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Effect of treatment for patent ductus arteriosus (PDA) on clinical and eccocardiographic variables of very low birth weight (VLBW) infants

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Introduction: The significance of PDA and indications for treatment of VLBW infants has recently been questioned.
Methods: Clinical and eccocardiographic variables were studied in 86 VLBW infants before (D-1) and after (D2, D4, D7) the day (D0) of pharmacologic or surgical treatment for PDA.
Results: Compared to D-1, infants given indomethacin or ibuprofen had an increase in both systolic (Ps, $p < 0.005$) and diastolic (Pd, $p < 0.001$) blood pressure on D4 compared to D-1), but needed more oxygen (FiO_2, $p < 0001$). In infants undergoing surgical ligation an increase in Pd ($p < 0.05$) and FiO_2 ($p < 0.001$) was also seen as well as increased need for high frequency ventilation ($p = 0.04$). Ductal diameter was significantly reduced on D2 ($p < 0.001$) and D4 ($p = 0.047$), but peak ductal blood flow or left atrium to aorta width (La/Ao-ratio) did not change. Although only 14.3% of infants treated with indomethacin or ibuprofen had a closed duct evaluated by eccocardiography on D7, only 51.4% needed additional treatment courses.
Conclusions: Treatment for PDA improves blood pressure but worsens pulmonary function, particularly after surgery. A significant reduction in ductal size does not improve other eccocardiographic variables. The associations between eccocardiographic findings and clinical symptoms in VLBW infants with PDA need further investigations.

Gender and dose dependent effects of caffeinated sonic hedge-hog on rat models with oxygen-induced retinopathy (OIR)

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Introduction: To determine the effects of dose and gender on caffeine action on Sonic Hedgehog (Shh) signaling pathway.
Methods: At birth, rat pups ($n = 18$ pups/group) were given hyperoxia (50% O_2) with brief hypoxia (12% O_2), or normoxia from P0-P14 with IP injections (P1-P14) of: 1) Caffeine citrate (20 mg/kg IP + 5 mg/kg/d; 2) Caffeine citrate (50 mg/kg IP + 10 mg/kg/d; or 3) equivalent volume saline. At P14, pups were euthanatized or placed in room air till euthanized at P21. Retinal ADPase stains and quantitative real-time PCR for expression of Shh genes signaling pathway were done.
Results: Shh, desert hedgehog (Dhh), Indian hedgehog (Ihh), and HH-interacting protein genes were upregulated at P14 in low Caffeine O_2 group. Expression profile differed by gender. Dhh and Shh were upregulated in males at P14 in response to both caffeine doses. In females, Shh was downregulated with low and upregulated with high dose. At P21, Shh remained downregulated in females and upregulated in males with both caffeine doses.
Conclusions: Caffeine exerts dose-dependent and gender-specific effects on Shh signaling and may re-

sult in differences in ROP outcomes between males and females.

Clinical characteristics of viral intestinal infection on preterm and term neonates

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Introduction: The clinical presentation of the viral enteric pathogens in newborn infants has not been adequately examined. The aim of this study was to evaluate the clinical characteristics of viral intestinal infections in newborn infants.
Methods: Clinical data of all term and preterm infants admitted to our tertiary neonatal intensive care unit from 1998 to 2007 with clinical signs of gastroenteritis (GE) or necrotizing enterocolitis (NEC) were retrospectively reviewed and compared between infants with different viral enteric pathogens in stool specimens.
Results: In thirty-four infants with signs of GE or NEC, enteropathogenic viruses were found in stool specimens. Rotavirus was detected in 12 cases, of which 2 infants had NEC. Compared with infants with rotavirus or norovirus, infants with astrovirus more frequently suffered from NEC ($p < 0.05$). In addition, an acute systemic inflammatory response was significantly more common in patients with astrovirus infection (astrovirus vs. rotavirus and astrovirus vs. norovirus $p < 0.01$ and $p < 0.05$, respectively). Of 8 children infected with norovirus, one infant had a systemic acute inflammatory response and NEC.
Conclusions: This study demonstrates that in newborn infants, intestinal rotavirus, norovirus, and astrovirus infections may be associated with severe illness such as hemorrhagic enteritis resulting in bloody diarrhea or even NEC.

Ureaplasma urealyticum in amniotic cavity cultures at birth is associated with an adverse neuromotor outcome of preterm infants at 2 years adjusted age

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Introduction: Intrauterine infection with *Ureaplasma* spp. has been associated with preterm delivery and chronic lung disease (CLD) in preterm infants. The aim of the present study was to assess the association between the presence of Ureaplasma spp. inside the amniotic cavity and the neuromotor outcome at 2 years adjusted age in preterm infants.
Methods: 114 infants, 23 to 33 weeks'gestational age, born to mothers with amniotic cavity culturing during cesarean delivery were evaluated with the Bayley Scales of Infant Development II and a standardized neurologic examination at 2 years adjusted age.
Results: 67 infants with negative amniotic cavity cultures were compared to 32 infants with isolation of Uu and 15 patients with other bacterial pathogens. Patients with isolation of Uu had a significantly higher risk for an adverse psychomotor development index (PDI) score (OR 4.1, CI 1.6–10.4, $p = 0.003$), an abnormal neurologic outcome (OR 5.7, CI 1.8–17.6, $p = 0.003$), and a higher probability for diagnosis of cerebral palsy (OR 6.5, CI 1.8–23.5, $p = 0.004$) at 2 years compared to patients with negative culture results.
Conclusion: Isolation of Uu from the amniotic cavity at birth is significantly associated with an abnormal PDI and an adverse neuromotor outcome in preterm infants, irrespective of gestational age and birthweight.

Short term effect of erythropoietin on brain lesions and aquaporin-4 (AQP4) expression in a hypoxic-ischemic (HI) neonatal rat model assessed by DWI and immunohistochemistry

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Introduction: Erythropoietin (Epo) has recently increased interest since its concept as a neuroprotective agent has emerged. The potential protective effect of human recombinant Epo (r-hu-Epo) on a HI pup rat model was studied (Vanucci-Rice model).
Methods: Brain lesions were assessed by DWI 3H after carotid ligation; r-hu-Epo (30000 U/kg-dose) intraperitoneal administration was realized just after the carotid ligature. To identify mechanisms underlying the effects of Epo, immunohistochemical detection of caspase3 and AQP4 was performed.

Results: r-hu-Epo limited both the HI-induced brain lesion area and the decrease in apparent diffusion coefficient in the lesion. No early apoptosis was detected; AQP4 up-regulation expression was observed only in HI-pups receiving r-hu-Epo.
Conclusion: This study demonstrates an early neuroprotective effect of Epo. One possible mechanism of Epo for decreasing brain edema and cellular swelling could be a better clearance of water excess in brain tissue, possibly mediated by AQP4.

Perinatal acid base status does not predict neurodevelopmental impairment in very low birth weight infants

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Introduction: In term and near-term infants with perinatal asphyxia, therapeutic hypothermia increases rates of survival without neurologic morbidity. Extending this new treatment to preterm infants is being debated, but the association of low pH and base excess (BE) at birth or admission, and evolving brain damage has not been investigated in preterm infants.
Methods: In a cohort of preterm 1137 infants (gestational age < 35 weeks, birth weight < 1500 g), we assessed outcome in relation to severe perinatal acidosis (pH $\leqslant 7.0$, BE $\leqslant -16$ mmol/l).
Results: Umbilical artery pH was not related to death or neurodevelopmental impairment (NI), as defined by developmental quotients $\leqslant 75$ at 12 or 20 months. pH or BE at admission were weakly predictive of death but not NI, while lowest BE during first 12 h of life was also weakly predictive for NI (positive predictive values 0.30 and 0.27 at 12 or 20 months, respectively).
Conclusions: Perinatal acid base status has a minor role in determining outcome of very preterm infants.

Early identification of the risk for free radical-related diseases in newborns

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Introduction: Oxidative stress (OS) is an unbalance in redox system playing a key role in the pathogenesis of free radicals diseases (FRDs) of the newborn. We tested the hypothesis that OS markers levels in cord blood may predict the onset of FRDs.
Methods: 168 preterm newborns of GA 24–32 weeks were consecutively recruited. Markers of potential OS risk (non protein bound iron, NPBI) and markers of OS-related damage (total hydroperoxides, TH; advanced oxidation protein products, AOPP) were assessed. Associations between FRDs onset and OS markers were checked through inferential analysis.
Results: The development of FRDs was significantly associated to high cord blood levels of TH, AOPP and NPBI (respectively $p = 0.000$, OR $= 1.025$; $p = 0.014$, OR $= 1.092$; $p = 0.007$, OR $= 1.269$).
Conclusions: High cord blood levels of TH, AOPP and NPBI are associated with increased risk for FRDs. OS markers allow the early identification of infants at risk for FRDs because of perinatal oxidant exposure. This can be useful in devising strategies to ameliorate perinatal outcome.

The milking mother of God: A health and life expectancy?

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Introduction: Hundreds of late Medieval, Renaissance paintings and sculptures depict the Virgin Mary with one breast exposed as she is nursing, or preparing to, the infant Christ. Whatever its origins are, representations of the breast feeding Virgin had acquired a new meaning in mid-14th-century Tuscany. In small communities, especially the ones under siege from plague, wars and malnutrition, the Virgin's bosom was a symbol of nourishment and care that sustain the life and salvation that promises the eternity.
Goal: To test the popular belief regarding the Holy Mother's Milk as a support of a healthy and safe life.
Methods: Authors studied 246 between pictures, sculptures and engravings, all concerning the breast feeding Mother of God. Those representations have been considered as a possible connection between the Iconography and the popular and historical idea of protection and defence of human being's life given by those images themselves.
Results: Among 246 images, 44 have been shown to be directly connected with the common belief of the milk as a power of saving and healing, as documented by numerous papers and books.
Conclusion: Results confirmed the goal.

Postnatal depression in mothers of infants admitted to a neonatal intensive care unit at birth: Comparison with mothers admitted in the maternity ward

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Introduction: Our aim was to apply a screening programme of Postnatal Depression (PND) in mothers of infants admitted at birth to the NICU in Cagliari and compare data obtained with a group of mothers of healthy full-term infants from the maternity ward of the same hospital, evaluating risk factors.
Methods: 113 mothers of newborns admitted to NICU (Group 1), 44 of whom VLBW and 69 with birthweight $>$ 1500 g. 101 mothers of healthy full-term infants (Group 2). The Edinburgh Questionnaire (EQ) (cut-off 10) was applied in screening for PND. The survey was conducted at least one month after delivery with further controls.
Results: The prevalence of PND was significantly higher Group 1 compared in Group 2 (23% vs 8%; $p <$ 0.001). PND was almost double in the VLBW group mothers.
Conclusions: Our results are similar to the very few obtained in similar studies. High tech is nothing without a high touch. Medical Humanities must improve in NICUs.

Incidence and distribution of pathogens in late-onset-neonatal-infection (LONI) in the era of antenatal antibiotics (AA)

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Introduction: In 2001, France issued new guidelines for the use of AA (GBS intrapartum antimicrobial prophylaxis, AA for PPROM). This study aims to determine their effects on the incidence and distribution of pathogens in LONI.
Methods: Population-based, observational study throughout Alsace (France), between 01 and 12–2007. All neonates with confirmed and probable LONI, treated with antibiotics for at least 5 days, were included. We analysed exposure to AA, clinical and microbiological data.
Results: Among the 22458 infants born in 2007, 139 infants (mean-GA 33 weeks) were included: 109 had confirmed infection, 30 had probable infection, 53 were preterm infants. The overall LONI, GBS and *E-coli* infections incidences were respectively 6.19, 0.36 and 3.12/1000 live-births. LONI were mainly *E-coli* urinary tract infections (52,5%) with 47.1% of AR-strains. The mortality rate was 3.6% (mainly due to GBS infections) 19.6% of mothers of infected newborns received AA (81% with amoxicillin).AA exposure was significantly associated with AR-*E-coli* infection ($p =$ 0.008).
Conclusion: GBS LONI has a low incidence but is associated with the worst prognosis. AR- *E. coli* LONI seem to be linked to AA.

Persistent coagulase-negative staphylococcal bacteraemia in a neonatal intensive care unit: Clinical and molecular profile

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Introduction: The aim of this study was to describe the clinical and molecular profile of a persistent form of coagulase-negative staphylococcal (CoNS) bacteraemia in a level III NICU.
Methods: Between 2006 and 2008, all neonates with CoNS bacteraemia were studied. Demographics, clinical, laboratory and molecular data were compared between neonates with persistent ($\geqslant$ 3 consecutive positive blood cultures) and non-persistent bacteraemia.
Results: Twenty nine cases with persistent and 43 with non-persistent bacteraemia were identified. The incidence of thrombocytopenia and maximum CRP levels were higher in the persistent group. Biofilm production was expressed by 80 strains (54 persistent, 26 non-persistent; $p = 0.013$). Endotracheal intubation and central vascular catheters were significant risk factors for persistent bacteraemia, but in a logistic regression model, only the biofilm production was significantly related to persistent bacteraemia ($p = 0.005$).
Conclusions: CoNS microbiological characteristics did not differ between persistent and non-persistent cases, however, biofilm-producing strains were associated with persistent bacteraemia.

The price of being born SGA or twin before 32 weeks of gestation

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Background: SGA and twins have variable prognosis according to their gestational age.
Objective: To compare infants born SGA ($\leqslant$ 2SD) to AGA of the same GA as well as singletons to twins in order to assess the extent and the type of neonatal pathologies related to deliveries before 32 weeks of gestation.
Methods: We analyzed the electronic data of all infants $<$32 wks born in our tertiary care perinatal center from 1998 to 2008, to evaluate morbidity and mortality.
Results: AGA vs SGA: 884 singleton AGA and 141 SGA were born. BW $= 1236 \pm 388$ vs 767 ± 225 ($<$ 0.0001). C/Section rate 43.9% vs 78.08% ($<$ 0.0001), mechanical ventilation 49.2% vs 65.2% ($<$ 0.0006), and mortality 10.2% vs 20.6% ($<$ 0.0009).
Singleton vs twins: S $= 893$, T $= 253$, BW $= 12044 \pm 398$ vs 1204 ± 348, C/Section 44.2% vs 74.7% ($<$ 0.0001), RDS 44.0% vs 62.1% ($<$ 0.0001), mortality 10.8% vs 15.4% (0.05).
Conclusions: Deliveries before 32 wks of gestation carry an increased risk of mortality and morbidity both for SGA and twin pregnancies compared to AGA singletons.

Are regional differences in the rate of BPD affected by survival rates at different gestational age?

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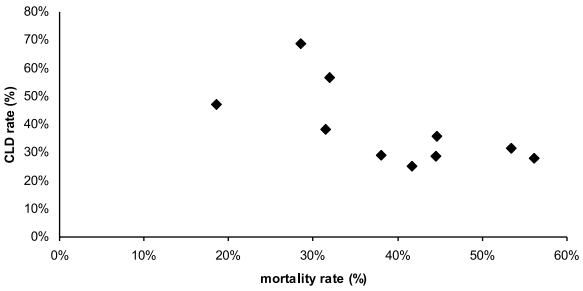
Aims: A considerable regional variability in the rate of bronchopulmonary dysplasia (BPD) has been reported, thus we attempted to identify the role of survival rate on these findings.
Methods: Out of a total of 4984 preterms $<$ 32 weeks, 4185 survived to 36 weeks in 10 European regions (the MOSAIC cohort). The regional differences of BPD were assessed and associated with mortality in 2 subcohorts of 24–27 and 28–31 weeks.
Results: The region specific crude rate of BPD ranged from 10.2% (Italian region) to 24.8% (UK Northern region), mortality rates from 7% (German region) to 20% (Polish region). In 24–27 weeks preterms mortality rate was negatively related with BPD rate (Spearman's rho $= 0.025$; Fig. 1), whereas in less immature neonates (28–32 weeks), no association could be demonstrated.

Region-specific rate of BPD vs. mortality (% each)



Conclusion: Different regional rates of BPD in extremely immature preterm neonates may be due to different survival rates.

Respiratory outcome after preterm birth in school age children with and without bronchopulmonary dysplasia

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Aim: To assess the pulmonary function and prevalence of atopy at school age in very low birth weight infants and to compare BPD and no-BPD patients.
Material and Methods: We studied 85 VLBW infants (34 M/ 43 F) at 84 (62–107) months of life. BPD was defined as oxygen dependency at 36 weeks gestational age. Lung function was evaluated using conventional spirometry (Vitalograph compact).
Atopy (skin-prick test) was considered when there was at least one positive skin test in a panel of the most common environmental allergens in our region.
Mann-Whitney, $\chi 2$ test or Fisher exact test were used.
Results: We compare BPD ($n = 13$) and no-BPD ($n = 64$) groups. Our data show no significant differences in lung function between BPD and no-BPD patients at school age and no evidence of association between atopy and BPD.
Conclusion: In spite of a greater morbidity in early life of children with BDP, our data point to a good respiratory outcome at school age in agreement with some studies that show an improvement in lung function with age.

H1N1 from simple flu to encephalitis and septic shock

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Introduction: To evaluate the clinical picture of H1N1infection.
Methods: Descriptive study from August till November 2009. Patients were screened with real time PCR on sputum, or nasal swab, or CSF.
Results: 12 patients were found to be H1N1 positive. 7(5M -9Y) had respiratory symptoms, of which two were intubated and ventilated. The signs were similar to those of RSV infections including wheezing, rhinitis and respiratory distress, X–rays ranged from simple infiltrates to ARDS patterns. All recovered after 5 to 10 days of treatment by Tamiflu. One child (9Y) was admitted for septic shock and severe hypothermia 35*C. Septic shock resolved after resuscitation within 48 hours. Tamiflu was initiated 12 hours after her admission. The remaining child presented with encephalitis, H1N1 PCR on C.S.F was positive, Tamiflu was given and patient regained consciousness and was a febrile and seizure free on day 2 of admission. 3 premature babies had rhinitis, apneas, and desaturation; none was intubated nor given Tamiflu.
Conclusions: H1N1 infection is now a possible cause of severe infection. Septic shock and encephalitis should be considered.

Prediction of apnoeic spells by means of automatic learning: A pilot study

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Introduction: Apnoeic spells (AS) in preterm infants are serious events and require a high level of alertness and additional workload. If AS could be predicted automatic arousal reactions could be initiated.
Methods: Recording of continuous 2-channel EEG signals and vital parameters (thorax impedance curve, oxygen saturation, heart rate) in 5 preterm infants $<$ 34 weeks g.a. Extraction and transformation of EEG signals to time-frequency representations of periods of 30 sec before an AS. Application to previously unseen episodes using neural (NN) and a Bayesian network (BN). Receiver operating characteristic (ROC) curve analysis (AUC).
Results: 60 AS and 297 non-AS episodes were analysed. NN analysis was slightly inferior to BN. Beta waves were more predictive of AS than alpha, delta, or theta waves with both. Analysis of signals from all wave bands together yielded an AUC between 0.72 and 0.88. When learning model of infants 1-4 was applied to infant 5, without downsampling of non-AS episodes (4 AS episodes versus 75 non-AS episodes) a recall of 1.0 was achieved, but the precision was only 0.1.
Discussion: Total number of AS episodes used in this study was too small for a final appraisal of the method. Additional physiologic parameters should be implemented.

Avoid mechanical ventilation (AMV-TRIAL): Surfactant via gastric tube in spontaneously breathing VLBW infants

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Introduction: Infants on nasal CPAP with oxygen demand and signs of RDS may benefit from surfactant.
Objective: To evaluate effectiveness/safety of surfactant instillation via a gastric tube.
Methods: Randomized multicenter study. Entry criteria: 26+0 to 28+6 weeks, age: $<$ 12 h, RDS with $FiO_2 > 0.30$, no malformations. Intervention: surfactant by gastric tube as previously described. Endpoint: rate of mechanical ventilation between 24 and 72 h.
Results: 108 infants received the intervention, 112 controls received standard treatment, i.e. continuation on CPAP and ventilation/rescue surfactant if indicated. 51/112 (45%) infants were put on mechanical ventilation in this group as opposed to only 30/108 (28%) in the intervention group ($p < 0.05$). No differences were observed in the rate of adverse events, including pneumothorax and intracerebral hemorrhage.
Conclusions: This study demonstrates a reduced need for subsequent mechanical ventilation following surfactant administration via a gastric tube while the infants are breathing on CPAP.

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Haemodynamic response in an experimental model of normocapnic hypoxia and resuscitation with different concentrations of O_2 in newborn piglets

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Introduction: To study the haemodynamic response in an experimental model of normocapnic hypoxia and reoxygenation with different concentrations of O_2 in newborn piglets
Methods: 40 male newborn piglets were premedicated, anaesthetized and instrumented for monitoring of mean arterial blood pressure (MAP) and central venous pressure (CVP). After stabilisation, normocapnic hypoxia (6–7%O_2) was induced until heart rate (HR) $<$ 60bpm. Piglets were reoxygenated, with 18%, 21%, 40% and 100%O_2 until HR reached baseline values. Acid-base balance was examined at stabilisation, hypoxia and reoxygenation.
Results: 14 piglets suffered asystole during hypoxia, 9 did not recover (5 of the 18% group). HR and MAP decreased from stabilisation to hypoxia and increased from hypoxia to reoxygenation in all groups, while no differences were observed between values at stabilisation and those at reoxygenation. CVP and PCO_2 increased from stabilisation to reoxygenation only in the 18% group. pH decreased from stabilisation to hypoxia and increased from hypoxia to reoxygenation in all groups except the 18% one.
Conclusions: Reoxygenation with $O_2 < 21\%$ is not beneficial in this experimental model.

Impaired lung development after choriamnionitis

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Introduction: Antenatal inflammation in utero may be associated with lung injury and subsequent aberrant lung development resulting in bronchopulmonary dysplasia (BPD). BPD has become a developmental disease with a uniform arrest in lung development and is the most common adverse outcome after preterm birth. Drug therapy of BPD is limited to postnatal treatment with vitamin A and caffeine since maternal glucocorticoids have no effect.
Methods: We developed a sheep model suitable for the study of lung development with respect to human development to explore antenatal therapeutic options. Chorioamnionitis was induced by a single injection of endotoxin into the amniotic cavity under ultrasound guidance.
Results: Endotoxin-induced chorioamnionitis caused a cascade of lung injury, pulmonary inflammation, and remodeling in the fetal lung similar to lung injury previously described in adult animal models. The structural changes and the reduced expression of growth factors in the fetal lung after chorioamnionitis resulted in alveolar and microvascular simplification similar to BPD.
Conclusions: Chorioamnionitis can induce structural changes in the fetal lung. The mechanisms of inflammation, structural damage and decreased expression of growth factors needs to be further studied to determine therapeutic targets.

Intrapulmonary pressure during tube suction in a neonatal lung model

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Objective: After introducing new suction devies in our NICU, we observed an increased rate of atelectasis. Here, we verifyed this impression and determined suction pressures using different devices.
Methods: Comparison of atelectasis rates in 2 periods employing an electric and a wall unit suction device; 30 ml-lung model study simulating suction with these devices at -200 mbar. Four endotracheal tubes (ETT) with and without the ETT adapter in place and 3 suction catheters (SC) were used, with 10 measurements for each SC/ETT combination.
Results: We confirmed an increased rate of atelectases with the new suction device (28/83 vs. 23/129 patients, $p < 0.01$). Suction pressure increased exponentially with increasing cross-sectional area ratio (SC:ETT), with only minor differences between pressure generators. Maximum negative pressure varied from -0.54 mbar (ETT 3.5/SC 5) to -58.9 mbar (ETT 3.0/SC 8 Ch with adapter). Suction with ETT adapter in place resulted in higher pressures. The time to reach 90% of the maximum negative pressure decreased with increasing SC:ETT cross sectional area.
Conclusion: Suction without the ETT adapter and with the smallest possible SC over a short time interval will minimize negative intrapulmonary pressure during suc-

tion, potentially affecting the risk of developing atelectasis in intubated neonates.

A parental questionnaire helps to improve follow-up rate of preterm infants to near completeness

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Introduction: Follow-up data of preterm infants are an important measure of quality in neonatal care. The significance of such follow-up data depends on their completeness because a high rate of drop-outs may underestimate the percentage of disabilities.
Methods: The outcome of 250 infants born $<$ 30 weeks' gestation or $<$ 1250 g born 1995-2000 at the largest level 3 perinatal centre in Munich, Germany, was evaluated. Data were derived from neurodevelopmental assessments by specialized paediatricians combined with a validated parental questionnaire about the infants' health and developmental status.
Results: Follow-up data were available from 97% of the survivors. Parental questionnaire and neurodevelopmental assessment gave identical results in 66% of cases. 31% were developmentally delayed in at least one area regarding motor functions, cognitive, language and social skills. An additional burden represented feeding (35%), behavioural (25%) and sleeping problems (21%).
Conclusion: A high completeness of follow-up data is important and achievable even under limited personal and financial resources.

Which artificial odors do premature newborns smell in their incubator? A French survey of healthcare/ cleaning products used in neonatal units

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Introduction: To evaluate the main determinants of the newborn's nosocomial olfactory environment.
Methods: An electronic questionnaire was sent to 99 French neonatal units to evaluate the nature and use of skincare products, lubricants, disinfectants used to clean materials, hand hygiene products.
Results: The response rate was 49.5%. Nine groups of products and 76 distinct commercial preparations were identified. Depending on their vulnerability, newborns infants were estimated to be exposed to nosocomial odours an average of 48 to 64 times daily. Higher levels were reported. Use of the products varied among centres. Newborns were most frequently exposed to aqueous alcoholic solutions.
Conclusion: Newborns are exposed to high levels of olfactory and trigeminal stimuli of nosocomial origin. Their impact on the well-being and development of newborns should be systematically evaluated. Although most of these products are necessary, a wise use of them is recommended. Consensus guidelines should be developed to regulate their use.

Capnography in infants with bronchopulmonary dysplasia

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Background: In adults with chronic obstructive pulmonary disease, there is a gradient between end-tidal CO_2 ($EtCO_2$) and $PaCO_2$, and the slope of the ascending phase is decreased on the capnogram, resulting from obstruction. There are no data in infants with bronchopulmonary dysplasia (BPD).
Objectives: To compare the PCO_2-$EtCO_2$ gradient and the capnogram shape in 2 groups of spontaneously breathing preterm infants: infants with BPD and infants without respiratory disease (controls).
Material and Methods: Sidestream capnography was performed in 20 infants at 36 weeks (BPD $=$ oxygen dependency: 12 cases, controls: 8 cases). Respiratory rate was measured. The PCO_2-$EtCO_2$ gradient was calculated using $EtCO_2$ and capillary sample values ($PcCO_2$). Capnograms were compared.
Results: In BPD, vs control infants: 1) Respiratory rate was increased (60 ± 16 vs. 43 ± 16 /min, $p = 0.009$); 2) A $PcCO_2$-$EtCO_2$ gradient was observed (13 ± 4 vs 0 ± 7 mmHg, $p = 0.0013$); 3) The ascending phase of the capnogram was not decreased, whereas the initial inspiratory phase was prolonged (0.32 ± 0.05% vs. 0.24 ± 0.04, $p = 0.001$).
Conclusions: In infants with BPD, compared with controls: 1) inhomogeneous alveolar ventilation-perfusion ratio was suggested; 2) the capnogram shape did not suggest the existence of airway obstruction.

Functional limitations, compensatory dependency and increased need of health services above routine, related to chronic diseases, at school age, in a cohort of extremely low birth weight (ELBW) or very preterm newborns (1998–2002)

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Introduction: The aim of this study was to evaluate the outcome at school age of a cohort of ELBW or < 28 weeks newborns, born in a 5 years period, in a central maternity hospital in Lisbon. The role of perinatal risk factors was also evaluated.
Methods: Caregivers were questioned by phone interviews, using a validated questionnaire (QuiCCC) related to chronic diseases. Neonatal data was prospectively collected as part of Vermont Oxford's Database.
Results: Survival until discharge was 71%. Fifty-two percent had neither limitations nor dependences. Prevalence of functional limitations, compensatory dependence and increased need of health services was, respectively, 34.2, 28.1 and 62.3%. Twenty-nine percent had cognitive problems and 6% neurosensorial deficits. Severe intraventricular haemorrhage was the most important predictor of functional limitations and compensatory dependency. Male sex and caregiver scholarship $\leqslant$ 10y were predictors of cognitive problems.
Conclusions: QuiCCC can be a useful and easy to use epidemiological tool to evaluate consequences of long-term morbidities that affect ELBW infants, despite improvements in survival rates.

Values of oxygen saturation in the first 25 minutes of life

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Introduction: Use of oxygen (O_2) in the delivery room has been subject for controversy.
Aim: To assess O_2 saturation during the first minutes of life.
Methods: Prospective, observational, cohorts study. A sensor of Signal Extraction Pulse Oxymeter Radical from Masimo was applied on the neonate's right hand. Results were collected at birth and registered sequentially during the first 25 minutes of life. Inclusion criteria – term and preterm healthy newborn infants not needing resuscitation.
Results: Eighty newborn infants were enrolled. GA and BW were respectively 39 weeks (33–41) and 3303 g (1516–4085); vaginal delivery-36%, vacuum extraction/forceps −35%, caesarean section- 29%; 94% of mothers had epidural analgesia.

Minute of life	Median (interquartil)	SpO_2 values
1	78%	(67–84)
2	74%	(65–84)
3	80%	(70–88)
4	82%	(74–92)
5	89%	(77–95)
10	95%	(88–98)
15	97%	(94–99)
20	98%	(95–100)
25	98%	(94–100)

Values of 90% and 95% were surpassed respectively by 7.5 and 15.5 minutes.
Conclusions: In transition to extra uterine life low levels of SpO_2 have to be considered as normal. This should be remembered when O_2 is used in the delivery room.

Lung function at school age of 60 children after twin-twin transfusion syndrome (TTTS)

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Objective: To evaluate how different intrauterine growth patterns influence lung growth and function in later life.
Methods: Lung function (bodyplethysmographie and spirometry) of 30 twin pairs with TTTS and a median gestational age of $34 + 4$ SSW were measured at a median age of 9 y 5 m according to the recommendations of the American Thoracic Society.
Results: A trend to higher total air way resistance and a reduced vital capacity in donor twins was observed. Significant differences were shown with lower FEV1% and lower MEF 25 in the donor subgroup.
Compared with patients' gestational ages at birth there was a significant correlation between MEF 25 and gestational age ($P = 0.027$) and an almost significant correlation between lower VC and lower gestational age ($P = 0.058$).

Conclusions: Donor twins show a trend to reduced VC and relevantly more signs of airway obstruction. Our observations indicate that intrauterine growth retardation in the first half of pregnancy has more negative influence on decreased air way dynamics than decreased lung volumes which could be explained by the fetal growth of lung tissue.
A lower gestational age at birth leads to both a reduced lung volume and signs of airway obstructions.

Deciphering the metabolic pathways perturbed by preterm birth

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Introduction: Metabolomic technologies provide a broad metabolic screen without prior pre-selection of analytes. Here we explore differences in the urinary metabolome between preterm and term neonatal and adult subjects.
Methods: In this cross-sectional study conducted with Research Ethics Committee approval we recruited neonates and adults aged 19–27y, born $\leqslant$ 32 weeks gestation, or at term. Urine samples were analysed using one-dimensional ^{1}H NMR spectroscopy, standard parameters and pre-processing algorithms, principal component analysis (PCA) and partial least square-discriminant analysis (PLS-DA).
Results: Significant differences in the urinary metabolome of preterm and term neonates was apparent in the first urine samples collected after birth and remained evident at term.There were also significant differences between term and preterm young adults. The most marked differences were in preterm young men (elevated methylamines and acetyl-glycoproteins; lower hippurate).
Conclusions: These data are indicative of persisting alterations in metabolic pathways initiated in early life. Metabolomic technologies offer a sensitive means to identify specific biological pathways affected, and may lead to the identification of biomarkers for interventional studies.

Intrapulmonary concentrations of vancomycin in critically ill neonates

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Introduction: In this study our objective was to determine the intrapulmonary concentration in critical ill mechanically ventilated neonates treated with intravenous vancomycin because of proven or suspected infection with Gram-positive bacteria.
Methods: Tracheal and serum samples were taken before the application of vancomycin as trough value. Vancomycin and urea concentrations in tracheal and serum samples were determined by HPLC. Urea was used as an endogenous marker (dilution marker) for calculation of the amount of the epithelial lining fluid (ELF) and subsequent of the concentration of vancomycin in the ELF.
Results: The median plasma and ELF concentration of vancomycin were 9.45 μg/ml (IQR 5.5–11.9) and 103.35 μg/ml (IQR 50.78–178.26). The vancomycin (ELF)/vancomycin (Serrum) ratio was 11.16 (IQR 8.34–25.79).
Conclusions: The results suggest that the intrapulmonary concentration of vancomycin are above the serum concentration and indicate that vancomycin is likely to be an effective agent for the treatment of pulmonary infections in neonates. The concentration of vancomycin in the ELF of neonates exceed the MIC_{90} of *S. epidermidis* and *S. aureus* including MRSA.

Effects of cord clamping on circulation in neonates (VLBWI)

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Introduction: Aim was to investigate the effects of late (LCC) vs. early cord (ECC) clamping on systemic circulation and cerebral blood flow velocity in neonates.
Methods: 19 neonates were studied 4 hours after caesarean section. In 11 neonates (birth weight: 1240 $\pm$ 290 g; gestational age: 30.0 $\pm$ 2 wks) the umbilical cords were clamped after 30s and the infants were placed 30 cm below placenta level (Late), and in 8 (1231 $\pm$ 350 g; 28.6 $\pm$ 2) the cord were clamped immediately (Early). MBP (mmHg), left ventricular output (LVO, ml/kg/min), mean cerebral blood flow ve-

locity (CBFV) in the Arteria carotis interna (ACI, m/s, hemoglobin (Hb, g/dl), and hematocrit (Hct, %) were measured. Systemic and cerebral hemoglobin transport (HbT), and systemic vascular resistance (SVR; mmHg/kg/min^{-1}) were estimated.

Results:

Parameters	ECC	LCC	*p-value
MBP	36 ± 4	44 ± 7	0.03
LVO	241 ± 38	245 ± 25	NS
ACA	0.16 ± 0.03	0.20 ± 0.05	NS
SVR	123 ± 40	145 ± 30	0.05
Hct	0.46 ± 0.4	0.55 ± 0.5	0.002
cerebral HbT	7.4 ± 1.8	11.1 ± 4.1	0.04
systemic HbT	154 ± 27	181 ± 24	0.05

Conclusions: LCC has the potential to avoid arterial hypotention and therefore improves circulation in VLBWI.

On the limit of viability

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Background: Survival is not an adequate measure of success when managing preterm infants $\leqslant$ 24 weeks gestational age (GA).
Aim: To evaluate neonatal morbidity, survival rate and outcome of preterm infants $\leqslant$ 24 weeks GA at birth, in our NICU.
Material and methods: Retrospective chart review, 1996–2009. Data collected included neonatal morbidity and mortality, follow-up at the outpatient department regarding to medical problems and neurodevelopmental and behavioural outcomes.
Results: 53 preterm neonates, 27M/ 26F, BW 630g (360–870), GA 23.5 wks (22–24), outborn 9 (17%), any antenatal steroid 57%. Neonatal morbidity was: hypotension 68%; RDS 98%; pneumothorax 11%; PDA 42%; noso sepsis 72%; NEC ($>$ 2A) 54%; IVH (III+IV) 34%; ROP ($>$ 2) 20%; BPD 71%. Mortality rate was 87% ($n = 46$). Seven (13%) survivors aged between 7 months and 14 years old (two $<$ 24 months) present at follow-up major sequelae 71% ($n = 5$), and normal "border line" development 29% ($n = 2$).
Conclusions: Based on these findings it seems that it is not worthwhile to pursue aggressive support of infants born at $\leqslant$ 24 weeks GA. It is important to combine data from other studies.

Results of the international TEST-Apgar study

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Background: There is considerable variation in assigning Apgar-scores. Definitions are required to apply Apgar-score under clinical conditions such as preterm delivery or resuscitation [ActaPaed'09:98;1433–36].
Aim: To test the prognostic value of a specified type of Apgar-score to predict short term neonatal outcome in a population of preterms.
Methods: An international prospective multicenter study, to compare the conventional Apgar with the specified type of Apgar-score and AAP-suggestion. Data were obtained: (A) perinatal characteristics; (B) description of the condition of the infant during first 10 minutes; (C) data on discharge.
Results: 2169 infants were screened in 20 NICU from 13 countries; 1855 infants were included, [median 89 per center (range 23–229)]. Included infants had the following birth characteristics: GA 28 $\pm$ 2.5 weeks, birth weight 1165 $\pm$ 401 g, pH 7.3 $\pm$ 0.1. The specified Apgar-score was significantly higher than the conventional. Comparison of infants who died or survived showed no differences in conventional Apgar-score [median (range) 7 (5–8) vs. 8 (7–9)], however, significant differences in the specified score [6 (4–7) vs. 9 (8–10)].
Discussion: The specified Apgar-Score has an improved prognostic value in infants who require support in the delivery room.
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Effect of hyperoxia on the pulmonary function of newborn rats

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Introduction: Hyperoxia and oxidative stress play an important role in the pathogenesis of bronchopulmonary dysplasia (BPD).
Methods: We studied two litters of Sprague-Dawley newborn rats divided into a control Group (CG): exposure to room air and Hyperoxia Group (HG): exposure to 60% of Oxygen from birth and during 14 days. Pul-

monary function tests were performed on day 15th in both groups by total body plethysmography. VEGF-A, was measured and compared between groups.
Results: 14 offspring in each group were studied. A significant decrease in tidal volume in the hyperoxia group compared to controls was found, HG: 0.0059 ml/g (SE: 0.000468 ml/g), CG: 0.0046 ml/g (SE: 0.000319 ml/g), p 0, 000) with a significant increase in the respiratory rate (HG: 310 rpm; CG: 266 rpm; p 0.03). VEGF-A, was statistically significant lower in the hyperoxia group, (HG: 4.84 pg/mg lung protein, CG: 5.43 pg/mg lung protein).
Conclusion: Prolong exposure of newborn rats to hyperoxia alters the spontaneously breathing pulmonary function test, by decreasing tidal volume with a compensatory increase in the respiratory rate.

Nationwide short-term outcome for VLGA infants in Estonia: Comparison of two cohorts
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Introduction: Changes in perinatal care and short-term outcome of all VLGA infants born in Estonia were identified.
Methods: A nationwide population-based study included all infants, gestational age of 22 to 31 completed weeks born in Estonia in 2002-2003 and in 2007-2008, until discharge or death.
Results: During the two periods 299 and 406 VLGA infants were born, live-born (88% vs 89%) were of similar mean gestational age (28.2 *vs* 28.1 weeks) and birth weight (1234 *vs* 1223g). Significally more live-born infants in 2007–2008 were admitted for care (98% vs 94%), including a higher ratio of infants of 22–23 (88% vs 54%) and of 24–25 GW (98% vs 84%). Survival to discharge increased from 78% to 85% ($p = 0.035$) and improved in more immature infants (OR adjusted for GA 1.8 (95% CI 1.1–3.1). Survival without morbidities predicting poor neurodevelopmental outcome remained unchanged.
Conclusions: Neonatal morbidity of VLGA infants in Estonia has not increased despite of better survival rate of more immature infants.

Neonatal treatments and early nephrotoxicity in very preterm infants
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Introduction: Preterm infants are at high risk of drug-induced acute kidney injury. We aimed to determine the impact of drugs prescribed to very preterm infants during the first week of life on glomerular filtration rate (GFR) during the first month of life.
Methods: Multicenter prospective cohort of infants aged 27-31 weeks gestation. GFR was measured on day 2, then weekly for one month. Infants were parted in "Low GFR" or "High GFR" groups according to their GFR on day 7, with regard to the median reference GFR for their gestational age. Statistical analysis was performed with a logistic regression and a repeated measure analysis.
Results: 269 infants were analyzed, 183 in "Low GFR" group and 86 in the "High GFR" group. Perinatal characteristics were similar in both groups. Aminoglycosides and glycopeptides did not show a nephrotoxic effect, even at high plasma concentrations, during the first week of life. Significantly more infants were treated with ibuprofen in "Low GFR" group than in "High GFR", respectively $n = 55$ (30.0%) versus $n = 15$ (17.4%).
Conclusions: Ibuprofen alone proved to be really nephrotoxic if prescribed during the first week of life.

The effect of healthcare associated infections in newborn period on atopic diseases in childhood
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Introduction: We aimed to investigate the effect of healthcare associated infections (HAIs) and antibiotic use in newborn period on atopic diseases.
Subjects and Methods: 73 children who had HAIs in NICU between January 2001 and September 2007, and their 41 siblings who were healthy in newborn period were included.
Results: Ventilator associated pneumonia (VAP) was observed in 32 (45.2%), blood stream infection (BSI)

in 28 (38.4%) and clinic sepsis in 12 (16.4%) of 73 children with HAIs. There were asthma in 24 (32.9%) children, allergic rhinitis in 3 (4.1%) and atopic dermatitis in 5 (6.8%) children in HAIs group. However, 2 children (4.9%) had asthma, 1 child had allergic rhinitis (2.4%) and 2 children (4.9%) had at least one atopic disease in sibling group. Asthma was significantly higher in HAIs group ($p < 0.001$).
When we compared atopic 29 children with non-atopic 85 children, children who had been hospitalized and treated with antibiotics in newborn period were almost 11.5 times as likely to have atopic disease.
Conclusion: Asthma was significantly higher in HAIs group, and atopic disease risk seems to increase in children treated with antibiotics for HAIs in newborn period.

Risk factors in preterm infants for chronic renal damage at a later age

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Introduction: To assess biochemical parameters of renal function and renal volume using ultrasound in preterm infants.

Methods: 69 children preterm born (mean age 5.7 $\pm$ 1.4 years) (BW $<$ 1500 gr) were categorized according to BW, in VLBW ($n = 43$) and ELBW ($n = 26$). ELBW had BW [850 (775–883) vs 1,315 (1,248–1,352) g] and GA [27.0 (26.3–27.7)vs30.1 (29.9–31.3) weeks] significantly lower than VLBW.
Results: No differences were found in age, BSA, BP, and RF at follow-up. Urinary excretion of α1-microglobulin/creatinine was significantly higher in children born with ELBW [0.16 (0.25–0.79) vs 0.00 (0.05–0.25) mg/mmol, $p = 0.008$].
AKI occurred in both VLBW (4/43) and ELBW (3/26). At birth, ELBW were more frequently treated with nephrotoxic drugs than VLBW: aminoglycosides (96.2% vs 46.5%), and ibuprofen (34.6% vs 7%). Children born ELBW showed reduced renal volumes [73.8 (69.0–80.7) versus 86.3 (84.1-97.1)cm^3], overall the left cortical thickness [1.00 (0.96–1.10) versus1. 20 (1.11–1.29) cm]. Children who received post-natal aminoglycoside (45) showed comparable total renal volume ($p = 0.209$) than who did not (24).
Conclusion: VLBW was associated with reduced renal volumes and aminoglycosides administration at-birth to an increased α1-microglobulin excretion at follow-up.