membrane depolarization (i.e. JC-1 flow analysis); no activation of caspase-9). Universal caspases inhibition and neutralization of FasL abrogated the stretch-induced apoptosis.

Conclusion Prolonged mechanical ventilation induces apoptosis of alveolar type II cells in newborn rats and the cellular mechanism involves activation of the extrinsic death pathway via the FasL/Fas system.

234 EFFECTIVENESS OF FETAL PERFLUOROCARBON THERAPY FOR LUNG HYPOPLASIA IN DIAPHRAGMATIC HERNIA

doi:10.1136/archdischild-2012-302724.0234

¹S Herber-Jonat, ²A Vuckovic, ³R Mittal, ³J Jani, ¹AW Flemmer. ¹Div. of Neonatology, University Children's Hospital, LMU Munich, Munich, Germany; ²Laboratory of Physiology and Physiopathology, Faculty of Medicine, Université Libre de Bruxelles; ³Department of Obstetrics and Gynecology, CHU Brugmann, Brussel, Belgium

Aims To assess the effects of fetal, intratracheal perfluorooctylbro-mid (PFOB) instillation on lung-mechanics and gene expression of Surfactant and developmental proteins in a newborn rabbit model of lung hypoplasia.

Methods On day 23/31, diaphragmatic hernia was induced by fetal surgery in two fetuses/doe. On day 28/31, the fetuses were randomly instilled with intratracheal PFOB (CDH-PFOB) or saline (CDH-saline). After term delivery, the fetuses were venti-lated (30min) and lung-mechanics were measured. Lung-to-body-weight-ratio (LBWR) and mRNA levels of different proteins were determined. Non-operated littermates served as controls. Gene expression was expressed as fold-induction relative to controls.

Results LBWR showed an increase in CDH-PFOB as compared to CDH-saline (p=0.05). Total lung capacity (TLC), static lung compli-ance (Cst), and RTq-PCR are shown below (+p<0.05 as compared to control, *p<0.05 as compared to CDH-saline):

Abstract 234 Table 1

Mean (95%-CI)	control (n=9)	CDH-saline (n=8)	CDH-PFOB (n=8)
TLC (μl/g)	33.34 (30.29; 36.38)	15.42 (10.25; 20.58)+	21.68 (18.64; 24.72)+,*
Cst (ml/cmH ₂ O*kg)	2.36 (2.12; 2.60)	1.20 (0.85; 1.55)+	2.08 (1.47; 2.70)+,*
SpA	1 (0.53; 1.88)	0.56 (0.24; 1.39)+	0.47 (0.15; 1.37)+
SpB	1 (0.44; 2.3)	1.55 (0.68; 3.29)+	0.76 (0.29; 1.72)*
SpC	1 (0.3; 3.3)	1.72 (0.88; 4.66)+	0.92 (0.29; 2.77)*
TGF-β2	1 (0.12; 8.5)	1.43 (0.10; 10.18)	0.92 (0.10; 9.03)
prepro α-1 coll 1	1 (0.44; 2.27)	1.64 (0.78; 4.30)+	1.04 (0.38; 3.14)

Conclusions In contrast to previous data addressing tracheal occlusion, PFOB improved TLC and Cst. PFOB also resulted in nor-malization of Surfactantproteins without inducing extracellularma-trix proteins. Thus, PFOB instillation appears to be a promising therapy for use in fetal lung hypoplasia.

235 ROLE OF EARLY PROTEIN INTAKE IN OBESITY DEVELOPMENT

doi:10.1136/archdischild-2012-302724.0235

MF Rolland-Cachera. UREN, University Paris 13, Bobigny, France

There is now convincing evidence that early life factors exert long-lasting influence on health. Birth weight and growth seem to be highly sensitive to nutritional factors during pregnancy and

in early life. The nutrient balance of the diet in the first years of life is likely to have important impact on growth and later health. Mother's milk contains a high proportion of fat (52%) and low proportion of protein (6%). After weaning, the infant diet in industrialized countries is in sharp contrast with the composi-tion of human milk. The fat content suddenly drops and the pro-tein content increases, reaching 3 to 4 times the protein needs. The beneficial effect of human milk could be attributable to its nutrient composition. Indeed, several studies have shown that the high protein content of the diet could have detrimental effects on growth. High protein intake is associated with an early adiposity rebound which predicts later health risks. However, the mechanisms and the cause-effect relationships remain to be elucidated. Low energy dense diet can affect leptin and ghrelin concentrations in early life and program later resistance. Besides, excessive protein intake might accelerate growth by increasing insulin-like growth factor. Optimal growth is desirable, as stunt-ing and rapid growth as well are risk factors for various diseases. These observations stress the importance of providing nutri-tional intakes adapted to nutritional needs at various stages of growth.

236 INTERMITTENT HYPOXIA: EFFECTS ON BRAIN STEM OF OXIDATIVE STRESS AND NRF2 TRANSCRIPTION FACTOR ACTIVATION IN A RAT PUP MODEL

doi:10.1136/archdischild-2012-302724.0236

¹M Vento, ²J Escobar, ³J Kuligowski, ⁴K Prabha, ⁴RJ Martin, ¹E Cubells, ⁴O Koroglu. ¹Division of Neonatology, University and Polytechnic Hospital La Fe; ²Neonatal Research Unit; ³Division of Neonatology, Health Reseach Institute La Fe, Valencia, Spain; ⁴Division of Neonatology, Rainbow Babies & Childrens' Hospital, Cleveland, OH, USA

Background Apnea of prematurity which is a common condi-tion in the neonatal period caused by immature brainstem respi-ratory neural output may result in intermittent hypoxia and cause of oxidative stress during this vulnerable developmental period.

Objective To test if chronic intermittent hypoxia (CIH) alters oxi-dative metabolism and resultant redox status in the medulla of rat pups.

Methods Litters of 10 rat pups and their dams were assigned to: normoxia (controls) and intermittent hypoxia (Hx). Exposure occurred from P1-P7. CIH consisted of exposing rat pups to alternating cycles of N2 and air: 45 seconds of hypoxia (nadir of 5% O₂) was administered every 5 minutes for 8 hours/day. For controls, animals were kept at air. On the eighth day, brainstems were harvested, snap-frozen in liquid nitrogen. Reduced (GSH) and oxidized (GSSG) glutathione, and precursors -glutamyl-cysteine (-G-cysteine) and L-cysteine in medulla were determined by UPLC-MS/MS and MDA in medulla was determined by HPLC.

Results GSH was significantly reduced in medulla of rat pups sub-mitted to chronic intermittent hypoxic (CIH) episodes associated with reduction in GSH/GSSG ratio. GSH precursors were also sig-nificantly lower in the brainstem of the Hx group.

Conclusions Intermittent hypoxic episodes in rat pups cause a sig-nificant reduction in GSH and its precursors in the developing brainstem. GSH and precursors are major determinants of redox status. These alterations may activate transcription factors relevant to the expression of antioxidant enzymes and inflammation. We speculate that oxidant stress may impair central respiratory control and contribute to further enhance recurrent apnea/impaired oxygenation.