in the newborn infant as neither skin potential responses nor changes in the skin potential level can be used to differentiate noxious from non-noxious stimuli.