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Gastro-oesophageal reflux (GER) and ALTE in babies : Role of Beta Endorphins? M.A. SERRE, P MONIN , F FEILLET, B. DOUSSET , M VIDAILHET Services de médecine Infantile , Laboratoire de Biochimie CHU de NANCY - BRABOIS , 54511 VANDOEUVRE FRANCE - Maternité régionale NANCY

GER is frequently observed during the first months of life and is now considered as a significant risk factor for ALTE or SIDS. To evaluate the potential role of Beta endorphins in the pathogenesis of ALTE in the presence of GER, 2 groups of babies are studied. Fifteen babies admitted for ALTE and presenting a GER (Gr 1) are compared to 15 siblings of SIDS patients also having a GER diagnosed at 1 month of age when investigated for risk factors (Gr 2) . GER was evaluated by oesophageal pH recordings. Plasma Beta endorphins levels were measured with radioimmunologic method (Allegro Beta endorphins Reagents - Nichols Institute Diagnostics USA) following ALTE in Gr 1 and on the day of evaluation at 1 month of age in Gr 2. The 2 groups were comparable for birth weight, gestationnal age and sex ratio. The severity of GER assessed by oesophageal pH was also similar in the 2 groups : acidity index (% of the recording period with pH below 4) was respectively of 10,6% + 3,5% in gr 1 and 13,9% + 5,6% in gr 2 . The number of reflux per hour was 11 + 6 and 16 + 5.Plasma B endorphin levels was 84.5 + 80 pg/ml in gr 1 (15-312 , median 47 pg/ml) and 25,9 + 31 pg/ml in gr 2 (5-91 pg/ml , median 14 pg/ml) $p < 0,01$. In group 1 ,4 babies had levels above 125 pg/ml (normal mean plasma level :29 pg/ml).

These data suggest

1) GER can be associated to an increased production of Beta endorphins probably in response to the oesophageal insult induced by acidity.

2) the depressive effect of B endorphins on respiration might increase the vulnerability of babies with GER to ALTE.

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MAY APNEA REFLEX INDUCE SUDDEN INFANT DEATH?

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Beta-endorphin may induce respiratory depression and bradycardia. Elevated hypoxanthine (HX) level in corpus vitreum humor (CVH) indicates hypoxia before death. We measured beta-endorphin immunoreactivity (BEI) in CSF and HX in CVH in SIDS victims (n=27) and in control infants (n=12). In a pilot study we measured BEI in CSF in piglets where the larynx reflex was induced by ammonium gas (n=4). BEI in CSF was also measured after brain hypoxia in piglets (n=6).

The BEI levels in CSF divided the SIDS victims into two subpopulations: one half with undetectable level <4.3 fmol/ml CSF, and the other half with high level 247 fmol/ml CSF (range 160-400). All the SIDS victims had elevated levels of HX in CVH 209 mikromol/l (range 53-419) compared with the controls that died a sudden death (accidental, cardial or strangled), which had 54 mikromol/l (range 0-188). In the subpopulation of SIDS victims with elevated BEI in CSF, we found a positive correlation between BEI in CSF and HX levels in CVH r=0.92 (p<0.001). In the control infants no correlation between BEI in CSF and HX in CVH was found. In piglets where the larynx reflex was excited, we found increased levels of BEI in CSF which correlated with the duration of the apneas r=0.84 (p=0.16). In the control piglets undetectable levels of BEI in CSF was found.

Conclusion: In SIDS victims with elevated levels of BEI in CSF, the BEI correlated with HX in CVH. The larynx reflex induced apneas, induced BEI increase in CSF in piglets.

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MEASURING BODY FAT IN INFANCY: ANTHROPOMETRY VERSUS TOTAL BODY ELECTRICAL CONDUCTIVITY (TOBEC)

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TOBEC is a rapid, safe and convenient method for the measurement of body composition. Cross-sectional measurement of body fat (BF) by TOBEC (BF-T) and by anthropometry including skinfold thickness[1] (BF-S) was performed in 423 normal, healthy caucasian infants, allowing comparison of these techniques with each other and with reference data on body fat[2] (BF-R). Results in percentage BF (% BF):

AGE	% BF-R		% BF-T		% BF-S	
months	boys	girls	boys	girls	boys	girls
1	15.1	16.2	13.0	12.4	10.3	9.1
2	19.9	21.1	18.5	18.1	14.6	13.8
3	23.2	23.8	20.3	21.4	14.8	15.5
4	24.7	25.2	24.0	24.4	17.0	17.1
5	25.3	26.0	24.4	25.6	17.5	17.0
6	25.4	26.4	24.6	27.1	16.7	19.1
9	24.0	25.0	25.6	27.6	18.9	20.1
12	22.5	23.7	23.8	25.4	19.7	23.5

BF-T was correlated with BF-S. Expressed in percentages $r = 0.550$ ($p < 0.0001$), expressed in grams $r = 0.780$ ($p < 0.0001$). Biological plus experimental scatter (expressed as CV) was much higher in the BF-S data. Conclusions: 1) BF-T in infancy were slightly lower, but in close agreement with reference data from Fomon et al. 2) BF-S values were consistently lower than BF-T values. 3) The difference between BF-T and BF-S may represent non-subcutaneous BF. [1]Dauncey et al. Arch Dis Child 52:223-227, 1977 [2]Fomon et al. Am J Clin Nutr 35:1169-75, 1982

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rHu-ERYTHROPOIETIN (rH-EPO) IN THE PREVENTION OF ANEMIA OF PREMATURITY: EFFECTS ON ENDOGENOUS ERYTHROPOIESIS.

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Introduction: rH-EPO has been studied as a new treatment regime for the anemia of prematurity in two multicentre studies in order to avoid red cell transfusion with its potential hazards. **Methods:** We randomly assigned 29 premature infants to 2 treatment schedules with rH-EPO or none. Infants in treatment group 1 (n = 8, mean BW 1436 +/- 357 g, mean GA 31 w) received 70 IU rH-EPO/kgBW/w upto day 25 of life by subcutaneous injection into thigh, those in treatment group 2 (n = 6, mean BW 1284 +/-148 g, mean GA 31 w) 750 UI/kgBW/w upto day 42 of life, those in the control group (n = 15, mean BW 1327 +/- 316 g, mean GA 30 w) received no treatment. All infants received supplemental iron orally from day 14 of life. **Results:** Mean number of packed red cell transfusions per patient during the study period were 1.4 units (controls), 1.6 units (70 IU group) and 0.17 units (750 IU group). Mean reticulocyte counts were at day 3 of life were 10.1 +/-5 % (controls), 8.8 +/- 4.4 % (75 IU group) and 8.2 +/- 6.5 % (750 IU group). In both the control and the 75 IU group mean reticulocytes count decreased during observation time to mean values between 3 and 4 %, while it increased in the 750 IU group to a highest value of 10.6 +/-2.3 % in week 3 and stayed at a high level of 7 to 8 % until week 5. Mean absolute normocyte count fell in a logarithmic manner but values were higher in both treatment groups. The biggest difference was observed in week 4 with a mean of 180 normocytes in the 750 IU group, 75 in the 75 IU group and only 16 in the control group. **Conclusion:** Low dose rH-EPO showed no sufficient effect for the treatment of anemia of prematurity. High dose rH-EPO prevents the need for transfusion in preterm infants, stimulates endogenous generation of normovolaemic hypochrome erythrocytes and does not stimulate other cell lines than the red cell line.

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MUTATIONAL ACTIVATION OF N-*RAS*-12 GENE IS ABSENT IN PEDIATRIC OSTEOSARCOMA.

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Activation of *ras* oncogenes is found in human cancers, overall it is observed in 15% of all neoplasms. OBJECTIVE: The purpose of this study was to assess the extent of involment of *ras* oncogenes in osteosarcoma. STUDY DESIGN: Tumor samples from a series of 53 pediatric patients diagnosed of osteosarcoma and treated at our institution were evaluated. Parraffin-embedded tumor samples from diagnostic biopsies, from tissue of tumor en bloc resection after neoadjuvant chemotherapy, and samples from metastases were examined for point mutations at the N-*ras*-12 gene by means of polymerase chain reaction (PCR), slot-blotting, and radioactive labelled specific DNA probes. RESULTS: A total of 133 archival samples were studied. No point mutations activating the N-*ras*-12 gene were found. CONCLUSIONS: In order to exclude the potential role of the *ras* gene family in the development of ostesarcomas codon 61 of the N-*ras* gene and codons 12 and 61 of genes H-*ras* and K-*ras* must evaluated. These studies are been performed. Archival tumor samples are adequate for PCR amplification. PCR greatly facilitates the study of oncogene activation in tumor samples.

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INTRAVENTRICULAR STREPTOKINASE INCREASES CEREBROSPINAL FLUID D DIMER IN PRETERM INFANTS WITH POSTHAEMORRHAGIC HYDROCEPHALUS

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Failure to lyse multiple small blood clots in the cerebrospinal fluid (CSF) reabsorption pathways may be one of the mechanisms leading to posthaemorrhagic hydrocephalus (PHH). A pilot study has suggested that intraventricular streptokinase may help to prevent PHH (1). However, nothing is known about the effects of intraventricular streptokinase on fibrin in neonatal CSF. The purpose of this study was to determine whether intraventricular administration of streptokinase produces an increase in fibrin degradation products in the CSF.

Six preterm infants with progressive ventricular dilatation (ventricular width 4 mm over the 97th centile) after intraventricular haemorrhage were studied. Ventricular CSF was collected before and during intraventricular treatment with streptokinase at 1,000 units/hour for 48 hours. D Dimer was measured by an ELISA technique.

In all 6 infants, CSF D dimer rose during streptokinase treatment. Median D dimer before treatment was 1642 ng/ml (range 550 - 2075) and during treatment rose to 5440 ng/ml (range 950 - 11,400) ($p < 0.05$). D dimer levels in CSF were considerably higher than those in plasma thus ruling out the possibility that D dimer had merely diffused into the CSF through a damaged blood brain barrier.

Conclusion. Intraventricular streptokinase produces a significant rise in CSF D dimer. This augmentation of local fibrinolysis may have therapeutic potential in the treatment of PHH.

1. Whitelaw A, Rivers R, Creighton L, Gaffney P. Low dose intraventricular fibrinolytic therapy to prevent posthaemorrhagic hydrocephalus *Arch Dis Child* 1992 ; 67: 12-4.