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.

### Abstract 234

**EFFECTIVENESS OF FETAL PERFLUOROCARBON THERAPY FOR LUNG HYPOPLASIA IN DIAGNOSTIC HERNIA**

doi:10.1136/archdischild-2012-302724.0234

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**Aims** To assess the effects of fetal, intratracheal perfluorocetylbro- 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 ventilated (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):

<table>
<thead>
<tr>
<th></th>
<th>Mean (95%-CI) control (n=9)</th>
<th>CDH-saline (n=8)</th>
<th>CDH-PFOB (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC (µl/g)</td>
<td>33.34 (30.29; 36.38)</td>
<td>15.42 (10.25; 20.58)*</td>
<td>21.68 (18.64; 24.72)*</td>
</tr>
<tr>
<td>Cst (ml/cmH2O*kg)</td>
<td>2.36 (2.12; 2.60)</td>
<td>1.20 (0.85; 1.55)</td>
<td>1.04 (0.78; 1.34)</td>
</tr>
<tr>
<td>SpA</td>
<td>1 (0.53; 1.88)</td>
<td>0.56 (0.24; 1.39)+</td>
<td>0.47 (0.15; 1.37)+</td>
</tr>
<tr>
<td>Spß</td>
<td>1 (0.44; 2.3)</td>
<td>1.55 (0.68; 3.29)+</td>
<td>0.76 (0.29; 1.72)*</td>
</tr>
<tr>
<td>SpC</td>
<td>1 (0.3; 3.3)</td>
<td>1.72 (0.88; 4.66)+</td>
<td>0.92 (0.29; 2.77)*</td>
</tr>
<tr>
<td>TGF-d2</td>
<td>1 (0.12; 8.5)</td>
<td>1.63 (0.10; 10.18)</td>
<td>0.92 (0.10; 9.0)</td>
</tr>
<tr>
<td>prépro α1 coll 1</td>
<td>1 (0.44; 2.27)</td>
<td>1.64 (0.78; 4.30)+</td>
<td>1.04 (0.36; 3.14)</td>
</tr>
</tbody>
</table>

**Conclusions** In contrast to previous data addressing tracheal occlusion, PFOB improved TLC and Cst. PFOB also resulted in normal- ization of Surfactantproteins without inducing extracellularoma- trix proteins. Thus, PFOB instillation appears to be a promising therapy for use in fetal lung hypoplasia.

### Abstract 235

**ROLE OF EARLY PROTEIN INTAKE IN OBESITY DEVELOPMENT**

doi:10.1136/archdischild-2012-302724.0235

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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 composition 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 adipo- sytis 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 stunting 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.

### Abstract 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

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**Background** Apnea of prematurity which is a common condi- tion in the neonatal period caused by immature brainstem respiratory 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 oxid- ative 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 oxidative stress may impair central respiratory control and contribute to further enhance recurrent apnea/impaired oxygenation.