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PROLACTIN AND HUMAN LUNG MATURATION

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We have recently shown that administration of prolactin (1 mg per fetus) to rabbit fetuses leads to an increase in the concentration of lung dipalmitoyllecithin (Hamosh, J. Clin. Invest. 59: 1002, 1977). In the present study we have tested the relationship between serum prolactin and cortisol levels and lung maturity in premature infants. Prolactin and cortisol levels were measured by radioimmunoassay in 40 premature infants between 26 and 37 weeks of gestation. Mixed cord blood was collected at delivery, centrifuged and the sera kept at -20°C until analysis. Prolactin levels ranged from 20 to 600 ng/ml; cortisol levels measured 25 to 350 ng/ml. Cord prolactin levels less than 140 ng/ml were associated with a high incidence of respiratory distress syndrome (RDS); of 18 infants with prolactin levels less than 140 ng/ml 16 (89%) had RDS. Only 27% of the infants with RDS had prolactin levels above 140 ng/ml. Two of the highest levels in this group were from infants with diabetic mothers. There was no correlation between cord serum prolactin and cortisol levels or between cortisol levels and the incidence of RDS. The data suggest that prolactin might be a trigger of lung maturation in the human fetus. (Supported by grant HD 11353 from the NIH)

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EFFECT OF ACUTE HYPOXIA ON CONVERTING ENZYME ACTIVITY IN CULTURED ENDOTHELIAL CELLS. S. Alex Stalcup, Joel S. Lipset, Jen Mei Woan, Philippe Leuenberger, Gerard

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Hypoxia inhibits converting enzyme (CE) activity in vivo in dogs (Fed. Proc. 36:630, 1977). To study the cellular basis of this phenomenon, we harvested endothelial cells by perfusing human umbilical cords, rabbit and pig lungs and calf aortas with a mixture of 0.1% collagenase, 0.1% trypsin and 1.0% chicken serum in Hank's Solution, and propagated the cells in medium 199. CE activity in monolayer cells was assessed by adding both bradykinin and angiotensin I to culture flasks and measuring residual peptide over time by radioimmunoassay. CE activity was fully inhibited by SQ20881. Flasks were equilibrated with varying hypoxic gas mixtures. Hypoxia rapidly inhibited CE activity (< 2 minutes) and room air rapidly restored it (< 2 minutes). All CE activity was inhibited at P_O₂ of 30 mm Hg. In all species, the extent to which CE was inhibited was a direct function of P_O₂ (r = 0.99, p < .001). The velocity of the reaction, calculated from 0 to 4 minutes of incubation, was 5.4 nmoles/hr/10⁶ cells when P_O₂ = 100, 1.6 at P_O₂ = 50, and < 0.11 at P_O₂ = 30. Commercial purified pig converting enzyme was unaffected by hypoxia (V_{MAX} = 2.2 nmoles/mg protein/hr at all P_O₂ levels from 100 to 0 mm Hg). We conclude that the inhibition of CE by hypoxia 1) takes place at the cellular level and 2) is not a characteristic of the enzyme per se but is a unique property of the endothelial cell membrane.

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DELAYED LUNG MATURATION IN FETUSES OF ALLOXAN DIABETIC RABBITS. Ilene R.S. Sosenko, Edward E. Lawson, Van Demottaz, and Ivan D. Frantz III,

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Maternal diabetes has been associated with an increased incidence of hyaline membrane disease. We have studied this relationship in rabbit does injected with alloxan and then mated. A total of 26 litters were studied. Fetuses from saline-injected control and diabetic litters were examined at 27.5 and 29.5 days gestational age. Pressure-volume curves were performed and surfactant from alveolar lavage fluid was quantified on a surface balance. Blood sugars of diabetic does ranged from 175-400 mg/dl throughout pregnancy as compared with 80-120 mg/dl in the controls.

Fetuses	% Total vol. on Deflation		Surfactant (µg/gm dry lung)
	15 cm H ₂ O	5 cm H ₂ O	
27.5 d. controls	70±5(SE)	26±1	168±57
27.5 d. diabetics	57±6	15±2	undetectable
p value	<0.02	<0.01	<0.01
29.5 d. controls	81±2	60±2	1724±299
29.5 d. diabetics	81±1	59±2	1264±120

We conclude that fetuses of diabetic rabbits have less deflation stability and quantitatively less surfactant when born prematurely but these effects are diminished close to term.

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RESPONSES TO MUSCLE PARALYSIS IN MECHANICALLY VENTILATED INFANTS. Ann R. Stark, Rebecca Bascom, Ivan D. Frantz, III. (Spon. by H. W. Taeusch, Jr.) Harvard

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To evaluate the subjective impression of improved gas exchange with muscle paralysis in some infants on mechanical ventilation, we observed 35 infants who received pancuronium while on Baby Bird ventilators. Pancuronium (0.1 mg/kg I.V.) was repeated until spontaneous respirations ceased in infants who had inadequate gas exchange with F_O₂ > 0.60, peak inspiratory pressure > 30 cm H₂O or who were "fighting" the ventilator. 27 infants received pancuronium within the first 48 hours of life, 15 within the first 24 hours. Infants remained paralyzed for a median of 36 hours. 27 infants had A-aP_O₂ > 300 torr before paralysis. A-aP_O₂ improved by > 100 torr within one hour of paralysis in only 2 of the 27 infants; it worsened in 2 infants within the same period. By 6 hours post-paralysis, 12 infants had improved, 5 of whom had had a worsening A-aP_O₂ before administration of pancuronium. PCO₂ decreased in 5 infants by > 10 torr within 1 hour of paralysis and increased in 8 infants with either unchanged ventilator settings or changes expected to improve ventilation. No significant changes were observed in blood pressure or heart rate. Only 4 of the 35 infants developed a pneumothorax while paralyzed. Since birthweight, gestational age, or diagnosis could not distinguish those who would respond, one can determine efficacy in a particular patient only by trial. Improvement, when it occurs, is most likely related to changes in right-to-left shunting or V/Q abnormality.

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CELLULAR AND BIOCHEMICAL COMPARISONS OF CHILDHOOD AND ADULT FORMS OF ALVEOLAR PROTEINOSIS. A. Spock, C.F. Lanning, J.A. Kylstra, Dept. of Ped. Anes. and Med., Duke University Medical Center, Durham, North Carolina.

Alveolar proteinosis is a rare disorder characterized by accumulation of large amounts of proteinaceous material in the lungs. Detailed examination of lavage fluid from these pts may provide a clue concerning the etiology of this disease. Two pts age 1 & 10 yrs had 5 bilateral lung lavages using the technique of Spock (Clin. Res. 24:77A, 1976) and the lung effluents were compared with effluents from 6 adult pts. Cellular material of the 10 yr old pt and the adult pts had decreased number of cells. The 1 yr old pt had 1x10⁶ cells/ml which was 7x as many cells as the adult pts. In all pts 50-70% of the cells were macrophages and with electron microscopic studies, the macrophages were enlarged and contained increased lysosomes. The remaining cells were monocytes and lymphocytes. 65% of lymphocytes were T-cells. Cell viability with Trypan blue was 65% with evidence of abundant cell debris. Biochemical: all pts had elevated levels of lactic dehydrogenase (LDH)-290 and alkaline phosphatase (ALP)-280 which paralleled the serum levels. In adult and pediatric pts, the relative composition of the insoluble airway secretions were similar--lipids 60%; carbohydrates 3%, and protein 35%. Soluble phase proteins: 20 proteins were analyzed and the effluents of the pediatric pts for the IgG, IgA and IgD values were elevated when compared with serum; however the IgM and Alpha 2 macroglobulin levels were decreased. Albumin represented 46% of the total protein. No significant differences were noted between the effluent soluble proteins in the pediatric and adult pts. Several proteins were not present in the effluents of normal volunteers and pts with asthma. All cultures were negative. The cellular and biochemical changes are suggestive of cellular destruction, however, the associated alteration of immunoglobulins may indicate a localized immunological process without cellular proliferation. The pediatric pts had normal humoral cellular immunity and no evidence of immediate hypersensitivity. Supp. in part by NIH Grant RR-30, GCRC Program, Div. of Res. Resour. HEW.

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NASOTRACHEAL INTUBATION: ABSENCE OF LONGTERM MORBIDITY. A.R. Stewart, R.R. Moriarty & N.N. Finer

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Clinical sequelae have been reported in up to 10% of intubated neonates. A prospective and retrospective analysis revealed 94 patients intubated for greater than 24 hours and alive at discharge, 92 of whom were ventilated. The mean birth weight was 2294 gm (1010 gm-4600 gm), mean gestational age was 35 wk (28 wk-44 wk) and mean duration of intubation was 178.5 h (29 h-830 h). The mean total oxygen exposure was 250 h (12.5 h-1310 h) and mean requirement of oxygen greater than 60% was 24.3 h (0 h-229h). Of these patients, 30 required greater than one intubation, 13 to replace the orotracheal tube used for resuscitation, 13 to replace the atelectasis occurred in 16 patients, 3 of whom required reintubation. There were 24 pneumothoraces of which 9 were present before intubation or as a result of surgery. All nasotracheal intubations were performed or supervised by experienced Pediatricians using the largest size possible non-tapered, non-cuffed, polyvinylchloride tube of size 3.0 mm or larger. Endotube position was determined clinically and confirmed roentgenographically. The only indication for tube replacement was accidental dislodgement (13) as no tube obstruction was documented in this series. Extubation was always performed in the morning, following Decadron 1 mg/kg. Follow-up has shown no evidence of tracheal stenosis or clinical stridor. Nasotracheal intubation by experienced physicians with appropriate tube care, without elective tube replacement will result in very low tracheal morbidity.