● 1700 PULMONARY EFFLUENT CELLS, CHEMOTAXIS, AND ELASTASE IN O_2 EXPOSURE.

T. Allen Merritt (Spon. by Donald L. Shapiro) University of Rochester School of Medicine, Strong Memorial Hospital, Department of Pediatrics, Rochester, NY

Influx of polymorphonuclear leukocytes (PMN) and alveolar macrophages (AM) into pulmonary effluent of infants developing bronchopulmonary dysplasia has been found at the 3rd & 7th day with exposure to F_iO_2>.6 & mechanical ventilation. The finding prompted an evaluation of these cells in O_2 exposed newborn guinea pigs (GP). Cell influx into pulmonary effluent, their chemotaxic response to 10^{-5}M N-formyl-methionyl-phenylalanine (FMP) using the double filter Boyden Chamber technique,& effluent elastase, a protease produced by both PMN and AM, measured by elastase activity against succinyl-L-alanyl-L-alanyl-L-alanine-p-nitroanilide was measured in GP after 72 hr. exposure to F_iO_2>.9 or .21.

GP	Cells/ml x10^6	% Chemotaxic to FMP	Elastase U/ml pulmonary effluent
Air n=8	2.44±1.07	15.5%	2.86
72 Hr O_2 n=11	6.01±4.21 p<.01	37.9% p<.01	1.51 p<.02

These data indicate that O_2 exposure in newborn GP increase PMN & AM influx into lung effluent & that these cells are more chemotaxic than in controls. Increased cell number & enhanced chemotaxis of lung effluent PMNs & AM may result in the release of toxins to airway epithelium. Effluent elastase activity is significantly reduced by 72 hrs of O_2 exposure, possibly as a result of depletion or degradation. (Supp. by HD-13279)

1701 PROGRESSIVE ONSET OF SPONTANEOUS AND INDUCED FETAL BREATHING.

Immanuela R. Moss and Emile M. Scarpelli. Pediatric Pulmonary Division, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, New York 10461.

Intratracheal pressure (P_{max}) and respiratory drive (dP/dt) from the occluded, liquid filled trachea of term fetal lambs in utero were measured for each breath during the onset of fetal breathing. Progressive breathing responses at the onset of fetal breathing were observed (1) during spontaneous breathing, (2) during sciatic nerve stimulation, (3) during induced hypercapnia by Fetal CO_2 Tests (Moss and Scarpelli, J. Appl. Physiol. 47:527, 1979) and (4) following naloxone administration. These responses were characterized by linear increase of both P_{max} and dP/dt for 6.8 ± 0.3 breaths ($\bar{x}$ ± SEM) over 13.9 ± 1.7 seconds, following which these parameters became stable. The rate of rise of P_{max} and dP/dt versus both breath number and absolute time was lowest and similar during spontaneous breathing and sciatic stimulation, but increased incrementally with hypercapnia and naloxone. Mechanical factors could not account for these responses in the liquid filled lung, nor did appreciable chemical changes occur during this period. These results suggest that progressive breathing responses at the onset of fetal breathing may stem from gradual recruitment of central respiratory neurons, and that the rate of rise of such recruitment depends on facilitation by natural or somatosensory induced "arousal" and by chemical stimulation,as well as on release from natural (endorphin) inhibition. (Supported by NIH HL 00688 (RCDA) and HL 23995).

1702 At what age is ipratroprium bromide an effective bronchodilator agent in childhood asthma?

A D Milner, I G C Hodges, G M Stokes and R C Groggins. University Hospital, Nottingham,UK.

Beta adrenergic stimulant drugs are rarely effective as bronchodilator drugs below the age of 18months in childhood asthma. We have previously shown that ipratroprium bromide, an anticholinic drug, is an effective bronchodilator agent in children over the age of three years, and produced a response similar to that of salbutamol. We set out to investigate whether this drug was effective in the first three years of life. Children under the age of three, admitted to hospital with wheezy bronchitis/asthma, were sedated and given a nebulised solution containing 250mc gms of ipratroprium bromide. Airways resistance (Raw), thoracic gas volume (TGV) and total respiratory resistance (R_T) were measured five minutes before and 20 minutes after the administration of the drug, using a total body plethysmograph and the forced oscillation technique. Twelve of 30 children under the age of 18 months showed a greater than 15% improvement in R_T and 10 of 22 an improvement in Raw, the youngest being six months of age. This preliminary work suggests that ipratroprium bromide may have a place in the treatment of the very young asthmatic.

1703 Onset of respiration after delivery by Caesarean section and the vagina.

A D Milner, H Vyas, I E Hopkin. University Hospital, Nottingham, UK.

Our previous work has shown that babies born by C section requiring resuscitation rarely achieve a functional residual capacity (FRC) immediately, unlike those born by vaginal delivery. As these differences could be due either to asphyxia or the mode of delivery, we have measured the first spontaneous breath in 21 babies born vaginally, measuring intrathoracic pressure with a micro pressure transducer on a 6fg catheter, and thoracic volume change on a pneumotachograph, from the time the baby's head was delivered on the perineum until regular respiration had commenced. We compared the results with data obtained on 12 babies born by C section, commencing measurements as soon as the baby's head was delivered through the uterine incision. Those delivered vaginally experienced prolonged squeeze of up to 237cm H_2O, compared to a transient pressure of 113cm H_2O on passage through the uterine scar. Inspiratory pressures and volumes were similar for the two groups, but only five of those born by C section had an FRC after the first breath, compared to 20 of the 21 vaginal deliveries. Opening pressures were rarely seen in either group. We conclude that passage down the birth canal does aid lung expansion at birth.

● 1704 RUNNING IMPROVES FITNESS IN ASTHMATIC CHILDREN WITHOUT CHANGING AIRWAYS REACTIVITY OR VENTILATORY MUSCLE FUNCTION.

B.G. Nickerson*, D.B. Bautista*, M.A. Namey*, W. Richards*, T.G. Keens* (Spons. R.M. McAllister) Childrens Hospital of Los Angeles, Sunair Home for Asthmatic Children, and Department of Pediatrics, University of Southern California, Los Angeles.

We studied the effect of running 3km/day, 4 days/week for 6 weeks on 15 children ages 7-14 years who had severe asthma. All took oral theophylline and inhaled beclomethasone and sympathomimetics and 2 took prednisone. We studied each subject before and after a 4 week control period and after 6 weeks of running with the following: spirometry, body plethysmography, maximum inspiratory pressure (MIP), ventilatory muscle endurance as the sustained inspiratory pressure (SIP) by a new technique we have developed, a maximum exercise stress test on a bicycle ergometer followed by repeat spirometry and body plethysmography and a 12 minute run on a different day.

M±SE N=15	12 min run (m)	FEV_1 (%pred)	Maximum pulse	ΔFEV_1 p exercise%	MIP cmH_2O	SIP cmH_2O
control 1	1605	71±5	185±4	-11±3	159±9	110±5
control 2	1573±53	71±5	180±5	-10±5	165±7	108±7
post training	1776±68	69±5	182±5	-11±4	164±9	113±7
significance	p<0.005	NS	NS	NS	NS	NS

The distance run in 12 minutes improved significantly without changes in pulmonary function or airways reactivity. The ventilatory muscle strength and endurance was initially greater than normal and did not increase. We conclude that running did not improve the pulmonary mechanics but did increase the specific muscle and cardiovascular fitness of these asthmatic children.

1705 FINDING SPECIFIC ABNORMALITIES IN NEAR MISS CRIB DEATH.

Dennis W. Nielson, David H. Rubin, Gregory P. Heldt, William H. Tooley. Cardiovascular Research Institute, University of California, San Francisco.

Many different abnormalities, including infection, gastroesophageal reflux (GER), and neurologic abnormalities, are proposed causes of crib death and near miss crib death. As the final common pathway, these abnormalities may all cause fatal apnea. Past studies have concentrated on proving the association between near miss crib death and some particular abnormality. Instead, we have elected to study each patient for many of these abnormalities. We evaluated 15 patients referred to us because of a history of near miss crib death with a careful history and physical exam, appropriate cultures and titers, EKG, EEG, chest radiogram, and a 4 hour sleep study in conjunction with a 12 to 24 hour esophageal pH study. During the sleep study, we continuously monitored sleep state, chest and abdominal movement with breathing, exhaled CO_2, skin surface PO_2 and PCO_2, and esophageal pH. We also studied each patient's response to 10 minutes of breathing 17% O_2 and 10 minutes of breathing 6% CO_2 in air. By history, 7 patients were premature. Of our 15 patients, 4 had severe obstructive apnea with GER, 3 had excessive periodic breathing, 2 had seizure disorders, 1 was septic, 1 had airway obstruction due to Beckwith's syndrome and a respiratory infection, 1 had both central and obstructive apnea with nasopharyngeal obstruction exacerbated by chronic use of nosedrops, and an abnormal response to CO_2, 1 had mild upper airway obstruction due to a small mandible, and 1 had moderate GER that was associated with agitation and perioral cyanosis, but not with apnea. We found mild neurologic abnormalities in 8/15. We did not find any specific abnormality in 1 patient.

Our results support the hypothesis that near miss crib death has many causes, and by doing an extensive evaluation, we were able to find at least one specific abnormality that could reasonably explain a history of near miss crib death in 14 of 15 patients.

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