†1735 A SERUM-FREE SYSTEM FOR THE STUDY OF MITOGEN EFFECTS ON TYPE II PNEUMOCYTES IN PRIMARY CULTURE.

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Isolated type II pneumocytes are reported not to divide in primary culture, and the cell number usually falls with time in culture. A serum-free culture system has been developed which allows the response of a stable type II pneumocyte population to exogenous mitogens to be studied over several days in culture.

Type II pneumocytes were isolated from adult rat lung. After a 36 hr plating period cell number, purity (>90%) and viability (>95%) remained stable over 7 days in a serum-free medium supplemented with fibronectin, insulin, transferrin and selenous acid (F.I.S.T.). Plating efficiency was 15-25%. Under serum-free conditions pneumocytes increase in number ($p<.01$) in response to EGF 50ng/ml, though there is a subsequent loss of adherent cells. The response to EGF is lost in the presence of 10% fetal bovine serum. The addition of 10% adult rat plasma, however, allows a sustained increase in cell number over 9 days in culture ($p<.05$).

After a brief period of conditioning with rat serum, type II pneumocytes maintained in serum-free medium respond to F.I.S.T. by a 60% increase in cell number over 8 days in culture. These studies have shown that type II pneumocytes can be maintained under serum-free conditions for several days in primary culture, and respond to known mitogens by an increase in cell number.

1736 BRONCHODILATOR EFFECTS ON NEONATAL CARDIOVASCULAR FUNCTION AND GAS EXCHANGE.

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The use of bronchodilators in newborn infants is common clinical practice; however, their effects on gas exchange and on the cardiovascular system have not been evaluated. The purpose of this study was to investigate the effects of Isoetharine (I) nebulization, given during the first 3 days of life, on transcutaneous PO2 (PtcO2) and PCO2 (PtcCO2), heart rate (HR) and blood pressure (BP) of 12 preterm infants with severe HMD treated with ventilator; BW 1570±537gm, GA 30±3wks. 2ml of I 0.08% were nebulized while connected to the ventilator at the same baseline mean airway pressure each day. Data obtained before (baseline) and 15 min after I were compared. There were no cardiac arrhythmias found during the study. HR, BP, and PtcO2 were not significantly different 15 min after I nebulization, however, PtcCO2 reduced from mean values of 45 to 43 mmHg in day 1 ($p<.05$) from 48 to 44 mmHg in day 2 ($p<.05$) and from 47 to 42 mmHg in day 3 ($p<.05$). The absence of cardiovascular effects after I are explained by its selective action on B2 receptors. The decrease in PtcCO2 suggests that I nebulization, given at constant mean airway pressure, improves ventilation either by relieving bronchoconstriction with an increase in minute ventilation or improvement in ventilation-perfusion matching. We conclude that I is an effective drug to improve ventilation without significant cardiovascular side effects in infants with severe HMD.

1737 FUNCTIONAL RESIDUAL CAPACITY (FRC) CHANGES IN PRETERM BABOONS WITH HYALINE MEMBRANE DISEASE (HMD).

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FRC, related to alveolar stability at end expiration, would be expected to improve with recovery from HMD. Intubated, paralyzed preterm (140±2 days) baboons with HMD were evaluated with serial FRC measurements by the He dilution method on Day 0, 3,7 and 9. Values on Day 0 were obtained within 4 hrs. of birth when all animals were ventilated by conventional ventilation (CV). Animals were then randomized to CV or high frequency ventilation (HFV). Mean values (±SD) obtained were:

Day	0	3	7	9
n	6	6	6	6
FRC(CV) ml	3.5±0.33	12.3±5.27	12.0±2.49	10.6±2.66
FRC(HFV) ml	4.1±2.87	11.6±3.77	11.7±1.52	11.3±1.61

On Day 0, FRC was not significantly different (ANOVA for repeated measures) between ventilator groups indicating groups of equivalent initial disease severity. Analysis of differences due to ventilator type and interaction between ventilator type and time proved nonsignificant. FRCs on Day 3, 7 and 9 were significantly improved ($P< 0.01$) over Day 0 values. Changes in FRC appear to reflect recovery in surviving preterm baboons with HMD treated with CV or HFV.

1738 OBSTRUCTIVE SLEEP APNEA IN A 7-YEAR-OLD BOY WHO HAD A NEAR-SUDDEN INFANT DEATH (N-SIDS) EPISODE AT 6 WEEKS.

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A 6-wk-old boy, the patient of Dr. Francis X. Lieb, was admitted to the hospital because of apnea. He was 38 wk gest., b wt 3490 g, with perinatal acidosis, hypoglycemia, prolongation of the Q-T interval on EKG. At 5 wk he cried out in his sleep, was irritable, had episodes of high-pitched cry, with his back arched and arms extended. At 6 wk at 6 AM he was found ashen, cold, unresponsive and limp, with periodic apnea. The BP was 76 mm Hg, the T 36.4°C (R). He required a ventilator. The blood pH was 6.88 when the initial plasma magnesium (Mg) was 2.4 mEq/L (Hosp. normal, 1.6-2.2). As the pH normalized, the Mg decreased to 1.7, then 1.3 mEq/L. The blood glucose was 157 mg/dl; the spinal fluid showed 8 RBC, 0 WBC/hpf; the urine gave a pH of 5, ++ protein, tr. glucose, and abnormal sediment. Bacterial and viral cultures were neg. On days 4-5 he retained 99% of an IM Mg load of 0.49 mEq Mg/kg body wt and was treated with 0.4 mEq Mg/kg for 5 days. He began oral fluids on day 10 and progressed well until he developed Staph. aureus pneumonia at 1 mo, and required a tracheostomy. A plasma Mg was 2.0 mEq/L, and he retained 21% of an IM Mg load. After discharge he was readmitted for chronic lower respiratory problems and post-tracheostomy subglottic stenosis. He attended school. At 7 yr a nocturnal polysomnogram showed obstructive and mixed apnea. This report suggests: 1) A possible link between N-SIDS and the adult sleep apnea syndrome, a hypothesis of Guilleminault and Dement (Adv. Sleep Res. 1: 345, 1974) and 2) A possible role for Mg deficiency in the pathogenesis of N-SIDS.

1739 THE EFFECT OF PULMONARY HYPERTENSION (PHN) ON LUNG COMPLIANCE (C_L) IN NEWBORN LAMBS.

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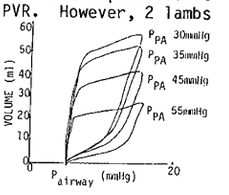
Some newborns with PHN appear to have noncompliant lungs until they receive a pulmonary vasodilating drug. We speculate that a stiff, hypertensive pulmonary vasculature may hold the lung in an erect state, thereby decreasing C_L. To test this hypothesis, 11 anesthetized and paralyzed newborn (0-3 days) lambs were ventilated at fixed rates and pressures. We instrumented them to measure C_L, pulmonary blood flow, and pressures in the pulmonary artery (Ppa), aorta, and left atrium. Pulmonary vascular resistance (PVR) was calculated.

In 9 lambs, we induced PHN (10-150% increase in Ppa) with either hypoxia (PaO_2 32.5±9.2 torr), infusion of HCl (arterial pH 7.26±0.03), or addition of CO_2 to the inspired gas ($PaCO_2$ 64.8±14.1 torr, pH 7.21±0.13). Decreases in C_L ranged from 7-24%, occured with 47% of the maneuvers, but were unpredictable and correlated poorly with rising Ppa and PVR. However, 2 lambs with unexplained, spontaneous PHN (50-80% increases in Ppa) had 28-36% decreases in C_L. Pressure-volume loops from one of these animals are shown at the right.



We conclude that PHN may alter C_L in newborn lambs, but the mechanism remains unclear. An improved model is needed to elucidate this mechanism.

●1740 LARYNGEAL MUSCLE ACTIVITY REGULATES EXPIRATORY FLOW AND LUNG VOLUME.

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In neonatal and adult animals, abduction of the vocal cords by laryngeal muscles regulates airflow by decreasing inspiratory and expiratory airway resistance. To determine if laryngeal muscles modify airflow in neonates, we recorded electromyograms (EMG) in the posterior laryngeal area(LAR) with electrodes attached to the tip of an esophageal catheter inserted 7-9cm beyond the nares. Simultaneous diaphragm(DIA) EMG was recorded from surface electrodes and airflow via mask pneumotachograph. Studies were performed in 12 healthy preterm infants(birthweight 1.6 ±.4kg, gestational age 32±2 weeks, postnatal age 21±8 days) without respiratory distress. Bursts of LAR EMG preceded onset of both DIA EMG and inspiratory airflow by 66±58msec($p<0.05$) and 175±75msec($p<0.001$), respectively. Retarded expiratory flow during early expiration(expiratory breaking) was observed in 9 infants. Onset of LAR EMG during late expiration in these subjects coincided with development of high end expiratory airflow and exhalation of 3-13cc of air. Thus, laryngeal breaking maintained an increased lung volume throughout most of expiration. In contrast, high flow throughout expiration(absence of breaking) coincided with increased expiratory LAR EMG. We conclude that laryngeal muscle activity regulates respiratory airflow. Control of laryngeal muscle activity maintains an elevated lung volume until end expiration in healthy preterm infants and may assume even greater importance in neonates with decreased functional residual capacity.

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