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80% OXYGEN ADMINISTERED TO NEWBORN PREMATURE INFANTS CAUSES PROLONGED CEREBRAL VASOCONSTRICTION.

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Hypothesis Low values of cerebral blood flow(CBF) in newborn, premature infants may partly be due to excessive oxygen administration at birth. Design In a prospective, randomized study of 70 preterm infants (GA<33 wks) we used 21%(GrI) or 80%(GrII) oxygen for the initial stabilisation in the delivery room. Infants in GrI received supplemental oxygen if clinically indicated. Two hours after birth, CBF was measured using the ^{133}Xe-clearance method and left ventricular output(LVO) was calculated using M-mode echocardiography and Doppler ultrasound velocimetry. Results No difference in GA(median 28wks), BW(mean 1125gr), umb. cord pH, AS, use of antenatal steroid or mode of delivery was found between the groups. 9(26%) of the infants in GrI required supplemental oxygen (FiO_2<0.40) in the delivery room. These infants were included in the analysis(GrI). Another infant required intubation before two hrs. of age and was excluded. At the time of measurements no significant differences in MABP, pCO_2, hemoglobine-conc., blood glucose or a/A-ratio were found.

Values are mean(SD)	GrI(n=34)	GrII(n=35)	p-value
CBF ml/100gr/min	17.4(5.2)	13.1(3.9)	0.0002
LVO ml/kg/min	235 (59)	217 (57)	0.24

ANCOVA revealed allocation to initial 80% oxygen as being the strongest and most significant factor (p<0.001).
Conclusion These results suggest cerebral vasoconstriction following a short period of oxygen administration at preterm birth, possibly related to a low antioxidant capacity of preterm infants.

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THE ANTIOXIDATIVE POTENTIAL OF ALVEOLAR SURFACTANT.

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Alveolar surfactant is exposed to a variety of oxidants that can oxidize functionally important lipids and proteins. We examined the hypothesis that the type II pneumocyte equips surfactant with antioxidants to counteract its oxidation.
Rat type II cells, cultured in the presence of ^{14}C-palmitic acid and either ^{3}H-vitamin E or ^{3}H-vitamin D, responded to stimulation with isoproterenol with a time-dependent increase in secretion of ^{14}C-labeled phospholipids and ^{3}H-vitamin E, but not of ^{3}H-vitamin D.
Plasmalogens - a subclass of phospholipids - also act as antioxidants in animal cells. Type II cells, cultured in presence of ^{3}H palmitic acid and ^{14}C hexadecanol, synthesize and secrete ^{3}H labeled phospholipids and ^{14}C labeled plasmalogens spontaneously and in response to isoproterenol stimulation.
In pharyngeal aspirates of healthy newborns vitamin E and plasmalogen contents range from 2-10 nmol/μmol polyunsaturated fatty acids (PUFA) and from 8-20 nmol/μmol PUFA respectively.
We conclude that alveolar surfactant is equipped with lipophilic antioxidants of its own during its formation in type II cells. These lipophilic components could be of use as clinical parameters to evaluate the antioxidative potential of alveolar surfactant.

Supported by BMFT Project "Risikoneugeborenes".

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EXCLUSIVE BREAST FEEDING AND WEIGHT GAIN IN PRETERM INFANTS.

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The advantages of breast feeding as against formula feeding have to be considered in developing countries in terms of adequate weight gain versus high risk of mortality and morbidity in artificially fed preterm and low birth weight infants. Infants born in our unit are discharged home on exclusive breast feeding. Preterm babies are given their own mother's breast milk once early neonatal problems are settled, gradually increasing the number of direct breast feeds. At discharge from the special care nursery these infants are exclusively breast-fed. The weight gain of 355 preterm low birth weight infants who were exclusively breast fed by their own mothers after discharge from the special care nursery was analysed prospectively over the first 25 weeks of infancy. The infants were divided into 4 categories - 30 weeks or less gestation with birth weight appropriate to the gestation (AGA), and small for gestation (SGA), over 30 weeks of gestation SGA and AGA. There were 22 infants of 30 weeks or less gestational age. All were AGA. 333 infants were between 31 weeks gestation to 36 weeks gestation. 106 were SGA and 227 were AGA. The growth velocity for all groups of babies varied between 20 to 30 gms per day. Less than 30 week AGA infants had a growth delay up to 3 weeks. Among the infants over 30 weeks the AGA infants had a more rapid growth than the SGA infants. All 3 groups had a brisk catch up phase and doubled their birth weight by 10 to 12 weeks of age and tripled by 16 to 18 weeks of age. The weights attained were compared to intrauterine growth rates. Thus exclusive breast feeding of preterm and low birth weight infants is appropriate to developing countries.

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CEREBRAL AUTOREGULATION IS A NONLINEAR TYPE CONTROL SYSTEM.

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Introduction. In neonates, low frequency (LF) cerebral blood flow velocity oscillations (CBFV-O) are commonly attributed to an underdampened immature cerebral autoregulation (AR). Peri-intraventricular hemorrhage (PIVH) is linked to this 'instability'. In contrast to linear type control systems, nonlinear type systems express a regular periodicity as a fundamental part of their *stable* function. Aims. To classify the AR, and to identify factors possibly responsible for PIVF by investigating the relationship between CBFV-O, heart rate variability (HR-V), and intermittent positive pressure ventilation (IPPV). Methods. In 5 preterm neonates (GA 26 to 30 w) we serially Doppler-traced arterial CBFV continuously for 12 min every 3 to 7 days between days 1 and 49 of life. Another 5 preterms (GA 26 to 35 w) were traced sporadically. The time series of both CBFV and HR were subjected to spectral analysis. Results. 46/47 tracings showed LF CBFV-O ($p<0.0001$, one sample z-test). For HR, cycling was observed in only 15/47 tracings. LF cycling in HR was not a prerequisite for LF CBFV-O. All patients with < 30 % of total power in the LF band of CBFV-O were on the ventilator. Three of these patients demonstrated a shift of spectral power from LF to a frequency equal or harmonic to the ventilator rate in the sense of entrainment. The range of entrainment encompassed 12 to 25/min stimuli. Conclusion. In analogy to thermo- and blood pressure regulation, CBFVO and entrainment classify the AR as a *nonlinear* system. HR-V has no direct impact on CBFV-O, whereas respiration acts on both HR-V and CBFV-O. We discuss that periodic high-amplitude stimuli (i.e. IPPV in RDS) may challenge the regulatory capacity of the CBF control system as reflected by entrainment. While fragile vascular matrix elements, severe central blood pressure changes, and high pCO2 are prerequisites, entrainment of CBFV-O might be one key event for cerebral damage.

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OPIATES AND INTERMEDIARY METABOLISM IN VENTILATED PRETERM BABIES

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There are few data which indicate benefit from the use of opiates during mechanical ventilation in preterm babies. We have investigated the effect of sedative doses of alfentanil on intermediary metabolism.

Ventilated preterm babies were randomised to receive alfentanil (20 ug/kg bolus & 5 ug/kg/hr) or placebo as a pilot study. Samples were taken pre-dose, 1 hour post-dose and twice daily during infusion. No other change in routine management occurred during the trial. Median birthweight of the study group was 1300g (r:726-2352g), gestation: 29 weeks (26-36 weeks).

Twelve babies received alfentanil from a median age of 16 hours (r:12-36) after birth and 12 babies a placebo infusion from 24 hours (r:10-32). No differences in heart rate, blood pressure or pH were seen between the study groups and similar rates of perinatal complications were seen in each group.

During the administration of alfentanil, glucose rose by 2.02 mmol/l (sem: 1.67) compared to a fall of 0.87 mmol/l (2.94) in the placebo group 1 hour post-dose, and remained on average 1.27 (1.71) mmol/l higher than baseline over the next 24 hours, compared to 2.64 (1.78) mmol/l less among controls. Similar rises in lactate, pyruvate, glycerol were observed in the alfentanil group which persisted over the next 24 hours, in contrast to the anticipated fall. There were no differences in urinary catecholamine excretion.

These data suggest that sedative doses of alfentanil may have no immediate metabolic benefit.

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THE EFFECT OF INOTROPIC THERAPY ON THE VERY PRETERM NEONATAL ELECTROENCEPHALOGRAM (EEG)

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Computerized analysis of the neonatal EEG provides a measure of cerebral function in the very preterm infant. This method has enabled observation of the effects of inotropic infusions on cerebral function in 13 sick infants between 24 and 30 weeks gestation. Inotropes used included dopamine, dobutamine and nor-adrenaline, either singly or in combination as dictated by the clinicians. On commencement of inotropic therapy, no deterioration in EEG was seen and improvement was noted in only 3 of 18 occasions. Monitoring during a further 12 increases in inotropic therapy showed associated improvement in the EEG in only one of these occasions. However, on reduction of the inotropic treatment, which was no longer deemed clinically necessary, there was an associated improvement in EEG in 12 of 16 occasions monitored. The EEG improvement on reduction in inotropic therapy appeared to be related to the duration of use of inotropes and to the duration of time normotension had been achieved. These results imply that withdrawal of inotropic therapy should perhaps be considered as soon as clinically feasible as this deleterious effect of inotropic infusions on cerebral function may be related to enchanced cerebro-vascular sympatho-adrenal tone.