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The in vitro effect of Granulocyte colony-stimulating factor on Interleukin-3-dependent proliferation of circulating haemopoietic progenitors in neonates.

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Background: Neonatal neutropenia and sepsis are closely linked. The haematopoietic colony-stimulating factors may be of use in enhancing neonatal host defence.

Aim: To compare the quantitative effects of G-CSF (granulocyte colony-stimulating factor) with GM-CSF (granulocyte-macrophage colony-stimulating factor) and IL-3 (Interleukin-3) on neonatal peripheral progenitor cells in-vitro.

Methods: Progenitor cells from 31 babies (median gestation 32 weeks; birth weight 1.57 Kg) were assayed using a modification of a standard method, in the presence of IL-3 alone; and IL-3 with G-CSF, GM-CSF or G-CSF and GM-CSF. On day 14 CFUg and CFUgm (granulocyte and granulocyte-macrophage colony-forming units) were counted.

Results: Total CFUg and CFUgm were significantly increased in G-CSF/IL-3 and G-CSF/GM-CSF/IL-3-supplemented culture systems ($p < 0.0001$ for both), and in GM-CSF/IL-3 supplemented cultures ($p = 0.0024$), compared to systems with IL-3 alone. There was no difference in total CFUg and CFUgm with addition of GM-CSF to G-CSF.

Conclusions: G-CSF had a positive effect on neonatal myeloid progenitor cells in vitro which was not synergistic with the effect of GM-CSF. G-CSF may be of therapeutic benefit in neutropenic neonates.

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SERUM ERYTHROPOIETIN (EPO) CONCENTRATIONS IN WELL NOURISHED PREMATURE INFANTS WITH AND WITHOUT EPO TREATMENT. Anne G Bechensteen, P Mary Cotes, Per Hågå, Sverre Halvorsen and Ludvig Daae. Departments of Pediatrics and Clinical Chemistry, Ullevål Hospital, University of Oslo.

In healthy AGA preterm infants (n=14, B.W. 900-1400 g) who were supplemented from 3 weeks of age with human milk protein (3g/kg/day), iron (18 -36 mg Fe^{++}/day) and s.c. EPO (Eprex, Cilag, 300IU/kg/week), the anaemia of prematurity was abolished. Control infants (n=15) also had a marked reticulocyte increase, and Hb was at nadir 9.9 g/dl. (Arch Dis Child, in press.)

To evaluate the EPO response to the anaemia serum immunoreactive EPO (siEPO) levels have been measured in these 29 preterm infants. At study start (3 weeks of age) siEPO was 11.5 mU/ml (range: 6.1-24.3). Normal adults: 15.3 mU/ml (9.5-25.8). In the treated infants siEPO was 59.1 mU/ml (31.9-128.0) 24 hours after s.c. injection. At 48 and 72 hours the levels were 19.8 and 10.8 mU/ml respectively. This suggests that EPO injected subcutaneously should be given with 48 hour intervals or shorter. In the controls siEPO was significantly increased 2 weeks after start of nutritional supplements with a mean maximum of 20.5 mU/ml (8.0-50.0) ($p < 0.05$). SiEPO correlated inversely with Hb. EPO decreased following blood transfusions in the 4 infants transfused. In contrast to previous studies, our results suggest that the hypoxia-erythropoietin mechanism operates in well nourished preterm infants.

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BRAIN SIZE AND NEONATAL GLUCOSE TURNOVER RATES

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The brain is probably the major glucose consuming organ in neonates. In adults brain glucose consumption is ± 5 mg/100 g brain tissue/min. In newborn infants with a brain size of ± 130 g/kg body weight this would account for 6.5 mg glucose /kg/min.

Infants: We measured glucose turnover rates in 42 infants on the first day of life , (gestational age 29 - 40 week range, 35.3 ± 3.2 mean ± SD, birth weight 0.88 - 4.77 kg range, 2.23 ± 0.97 mean ± SD) using a stable isotope dilution technique with [6,6 $^2H_2$]glucose. Brain weight was calculated from the head circumference by the method of Cooke et al. (EHD 1977; 1/2: 145-9).

Results: Brain weight was 306 ± 79 g (mean ± SD, range 155 - 435 g). Whole body glucose turnover was 5.4 ± 1.1 mg/kg/min (mean ± SD, 3.1 - 8.2 mg/kg/min range) The amount of glucose theoretically available for brain tissue consumption ranged from 1.85 mg/100 g brain tissue per min in infants with the highest brain size (19.9 % of bodyweight, SGA infants) to 7.02 mg glucose/100 g brain tissue per min in infants with the lowest brain size (8 % of body weight)

Conclusion: Brain tissue glucose consumption in neonates, particularly in SGA infants must be lower than in adults.

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SURFACTANT THERAPY FOLLOWED BY HIGH FREQUENCY OSCILLATION (HFO) IN NEONATAL RESPIRATORY DISTRESS SYNDROME (RDS) : EFFECTS ON GAS EXCHANGE. O. CLARIS, A. BAKR, A. LAPILLONNE, B.L. SALLE. Neonatal Department, Hôpital Edouard Herriot, LYON, FRANCE.

Pulmonary function as assessed by FiO2, Mean Airway Pressure (MAP) and PaO2 was prospectively studied in 57 term and preterm neonates developing RDS and receiving exogenous surfactant followed by HFO. Mean (m ± SD) birthweight was 1554 ± 654 g and m gestational age was 30.2 ± 2.9 weeks. 51 babies received Exosurf at a m post-natal age (PNA) of 3 ± 2 hours (h), a 2nd dose of Exosurf being given to 43 of them at a m PNA of 16 ± 3 h. Curosurf was administrated in 6 neonates at a m PNA of 3 ± 2 h. HFO was initiated at a FiO2 ≥ 0.5 in order to maintain a PaO2 > 7 kPa, at a m PNA of 8 ± 9 h, and lasted for 37 ± 19 h in the Exosurf group, and 4 ± 2 h and 37 ± 19 h respectively in the Curosurf group. a) Exosurf group : FiO2 was significantly reduced from 0.71 to 0.51 (p = 0.003) in 3 h of HFO and reached 0,26 at a PNA of 72 h. MAP was stable during the first 3 h of HFO (13.3 vs 13.7 cm H2O) and was significantly lowered to 12.7 cm H2O 3 h later (p = 0.031), and reached 7 cm H2O at a PNA of 72 h. b) Curosurf group : FiO2 was 0.73 before HFO, 0.45 6 h later (p = 0.022) and 0.30 at 72 h of life. MAP and PaO2 were respectively 13.7, 11.8 (p = 0.031) and 6.4 cm H2O, and 6.6, 7.9 (p = 0.016) and 10.2 kPa. 10 (18%) neonates died, but none because of respiratory problems (9 severe brain haemorrhagic-ischemic lesions, 1 haemorrhagic disease), 1 (2%) developed air leaks an 1 (2%) chronic lung disease. In conclusion : HFO can be safely and efficiently used after surfactant administration in RDS, even with a high MAP.

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INCREASED BLOOD PRESSURE AT BIRTH AND INFANCY IN CHILDREN OF SMOKING MOTHERS. N G Beratis, D Panagoulias, Anastasia Varvarigou. Dept Ped, University of Patras Medical School, Patras, Greece.

Smoking (S) during pregnancy causes several adverse effects on the fetus and child including compromised placental and fetal circulation.Three blind blood pressure (BP) measurments were made using a Dinamap oscillometric recorder. The mean systolic BP±SD mmHg in 32 neonates of S and in 155 neonates of non-S mothers are listed in the Table (*Compared with BP of neonates of non-S mothers).

Age h	Non-S BP	5-15 Cigarettes/ day BP	p*	>15 Cigarettes / day BP	p*
1	62.4±7.3	64.3±5.8	> 0.1	65.9±9.0	≤ 0.05
24	66.4±7.0	68.5±6.4	> 0.1	73.5±9.2	≤ 0.0005
48	69.1±6.6	72.4±5.8	< 0.05	79.5±9.0	≤ 0.0005
72	71.2±5.5	80.0±5.0	< 0.0005	82.4±7.7	≤ 0.005

Similar differences were observed in the diastolic BP. The mean BW±SD in the newborns of the S and non-S mothers was 3124±440 and 3330±418 g, respectively. Neonates of mothers who quit S after conception had normal BP. On reexamination at 4 mos 5 d to 8 mos 25 d of life (mean±SD 6.5±1.7 mos) the mean systolic BP in 10 children of S mothers (>15 cigarettes/ day) and 10 matched controls (similar age and weight) of non-S was 102.3±5.2 and 94.8±7.6, respectively ($p<0.01$). The diastolic BP was 64.6±5.6 and 58.6±4.7, respectively ($p<0.01$). The findings demonstrate increased BP in newborns of S mothers which is maintained at least during the first 6 months of life.

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OXIDATIVE STRESS AND LIPID PEROXIDATION IN THE NEWBORN Giuseppe Buonocore, Stefano Zani, Maria Angela Farnetani, Franco Bagnoli, and Rodolfo Bracci. Division of Neonatology, University of Siena, Siena, Italy

Increasing appreciation of the causative role of oxidative injury in the development of many severe diseases of the newborn places great importance on the reliable assessment of lipid peroxidation. Lipid peroxidation in the erythrocyte membrane has been widely investigated but little has been reported on lipid peroxidation in the plasma. The aim of the present paper was to evaluate lipid peroxidation and peroxidation tissue injury in the plasma of newborns using the concentration of Malondialdehyde (MDA), one of the several substances formed when lipid hydroperoxides break down in biological systems. Twenty-one, healthy, full-term newborn infants, (10 male and 11 female), with an Apgar score of more than 8 at 1 min., were studied. Fifteen were born by vaginal delivery (VD) and 6 by elective cesaerean section (ECS). Heparinized blood samples were taken at birth from the cord blood and on the 4th day of life from a peripheral vein. MDA levels were determined by fluorometric assay using the MDA Kit (Sobioda, Grenoble, France). We found significantly lower concentrations of MDA at birth (2.81±1.34 nmol/mL, mean±1SD) than on 4th day of life (4.35±1.98, $P<0.0003$) in total population. This difference was also observed in the two mode of delivery when considered separately. No statistically significant differences were found between the two groups nor between the sexes. These results clearly demonstrate a significant increase in lipid peroxidation after birth. We speculate that environmental changes in O_2 concentration from fetal to postnatal life are sufficient to produce an increase in aerobic metabolism and in the rate of free radical generation. The deficient antioxidant mechanisms at birth could impair normal fetal equilibrium between oxygen free radical generation and free radical detoxification.