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THE PERSISTENCE OF NON-PROTEIN-BOUND PLASMA IRON IN PRETERM INFANTS.

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Non-protein-bound iron (npb-iron), a potent prooxidant, is present in newborn plasma, and can induce peroxidation of surfactant (Moison et al, Lancet 1993;341:79). This study assessed the persistence of npb-iron (bleomycine assay) in 26 infants (GA; 26-34 wks) for the first 10 days of life. Npb-iron was present in 10 (38%), 7 (27%) and 2 (8%) infants at day 1, 4 and 10 respectively. In 5 babies npb-iron was not present at day 1 but developed at day 4, and in 2 of them it persisted until day 10. Npb-iron was more frequently present in the more immature babies ($p<0.01$) and in babies with a longer duration of O_2 therapy (mean(SD): npb-iron pos 121.4 (174.8), npb-iron neg: 22.3 (40.0) hrs, $p<0.01$), whereas the level of the peroxidation product TBARS did not differ in infants with or without npb-iron. The babies who developed npb-iron at day 4 had a longer duration of O_2 therapy than babies with npb-iron already present at day 1 ($p<0.01$). Npb-iron induced oxidative damage could play a role in the pathogenesis of acute and chronic lung disease in the newborn.

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INCREASED PULMONARY GRANULOCYTE ACTIVATION IN PATENT DUCTUS ARTERIOSUS IN PREMATURE INFANTS

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In premature infants patent ductus arteriosus (PDA) is associated with the development of chronic pulmonary complications such as bronchopulmonary dysplasia. The precise pathogenesis of these complications is unknown.

We followed 13 infants (GA 26±2 weeks, b.w. 903±290 g, mean±SD) with PDA treated by indomethacin during the first week of life. As matched controls served 13 infants without PDA (GA 27±1 weeks, b.w. 1041±430 g). Tracheal aspirates were analyzed for myeloperoxidase (MPO) as an indicator of granulocyte activation. In patients with PDA before indomethacin treatment, tracheal MPO was 14.7±2.9 μg/mg prot, compared with 5.4±3.6 in controls ($p<0.01$). After indomethacin treatment in PDA patients MPO decreased to 4.6±5.6 ($p<0.001$), whereas in untreated controls it remained unchanged 5.4±4.1 (N.S.).

Increased granulocyte activation in the lungs may contribute to the development of pulmonary complications in preterm infants with PDA.

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RECOMBINANT ERYTHROPOIETIN (rhEPO) REDUCES THE NEED FOR TRANSFUSION IN VERY LOW BIRTH WEIGHT (VLBW) INFANTS.

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The anaemias of prematurity are characterized by inadequate erythropoietin response and require frequent transfusions. **Methods:** In a 12 centre blinded trial, VLBW infants were randomized into rhEPO ($n=120$) or control group ($n=121$) on day 3 of life. Blinding was ensured by two independent teams in each centre. rhEPO was given 3 x 250 IU/kg/week s.c. from day 3 to day 42 of life (17 single doses). Oral iron started in both groups on day 14 with 2 mg/day and was adjusted according to serum ferritin levels. **Results:** Reticulocyte (%) and neutrophil counts ($x10^9/l$) at start and end of the study period were (mean±SD):

	reti day 3	reti day 42	neutro day 3	neutro day 42
rhEPO	7.6±5.7	6.4±4.9	7.7±7.8	2.6±1.5
Control	9.6±9.1	4.4±4.3	6.4±4.3	2.7±1.7

Of 177 infants completing the study period, 40 (47%) infants in the rhEPO and 24 (26%) in the control group remained without any transfusion from day 3 to 42 ($p<0.01$). Median cumulated volume of transfused red cells (ml per kg and day) was 0.27 in the rhEPO and 0.47 in the control group ($p<0.05$).

Conclusion: rhEPO, given in a dose of 750 IU/kg/week from day 3 of life, effectively reduces the need for transfusion in VLBW infants.

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HYALURONAN AND WATER CONTENT IN THE LUNGS OF TERM RABBIT PUPS KEPT IN AIR OR OXYGEN.

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Increased lung water is considered to be an important component in neonatal respiratory distress. In adult respiratory distress increased lung water is accompanied by high levels of hyaluronan concentrations in broncho-alveolar lavage fluid (Am Rev Resp Dis 1989;139:682-87). Little is known about lung hyaluronan content in the perinatal period. In rabbit pups lung hyaluronan concentration decreases just before term and lung water decreases at term (Am J Physiol 1991;260:H1449-54). Data on preterm rabbits have been presented previously (Ped Res 1992;32:635. The present study was undertaken to study the effect of oxygen exposure on lung hyaluronan concentration and lung water in rabbit pups born at term. Some pups were kept in oxygen and some were kept in air. Pups were sacrificed and lungs were taken at an age of 4-6 days. The water content was measured as wet/dry weight, and the hyaluronan concentration with a radiometric assay kit (HA 50, Pharmacia, Uppsala).

Results: In the lungs from pups kept in oxygen significantly higher hyaluronan concentrations were seen both at 4 ($p<0.001$;$n=14$) and 6 ($p<0.01$;$n=17$) days of age compared to the lungs from the pups kept in air ($n=15$ and 29, respectively). This was accompanied by a higher lung water content ($p<0.001$) than in pups kept in air at 4 days of age.

Conclusion: In term rabbit pups lung hyaluronan concentration and lung water content increase during oxygen exposure.

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PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN (PPHN) IS SELECTIVELY LOWERED BY PROSTACYCLIN (PC).

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PPHN is a common indication for ECMO because of severe hypoxemia and mortality risk. We studied the effects of PC in 8 infants (b.wt.2540-4130 g, gest. age 34-42 wk) with respiratory failure and PPHN. At mean age 19 (range 3-32) h, despite maximal ventilator therapy and FiO2 of 1.0, mean paO2/PAO2 was 0.07 (range 0.04-0.10) and AaDO2 614 (521-640) mmHg. Mean pulmonary artery pressure (PAP) by echocardiography was 68 (64-80) and syste-mic pressure (BP) 59 (51-64) mmHg. After volume correction and during dopamine infusion, PC was increased stepwise from a mean of 10 to 55 (max. 120) ng/kg/min in 4-12 h, at which time PAP had decreased to 49 (45-55) and BP to 53 (42-63) mmHg, PAP thereafter remaining below BP. After 72 h PAP was 50 (25-86), BP 66 (55-72), paO2/PAO2 0.14 (0.08-0.40), and AaDO2 429 (83-605) at FiO2 of 0.59. All patients survived without ECMO, PC was stopped at 5.3 (3-10.5) d and ventilator therapy at 7.8 (4-13) d. At 6-12 mo, none have CNS complications but 2 have BPD. We conclude that PAP is decreased, right-to-left shunt reversed and oxygenation improved by PC. Adequate plasma/red cell and pressor infusion are able to maintain systemic blood pressure.

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ECONOMICAL EFFECTS OF SURFACTANT TREATMENT

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The effect of surfactants in treatment of neonatal RDS is well known. However, the favourable results increase the demand for neonatal intesive care.

We collected retrospectively clinical and follow-up data of all 29 very low birthweight (VLBW) infants who received surfactant in the OSIRIS-study (from March 1991 to November 1991) and of 30 VLBW patients born during the previous year who did not receive surfactant treatment. Patients were eligible to the control group if they had at least once arterial/alveolar oxygen ratio <0.22.

The gestational age, birthweight and blood pressure, were similar in both groups. Only 6 infants in the control group survived and only 2 of them did not have any neurological sequelae. In the OSIRIS group 20 survived, 9 without neurological complications. The mean duration of neonatal intensive care was 10.2 days in the controll group and 26.8 days in the OSIRIS group. The mean duration of neonatal intensive care of the survivors was 32 days in both groups. A similar effect was observed on the time on respirator, and on the duration of oxygen therapy and of hospital care.

The costs of neonatal intensive care were in 1992 about 1500 US$ and the cost for care on a paediatric ward were about 400 US$ per day. Thus giving a VLBW infant surfactant will increase the costs with at least 36 000 US$. The costs per survivor were without surfactant about 3110 US$ and with surfactant 2730 US$. The costs per healthy survivor were 9330 US$ and 6670 US$, respectively.

This study illustrates the economical problems associated with improvments of neonatal intensive care. Although the price per survivor decreases the increase of total costs is very large. The price of surfactant itself is almost negligible.