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ISONIAZIDE (INH) INDUCES SUPEROXIDE (O_2^-) PRODUCTION IN CULTURED HUMAN MONOCYTES

P. Megyeri*, M.J. Pabst
Department of Pediatrics, Albert Szent-Györgyi University Medical School, H-6725, Szeged, Korányi fasor 14-15, Hungary*, Department of Biochemistry University of Tennessee, Memphis, USA.

The tuberculostatic drug INH has been implicated in inducing a number of idiosyncratic reactions such as hepatitis and lupus. Monocytes, freshly isolated from blood as a mixed cell population were cultured in endotoxin-free non-adherent conditions in Teflon bags for 3 days. The cells produced large amounts of O_2^- (60-80 nmol/million Mo) in response to stimulation by PMA (1 μg/ml) or LPS (10 ng/ml) as measured by the reduction of the added cytochrome C. Addition of INH (5 or 25 μg/ml) resulted in *7.1 ± 0.07 and **11.2 ± 1.48 nmol/million Mo O_2^- production respectively, compared to the 5.7 ± 0.02 nmol/million Mo O_2^- produced during the one our experiment by the non-treated controls. (p* N.S., p** < 0,001, n = 20). The production of O_2^- and possibly other reactive radicals by INH might be implicated in the bacteriostatic such as in some of the adverse reactions of INH. Based on our earlier studies (Acta Paediatr.Scand. 75:668-669, 1986) we speculate that INH might have a beneficiary effect in clinical conditions where the lack of O_2^- production is responsible for the impaired host defence i.e. in chronic granulomatous disease.

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β-SYMPATHOMIMETICS GIVEN ANTENATALLY MAY INFLUENCE THE DEVELOPMENT OF RETINOPATHY IN THE PREMATURE.

Colin A. Michie, Sally Braithwaite, Edward Schullenberg, David Harvey.
Department of Paediatrics and Neonatal Medicine, Hammersmith Hospital, LONDON.

Infants requiring oxygen therapy for over 60 days on our neonatal unit were reviewed in a retrospective study. A consultant opthalmologist (ES) had examined all these at 2-weeky intervals from the second week of life and identified 14 cases of retinopathy (ROP) greater than stage 3 between 1990 and 1993. The ROP cases were matched for gestation (±1 week), gender, ethnic group and birth weight (±50g) with other infants who also had oxygen requirements for more than 60 days and were on the unit during the same time-period. Comparison of these groups over the first two months of life demonstrated that the ROP group received significantly larger numbers and volume of transfused blood ($p<0.04$, $p<0.05$ respectively, Wilcoxon); this is not a new observation. However mothers of eight of the retinopathy group received β-sympathomimetics (7 ritodrine, 1 salbutamol) to arrest premature labour; only one of the non-retinopathy group had received this treatment ($p<0.01$). In the premature infant antenatal changes in retinal perfusion caused by β-sympathomimetics may be exacerbated by large swings in haematocrit and oxygen tensions resulting in an increased tendency to develop retinopathic changes. This observation casts further doubt as to the value of β-sympathomimetics in the treatment of premature labour.

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INCREASED APOPTOSIS IN THE BRAINS OF NEWBORN PIGLETS FOLLOWING TRANSIENT HYPOXIA-ISCHAEMIA.

Huseyin Mehmet, Xu Yue, M. Valerie Squier* and David Edwards.
Department of Paediatrics and Neonatal Medicine, Royal Postgraduate Medical School, London and *Department of Neuropathology, Radcliffe Infirmary, Oxford. On behalf of the UCL/RPMS Perinatal Brain Research Group.

This study examined the relationship between the severity of perinatal hypoxia-ischaemia (HI) as determined by ^{31}P magnetic resonance spectroscopy, and the fraction of cells showing evidence of apoptosis (morphological changes and DNA fragmentation). Ten newborn piglets were subjected to HI which caused cerebral total nucleotide triphosphate concentration ([NTP]) to fall to less than 30% of baseline, then resuscitated and observed for 48 hours. Six further animals underwent sham surgery. Brains were examined after staining with haematoxylin and eosin, and by *in situ* end-labelling of DNA.

Results: Zero to 27% (median 10) of cells showed the features of apoptosis: this fraction was related positively to the time integral of the decrement in [NTP]: exchangeable phosphate pool ratio (a measure of ATP depletion) during HI, and negatively to minimum phosphocreatine: inorganic phosphate ratio (a measure of the severity of secondary energy failure) following resuscitation ($p < 0.01$).

Conclusion: These results demonstrate a relation between impaired cerebral energy metabolism and the appearance of cells undergoing apoptosis, suggesting that perinatal brain injury resulting from HI may be due, in part, to the excessive or inapprpropriate activation of apoptosis.

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ASSESSMENT OF TOTAL BODY WATER AND WEIGHT IN NEONATES USING BIOELECTRICAL IMPEDANCE ANALYSIS. Wing Tang, Neena Modi, Deborah Price, Donna Cowan. Department of Paediatrics, Royal Postgraduate Medical School, Du Cane Road, London, W12 ONN, UK.

Bioelectrical impedance analysis (BIA) is a non-invasive technique that has been used to measure total body water (TBW). In view of the close relationship between TBW and weight in newborn babies, we hypothesised that it might also be possible to derive an estimate of weight from BIA. Twenty eight babies (median gestational age 30.5 weeks (range 24 - 38); median birth weight 1.388 kg (range 0.690 - 3.510)) were studied once during the first week after birth. TBW was assessed by dilution of isotopic water ($H_2{}^{18}O$). Bioelectrical measurements were made using the tetrapolar surface electrode method. The model, TBW = 0.135 + 0.516 wt + 4.074 L^2/R accounted for 99.4% of the variation in TBW and log TBW = -0.188 + 0.895 log wt, 98.8% of this variance. The former model improved prediction of TBW in larger babies but there was no difference in prediction between the two models in smaller babies. The model, body weight = 0.018 + 0.809 birthweight + 3.49 L^2/R accounted for 99.6% of the variation in body weight (TBW, litres; wt, body weight on study day in kg; L, foot length in cm; R, resistance at 50 kHz in ohms.)

In the most immature babies, the prediction of TBW from BIA, offers no improvement over prediction from body weight alone. It does improve prediction in larger babies. BIA may have a clinical role in the longitudinal assessment of body weight if, as is often the case, a baby is too unwell to be weighed formally.

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CARNITINE DEPENDENT CHANGES OF METABOLIC FUEL CONSUMPTION IN CHRONIC VALPROATE TREATMENT. Bela Melegh, Maria Pap, Eva Morava, Denes Molnar, Maria Dani. Department of Pediatrics, University Medical School of Pecs, Pecs, Hungary.

Composition of energy metabolism was determined in children receiving chronic valproate treatment with indirect calorimetry. In eight of ten randomly selected subjects the resting respiratory quotient (RQ) increased as compared with age and sex matched controls (0.91±0.01 vs 0.87±0.01). A shift was observed in the metabolic fuel consumption, decrease was found in fats oxidised (0.68±0.23 vs 1.18±0.18 g/kg/day) and the utilisation of carbohydrates increased (5.31±0.79 vs 3.81±0.39 g/kg/day), with no significant change of the urinary output of nitrogen compounds. The resting total energy expenditure was not affected by the treatment. The children showing altered energy consumption pattern received carnitine supplementation for a month. After the carnitine administration the RQ value decreased (0.87±0.02) and an increase was in the oxidation of fats (1.42±0.25), the consumption of carbohydrates decreased (3.87±0.79). The resting energy consumption was not affected by the treatment. The results show, that carnitine depletion, which is a known adverse effect of valproic acid administration, may result in inhibited fatty acid oxidation leading to a shift from fats to carbohydrates in composition of substrates utilised.

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Acute Blood Pressure Effects of Surfactant Replacement in Newborn Piglets

[a]Atle Moen, [a]Terje Rootwelt, [b]Tore Curstedt, [c]Bengt Robertson, [a]Ola Didrik Saugstad.
[a]Dept. Pediatr. Res. Rikshospitalet , Oslo Norway. [b]Dept Clin.Chem. Danderyd Hosp. Danderyd Sweden. [c]Res.Unit Exp. Perinatal Pat. Karolinska Hosp. Stockholm, Sweden

As part of a study on cerebral blood flow and hemodynamics after replacement therapy with a natural porcine surfactant, we present preliminary data on acute changes in blood pressure. Three groups of piglets, age 3-6 days chosen to secure closed ductus arteriosus, underwent lung lavage with 0.9% saline. Group 1 was normovolemic and normoxic before surfactant was given. Group 2 was normoxic and made hypovolemic by bleeding 20% of estimated blood volume. Group 3 was normovolemic and hypoxic. Mean blood pressure (MBP) was measured continuously and is given as mean ±SD. ΔMBP is the difference between MBP immediately before surfactant and at lowest MBP after surfactant

	ΔMBP mmHg	ΔMBP p-value	a/APo2-ratio before surf	a/APo2-ratio at min. MBP	Δa/APo2-ratio p-value
Group 1 (n=7)	15.7 (11.2)	<0.05	0.13	0.10	NS
Group 2 (n=5)	33.8 (12.1)*	<0.01	0.18	0.11	<0.05
Group 3 (n=6)	31.3 (10.8)*	<0.01	0.06*	0.07	NS

*Significantly different from Group 1 ($p < 0.05$)

Blood pressure decreased significantly in all three groups reaching a minimum value at 4 minutes ±1.5 after surfactant instillation. The blood pressure decreased significantly more in group 2 and 3 than in group 1. MBP was restored to pre-surfactant values within 22 min ±13 min. a/APo2-ratio decreased significantly in group 2. Later a/APo2 ratio increased beyond pre-surfactant value in all three groups. We conclude that in normovolemic, normoxic piglets MBP decreased significantly less than in hypovolemic and hypoxic piglets treated with natural porcine surfactant.The change in MBP was independent of changes in pO_2 and not related to a persistent ductus arteriosus.