ALPHA$_1$-ANTITRYPSIN SERUM LEVELS AND PULMONARY FUNCTION IN ASTHMATIC CHILDREN. D. M. Cooper, D. W. Cox and H. Levison. Dept. of Peds. University of Toronto, Research Inst., Hospital for Sick Children, Toronto.

To define a possible role of alpha$_1$-antitrypsin deficiency in bronchial asthma, 181 children were studied. Alpha$_1$-antitrypsin typing and serum levels were performed in all and pulmonary function testing in 120 of them. Static and dynamic lung volumes and blood gases were measured. No increased incidence of either homozygous or heterozygous deficient types was found. The range of alpha$_1$-antitrypsin levels (242-688, Mean 372± 59) did not differ significantly from those in a healthy non-asthmatic population. No correlation was found between serum levels of alpha$_1$-antitrypsin and pulmonary function tests. This evidence indicates that alpha$_1$-antitrypsin plays neither a quantitative nor a qualitive role in the aetiology of childhood asthma.

SUPPRESSION OF THE FETAL RESPIRATORY RESPONSE IN SHEEP: AN EFFECT OF PHYSIOLOGIC HYPOXIA?
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The respiratory center of the in situ fetus is responsive only to extremes of acidemia and hypercarbia. Recent observation by Brady (Peds:50, 219, 1972) suggest that apnea in the immature newborn is related to hypoxia.

To test the thesis that physiologic fetal hypoxia might suppress the medullary responses we placed chronic catheters in the aorta and ventral lateral medulla of 10 in situ 130 day lamb fetuses.

Respiratory exscursions were monitored via tracheal cannulation. Infusion of buffered artificial CSF between a pH of 7.20 and 7.35 resulted in no change in spontaneous respiratory activity in the normoxic fetus (P_aO_2~25 TORR). When the ewe was placed in a hyperbacric chamber and the pressure and F_IO_2 adjusted to maintain fetal P_aO_2~100 TORR, infusion of artifical CSF in the same pH range resulted in a fetal respiratory rate between 20 and 80 and a response curve similar to that of the newborn lamb. Thus it appears that physiologic hypoxia may serve to depress the medullary response to hydrogen ions in the immature fetal lamb.

THE EFFECT OF POSITIVE PRESSURE BREATHING ON a-A.DN_2 IN HYALINE MEMBRANE DISEASE. Anthony Corbet *, Jane Ross, Pierre Beaudry and Leo Stern **. McGill University, Montreal Children's Hospital Research Institute, Montreal, Quebec.

In 7 subjects with hyaline membrane disease breathing 40-70% oxygen in nitrogen, the effect of continuous positive pressure breathing (C.P.P.B.) was examined by application of a continuous negative pressure (10 cm. water) about the thorax and measurement of the changes in PaN_2, PaO_2 and $PaCO_2$. On C.P.P.B. all sugjects showed improvement, the PaO_2 was a mean 38 mm Hg. higher, the SaO_2 was 9% higher, the A-a.DO_2 was reduced from 279 to 235 mm Hg. and the a-A.DN_2 was reduced from 23 to 14 mm Hg. Assuming values for the composition of mixed venous blood, this meant that on C.P.P.B., the total venous admixture (Qva/Qt) was 0.20 lower, the true right-to-left shunt (Qs/Qt) was 0.19 lower and the venous admixture produced by open low V/Q units ($\dot{Q}o/Qt$) was 0.01 lower. Whilst recruitment of collapsed alveoli certainly occurred and was responsible for some of the improvement in A-a.DO_2, consideration of the La Place relationship and the overall decrease in a-A.DN_2 indicates that another important mechanism was improvement in ventilation of an open, extremely low V/Q compartment. This could be responsible, particularly by relief of local alveolar hypoxia, for reduction of the pulmonary vascular resistance and the true right-to-left shunt.

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SOLUTE PERMEABILITY OF THE ALVEOLAR EPITHELIUM. Edmund A. Egan and Richard E. Olver. University Hospital College Medical School, Dept. of Ped., London, England (Intr. by Donald V. Eitzman).

Investigations were made of the permeability of the in vivo mammalian alveolar epithelium to determine if restriction of solute diffusion could explain the ability of the alveolar lining cells to maintain the separation of the gas phase of the alveolus from the liquid phase of interstitial and vascular spaces of the lung. Using a split lung preparation, trace amounts of non-electrolyte, lipid insoluble solutes dissolved in normal saline were infused into one lung which was then inflated. Transfer out of the alveolar space was determined by serial samplings of the alveolar liquid and transfer constants were calculated from the change in concentration of each substance with time. The rates of transfer of the various sized substances were analyzed in terms of pore theory to determine an equivalent pore radius for the alveolar epithelium. Individual animals had an equivalent pore radius across the alveolar barrier of 20-40 Å with an average of 26 Å. The total area of the solute movement was estimated to be only $2x10^{-8}$th of the total alveolar surface area, pointing to the intercellular junctions as the anatomic site. Pores of this size impose virtually complete restriction to protein movement, significantly restrict NaCl diffusion, and produce an osmotic gradient favoring free water absorption from the alveolus.

A NEW METHOD OF EVALUATING THE CHEMOSENSITIVITY OF THE RESPIRATORY CENTRE IN CHILDREN. J. Cosgrove, D. Cooper, A.C. Bryan, N. Neuburger and H. Levison. Dept. of Peds., Research Institute, Hosp. for Sick Children, Univ. of Toronto.

Decreased ventilatory response to carbon dioxide is often present in lung disease. This can be due to a reduction in the output of the respiratory centre or an inability of the respiratory pump to respond to a normal output because of the size or impedance of the pump. To separate these mechanisms we have measured the isometric force developed by the respiratory muscles during brief airway occlusion, by measuring the pressure generated at 100 milliseconds (P_{M100}). We have found a linear rise of P_{M100} with rising PCO_2 during rebreathing CO_2 response curves. There is a wide range in the slope of P_{M100}/PCO_2 in children indicating a wide range in sensitivity of the respiratory centre, but no relationship to age or size. In contrast the ventilatory response either assessed as $\dot{V}_E/CO_2$ or $\dot{V}_T/PCO_2$ depended on lung size. Correction for lung size does produce a linear relationship ($\dot{V}_E$/TLC = 0.37 CO_2 + 1.09 $P < 0.02$; $\dot{V}_T$/TLC = 0.013 CO_2 + 0.01 $P < 0.001$). These results suggest that comparison of P_M/PCO_2 and $\dot{V}_E/PCO_2$ can differentiate abnormalities of the respiratory centre from abnormalities of the pump, particularly in children, where response depends on lung size.

AIRWAY RESPONSE TO EXERCISE IN INTRINSIC AND EXTRINSIC ASTHMA. Peyton A. Eggleston, Jerry W. Miller, Department of Pediatrics (Intr. by Diane M. Komp), University of Virginia, Charlottesville.

Although intrinsic, non-allergic asthma has a poor prognosis and requires a different treatment rationale than extrinsic asthma, there is no simple means of differentiating them at present. This study was designed to evaluate exercise-induced bronchospasm (EIB) as a differential test.

Fifteen subjects with extrinsic asthma and six with intrinsic asthma were studied. Five minutes of treadmill exercise adequate to raise heart rate to 90-95% of maximum predicted was performed several times at 2-3 day intervals by each subject. VC, FEV_1 and MMEFR were measured prior to exercise and at 1, 5, 10, 15 and 20 minutes after exercise.

The percent fall in spirometry following 49 exercise periods in extrinsic asthmatics and 22 exercise periods in intrinsic asthmatics is seen below.

	VC	FEV_1	MMEFR
Extrinsic	10.3±1.2	23.1±2.0	41.6±2.8
Intrinsic	5.5±1.1	15.4±2.5	21.5±4.5
p	< .001	< .01	.001

Intrinsic asthmatics often responded to exercise with bronchodilation. Extrinsic asthmatics had greater exercise-induced bronchospasm during a significant pollen season.

We concluded that EIB is more pronounced in extrinsic than in intrinsic asthma and may serve to differentiate the two entities.