592 RESPIRATORY DISBIOSES IN THE CHILDREN WITH FIRST DIAGNOSED TUBERCULOSIS

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Background and Aims Second disbioses of the respiratory play the presentative role and had negatively influence on the result of duration of infectious diseases and assists development of immune disbalance of mucous membranes of respiratory tract.

Methods We investigated 24 children with the Frst Dagnosed Pulmonary Tuberculosis (FDPT) in the age from 1–16 years. Research of microflora of respiratory tracts was conducted by a bacteriologic examination of native material (expectoration).

Results The inspected contingent had Pulmonary form of the first diagnosed tuberculosis. The patients concluded: childs to 3 years - 50.00%. other 50.00% children contained the group of pubertat period. Distributing on the forms of tubercular process: primary tubercular complex - 25.00%, pulmonary focus tuberculose 12.50%, disseminated tuberculosis - 25.00%, infiltrative tuberculosis - 37.50%. 58.30% children had assotiatin pathology with the FDPT: anaemia in 25.00% cases, pneumonia - 8.30%, HIV - 8.30%. In microbiological culture was confirmed presence of M. tuberculosis in 33.30% cases. The destructive chang in lung 16.70% cases was identificated. N.sicca was presented in 40.00% children with the normal microflora and S.epidermidis - in 60.00%. In 50.00% cases of children with the FDPT disbioses violations was identificated after the beginning of using of antiphthisic treatment. Disbioses as a monoculture found in 83.3% cases, in 16.70% cases - as associations of cultures. In 33.30% cases found out Escherichia coli, in the 16.70% - K.pneumonia, in the 50.00% cases - Candida A.

Conclusions On the basis of the conducted researches are set presence of respiratory dysbiosis in children with the FDPT.

593 PERSISTENTLY ELEVATED RIGHT VENTRICULAR INDEX OF MYOCARDIAL PERFORMANCE IN PRETERM INFANTS WITH INCIPIENT BRONCHOPULMONARY DYSPLASIA

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Objectives Elevated pulmonary vascular resistance occurs during the first days after birth in all newborn infants and persists in infants at risk for bronchopulmonary dysplasia (BPD). Pulmonary vascular resistance is higher during the first days after birth and in preterm infants with incipient bronchopulmonary dysplasia (BDP). It is difficult to measure in a non-invasive fashion. We assessed the usefulness of the right ventricular index of myocardial performance (RIMP) to estimate pulmonary vascular resistance in very low birth weight infants.

Study Design Prospective echocardiography on day of life (DOL) 2, 7, 14, and 28 in 121 preterm infants (median [quartiles] gestational age 28 [26–29] weeks, birth weight 998 [743–1225] g) of whom 36 developed BPD (oxygen supplementation at 36 postmenstrual weeks).

Results RIMP derived by conventional pulsed Doppler technique was unrelated to heart rate or mean blood pressure. RIMP on DOL 2 was similar in infants who subsequently did (0.39 [0.33–0.55]) and did not develop BPD (0.39 [0.28–0.51], p= 0.467). RIMP declined steadily in non-BPD infants but not in BPD infants (DOL 7: 0.31[0.22–0.39] vs. 0.35[0.29–0.48], p=0.014; DOL 14: 0.23[0.17–0.30] vs. 0.35[0.25–0.43], p<0.001; DOL 28: 0.21[0.15–0.28] vs. 0.31 [0.21–0.35], p= 0.015).

Conclusions In preterm infants, a decline in RIMP after birth was not observed in those with incipient BPD. The pattern of RIMP

measured in preterm infants is commensurate with that of pulmonary vascular resistance.

594 A NEONATAL RAT MODEL OF BRONCHOPULMONARY DYSPLASIA INDUCED BY PRE- AND POSTNATAL INFLAMMATION WITHOUT EXPOSURE TO HYPEROXIA

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Purpose We tested if pre- or postnatal inflammation can develop BPD per se and if there are any interaction between prenatal and postnatal inflammation.

Methods Two days before delivery (E20), 1 µg of lipopolysaccharide (LPS) or vehicle (V) was injected into each amniotic sac, and after birth 0.25 mg/kg of LPS or vehicle was injected into peritoneum on P1, P3, and P5. This led to four experimental groups. On P7 and P14, their lungs and hearts were harvested, and alveolarization and lung vascular density were evaluated.

Results Morphometric analysis of P7 lungs revealed that both preLPS+postLPS group and V+postLPS group had significantly larger and less complex airspaces and small alveolar surface area than V+V group. On P14, only V+postLPS group had significantly larger and less complex airspaces than V+V group. Howevere, alveolar surface areas were significantly smaller both in preLPS+postLPS group and V+postLPS group than in V+V group. Lung vascular density of both preLPS+postLPS group and V+postLPS group was significantly lesser than V+V group.

Conclusions At these intra-amniotic and postnatal systemic LPS doses, prenatal intra-amniotic LPS injection per se did not affect postnatal alveolar and pulmonary vascular development, while postnatal systemic LPS injection significantly inhibited alveolar and pulmonary vascular development regardless of whether prenatal intra-amniotic LPS was injected or not. There was no definite interaction between intra-amniotic LPS and postnatal systemic LPS on the lung development. This rat model of BPD could be used as a valuable tool for testing the effect of anti-inflammatory agents on the prevention of BPD.

595 RISK FACTORS FOR BRONCHO-PULMONARY DYSPLASIA IN VERY-LOW-GESTATIONAL-AGE INFANTS

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Background BPD is a severe condition that has decreased in severity but remains a major long-term adverse outcome of surviving Very Low Gestational Age (VLGA) infants.

Aim To determine the BPD rate and evaluate its predictive and associated factors.

Methods BPP (need for supplemental O_2 at 36 wks CGA) rate and associated risk factors were analysed in a cohort of 24,087 VLGA infants admitted from 2006 to 2010 to 174 EuroNeoNet NICUs. Non-parametric independent tests and logistic regression models were performed to predict BPD, using crude and adjusted odd ratios (OR) to determine perinatal and early neonatal associations. Predictive capacity was assessed by Hosmer-Lemeshow test and discrimination by area under ROC curve (AUC).

Results BPD was diagnosed in 16% (95%CI: (15.4%–16.1%)) of infants, who had significantly lower GA, BW and Apgar scores. They were more frequently male, from single pregnancies, more often had

congenital anomalies, late-onset sepsis (LOS) (57.8% vs. 23.8%; OR:4.40; 95%CI:4.0–4.84) and symptomatic PDA (56.0 vs. 30.6%; OR:2.9; 95%CI:(2.6–3.2)). After adjusting for all BPD predictive perinatal risk factors (BW, GA, Apgar scores, gender and congenital anomalies (AUC:0.8, 95%CI:0.79–0.81), the factors strongly associated with BPD, other than BW and GA, were LOS (OR:2.54; 95% CI:2.27–2.83) and symptomatic PDA (OR:1.54; 95%CI:1.38–1.73).

Conclusion In this large cohort of VLBW/VLGA, the rate of BPD was 16% (15.4–16.1%), strongly associated with GA and BW but also with LOS and symptomatic PDA.

596 EARLY PREDICTION OF BRONCHOPULMONARY DYSPLASIA (BPD) BY AN EASILY AVAILABLE RISK SCORE

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Background Early prediction of BPD is important for identifying high risk patients likely to benefit from preventive treatment approaches and for providing prognostic information. Therefore we aimed to develop a risk score for BPD based on early available clinical parameters.

Patients and methods: All infants born at the University Hospital of Lausanne < 32 weeks of gestation (WG) between 1998 and 2007 (n=936) were included. Patients diagnosed with RDS (n=232) were divided in two groups, either developing BPD or not. Independent risk factors for the development of BPD were searched by multivariate logistic regression analysis. The β-coefficients (β=log(OR)) derived from the fitted multivariate model were used to build a scoring system. An internal validation was performed using a two-fold cross-validation technique with two subgroups: two thirds of the patients were used as training set for model calibration and one third as prediction set.

Results BPD-risk score was developed based on five covariates: intubation in the delivery room, early neonatal infection, duration of invasive mechanical ventilation in days, birth weight and gestational age, weighted according their β-coefficients. Area under curve (AUC) was 0.896. Sensitivity and specificity reached 82.7% and 82.6% with a score cut-off of –8 (range –25 to +17). Internal calibration proved a good prediction: AUC for the same cut-off was 0.882 for the training set and 0.927 for the prediction set.

Conclusions A simple scoring system available within the first postnatal week can reliably predict the probability of developing BPD in infants born < 32 WG.

597 VALPROIC ACID-MEDIATED PROTECTION AGAINST HYPEROXIC LUNG INJURY VIA HISTONE DEACETYLASE INHIBITION IN A NEONATAL RAT MODEL

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Epigenetic mechanisms might play an important role in development of BPD. The aim of this study was to evaluate the protective effect of valproic acid (VPA), an histon deacetylase inhibitor, in hyperoxic lung injury in neonatal rat model.

Methods A total of 30 rat pups (0 days old) were divided equally into 3 groups: control, hyperoxia and hyperoxia+VPA groups. In hyperoxia groups, pups were maintained in 95% O_2 for 10 days while control group was maintained in room air. VPA was administered intraperitoneally once daily for the first 10 days of life. On day 10, histopathological score, radial alveolar count, lamellar protein count, histone deacetylase activity (HDAC), proinflammatory cytokine concentrations were determined with ELISA, whereas acetylated H4 protein and caspase-3 expression were evaluated with Western-Blot analysis. Also apoptosis was evaluated with TUNEL method.

Results The histopathological score, radial alveolar count, lamellar protein count of the pups in VA group were significantly higher. VPA also preserved alveolarization significantly and fibrosis was significantly decreased in rat pups exposed to VPA treatment. HDAC activity significantly reduced with VPA treatment. The proinflammatory markers, caspase-3 expression and number of TUNEL positive cells were also significantly decreased with VPA treatment. Acetylated H4 protein expression was significantly higher in the hyperoxia+VPA group.

Conclusion All these data suggest that VPA might provide possible protective effect against hyperoxic lung injury as an histone deacetylase inhibitor. VPA exhibit these effects by preserving alveolarization, decreasing fibrosis and inflammation via decreasing HDAC activity, increasing acetylated H4 protein expression and reducing inflammation.

598 EFFECTS OF CATALYTIC ANTIOXIDANT MNTBAP ON PULMONARY ANGIOGENIC AND OXIDATIVE GENE EXPRESSION TO HYPEROXIA IN NEWBORN MICE

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Background Development of lung injury during prolonged O_2 exposure is a complex process, associated with changes in expression of a number of genes important in the adaptive response to hyperoxia. MnTBAP is a compound with strong antioxidant properties.

Objective To study the effects of MnTBAP on angiogenic and oxidative gene expression in C57BL6 neonatal mice following hyperoxia.

Design and methods: Newborn mice litters were randomized on postnatal day 4 to hyperoxia (> 95% O_2)(OX) or room air (RA) for 72 hrs during which they received MnTBAP (MN) 10mg/kg or saline (SL) daily by IP injection for 3 days and then were sacrificed. Whole lung angiogenic and oxidative gene expression profiling (84 related genes for each) was done by real-time, reverse transcription, quantitative PCR (n=4). Data was processed and analyzed using SA Biosciences PCR array data analysis web portal.

Results Hyperoxia significantly upregulated peroxiredoxin 6 expression compared to room air exposed newborn mice. Treatment with MnTBAP downregulated the expression of myeloperoxidase and Prdx6-rs1. Hyperoxia downregulated the expression of angiogenic genes such as angiopoietin 1 & 2, TGF 1, TGF 3 and HGF; MnTBAP treatment during the hyperoxia exposure reversed this effect and these genes were upregulated.

Conclusions The catalytic antioxidant MnTBAP reversed the effects of hyperoxia on angiogenic gene expression in newborn mice. The protective effects of antioxidants in newborn hyperoxia models need to be studied further to provide additional understanding of the management of bronchopulmonary dysplasia.

599 CARDIOVASCULAR CONSEQUENCES OF BRONCHOPULMONARY DYSPLASIA IN PREMATURELY BORN PRESCHOOL CHILDREN

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