It is over twenty years since epidemiological studies revealed that there was a relationship between patterns of early growth and risk of developing type 2 diabetes in later life. Studies of identical twins, individuals who were *in utero* during periods of famine and animal models have provided strong evidence that the early environment, including early nutrition, plays an important role in mediating this relationship. The concept of "early life programming" is therefore widely accepted. However the mechanisms by which a phenomenon that occurs in early life can have long-term effects on the function of a cell and therefore metabolism of an organism many years later are still emerging.

These include:

1. Permanent structural changes in an organ due to exposure to suboptimal levels of essential hormones or nutrients.
2. Permanent effects on regulation of cellular ageing through increases in oxidative stress and mitochondrial dysfunction leading to DNA damage and telomere shortening.
3. Persistent alterations in epigenetic modifications (including DNA methylation, histone modifications and miRNAs) leading to changes in gene expression.

Several transcription factors have been shown to be susceptible to programmed changes in gene expression through such epigenetic mechanisms. These are conceptually attractive targets of programmed epigenetic regulation, as through regulation of their expression a network of other genes will be regulated. Further understanding of the extent and nature of these programming mechanisms could enable the development of preventative and intervention strategies to combat the burden of diseases such as type 2 diabetes.

176 THE ROLE OF FGF10 FOR ALVEOGENESIS IN BRONCHOPULMONARY DYSPLASIA

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Background and aim Bronchopulmonary dysplasia (BPD) is associated with impaired alveolar growth and pathologic vascularization. As a chronic lung disease it remains an important complication for preterm infants, especially born before 28th week of gestational age. *Fibroblast-growth-factor 10* (*Fgf10*) is known to play an important role in lung morphogenesis. We aim to investigate the role of *Fgf10* for alveogenesis in a mouse model of BPD.

Methods Using an inducible double transgenic mouse line (*SPC-rtTA; tet(O)Fgf10*) we established a BPD model by exposing the pups to 85% oxygen (experimental and control group) and normoxia (control group) for 28 days. Activation of the transgene *Fgf10* was done after birth (P0) by doxycycline treatment. Gene expressions for *Fgfr2b* and *Fgf10* were analyzed by quantitative real-time PCR. To study lung morphology histology, mean linear intercept (MLI) and radial alveolar count (RAC) were performed.

Results Real-time PCR results showed a significant decrease of *Fgfr2b* and *Fgf10* expression in the hyperoxia group at day 21 and day 28 indicating epithelial cell damages. The histology showed a simplification of alveoli in the hyperoxia group (85% oxygen) but not in the normoxia group after 14 days. In contrast, the hyperoxia group with overexpression of *Fgf10* showed less simplification of alveoli. These findings were confirmed by MLI and RAC.

Conclusion We conclude that *Fgf10* may have a protective/regenerative effect on lung injury by increasing secondary septa formation.

177 AUTOMATION OF RESPIRATORY SUPPORT IN THE NEONATE: FACT OR FICTION

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Premature infants frequently present with respiratory instability that is associated with fluctuations in ventilation and gas exchange. Frequent adjustments of respiratory support to match the infant's needs are time consuming and are limited by staff availability and workload. Hence, automation is being developed as a way of improving the care of the premature infants and reduce staff workload.

Some of these automated modes of respiratory support are becoming available for clinical use in preterm infants. These include volume targeted ventilation where peak inspiratory pressure is automatically and continuously adjusted to deliver a preset tidal volume. Another modality is targeted minute ventilation where the ventilator rate is adjusted automatically to maintain a preset minute ventilation. Proportional assist ventilation is another modality where airway pressure is adjusted in proportion to flow or tidal volume generated by the infant. Using this principle recently NAVA has been introduced for use in neonates where the airway pressure generated by the ventilator is proportional to the electrical signal captured from the diaphragm. Finally, automated adjustment of inspired oxygen concentration is becoming available in some ventilators to adjust FiO₂ and maintain oxygen saturation within a preset range. These modes are expected to compensate for some of the limitations that exist in the present forms of respiratory support. Available evidence and preliminary findings for short term effects are promising but further investigation is needed to determine the effects of these modalities on the long term outcome of preterm infants.

178 CIRCUMSTANCES SURROUNDING END OF LIFE OF INFANTS WITH PERINATAL HYPOXIC-ISCHEMIC ENCEPHALOPATHY (HIE)

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Objective To analyze circumstances of all consecutive neonatal deaths by HIE over a 10 year period and examine changes along time setting. Level III Neonatal Intensive Care. Madrid, Spain.

Design Retrospective chart review of all neonatal cases with HIE who died from 2000 to 2010 within the neonatal period.

Results Of a total 70 infants with HIE, 18 died during the neonatal period. All of them had severe HIE and the mean age of death was 64.4±51 hours of life. In 17 (94%) the death was preceded by an end-of-life decision based on the bad prognosis; 15 by withdrawal or limitation of therapy (W/LT) while ventilated, and 2 by decision of parents not to resuscitate if cardiac arrest. All patients had coma and at least one of the following studies severely altered: EEG-aEEG, US/Doppler or CSF-NSE. The first interview for W/LT happened at 25.7±28.9 hours and the mean time interval since W/LT was initiated until death was 10.5±14 hours. Ten infants (56%) had sedation or analgesia during W/LT and presence of the family at the bedside

was reported in 5 (28%). There were no changes along the ten years reviewed.

Conclusion Most deaths in infants with HIE are preceded by a clear decision of W/LT, usually within the first three days of life. The W/LT may last usually a few hours to days. We did not find changes surrounding end of life during the decade.

179 END-OF-LIFE ETHICAL ISSUES: PAEDIATRIC INTENSIVISTS DIFFER FROM NON-INTENSIVIST PAEDIATRICIANS

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Background Ethical issues often arise near the end-of-life (EOL) because of concerns about what is appropriate care and who should decide. Differences may exist between paediatric intensivists and non-intensivist paediatricians.

Aim The aim of study was to assess if the approach toward EOL ethical issues differ between paediatric intensivists and non-intensivist paediatricians.

Methods Questionnaire was given to intensivists working in the Slovene paediatric ICUs and to paediatricians participating at a yearly meeting on issues in critically ill child. The questionnaire was assessing the opinion about EOL ethical issues and experiences with them.

Results Twenty-four out of 30 Slovene paediatric and neonatal intensivists and 35 out of 65 non-intensivist paediatricians responded. The average ages in both groups were 42 years. Over 90% of intensivists as compared to less than a third of non-intensivists knew whom to counsel in ethical dilemmas ($p=0.004$). Eighty-three percent of intensivists accepted withdrawing of treatment as ethically appropriate as compared to 53% of the non-intensivists ($p=0.0002$). Do-not-resuscitate order was always followed by 59% of paediatric intensivists. Neither group found physician's religious and cultural beliefs to be very important in decision-making process (69% and 66%).

Conclusions Substantial differences existed between paediatric intensivists and non-intensivist paediatrician in EOL ethical issues. Since only a third of non-intensivist paediatricians knew whom to counsel when facing an ethical dilemma and only around half of them accepting withdrawing of care as ethically appropriate, better ethical training is needed. Interestingly, neither group considered physician's religious and cultural beliefs to be very important.

180 PARENT'S PERCEPTION OF END OF LIFE IN BRAZILIAN PEDIATRIC INTENSIVE CARE UNITS

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Objective Assess the parents perception of patients who died in the Pediatric Intensive Care Unit (PICU) about the care given by health staff in the moments preceding the children's death.

Methods Exploratory-descriptive study with a qualitative approach. Settings: 2 PICU in southern Brazil. Subjects: 15 parents of children who died from April to September 2008. Data collection was performed through 3 steps:

- The researchers contacted the parents by phone call to invite them to attend to the hospitals,
- The doctors who assisted the children clarified doubts about the therapy offered.
- A semi-structured interview, was carried out by researchers who had not participated of the care.

Results The analysis resulted in 4 categories:

- the moment of death in the PICU;
- talking with the attending physicians;
- parental involvement in decision making;
- parental participation in research.

The results show that parents lack a peaceful environment where they can adequately carry out the goodbyes at the time of death of their children. They emphasized the solidarity provided by the nursing staff at this point and the little involvement of the medical team. The opportunity to revisit the process of their children's death with the team physician was considered positive. Parents felt that they did not have an effective participation in decision taking.

Conclusion The research shows that the difficulty of communication between health staff and parents is a factor that impacts negatively on the decision taking and grieving processes.

181 RESUSCITATION OF NEONATES AT 23 WEEKS GESTATIONAL AGE: A COST-EFFECTIVENESS ANALYSIS IN THE UNITED STATES

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Background and aims The appropriateness of intensive care for extreme prematurity continues controversial. In neonatal intensive care, an increasingly common choice is whether or not to resuscitate at 23 weeks gestational age. We sought to investigate whether such an intervention is cost effective.

Methods A decision analytic model was designed comparing resuscitation vs. non-resuscitation from a societal perspective for pre-term deliveries at 23 weeks. Estimates of death (74%) and neurodevelopmental disability (84–91%) in the setting of resuscitation were taken from the existing literature. Utilities were applied to discounted life expectancy to generate QALYs. All costs and QALYs were discounted at 3%. A cost-effectiveness threshold of \$100,000 per QALY was utilized. Sensitivity analysis included univariate and bivariate comparisons and Monte Carlo simulations.

Results Non-resuscitation is the dominant strategy, as it is both less expensive (\$71,036 v. \$259,358) and more effective (24.7 QALYs v. 24.4 QALYs). While resuscitation would lead to 240 live infants, in a theoretical cohort of 1,000 cases, there would be 100 severely disabled, 70 moderately disabled, and 90 non-disabled survivors. In univariate sensitivity analysis, non-resuscitation was the cost-effective strategy at all reasonable ranges of the inputs for the cost of NICU care and risk of mortality and disability.

Conclusions From a societal perspective, it does not appear cost-effective to resuscitate 23 week neonates over a wide range of assumptions. In our model, even if NICU care is free, resuscitation is not cost effective at baseline due to extreme long-term costs.

182 NEC PATHOGENESIS - NEWS FROM PRETERM PIGS

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Nutritional, microbiological and immunological dysfunctions all play a role in NEC etiology but the relationship among these determinants is not understood. The preterm gut is very sensitive to enteral feeding which may either promote gut adaptation or induce gut dysfunction via bacterial overgrowth and inflammatory reactions. Tumor necrosis factor alpha, toll-like receptors and heat-shock proteins are identified among the immunological components of the early mucosal dysfunction. It remains difficult, however, to