11 FIBRINOLYSIS IN THE CSF FOLLOWING INTRAVENTRICULAR HAEMORHAGE

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Current therapies for posthaemorrhagic hydrocephalus (PHH) such as surgical shunting, repeated tapping and acetazolamide all have major problems and so we are exploring the possibilities of lysis of the obstructing clots. X oligomers, as indicators of fibrinolysis, were measured in CSF from 5 normal preterm infants (mean 102 ng/ml), 6 preterm infants with IVH but no PHH (mean 315 ng/ml) and 8 infants with progressive PHH (mean >500 ng/ml). Serial CSF samples from one infant with IVH showed a peak X oligomer level over 1,000 ng/ml after 15 days.

4 infants were treated with repeated intraventricular injections of urokinase or streptokinase (2,500 or 5,000 units). CSF taken 2-3 days post-injection showed no change in the levels of X oligomers (already very high). Repeated doses were not associated with bleeding problems but hydrocephalus resolved in only one infant.

Conclusions: There is considerable natural fibrinolytic activity in the CSF after IVH. Single intraventricular injections of modest doses of fibrinolytic agents do not have a sustained effect on CSF fibrinolysis or hydrocephalus. Larger doses by infusion look more promising.

12 GASTRO-ESOPHAGEAL REFLUX AND APNEA IN PREMATURELY BORN INFANTS, DURING WAKEFULNESS AND SLEEP

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Apnea of infancy may be caused by gastro-esophageal reflux (GER). We tested the hypothesis that GER may similarly account for cases of persistence after term, of apnea of prematurity (AOP), which usually ceases before. 20 prematurely born infants (GA 31.6±2.8 wks) were selected because they still had apneas of duration ≥ 10s, or regurgitations, at 38.9±1.7 wks of post conceptional age (mean ± SD). GER was identified using esophageal pH monitoring. Recordings of chest and abdominal movements and of nasal airflow enabled apneas to be classified as central (CA), obstructive and mixed (OMA). Wakefulness (W), active sleep (AS) and quiet sleep (QS) were identified using EEG and assessment of eye movements. Results GER occured in the 20 subjects, in W and AS more frequently ($p < 0.02$) than in QS (n of events : 2.77±1.97;2.79±1.99 and 1.46±2.01 per 100 min). OMA (n=113) were predominant. They occured more in AS than in QS ($p < 0.01$). OMA did not occur more during than without GER ; and their number was not correlated with that of GER or with its duration. Conclusion In prematurely born infants with persisting AOP, GER occurs frequently in wakefulness and in AS. Usually, it is not the direct cause of apneas.

13 THE METABOLIC ADAPTATION OF HEALTHY TERM INFANTS IN THE FIRST POSTNATAL WEEK.

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In the light of recent controversy regarding the definition of neonatal hypoglycaemia, it is important to document blood glucose (BG) levels of healthy neonates in relation to other metabolic fuels. A cross sectional study was performed, taking pre-feed samples from 149 infants in the first seven days.

The overall mean BG concentration for the week was 3.67 mmol/l (range 1.50 - 6.18 mmol/l). The widest range of values was seen on the first day. 14% of all infants studied had BG levels ≤ 2.6 mmol/l, with all but two such low levels occurring within the first three days. The maximum mean ketone body levels were found on days 2 and 3 (max. level 2.568 mmol/l). The ketone body: glucose ratio is low on the first day, despite low blood glucose levels, indicating an immaturity of counterregulatory ketogenesis. The ratio rises to a maximum on the second postnatal day.

We conclude that a significant number of infants has low blood glucose levels in the first postnatal week, with an early immaturity of ketogenic response. Longitudinal studies of neonatal metabolic adaptation are required, as well as studies to establish the relationship between metabolic adaptation and neurological function.

14 THE DURATION OF INDOMETHACIN-INDUCED RENAL BLOOD FLOW DISTURBANCES IN PREMATURE INFANTS: ASSESSMENT WITH COLOR-DOPPLER FLOW IMAGING.

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Indomethacin treatment causus renal dysfunction probably secondary to impairment of renal blood flow. We measured renal artery blood flow velocity (RBFV) in 15 preterm infants with symptomatic patent ductus arteriosus before and during the first 12 h after a single intravenous dose of 0.1 mg/kg of Indomethacin. RBFV was serially measured by Color-Doppler Flow Imaging and was used as a relative measure of changes in renal blood flow.

Indomethacin treatment led to a sharp decrease in RBFV, which was maximal at 10 min post-indomethacin and was followed by a slow recovery until baseline values were attained at 4 h. RBFV (mean ± SD) decreased from 25.2 ± 1.9 cm/sec pre-indomethacin to 15.2 ± 3.1 cm/sec at 10 min. and rose 22.3 ± 2.2 cm/sec at 2 h. Mean arterial pressure, heart rate, PaO2 and PaCO2 were stable during the study period. Plasma-Creatinine (mean ± SD) rose from 82 ± 18 umol/ml pre-indomethacin to 95 ± 20 umol/ml post-indomethacin with a decrease in urine production.

We conclude that indomethacin can impact on renal circulation of the preterm infant for a period of 2 h.

15 CEREBRAL- (CBFV) AND AORTIC BLOOD FLOW VELOCITY (AoBFV) IN PRETERM INFANTS DURING AND AFTER SURFACTANT (SF) TREATMENT.

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Cerebral and systemic hemodynamics may be effected by SF-treatment. In 27 infants (GA 30 weeks), enrolled in a profylactic SF-study (curosurf), serial determinations of CBFV, CBFV-variability (CBFV-var) and AoBFV were performed from birth until day 5 using Duplex US. CBFV was derived from the mean velocity of the internal carotid artery and CBFV-var from the variation coefficient of the peak velocity. AoBFV was obtained from the descending aorta. 14 Infants received SF within 10 min after birth (SF-group). 13 Comparable infants served as controls (C-group). In the SF-group PCO2 decreased and FiO2 improved. CBFV increased with a peak at 5 minutes after SF-instillation. After the first 30 min no differences in CBFV were found between the SF-group and controls. CBFV-var was stable in both groups (10%). Only during SF-application CBFV lowered with an increase in CBFV-var, indicating a fluctuating CBFV. After SF treatment AoBFV wave form showed a persistent diastolic reverse flow in all cases and abnormally low diastolic CBFVs, indicating ductal steal. Mean arterial pressure did not differ between groups. Hemodynamic important ductus arteriosus occurred in 9 infants (6 SF-gr) and intraventricular hemorrhage in 5 (3 SF-gr).

We conclude that 1) cerebral blood flow is affected during and up to 30 min after SF-application, 2) left-to-right ductal shunting is a common event following SF-treatment.

16 PENTANE AS INDICATOR OF INCREASED LIPID PEROXIDATION IN BB RATS DURING DEVELOPMENT OF INSULIN DEPENDENT DIABETES.

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Free oxygen radicals (FOR) are hypothesized to take part in the destruction of the ß-cell in type I diabetes (DM). As a volatile product of lipid peroxidation, we followed breath pentane (P)(Lipids 24: 157-9, 1989) twice weekly of 8 endogenously DM prone BB Wistar rats from the age of 45 d until 90 d of age. 12 age-matched non-DM rats served as controls (Co) and were measured between 50 and 90 days of age. Of them 6 were treated with streptozocin (STZ) 65 mg/kg intravenously at age of 75 d. DM was treated with insulin.

P of the Co group was constantly low 1.9 ± 0.8 pmol/100g/min (mean±SD). All STZ-rats developed DM within 36 h after injection. Omitting insulin for 4 d caused heavy ketosis on the 90th d of life. Despite this P remained at 1.5±0.7 pmol/100g/min. All BB-rats developed DM at 71.1±7.7 d. 35-20 d before glucosuria P was 2.1± 0.2, 10 d before onset of DM P rose to 2.9± 0.6 ($p<0.005$ from Co) and 1-25d after DM P was 5.3±0.6 pmol/kg/min ($p<0.0001$ from Co).

We propose that FOR have an important role during the destruction of ß-cells in BB-rats developing diabetes. This mechanism is not reproduced by STZ toxicity.