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24HR PH-STUDY AND MULTIPLE INTRALUMINAL IMPEDANCE (MII) FOR THE DIAGNOSIS OF GASTROESOPHAGEAL REFLUX AND EVALUATION OF RELATED SYMPTOMS IN CHILDREN (ITALY)

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Background and aim: PH-monitoring is the most widely accepted tool for the diagnosing of gastroesophageal reflux (GER); however it does not detect non acid refluxes. MII is a new method for pH-indipendent detection of GER however, few data are available in childhood. Our aim was to compare the 24hr pH-study versus the combined 24-hrs pH and MII monitoring for the assessment of GER and related symptoms in children.

Methods: Fourteen children [M 7; mean age: 1,2 y (range 0,42 y - 10,4 y)] with symptoms suggestive of GER, underwent 24hr pH-study/MII recording. Reflux episodes revealed by 24hr pH-study were analysed at the light of the retrograde bolus movements detected by MII. The symptom index (SI) and the symptom sensitivity index (SSI) were calculated for both the techniques and according with the type of symptoms (typical or atypical).

Results: In the 14 children studied, the MII detected 1145 episodes of reflux of which 660 (58%) were associated with decreases in pH less than 4.0. The analysis of the 24hr pH-study blinded to the impedance data revealed a total of 1232 reflux episodes; of these only 660 were also associated with retrograde bolus movement detected by MII (SS and PPV of 24hr pH-study compared to MII: 54% and 58%). A total of 109 symptoms were reported: 58 typical and 51 atypical. The SI and SSI were significantly higher for the MII as compared to 24hr pH-study [(total symptoms: 58% and 5,5% vs. 28% and 2,5%; $p<0,00002$ and $p<0,0004$ respectively), (typical symptoms: 62% and 3,1% vs. 40% and 1,8%; $p<0,01$ and $p<0,05$ respectively) and (atypical symptoms: 53% and 2,4% vs. 18% and 0,7%; $p<0,0004$ and $p<0,002$ respectively).

Summary and conclusions: More than 40% of reflux episodes detected by pH-monitoring are not associated with retrograde bolus movement (false positive) and are responsible for the low PPV of the 24hr pH-study. SI and SII are significantly higher if assessed by MII especially for atypical symptoms, demonstrating the superiority of MII for the study of atypical manifestation of GER.

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REVISED APPROACH TO SUSPECTED LATE-ONSET SEPSIS IN NEONATES: ADDED VALUE OF C-REACTIVE PROTEIN AND STAPHYLOCOCCUS-SPECIFIC PCR.

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Background: Standard laboratory methods for early confirmation of late-onset sepsis (LOS) in neonates are time-consuming, flawed with poor sensitivity and specificity, and not helpful in decision-making regarding selection and initiation of empiric anti-microbial therapy (AMT).

Aim: To evaluate the predictive value of relevant clinical and laboratory parameters [complete blood count, serum C-reactive protein (CRP), procalcitonin (PCT) and Staphylococcus-specific PCR] in neonates suspected of having developed LOS.

Patients and Methods: NICU neonates were prospectively followed for suspected septic events. During the study period, 111 neonates developed 148 suspected septic events beyond 3 days of age, and comprised the study population. Clinical signs and laboratory abnormalities at onset of sepsis were recorded, including serum levels of CRP and PCT, results of Staphylococcus-specific PCR, microbiological data and the AMT instituted.

Results: Of the 148 events of suspected LOS, 26 (17.6%) had positive blood cultures (proven LOS) with gram-positive bacteria, gram-negative bacteria and Candida, accounting for 65.4%, 23.1% and 11.5% of the events, respectively. Variables that were significantly associated with subsequently confirmed LOS included hypotension [relative risk (RR)=5.6; 95% confidence interval (CI): 3.29–9.53]; mechanical ventilation (RR=2.46; 95%CI: 1.24–4.86); immature/total neutrophil ratio (I/T) > 0.2 (RR=5.13; 95%CI: 2.54–10.31); CRP >1.0 mg/dL (RR=2.85; 95%CI: 1.32–6.15); and, small for gestational age status (RR=2.13; 95%CI: 1.03–4.38). PCT was not significantly associated with LOS. For detection of Staphylococcal bacteremia, Staphylococcus-specific PCR demonstrated a sensitivity of 57.1%, specificity 94.7%, a positive predictive value of 53.3%, and a negative predictive value of 95.4%.

Conclusions: Hypotension, mechanical ventilation, I/T >0.2, CRP >1.0 mg/dL and SGA status at onset of sepsis are significant predictors of proven LOS in neonates. Staphylococcus-specific PCR is of value only in ruling out Staphylococcal sepsis. We propose an amended protocol for the approach to neonates with suspected LOS.

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MICROBIAL PRESENTATION AT THE EPITHELIAL LININGS: A STRATEGIC WAY TO PROMOTE THE GENERATION OF IMMUNITY AT BIRTH.

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Background: Epithelial linings in the human body are constantly populated by different microbes, an active process where innate immunity plays a pivotal role. We have previously reported that there is an upregulation of innate immunity in the skin of the healthy newborn infant. This event may be seen as a rash, known as Erythema Toxicum and is most probably a response to commensal skin colonization at birth. Now we postulated that the hair follicle immune system constitutes the physiologic room where microbes are presented to immune competent cells.

Design: Microbial cultures were collected from 70 healthy 1-day infants, skin punch-biopsies were analysed with transmission electron microscopy (TEM) and with immunohistochemistry by staining for Toll-like receptor (TLR) 2 and 4.

Results: We found that 84% of all of healthy 1-day old infants were colonized with coagulase-negative Staphylococci, remaining were positive for Staphylococcus aureus, Alfa-streptococcus, group B streptococcus and Enterococcus species.We also found that TLR 2 and TLR4 were expressed in the epidermis and in the epithelial layer of the hair follicle. In the lesions of Erythema Toxicum, TEM revealed microbe-like material into phagosomes of epithelial cells and into immune cell located in proximity to the hair follicles.

Conclusion: At birth, there is a penetration/presentation of commensal microbes at the epithelial linings. This exposure provides signals, possibly mediated by the TLRs, that alert the immune system and promotes a protective immune response.

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MAGNESIUM SULPHATE GIVEN FOR NEUROPROTECTION BEFORE PRETERM BIRTH

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Background: In some human observational studies, magnesium sulphate (MgSO4) is associated with a significant reduction of pediatric mortality and cerebral palsy.

Aim: To assess if prenatal MgSO4 given to women in labor before 33 weeks'gestation is neuroprotective for the infant.

Methods: 564 consenting women in 13 french centers whose birth was planned or expected within 24 hours were randomised to receive a sole dose of 4 g of MgSO4 or 4 g of isotonic sodium chloride solution for 30 minutes. In 660 out of 688 very preterm newborns who had at least one cranial ultrasonographic study (US), the primary outcome measures were the rates of mortality up to discharge of hospital, of the severe white matter injury (WMI) (defined by the presence of cavitations and/or intraparenchymal haemorrhage) and the combined of death and severe WMI. The secondary outcome measures were the rates of WMI (defined by severe WMI or persisting hyperechogenicities at two US more than 14 days and/or isolated ventricular dilatation), and of non-parenchymal haemorrhages.

Results: Mortality up to discharge (9.4% vs 10.5%; RR 0.85, 95% CI 0.56 - 1.28), severe WMI (9.7% vs 11.8%; RR 0.74, 95% CI 0.47 - 1.14), combined death and severe WMI (16.3% vs 18.0%; RR 0.85, 95% CI 0.63–1.15) were not significantly different between both groups. In the MgSO4 group, significant increases in the rates of preterm rupture of membrane more than 18 hours ($p = 0.077$) and of materno-fetal infection ($p = 0.025$) were observed. No women had life threatening events due to magnesium infusion; moderate or mild side effects were reported in 16.6 % of women given MgSO4 and in 1% of women given placebo. No severe side effect was reported in infant.

Conclusion: In this trial, even if there is a trend towards a beneficial effect of magnesium, no significant differences were observed between both groups. Financial support : Grants of the French ministry of Health and of the Centre Hospitalier Universitaire of Rouen 1997; Study approved by the ethical comittee of Haute-Normandie, France.

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PROTON MR SPECTROSCOPY (1H-MRS), DIFFUSION WEIGHTED IMAGING (DWI) AND ULTRASONOGRAPHY (US) IN NEONATAL HYPOGLYCAEMIA: A CASE REPORT

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Introduction: several neuropathological studies have documented brain damage following hypoglycaemia. In a few cases damage has been reported in vivo using CT, MRI and US. Here we report a functional and anatomic study of the brain in a case of transient symptomatic hypoglycaemia.

Case report: term newborn, AS 9–10, LGA, of a non-diabetic primigravida was referred to NICU at 51 hrs of age due to hypoglycaemia (12 mg/dl); a bolus of 200 mg/kg followed by an infusion of 5 mg/kg/min of e.v. glucose was administered and blood glucose reached a normal value (> 40 mg/dl). Clinical and electric seizures were diagnosed on arrival in NICU and continued for 24 hrs despite glycemic normalisation and phenobarbital treatment. HIE, other metabolic diseases and meningoencephalitis were excluded. At age 3 days cranial US showed a patchy hyperecogenicity of the periventricular and subcortical white matter at the parieto-occipital level; ventricles were split-like. Lesions were confirmed by MRI and resolved at about one month of age without developing ventriculomegaly. The infant underwent 1H-MRS and DWI at 4, 11, 17 and 31 days after birth. N-acethyl aspartate/Creatine (NAA/Cr) reduction and severe lactate and lipid accumulation were present in the occipital cortex; adjusted diffusion coefficient in the occipital lobes was severely reduced (-50%) at first examination and progressively recovered at all later time points. Clinical follow-up at 4 years of age is normal.

Discussion: for the first time by combining 1H-MRS, DWI and traditional imaging we have detected severe, transient, occipital lobe metabolic abnormalities in a hypoglycaemic neonate with a normal outcome at 4 years of age. US and MR were able to first detect these lesions and may be a good initial study in the hypoglycaemic neonate.