pneumonia and 10 no lung disease. Gestational age and birth weights were similar (38.3 ± 2.0 wks and 2782 ± 724 g). All newborns received intra-tracheally 2 mg kg^{-1} U^{13}C -DPPC mixed with 2 to 5 mg kg^{-1} of exogenous surfactant. We collected sequential tracheal aspirates from the start of the study (before the tracer administration) and isotopic enrichments of DPPC palmitate moieties were measured from serial tracheal aspirates by gas chromatography mass spectrometry. Data are expressed as median (interquartile range) and comparisons are performed by Mann-Whitney test. $p < 0.05$ was regarded as statistically significant.

Results: Median and interquartile range of DPPC pool size in newborns with pneumonia was 3 mg kg^{-1} ($1.5\text{-}14.0$) and 26.7 mg kg^{-1} ($18.3\text{-}44.0$) in control group. The difference was statistically significant ($p=0.041$). Median DPPC half life was 10.1 h ($7.6\text{-}13.9$) in pneumonia and 22.5 h ($18.2\text{-}36.1$) in controls. The difference was highly significant ($p=0.004$).

Conclusions: Term newborns with pneumonia exhibited a smaller pool size and shorter DPPC half life than controls suggesting a markedly faster surfactant turnover presumably triggered by neonatal pneumonia.

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NEW ANTI-INFLAMMATORY THERAPY FOR NEONATAL ACUTE LUNG INJURY: VARESPLADIB (A-001) INHIBITS EX-VIVO SECRETORY PHOSPHOLIPASE

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Background: Secretory phospholipase A2(sPLA2) is crucial for surfactant catabolism and inflammation. We demonstrated high sPLA2 activity during infection related respiratory failure (IRRF), hyaline membrane disease (iRDS), RSV-triggered ARDS. sPLA2 is also responsible for lung damage during

meconium aspiration syndrome (MAS). Varespladib is the first new anti-inflammatory drug able to directly inhibit sPLA2 and it resulted efficacious in animals and promising in adults.

Aim: To test varespladib efficacy in an ex-vivo model of direct endotracheal administration in various types of neonatal acute lung injury.

Methods: 24 neonates affected by iRDS, 12 with IRRF, 5 with MAS have been subjected to non-bronchoscopic broncho-alveolar lavage according to European Respiratory Society advices. Supernatant has been subdivided in aliquots which have been added with various concentrations of varespladib or equivalent volumes of saline. Real time sPLA2 activity and total protein content have been measured. Enzyme activity has been corrected for dilutional factors and varespladib absorbance. Clinical data were registered up to the intensive care unit discharge.

Results: Varespladib reduces sPLA2 during iRDS (-20% ; $p < 0.0001$), MAS (-23% ; $p=0.04$), IRRF (-15% ; $p=0.003$). Varespladib efficacy is higher when a lower capillary extravasation is present (ratio sPLA2 activity reduction/total proteins = 2.17 in iRDS; 0.59 in IRRF, 0.53 in MAS). IC50 has been calculated and varespladib efficacy correlates with the basal enzyme activity ($\rho = 0.375$; $p=0.017$). No correlations with gestational age, birth weight, surfactant cumulative need, mechanical ventilation and oxygen therapy duration were found.

Conclusions: Varespladib efficaciously inhibits sPLA2 in an ex-vivo model of direct administration. This might have important anti-inflammatory effects and spare surfactant from its catabolism.

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REGULATION OF AGE-DEPENDENT TYPE II CELL EPITHELIAL MESENCHYMAL TRANSITION BEHAVIOR

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Background and aims: Epithelial- Mesenchymal Transition (EMT) is a process where epithelial cells acquire a mesenchymal cell phenotype. EMT is activated in association with tissue repair and remodeling after injury in multiple organs including

the lung. In adult lungs, EMT is associated with fibrosis. In contrast, fetal tissue is capable of wound repair without scarring or fibrosis. We previously showed that MLE12 cells, similar to primary adult type II cells, undergo EMT with expression of mesenchymal cell phenotype after transforming growth factor beta (TGF β) 1 and epidermal growth factor (EGF) treatment. In contrast, fetal rat 21d type II cells did not undergo EMT with these treatments.

We hypothesize that ErbB receptors are important in the age-related regulation of EMT.

Methods: Primary isolated fetal d21 rat type II cells (>95% pure) were pretreated with cis-OH-proline to eliminate remaining fibroblasts, followed by a 5-day treatment with 2.5 ng/ml TGF β -1, 10ng/ml EGF, or both. Cells were then harvested for Western Blot analysis. MLE-12 cells were used as an adult lung epithelial cell model and treated similarly.

Results:

	MLE12 cells	Fetal Type II Cells
ErbB2 receptor	Increased receptor phosphorylation and protein expression after TGF β -1	Significantly decreased receptor phosphorylation (70%) and protein expression (81%) after TGF β -1
ErbB4 receptor	Significantly decreased phosphorylation (68%) and protein expression (85%) after TGF β -1	Significantly increased receptor phosphorylation and protein expression (130%) after TGF β -1

[ErbB expression after treatment]

Conclusions: These data suggest a mechanistic role of ErbB receptors in regulating the age-related induction of EMT.

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COMPARISON OF NORMAL SALINE, HYPERTONIC SALINE AND HYPERTONIC COLLOID RESUSCITATION FLUIDS IN AN INFANT ANIMAL MODEL OF HEMORRHAGIC-HYPOVOLEMIC SHOCK

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Background: Few studies have analyzed the effect of resuscitation fluid composition in infant animal models of hemorrhagic-hypovolemic shock. Our hypothesis was that hypertonic and hyperoncotic fluid will achieve goal-directed hemodynamic endpoints with less volume infusion than normal saline.

Methods: Prospective, randomized study in 34 two month-old piglets (9.9 $\pm$ 2kg). Following anaesthesia, paralysis and mechanical ventilation, hypovolemia was induced by controlled 30 ml/kg bleed. After 30 min, pigs were randomized to receive: Normal Saline (S0.9%) 30 ml/kg, n=11, Hypertonic 3% Saline (S3%) 15 ml/kg n=12, or Albumin 5% plus Hypertonic 3% Saline (A5%-S3%) 15 ml/kg, n=11. Hemodynamic (heart rate (HR), mean arterial pressure (MAP), cardiac index (CI)), brain tissue oxygenation by near infrared spectroscopy (bStO₂) and tissue perfusion (arterial lactate and gastric pHi) parameters were compared by ANOVA.

Results: 30 min. after bleeding, high baseline HR: 192 $\pm$ 37, and low MAP 72 $\pm$ 19 mmHg, CI 2.8 $\pm$ 1L/min/m², bStO₂: 44 $\pm$ 8%, gastric pHi 7.1 $\pm$ 0.2 and lactate 3.4 $\pm$ 2.3 mmol/L were recorded with non significant differences between groups. 30 min after infusion there were non significant differences between groups for HR (S0.9%: 188 $\pm$ 14, S3%: 184 $\pm$ 14, A5%-S3%: 151 $\pm$ 14 bpm); MAP (S0.9%: 80 $\pm$ 7, S3%: 86 $\pm$ 7, A5%-S3%: 87 $\pm$ 7 mmHg); CI (S0.9%: 4.9 $\pm$ 0.5, S3%: 5.1 $\pm$ 0.4, A5%-S3%: 5.3 $\pm$ 0.4 ml/ min/m²); lactate (S0.9%: 2.8 $\pm$ 0.7, S3%: 2.3 $\pm$ 0.6, A5%-S3%: 2.5 $\pm$ 0.6mmol/l); bStO₂ (S0.9%: 43.9 $\pm$ 2.2, S3%: 40.1 $\pm$ 2.5, A5%-S3%: 45.7 $\pm$ 2.3 %); and pHi (S0.9%: 7.07 $\pm$ 0.6, S3%: 7.25 $\pm$ 0.5, A5%-S3%: 7.23 $\pm$ 0.5).

Conclusion: In this model of pediatric hypovolemic shock, both hypertonic (S3%) and hyperoncotic (A5%- S3%) fluids achieved similar hemodynamic endpoints, requiring half of the volume compared to normal saline.