1164

TRANSPLENTAL EFFECTS OF A THYROID ANALOG ON PHOSPHOLIPID SYNTHESIS IN FETAL RABBIT LUNG. Philip L. Ballard, Arlette Brehier, Bradley J. Benson, Barbara

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To investigate the possible role of thyroid hormones in fetal lung maturation, we treated pregnant rabbits with 3,5-dimethyl-3'-isopropylthyronine (DIMIT), a thyroxine analog which binds to nuclear receptors in fetal lung. On days 24 and 25 of gestation, does received diluent or 0.05-1 mg/kg DIMIT im; fetuses were studied on day 26. We found no effect of DIMIT on viability, body weight, lung weight, lung wet/dry ratio, or fetal plasma cortisol levels. NADPH-cytochrome C reductase, a known T₄ inducible enzyme, was increased 64% (p<0.01) in fetal liver with 1 mg/kg DIMIT. Mean±SE values for the rate of ³H-choline incorporation into lecithin (pmol/mg tissue/h) by minced fetal lung and activity of phosphatidic acid phosphatase (PAPase, nmol/mg prot/min) in lung homogenate are shown below (*p<0.001):

	Control	0.05 mg/kg	0.5 mg/kg	1 mg/kg
Choline Incorp.	32.9±1.2	29.7±1.3	41.1±1.4*	52.0±1.8*
PAPase	6.1±0.3	--	5.7±0.2	13.6±0.6*

Similar results were found for incorporation of ³H-glycerol.

We conclude that DIMIT crosses the rabbit placenta and stimulates lecithin synthesis and PAPase activity in fetal lung. Since similar effects occur with glucocorticoid treatment, these two hormones may act in part by controlling the same enzyme.

1167

A NEUROMUSCULAR MECHANISM PREVENTING AIRWAY OBSTRUCTION. Robert T. Brouillette and Bradley T. Thach

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To function as a conduit for air, the extrathoracic airway (ETA) must resist closure when intraluminal pressure decreases during inspiration. Previous work (Fed. Proc., in press) suggested that a neuromuscular mechanism opposes ETA closure. Current experiments elucidate this mechanism. The ETA segment most vulnerable to passive closure was determined. Closing pressure (CP) was defined as that negative intraluminal pressure at which pressure changes are no longer transmitted across the ETA. In 5 rabbits, 30-32 days old, post mortem CP of the ETA was -6.0 ± 1.8 cm H₂O; in each case, the nose and trachea remained open at -40 cm H₂O, thus implicating the pharynx or larynx as the site of closure. In anesthetized rabbits, forward inspiratory movement of the hyoid bone and associated soft tissues was observed. Electromyography of muscles which pull the hyoid and tongue forward (mylohyoid, geniohyoid, genioglossus) demonstrated phasic inspiratory activity which increased during asphyxia from airway occlusion. Post mortem, the action of these muscles was simulated by traction on the hyoid. CP of the ETA with hyoid traction was -14.2 ± 3.1 cm H₂O compared to -6.0 ± 1.8 cm H₂O without traction (N=5, p<.01, paired t-test). This difference in CP with and without traction suggests that the mylohyoid, geniohyoid and genioglossus muscles function as accessory muscles of respiration to prevent inspiratory airway obstruction.

1165

PROSPECTIVE STUDY OF LUNG FUNCTION IN YOUNG CHILDREN FOLLOWING CROUP (C) AND BRONCHIOLITIS (B)

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Retrospective studies have suggested that infants who had C and B may have residual lung disease. Thirteen asymptomatic children were studied prospectively following hospitalization for C (mean age 18.5 months) and B (mean age 7.5 months). Initial and follow-up studies included viral cultures, serum IgE, allergy skin tests and lung function tests. Functional residual capacity (FRC), maximal flows at FRC (V_{max} FRC) derived from partial flow volume curves and response to exercise were measured in these subjects and 7 age-matched normals (N) at the age of 4-7 years.

Initial Illness			Follow-up				
Proven	IgE	FRC	Asthma	Skin	IgE	V _{max} FRC	Exercise
Viral	(#Abn)	(#Abn)	Tests	(#Abn)	(#Abn)	(#Abn)	Test
C(n=6)	5/6	4/4	5/6	0/6	0/6	3/5	1/6
B(n=7)	4/7	4/6	2/3	1/7	2/7	5/7	2/2

FRC was abnormal in 78% of subjects 2-4 weeks after the initial illness. At 4-7 years of age, baseline abnormalities in V_{max} FRC were demonstrated in 46% of C and B children but in none of the N group. Exercise-induced bronchospasm (EIB) was found in all B and C subjects (5/5) but in only 1/7 N subjects challenged (p<.05). Lung function abnormalities occurred independent of allergies. These data suggest that asymptomatic children who have been hospitalized with C and B have an increased prevalence of airway obstruction and EIB 3-6 years following their illness. Supported by NHLBI Grants 14136 and 17153. R. Beckerman is a Fellow of the American Lung Association.

1168

THE HEMODYNAMIC RESPONSE TO CONTINUOUS POSITIVE PRESSURE BREATHING (CPPB) IN NEWBORN PIGLETS. David

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The cardiovascular effects of CPPB were examined in 11 anesthetized 1 week old piglets. Mean aortic pressure (BP), heart rate (HR), central venous pressure (CVP), carotid (C), femoral (F) and renal (R) flows (f) and resistances (r), were determined at three levels of positive end expiratory pressures (PEEP) 1.5, 5.0, and 10 cm H₂O. The peak airway pressures at each PEEP were selected to maintain constant ventilation. The results are expressed as percent change ± SE between levels of PEEP: (*p<.05)

% Δ	1.5 to 5.0 cm	5.0 to 10 cm	1.5 to 10.0 cm
BP	-0.78 ± 2.79	9.56* ± 3.11	12.64* ± 4.03
HR	-0.48 ± 1.15	19.62* ± 6.10	22.23* ± 4.50
Cf	-8.18* ± 1.73	-26.26* ± 5.46	-12.53* ± 2.76
Cr	9.74* ± 4.13	34.43* ± 8.54	33.26* ± 9.28
Ff	-13.26* ± 5.59	-13.18* ± 1.18	-15.73* ± 4.80
Ff	10.96* ± 3.11	17.48* ± 6.16	27.26* ± 4.43
Rf	-3.22 ± 1.93	-16.88* ± 6.40	0.74 ± 3.15
Rr	4.84 ± 2.99	21.49* ± 6.77	13.59 ± 5.67
CVP	47.80* ± 15.00	57.30* ± 6.00	77.80* ± 27.30

These data demonstrate increases in HR, BP, CVP and r with falls in all flows as airway pressure increases. The newborn piglet responds in part to CPPB by vasoconstriction, with resultant diminution in blood flow in at least three major vessels.

1166

EFFECTS OF LABOR AND TYPE OF DELIVERY ON DRAINAGE OF FETAL LUNG LIQUID IN RABBITS. Richard D. Bland, Michael A. Bressack, and Douglas D. McMillan. Univ California

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Published reports suggest that drainage of fetal lung liquid begins immediately at birth, usually is complete in 4-6 h, but is delayed by cesarean section (CS). To re-examine this process, we measured pulmonary blood volume (PBV), extravascular lung water (EVLW), and size of perivascular fluid cuffs in frozen lung sections of 152 full-term rabbits born vaginally or by CS. We killed the rabbits before they breathed or at varying intervals, up to 24 h, postnatally by immersion in liquid N₂ after intraperitoneal barbiturate. Ten additional rabbits, killed before breathing, had CS after labor. CS rabbits (n=83) weighed 50 ± 7 g, vaginally-born (n=69) weighed 51 ± 8 g. Results: (1) a comparable increase in PBV after breathing in both groups; (2) EVLW significantly less (by 17%) in fetuses born vaginally, compared to those born by CS without labor, but no difference in EVLW for fetuses born either vaginally or by CS after labor; (3) no postnatal decrease in EVLW until 30-60 min of age irrespective of type of delivery; thereafter, decrease in EVLW over 24 h was similar for the 2 groups; (4) maximal perivascular cuffing at 30 min of age, virtually absent by 2-4 h after birth for both groups. Our results suggest that lung liquid content of fetal rabbits decreases during labor, but does not diminish further until 30-60 min after birth; a compliant perivascular tissue space accommodates excess fetal lung liquid until its later removal; and type of delivery has no effect on the pattern of postnatal lung liquid drainage.

1169

DISADVANTAGES OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) OBSERVED DURING CONTINUOUS MONITORING OF OXYGEN TENSION. Edwin G. Brown, Francis E.

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Nasal CPAP was employed in the treatment of infants with RDS while arterial oxygen tension (PaO₂) was continuously monitored by a special oxygen sensing electrode embedded in the wall of an umbilical artery catheter or transcutaneous oxygen tension (TcO₂) was continuously monitored by a Roche sensor.

With nasal CPAP, some infants demonstrated wide fluctuations of PaO₂ and TcO₂ during crying or when the mouth was open. Oxygen tension fell as much as 60%. These changes of oxygen tension are much greater than the reported changes from crying without CPAP. When these problems occurred a pressurized head hood was substituted for the nasal device, and the same pressures, pressure control system and gas flow were used. Following the change of equipment there was improvement and stability of the TcO₂ and PaO₂ when the mouth was open and during crying. In some instances oxygen tension during quiet periods with the hood in place was more than 4-fold those found during quiet periods with nasal CPAP; increases were never less than 2-fold. Every infant who we monitored continuously with an oxygen sensor demonstrated the above changes.

These findings support our previous clinical observations that there are infants in whom nasal CPAP is ineffectual whereas other forms of CPAP administration are effective and raises the question as to whether nasal CPAP is the best means of CPAP application.