**1243** ALTERATIONS IN LUNG MECHANICS AND THE WORK OF BREATHING OF PRETERM LAMBS ON POSITIVE END EXPIRATORY PRESSURE (PEEP). Thomas H. Shaffer, Peter A. Koen, James D. Ferguson, and Maria Delivoria-Papadopoulos. University of Pennsylvania School of Medicine, Departments of Pediatrics and Physiology, Philadelphia, PA 19174.

The effect of PEEP on lung mechanics and on the work of breathing was studied in 8 preterm lambs delivered by cesarean section at 134 days gestation. Indwelling arterial, venous, and tracheal cannulae were placed before clamping the cord. Assisted mechanical ventilation was performed at a tidal volume of 15/ml/Kg and a rate of 30-40/min at $F_IO_2$ of 0.95. Measurements of intraesophageal and tracheal pressures, air flow, tidal volume, and functional residual capacity enabled calculation of dynamic compliance ($C_L$), specific compliance ($C_S$), inspiratory resistance ($R_I$), expiratory resistance ($R_E$), and work of breathing at 0, 3, 6, and 10 cm $H_2O$ PEEP. Dynamic compliance and $C_S$ decreased by 0.11 ml/cm $H_2O$/Kg and 0.0051 l/cm $H_2O$ per cm $H_2O$ PEEP respectively for PEEP above 3 cm $H_2O$. Functional residual capacity increased ($p<0.005$) by 1.6 ml/Kg per cm $H_2O$ PEEP. Inspiratory resistance increased significantly ($p<0.05$) only between 0 and 6 cm $H_2O$ PEEP while $R_E$ increased ($p<0.05$) between 0 and all higher levels of PEEP (3, 6, and 10 cm $H_2O$). As compared to 0 cm $H_2O$ PEEP (11.9 ± 2.5 SE x $10^6$ ergs/min), the work of inspiration per unit time decreased 17% at 3 cm $H_2O$ and increased 10% and 80% at 6 and 10 cm $H_2O$ PEEP respectively. These data suggest that it is mechanically easier to breathe at low levels of PEEP (3 cm $H_2O$) than without PEEP or at high levels of PEEP (10 cm $H_2O$). (Supported by USPHS Grants HL19402 & HL15061)

**1244** PHOSPHOLIPID BIOSYNTHESIS AND SECRETION IN CULTURES OF TYPE II ALVEOLAR EPITHELIAL TUMOR CELLS: THE EFFECT OF THEOPHYLLINE. Donald L. Shapiro, Seamus A. Rooney, Linda L. Nardone, E.K. Motoyama, J. Munoz (Spon. by J.B. Warshaw) Yale University School of Medicine, Department of Pediatrics, New Haven, Connecticut.

A continuous cell culture line derived from a human lung tumor which has morphological characteristics of type II alveolar epithelial cells was studied for the ability to synthesize and secrete phospholipid. The cells contained 0.213 mg lipid/mg protein of which 41% was phosphatidylcholine (16% of the phosphatidylcholine was disaturated). The specific activities of choline kinase and choline phosphotransferase were 381 and 1030 pmoles/min/mg protein, respectively. The cells incorporated choline into phosphatidylcholine (28% of the phosphatidylcholine was disaturated) and secreted phosphatidylcholine into the culture medium (28% of the phosphatidylcholine was disaturated). To study the influence of the adenylate cyclase-cyclic AMP system on these processes, cells were cultured in the presence of $10^{-3}$M theophylline. Lipid content and composition were not significantly changed. Choline kinase and choline phosphotransferase specific activities were 172% and 88% of control values, respectively. Choline incorporation into phosphatidylcholine was 209% of the control value (28% of the phosphatidylcholine was disaturated). Acute stimulation of phospholipid secretion was not produced by theophylline addition. Homogeneous cell cultures can be used to study the effects of hormones on phospholipid biosynthesis and secretion.

**1245** PULMONARY WASHINGS AND BLOOD IN PULMONARY ALVEOLAR PROTEINOSIS (PAP). Lance Sieger, Joan A. Stratton and Karlman Wasserman (Spon. by Bascom F. Anthony) UCLA Sch. Med., Harbor Gen. Hosp., Depts. Peds. & Med., Torrance, Ca.

Pulmonary alveolar proteinosis is a diffuse pulmonary disease of obscure etiology characterized by abnormal accumulations of phospholipids in the lung. Despite severe pulmonary disabilities there is a striking absence of inflammatory cells and fibrosis in the lungs of these patients. We have examined the lung washings and blood from five patients with this disease in an attempt to discover whether there are any inhibitors of the normal inflammatory responses locally or systemically. The complete peripheral blood counts and numbers of T and B lymphocytes and monocytes were entirely normal in all patients. The cellular components of the lung washings were primarily mononuclear cells which exhibited histochemical and surface characteristics typical of alveolar macrophages (AM). Morphologically, these AM were many times larger than AM from control patients and were filled with amorphous material. The lung washings of the patients inhibited Con A and pokeweed mitogen stimulation of allogenic peripheral blood lymphocytes by >90%, but had no significant effects on PHA stimulation. Their sera inhibited stimulation by all three mitogens >95%. This inhibition was not due to cytotoxicity. When the lung washings were injected into normal rabbit peritoneal cavities, there was no inhibition of accumulation of either PMNs or peritoneal macrophages as stimulated by mineral oil. In addition, the lung washings stimulated RNA synthesis in vitro by rabbit AM.

**1246** PLASMA RENIN ACTIVITY IN THE RESPIRATORY DISTRESS SYNDROME. Richard L. Siegler, Margaret B. Walker, William Jubiz (spon. by Lowell A. Glasgow). Univ. of Utah Col. of Med., Univ. and VA Hosp., Dept. of Ped. and Med., Salt Lake City.

There is general agreement that long-term hypoxemia stimulates the renin-angiotensin system, but the effects of short-term hypoxemia are less certain. For these reasons, we measured plasma renin activity (PRA) by radioimmunoassay in 14 hypoxemic infants, age 2-3 days, with severe respiratory distress syndrome (RDS). The same studies were repeated 5-7 days later, after the infants' condition had improved markedly. Comparisons were also made with a group of age and weight matched normal premature infants (n=6), and with a group of age matched normal term infants (n=10). The following results (mean±SE) were obtained.

| PRA (ng/ml/hr) | | | |
|---|---|---|---|
| RDS Infants 2-3 days age | RDS Infants 7-10 days age | Normal Prematures | Normal Term Infants |
| 12.9±2.6 | 11.4±2.7 | 10.8±2.3 | 11.8±2.0 |

The PRA in the 2-3 day old infants with severe RDS did not correlate significantly with their $PO_2$; and did not differ significantly from the PRA levels obtained following their clinical improvement 5-7 days later. Moreover, the PRA in the RDS infants did not differ significantly from the levels in the normal premature and term infants. Thus, short-term hypoxemia secondary to RDS does not appear to stimulate PRA.

**1247** THE ROLE OF PULMONARY STEROID 11-REDUCTASE ACTIVITY IN LUNG MATURATION IN THE FETAL RAT Barry T. Smith (Spon.by H.W.Taeusch) Queen's Univ., Dept. of Paediatrics, Kingston, Ontario, Canada.

Fetal glucocorticoids play a role in the biogenesis of adequate pulmonary surfactant. The fetal lung possesses the necessary enzyme (11-reductase) to convert inactive but abundant 11-keto steroids to their active 11β-hydroxy configuration.

Fetal rats were injected on day 17 with 11-ketoprogesterone which blocks 11-reductase activity. On day 21 injected fetuses had larger lungs than vehicle-injected controls (147.6±9.8 mg vs 132.8±9.5, $p<.001$) with reduced 11-reductase (9.9±3.3% vs 51.7±6.1, $p<.001$). Lungs of injected fetuses did not retain air upon inflation as did controls and their content of saturated phosphatidylcholine was reduced whether considered as content/unit lung weight (1.42±.09 mgP/g wet weight vs 1.77±.11, $p<.001$) or as content per fetus (.20±.02 mgP/lung vs .24±.02, $p<.001$). Vehicle injected controls showed increased saturated phosphatidylcholine compared to unoperated controls (1.77±.11 mgP/g wet weight vs 1.66±.11, $p<.01$), suggesting stress induced acceleration of lung maturation.

These results suggest that pulmonary steroid 11-reductase activity facilitates fetal lung development perhaps by maintaining high pulmonary concentrations of active glucocorticoid. (Supported by the M.R.C.).

**1248** VENTILATION AND PERFUSION ASSESSMENT BY ELECTRICAL IMPEDANCE PLETHYSMOGRAPHY. James A. Spence, Tzong R. Weng, George Polgar and Jan Nyboer. Wayne State Univ. Sch. of Med. Childrens Hosp. Mich. Dept.Peds. & Physiol, Detroit

Tetrapolar electrical impedance plethysmography has been employed in an attempt to describe regional and total ventilation and perfusion profiles at tidal volume range in patients with different pulmonary pathology. Atraumatic and requiring minimal cooperation, the determinations were performed on patients ranging in ages from 8 mo to 18 yrs. Resistive impedance changes of a 0.8 ma,50 kHz constant current were detected from 1.5 $cm^2$ electrodes linearly mounted in adhesive belts. These belts were applied horizontally above the diaphragm in 6 areas corresponding to upper, mid, and lower regions of the lungs. Interelectrode distances were varied to suit both patient size and the depth of tissue to be studied. Even current distribution found from isoresistance studies allowed the assumption of favorable resolution within the sample region. Deflections representing ventilatory and perfusion events were recorded simultaneously with their derived velocities. From these blood flow pulses could be obtained using a forward extrapolation method. The data was then converted into ventilation and perfusion indices. The regional distribution of the ratios of ventilation and perfusion values was different from that of other methods because these values were not corrected for unit volume. In 6 cases of atelectases, hypoperfusion, consolidation, and lung abscess confirmed by conventional methods, low ventilation and perfusion impedance indices corresponded with diseased areas, whereas they were higher in more normal lung fields.