

1768

ANIONIC CHARGE SITES IN NEONATAL ALVEOLAR-CAPILLARY BASEMENT MEMBRANES. Bruce Ferrara, Susan Sisson, and Robert L. Vernier. University of Minnesota Medical School, Department of Pediatrics. Minneapolis, MN. We have developed a method for demonstration and quantitation of the anionic charge sites in human alveolar-capillary basement membrane (ABM). Fixed-frozen sections of normal lung were incubated with the cationic polymer polyethylenimine (PEI) and processed for electron microscopy using methods recently described for kidney (NEJM 309:1001, 1983). Results:

| Age Post- Conception | Condition | Molecular wt PEI | Anionic Charge Sites per 1000 nm of ABM (LRE) |
|-------------------------|--------------|---------------------|--------------------------------------------------|
| 44 wks | resolved RDS | 600 | 24.5 |
| | | 1200 | 24.7 |
| 38 wks | normal | 1200 | 24.4 |
| 22 wks | normal | 600 | 24.5 |
| | | 1200 | 23.2 |
| 24 wks | normal | 1200 | 25.6 |
| | | 40-60,000 | 24.0 |
| | | | mean 24.41 ± .72 |

The number of anionic sites in the lamina rara externa (LRE) of the ABM is remarkably consistent in multiple random samples of normal lung of differing ages and is not influenced by the molecular weight of the probe. Smaller numbers of sites are also present in the lamina rara interna and on cell membranes. Alteration of anionic charges in the ABM may influence permeability of negatively-charged protein across the membrane. This hypothesis can now be assessed in man by this method.

1769

MEMBRANE POTENTIAL RESPONSES OF TYPE II CELLS DURING SURFACTANT SECRETION. Jacob N. Finkelstein, Richard L. Gallo, Robert H. Notter and Donald L. Shapiro. University of Rochester School of Medicine, Department of Pediatrics (Neonatology), Rochester, NY

We studied membrane potentials of the plasma (Ep) and mitochondrial (Em) membranes of isolated type II alveolar epithelial cells under basal conditions and during surfactant secretion. Ep and Em of freshly isolated rabbit type II cells was measured by determining the distribution ratios of the labeled ionic probes triphenylmethylphosphonium (TPMP⁺) and Rb⁺, under conditions which eliminate potential-independent accumulation of probes. Under basal conditions Ep was found to be -63±4mV, similar to values obtained in other secretory epithelial cells. Stimulation of secretion by β-adrenergic agonists caused a 20% hyperpolarization of the cells measurable from 5 to 60 minutes after stimulation. The dose response relationship for the potential change was identical to that observed for secretion with a maximum at 10⁻⁵ terbutaline. Both secretion and potential changes were completely inhibited by use of the β-blocker propranolol. Through the use of potential selective poisons the change in potential could be attributed to a change in Ep occurring via the activation of an electrogenic membrane bound Na-K-ATPase. These results suggest that ionic movements across the plasma membrane play a role in the secretion of surfactant from type II cells.

1770

NECROTIZING TRACHEO-BRONCHITIS: A NEW COMPLICATION OF NEONATAL MECHANICAL VENTILATION. Jonathan Tolkin, Hareesh Kirpalani, Pam Fitzhardinge, Paul Swyer, Ernest Cutz, Tom Higa. Univ. of Toronto, Depts. of Pediatrics, Pathology, Mount Sinai Hosp., Hosp. for Sick Children, Toronto.

In 1982-83 7 neonates in 2 hospitals have developed sloughing of tracheal mucosa while on assisted ventilation. Gestation ranged from 26-40 wks; weight from 0.9-3 kg. Primary diagnosis was RDS in 4, persistent fetal circulation in 2 and aspiration in 1. 5 died at 1-4 days of age. At autopsy a thick basophilic membrane of necrotic epithelium and submucosa involved the distal part of the trachea and bronchi totally obstructing the airway in 2 patients. Repeated bronchoscopy in the survivors removed the obstructive plugs. Clinically all cases showed upper airway obstruction with poor chest movement, air trapping and severe CO₂ retention. Pressure limited conventional ventilators were used initially followed by a trial of high frequency oscillation in 3. Peak pressures >35 cmH₂O were used in 6. Hand bagging using dry 100% O₂ was given for periods of 10-90 min. to all.

An iatrogenic cause is suspected but not proven. No abnormalities or contaminants were found in the equipment, humidification, tubing or gas system in either hospital. Similar lesions were produced in adult rabbits by using either dry gas, overheated gas (>42°C) or high flow rates suggesting the possibility of multiple etiology. Units are advised to be on the alert for a possible iatrogenic lesion which may be alleviated by bronchoscopy. Further studies on etiology and treatment are required.

1771

DEXAMETHASONE STIMULATES FETAL RAT LUNG ANTIOXIDANT ENZYME ACTIVITY IN PARALLEL WITH SURFACTANT STIMULATION. Lee Frank, Pamela Lewis and Ilene Sosenko. Univ. of Miami Sch. of Med., Pulm. Res., Dept. of Med., Miami.

In fetal rabbits, a late gestational rise in lung antioxidant enzyme activity [superoxide dismutase(SOD), catalase(CAT), glutathione peroxidase(GP)] occurs which parallels surfactant development, and which may represent another important "preparation for birth" phenomenon (Peds. Res. 17:132A,1983). We have now injected time-pregnancy rats with Dexamethasone(DEX)(0.2mg/kg) or saline at 48 and 24 hrs prior to delivery of fetuses at days 19, 20,21 and 22 (term). We measured lung phospholipid(PL), disaturated phosphatidyl-choline(DSPC), and antioxidant enzymes to determine whether DEX, in addition to stimulating surfactant production, would also affect O₂-protective enzyme development. Results are expressed as mean values SALINE/DEX (2-3 expts./age group; n=3-4 samples/expt; *p<0.05, DEX vs. SALINE):

| GESTATION | DSPC(mg/gm lung) | SOD | CAT | GP(U/mgDNA) |
|-----------|------------------|------------|----------|-------------|
| Day 19 | 34.5/37.7 | 22.4/24.4 | 423/454 | 1.38/1.49 |
| Day 20 | 46.4/65.4* | 32.7/38.9* | 432/626* | 1.30/1.89* |
| Day 21 | 79.1/113* | 39.8/49.7* | 456/628* | 2.07/2.79* |
| Newborn | 112/114 | 70.4/76.5 | 650/643 | 2.40/2.10 |

Thus, prenatal DEX treatment results in an acceleration of the normal developmental increase in lung antioxidant enzyme activity which occurs late in gestation in the rat (as in the rabbit). The DEX-treated prematurely-born may thus be in a more favorable biochemical state to avoid toxic lung changes associated with (the relatively O₂-rich ex utero environment and) any supplemental hyperoxic treatment it may require.

1772

ALVEOLAR PRESSURE AND TIDAL VOLUME DURING HIGH FREQUENCY VENTILATION. Ivan D. Frantz III and Richard H. Close. Harvard Medical School, The Children's Hospital, Department of Pediatrics, Boston.

Alveolar pressures and tidal volumes have not been quantified during high frequency ventilation. We have measured dynamic and mean pressures at the airway opening, trachea, and alveoli as well as delivered volumes and blood gases in vivo in closed-chest adult rabbits ventilated at rates of 2-37.5 Hz with the Emerson flow-interrupting high frequency ventilator. Alveolar pressure was measured by opening the chest, gluing an adapter to the visceral pleural surface, puncturing the pleura and lung surface through the adapter, closing the chest, and attaching a pressure transducer. Delivered volume was measured with a pressure plethysmograph. As frequency increased, alveolar pressure swings decreased from 26 to 8% of pressure swings at the airway opening, and 100 to 42% of those in the trachea. Delivered volume decreased from 5.3±0.5 to 0.6±0.1 ml/kg as frequency increased. Respiratory system impedance fell initially with increasing frequency, then tended to remain relatively stable with no resonance seen. Lung tissue plus chest wall impedance behaved as an elastance and fell as frequency increased. Muscle paralysis had no effect on alveolar pressure swings, but excision of the rib cage resulted in a decrease. Mean pressures were equal at the airway opening, trachea and alveoli at all frequencies. The clinical implication of these results is that if gas exchange can be maintained with constant tracheal pressure swings, alveolar barotrauma may be minimized by choosing the highest possible frequency for ventilation. (Supported in part by HL 27372.)

1773

LUNG VOLUME, TIDAL VOLUME, AND ALVEOLAR PRESSURE DURING JET VENTILATION. Ivan D. Frantz III and Richard H. Close. Harvard Medical School, The Children's Hospital, Department of Pediatrics, Boston.

We have measured lung volume (FRC), tidal volume delivered (V_T), and alveolar pressures (P_A) during jet ventilation of rabbits. The rabbits were ventilated with room air using the Healthdyne jet ventilator at a driving pressure of 4 psi and frequencies from 2 to 15 Hz. The 0.98 mm ID jet cannula was inserted 2 cm into a 3.5 mm endotracheal tube. Pressure was measured in the trachea (P_T) just distal to the endotracheal tube tip, and in the alveoli. Alveolar pressure was measured by gluing an adapter to the pleural surface which had been exposed through a thoracotomy. After closing the thoracotomy, pleural punctures were made through the adapter and a pressure transducer was inserted. Volume was measured with a pressure plethysmograph. The animals were ventilated at 2, 5, 10 and 15 Hz, with inspiratory times (T_I) of 10, 30 and 50%. There was a marked increase in FRC during jet ventilation, to 80% or more of total lung capacity at 50% T_I. The increase in FRC was related to mean expiratory flow rate. Mean P_A and P_T were equal and exceeded mean pressure at the airway opening. Tidal volume diminished with increasing frequency, and was greatest at 30% T_I at any frequency. V_T exceeded estimated dead space below 10 Hz. P_A swings were equal to P_T swings, fell with increasing frequency and were least at 10% T_I. We conclude that dangerously large increases in FRC may occur during jet ventilation, and that measurement of pressure at the airway opening is an inadequate means of monitoring airway pressures during jet ventilation. (Supported in part by HL 27372.)