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MULTIPLE ISCHEMIC INSULTS SENSITISE THE FETAL BRAIN TO INJURY AND ALTER THE DISTRIBUTION OF DAMAGE.

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We have previously shown that an isolated 30 min ischemic episode in fetal sheep results in neuronal loss primarily in the cortex and hippocampus with only minimal damage in the striatum, while a single 10 min ischemia causes trivial neuronal loss (Ann Neurol.31:14, 1992). However, striatal injury occurs in the perinate. Recent evidence in the adult (BrainRes.528:114,1990) suggests that multiple ischemic episodes have an additive effect on neuronal loss. The objective of this study was to determine whether brief episodes of ischemia repeated at different intervals sensitise the fetal brain to injury and alter the pattern of damage.

Methods: Chronically instrumented fetal sheep were subjected to 3 episodes of 10 min ischemia by transiently occluding the cerebral vasculature, either at 1h (n=8) or 5h (n=5) intervals. Histological outcome was evaluated 72h later.

Results: Repeated insults caused significantly more striatal damage than a single 30 min ischemia ($p<0.01$). Total cerebral damage was more severe following 1h apart than 5h apart occlusions ($p<0.01$).

Conclusion: Brief repeated insults cause cumulative neuronal loss, particularly if the insults are frequent. Increased striatal damage is a feature of multiple but not single insults.

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NEURON SPECIFIC ENOLASE (NSE)IN PRETERM BABIES WITH BRAIN DAMAGE.

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Preterm babies are at risk for mental and developmental retardation. NSE represents the 1.4% of the total soluble protein of the brain. An increase in the CSF level of NSE may indicate neuronal damage. We hypothesized that the documented brain damage in preterm babies by cerebral ultrasound (CUS), is not only restricted to the white matter, and thus an increase in the CSF-NSE level would therefore be expected. 39 babies with known risk factors for brain damage were included. Mean gestational age and weight were 29.4±2.2 wk and 1153±255 g, respectively. CUS were initially performed in the first 12 h and then serially. CSF samples were collected at 72 h. NSE was measured by enzyme immunoassay. Infants were classified: group I, babies with normal CUS or grade I Periventricular hemorrhage (PVH). Group II included those with grades II and III. Group III was formed by those babies with PVH with parenchymal involvement. Group IV were patients with PVL.The results were (NSE expressed as ng/ml±SEM):

	Gr.I (n=7)	Gr.II (n=17)	Gr.III (n=6)	Gr.IV (n=9)
NSE	26.2±8.1	34.7±12.8	144.8±21.5*	120.8±49.7

***p<0.005 (Gr.III vs Gr.I and II.)**

The increase in CSF-NSE in Gr.III as compared to the CSF-NSE in Gr.I and II was statistically significant.

CONCLUSION: The high levels of NSE in CSF in infants with parenchymal injury suggests a more extensive brain involvement than just PV brain damage. (Sup. by CICYT. SAL 89-0916).

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PROLACTIN (PRL) AND GROWTH HORMONE (hGH) IN PERINATAL ASPHYXIA.

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Perinatal asphyxia is thought to damage the "hypothalamus-hypophysis axis" (J. Pediatr. 96:397, 1980) and found to increase PRL in the cord serum (Horm. Res. 25:125, 1987).

We investigated the serum levels of PRL and hGH 2-4 h after birth in 28 fullterm (FT) and 15 preterm (PT) infants with perinatal distress, and in 20 FT and 15 PT normal infants. PRL and hGH were correlated to the severity of hypoxic-ischaemic encephalopathy (HIE).

PRL and hGH were assayed in duplicate by IRMA.

Results: The mean PRL value ± SD in the asphyctic FT newborns was 189.9 ± 46.6, whereas in the control it was 117.4 ± 46.9 (t=5.30, $p \leq 0.0005$). The PRL in the asphyctic PT newborns was 166.4 ± 59.3, and in the control 94.1 ± 46.0 (t=3.43, $p \leq 0.005$). In the FT newborns a significant difference was maintained at 24 h (t=2.38, $p \leq 0.025$) and 48 h (t=2.95, $p \leq 0.005$), but not at 96 h. The hGH in the asphyctic FT newborns was 49.6 ± 36.2 after birth,and in the control 23.3 ± 15.6 (t=2.66, $p \leq 0.001$). In the asphyctic PT infants it was 63.5 ± 37.8, whereas in the control it was 29.1 ± 13.2 (t=3.03, $p \leq 0.005$). There was no significant difference at 24, 48 and 96 h in the hGH between asphyctic and normal FT and PT newborns. The increased levels of PRL and hGH were observed in all three degrees of HIE.

Conclusion: Perinatal asphyxia increases the PRL and hGH levels in FT and PT newborns. The differences are not significant on the fifth day of life for PRL and 24 h after birth for hGH.

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PRODUCTION OF SUPEROXIDE ANION (O_2^-) BY NEUTROPHILS (PMNS) FROM CORD, NEONATAL AND ADULT BLOOD.

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Previous investigations have shown that cord blood PMNs produce more O_2^- than adults cells when stimulated with a chemotactic peptide (FMLP) and a priming effect of labor was advocated. However little is known about O_2^- production rate by neonatal PMNs. We have measured the O_2^- production in PMNs from a) cord blood of 15 vaginally delivered healthy term neonates, b) cord blood of 7 vaginally delivered and moderately distressed neonates, c) blood of 16 healthy term neonates aged 4-5 days and d) blood of 8 adults. In 5 cases blood was taken twice, from the cord and the neonate 4 days later. The O_2^- was measured using 10^{-7}M FMLP as a PMNs stimulus.

Results: An increased O_2^- generation (nmol $O_2^-/5x10^5$ cells) from neonatal PMNs (13±2,6) compared to that of cord (11.4±1.7 $p<0.05$) and of adult (7.8±1.6 $p<0.001$) was found. This increase was confirmed in the 5 cases of paired blood samples (cord 10.8±2.1 and neonate 14± 2.7). PMNs from cord of distressed neonates (9.0±1.8) produce less O_2^- that those of nonstressed neonates (11.4±1.7 $p<0.05$).

Conclusion: It appears that during labor a depressive effect on neonatal PMNs is exerted and this effect is more pronounced in cases of complicated labor. This may be related to the severity of perinatal infections especially in the asphyxiated neonates.

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EFFECT OF MASK VENTILATION ON CEREBRAL BLOOD VOLUME (CBV) IN PRETERM INFANTS STUDIED BY NEAR INFRARED SPECTROSCOPY (NIRS).

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Mask ventilation has been reported to cause cerebral haemorrhage in preterm infants, possibly due to head compression. We used NIRS (1) to measure the effect of mask ventilation on CBV in 8 preterm infants born at 23-32 (median 27) weeks of gestation and studied aged 10-67 (23.5) days. The mask (Laerdal) was gently attached with ties and a wool bonnet. Observations were made in random order during spontaneous breathing with the mask either loosely applied, or tightly - with or without continuous positive airway pressure (CPAP) of 2-4 cm H_2O or intermittent positive pressure ventilation (IPPV) at a peak airway pressure of 10-14 cm H_2O, using a pressure limited ventilator. CBV changes from the loose mask mode were recorded from observations made over 5 minute periods during each mode of ventilatory support (table).

	mask loose	mask tight	CPAP	IPPV
ΔCBV±SD(ml.100g^{-1})	0.00±0.07	0.01±0.10	0.05±0.13	0.02±0.15
ΔCBV±SD(%)	0.03±2.93	0.15±3.82	1.60±5.17	0.60±6.71

The changes were very small, although ANOVA with the Scheffe test showed that CBV during CPAP differed significantly from the other periods ($p<0.05$). We conclude that mask ventilation had no important effect on CBV.

(1) J.S.Wyatt et al. J Appl Physiol 1990;68:1086-1091.

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THE EFFECT OF Ca-BLOCKADE WITH NIMODIPINE ON REGIONAL CEREBRAL BLOOD FLOW AFTER EXPERIMENTAL HYPOXEMIA IN THE NEWBORN PIGLET.

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The effect Ca-blockade (Ca-B) (continuous infusion of nimodipine, 15 microg./kg/min) on mean arterial blood pressure (MABP) and cerebral blood flow (CBF) after hypoxemia (HO, 10% O2) was studied in 29 newborn piglets with the microsphere method. CBF was measured in brainstem (BS), cerebellum (CBL) and cerebrum (CBR) at baseline (BL), during HO or baseline 2 (BL2, Ca-B group), 20 min after HO (20') or after the start of Ca-B, and 30 (30') and 60 min (60') after HO. Results were: Blood flow in BS (ml/100g/min, mean±SD) and MABP (mm Hg, mean±SD):

		BL	HO/BL2	Ca-B/20'	30'	60'
HO	BS	67±15	198±108*	78±19	66±15	77±47
	MABP	79±11	48±21†	77±11	77±12	81±14
Ca-B	BS	89±30	71±12	88±23	107±34	125±25§
	MABP	80±7	72±8	67±10	57±3§	51±7§
HO+ Ca-B	BS	63±15	253±61†	88±22†	86±19*	91±18*
	MABP	74±9	59±15†	52±11†	47±12†	46±10†

* $p<0.05$ from BL, † $p<0.01$ from BL, § $p<0.01$ from BL2

No effects of Ca-B on flow in CBL and CBR were found.

Conclusion: In spite of a significant reduction in MABP during nimodipine infusion an increased BS blood flow was found. This indicates a significant effect of nimodipine on cerebral vascular resistance.