population. DNA was extracted from whole blood and Guthrie card specimens. Surfactant single nucleotide polymorphism (SNP) genotyping was arranged using the Taqman technique. ACE gene primers were obtained for the previously known insertion/deletion polymorphism and PCR analysis was performed.

**Results**

236 infants born prematurely survived to 28 days postnatal age and contributed to genotype analysis. 106 infants did not develop BPD and 130 infants did develop BPD (54 mild, 29 moderate, 47 severe). Both gestational age and birth weight were significantly different between those infants who did and did not develop BPD and predicted BPD development with an area under the ROC of 0.88 and 0.82 respectively. We demonstrated using multifactorial statistical analysis that the inclusion of the ACE genotype to a predictive statistical model of BPD development improves the predictive potential of the model (area under ROC curve 0.88).

**Conclusion** The presence of the ACE DD genotype is associated with a higher likelihood of developing BPD.

**PS-209**

**BCG VACCINATION CAN PREVENT HYPEROXIC LUNG INJURY**

**Introduction**

The aim of this study effects of BCG vaccine on the histopathological and gene expression changes seen in hyperoxia induced neonatal rat lung injury.

**Method**

Twenty-three rat pups were divided into four groups: air-exposed control group (n = 5), hyperoxia-exposed placebo group (n = 7), hyperoxia-exposed BCG-vaccinated group (n = 7), and air-exposed BCG-vaccinated group (n = 4). Neonatal hyperoxic lung injury model was established according to the previous studies. Measurement of alveolar surface area, quantification of secondary crest formation, microvessel count, evaluation of alveolar septal fibrosis, and smooth muscle actin immunostaining were performed. Measurement of alveolar surface area, quantification of secondary crest formation, microvessel count, evaluation of alveolar septal fibrosis, and smooth muscle actin immunostaining were performed to assess hyperoxia-induced changes in lung morphology. The gene expression level was evaluated by RT-PCR.

**Results**

The alveolar surface areas were significantly different between the oxygen exposed placebo group and oxygen exposed BCG vaccinated group (alveolar surface area; 0.29 ± 0.02 μm² and 0.52 ± 0.04 μm² p < 0.05 respectively). Number of crests and microvessel count was found to be significantly increased in the oxygen exposed BCG vaccinated group compared with the animals in the oxygen exposed placebo group (p < 0.05). Exposure to hyperoxia resulted in a significant decrease in mean alveolar surface area and number of crests formed compared with air-exposed animals (p < 0.05). The degree of fibrosis was found to be significantly increased in the oxygen exposed placebo group compared with the animals in the oxygen exposed BCG vaccinated group (degree of fibrosis: 1.88 ± 0.33 and 0.91 ± 0.66 p < 0.05 respectively). Immunostaining revealed that SMA demonstrated hyperoxia-exposed animals with BCG vaccine in a significantly decrease in smooth muscle content compared with hyperoxia-exposed placebo animals (p < 0.05). The expression of VEGF, FGF1, IL13, NFκB1 and TNFα in the lungs of vaccinated animals was significantly higher than that of non-vaccinated animals (p < 0.05).

**Conclusion**

Our results suggest that BCG vaccination can be a new protective strategy against neonatal hyperoxic lung injury. These beneficial effects may be interpreted with its immunomodulatory effects on proinflammatory-antiinflammatory cytokine balance and expression of growth factors.

**PS-210**

**ALVEOLAR CAPILLARY DYSPLASIA: A GENETICALLY DETERMINED DISRUPTION OF THE ALVEOLAR/MESENCHYMAL CROSS-TALK CAUSING NEONATAL HYPOXIC FAILURE**

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**Background/aims**

Alveolar capillary dysplasia (ACD) is characterized by pulmonary veins misalignment, capillary paucity and alveolar misdevelopment, and caused by FOXF1 mutations only in 40% of cases. Objectives were 1. to identify known and new gene defects and 2. to correlate them with molecular/cellular mechanisms.

**Methods**

We recruited a cohort of 23 pathology-confirmed cases. When DNA was available, genome-wide copy number variation was analyzed through Array Comparative Genomic Hybridization (aCGH). Mutations were tested by direct sequencing of FOXF1 and candidate genes identified by aCGH; Molecular pathways were analysed by multi-channel immunofluorescence microscopy of ACD cases compared to human fetal/neonatal lung tissue at various development stages.

**Results**

1. Genomic deletions or mutations were identified in 57% of tested cases. Besides FOXF1, two of the genes involved stand out as potential candidates: MEOX2 and TBX4.

2. ACD cases showed a markedly decreased expression of c-kit, a marker expressed in pulmonary small arteries and capillaries in fetal lung controls. In normal fetal lungs FOXF1 and TBX4 were prevalently expressed at the mesenchymal-epithelial border, and MEOX2 in pulmonary vascular smooth muscle cells (PVSMC). Their expression pattern and intensity were altered in all ACD cases, indicating that decreased FOXF1 and/or its downstream transcription factor TBX4 disrupt lung micro vessel formation and homing to alveolar epithelium, and that a similar phenotype may derive from dysregulated PVSMC proliferation and angiogenesis related to MEOX2 insufficiency.

**Conclusion**

Genetic defects affecting the FOXF1 pathway affect the mesenchymal, endothelial and epithelial cross-talk leading to lung developmental disruption, pulmonary hypertension and hypoxic respiratory failure.

**PS-211**

**EARLY POSTNATAL SYSTEMIC LIPOPOLYSACCHARIDE INCREASES PRO-INFLAMMATORY CYTOKINES AND ANGIogenic GROWTH FACTORS IN THE LUNGS AND LEADS TO THE PHENOTYPE OF NEW BPD IN NEONATAL RATS**

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**Background/aims**

Lipopolysaccharide (LPS) is a proinflammatory mediator that induces microvascular injury and contributes to the development of neonatal lung injury. The aim of this study was to evaluate the systemic LPS-induced effects on the developing neonatal lung and the link to the pathogenesis of bronchopulmonary dysplasia (BPD).

**Methods**

0.1 mg/kg LPS (Escherichia coli 0111:B4) was intravenously administered to neonates 24 hours after birth. Blood samples were collected at different time points and analyzed for levels of proinflammatory cytokines. Lung tissue was harvested for histological and immunohistochemical analysis.

**Results**

Systemic LPS administration led to an increase in proinflammatory cytokines, such as tumor necrosis factor-alpha (TNFα) and interleukin-1β (IL-1β). These cytokines were significantly elevated in the lungs of pups that later developed BPD, compared to control animals.

**Conclusion**

Early postnatal systemic LPS exposure results in increased proinflammatory cytokine levels and angiogenic growth factor expression in the lungs of neonatal rats. This may contribute to the development of neonatal lung injury and the pathogenesis of bronchopulmonary dysplasia.
Background Recently bronchopulmonary dysplasia (BPD) occurs not infrequently without an exposure to hyperoxia and/or mechanical ventilation in very preterm infants. To simulate the recent pattern of BPD, novel animal model of BPD induced by inflammation alone is needed. We were to establish a rat model of BPD induced by postnatal systemic lipopolysaccharide (LPS) administration alone.

Methods Two days before delivery, 1 μg of LPS or vehicle (V) was injected into each amniotic sac, and after birth 0.25 mg/kg of LPS or V was injected into peritoneum of pups at P1, P3, and P5. At P7 and P14, bronchoalveolar lavage (BAL) and lung harvest were performed. BAL fluid (BALF) and peripheral blood (PB) were examined for blood cell counts and lung tissue was examined for morphometry, vascular density, neutrophil infiltration, and expressions of pro-inflammatory cytokines and angiogenic growth factors.

Results Postnatal systemic LPS significantly increased the neutrophil counts in PB, BALF and within the alveoli and expressions of pro-inflammatory cytokines and angiogenic growth factors at P7. When postnatal systemic LPS was preceded by intra-amniotic LPS administration, these findings were not observed. Postnatal systemic LPS led to significant disruption of alveolar and pulmonary vascular developments at P14.

Conclusions Early postnatal systemic LPS induced systemic and pulmonary pro-inflammatory responses and disrupted alveolar and pulmonary vascular developments. This rat model of new BPD induced by early postnatal inflammation per se without an exposure to hyperoxia can be used to test the effects of anti-inflammatory agents for BPD.

Background and aims Neonatal infection is a major cause of morbidity and mortality. The ongoing Swiss Paediatric Sepsis Study prospectively evaluates the epidemiology of blood culture-proven sepsis in newborns and children in Switzerland.

Methods Newborn infants admitted to nine Swiss neonatal intensive care units (NICUs) and presenting with culture-proven sepsis between 9.2011–2.2014 were prospectively enrolled. Early-onset sepsis (EOS) was defined as infection occurring.

Results We identified 189 episodes of blood culture-proven sepsis in 186 patients. Thirty seven episodes were classified as EOS and 152 episodes were classified as LOS. Median gestational age at birth was 34 weeks for EOS, and 28 weeks for LOS. Mortality was 14% in EOS and 9% in LOS. Forty six percent of patients required mechanical ventilation during the sepsis episode, and 4% required catecholamine treatment for arterial hypotension.

Group B Streptococcus (GBS) and Escherichia coli were the most frequently isolated pathogens in EOS, accounting for 35% and 16% of episodes. Coagulase-negative staphylococci were the most frequently isolated pathogens in EOS, accounting for 35% and 16% of episodes. Coagulase-negative staphylococci were the leading pathogens in LOS (36%), followed by Staphylococcus aureus (18%), Escherichia coli (16%), and GBS (11%). The proportion of hospital-acquired LOS due to Coagulase-negative staphylococci, Staphylococcus aureus and Escherichia coli varied between 10–68%, 0–45% and 0–30% in different NICUs.

Conclusions This national study confirms that neonatal sepsis continues to cause high morbidity and significant mortality. GBS is the most common cause of EOS. There are important differences in the aetiology of LOS in different institutions.

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