decade. In other families alpha₁-antitrypsin deficiency has been accompanied by cirrhosis in infancy or childhood, without clinical pulmonary disease. A 13-year-old girl has recently been studied, who has had recurrent pulmonary infections and progressive dyspnea since age 18 months. Chest x-rays show bullous emphysema and pulmonary function tests reveal severe airway obstructive disease with a low diffusing capacity. Lung biopsy done 5 years ago show emphysema and smooth muscle hypertrophy of the small bronchioles. Immunoglobulins, sweat electrolytes and liver function studies have been normal. Biochemical and electroimmunodiffusion studies of serum reveal a deficient level of alpha₁-antitrypsin and biochemical studies show a deficiency of inhibition of elastase. Family studies indicate that the deficiency is inherited in an autosomal recessive manner. The emphysema associated with hereditary alpha₁-antitrypsin deficiency may become symptomatic in early childhood and should be considered in the diagnosis of obstructive pulmonary disease in infants and children.

- 166 *Abnormal Erythrocyte Sodium Transport in Cystic Fibrosis (CF)*. ALLEN LAPEY and JERRY D. GARDNER, NIH, Bethesda, MD (introduced by Paul A. di Sant'Agnese).

To further explore the recently reported erythrocyte cation transport defect in cystic fibrosis (CF) patients and their parents [BALFE *et al.*, Science, 00: . . ., 1968], we have measured sodium (Na) content and the major components of Na outflux in erythrocytes from 21 normal young adults, 22 CF patients (ages 7-27), and 20 obligate heterozygotes.

Na content of red cells from patients and heterozygotes was normal. Of the various components of Na outflux measured, there was no difference between heterozygotes and their normal male or female counterparts.

Of the major components of Na outflux, that portion sensitive to ouabain (0+) was normal in all CF groups. Abnormalities of Na outflux in CF were primarily due to that portion which was insensitive to ouabain and sensitive to ethacrynic acid (0-/E+). 0-/E+ fractional outflux was decreased in CF males of all ages ($0.027 \pm 0.02/h$) relative to male controls (0.051 ± 0.02). 0-/E+ was decreased in 7 CF females over the age of 16 (0.012 ± 0.005) compared to female controls (0.023 ± 0.01). However, in the 4 CF females under 16, 0-/E+ outflux (0.057 ± 0.003) was greater than that of older CF females.

The normal data from heterozygotes indicate that erythrocyte Na outflux cannot be used as a 'genetic marker' for CF. These data document altered cation transport in non-exocrine tissue from males and older females with CF. Furthermore, this abnormality does not simply reflect a general alteration of erythrocyte cation transport, but is localized to a single specific component of Na outflux, which has a characteristic requirement for metabolic substrates as well as distinctive kinetic parameters. Studies of this transport system in other tissue from patients with CF may permit a characterization of the disease at the molecular level.

- 167 *The Distribution of Fluid Intake from Mist Tent Therapy*. NORMAN ASPIN, SAMUEL K. BAU, HENRY LEVISON and DONALD E. WOOD, Dept. of Paed., Hosp. for Sick Children, and Div. of Nucl. Med., Toronto Gen. Hosp., Toronto (introduced by Andrew Sass-Kortsak).

Mist tent therapy is widely used in the treatment of cystic fibrosis to increase deposition of fluid in the lower airways of the lung. To measure the time course and extent of this fluid uptake we have introduced a solution of radioactive ^{99m}Tc into the fluid reservoir of an ultrasonic nebulizer. Subjects breathed in the mist tent for periods up to 5 h following which the distribution of inhaled radioactivity was measured with a whole body counter and a rectilinear scanner. The results show that less than 5% of the radioactive aerosol entering the tent is inhaled by the subject. Of the inhaled aerosol 90% is initially trapped by the nasopharynx and later much of this radioactivity appears in the stomach. It is difficult to detect radioactivity in the lung. Similar results have been obtained in ten subjects using three different ultrasonic nebulizers. This work indicates that very little fluid from a mist tent reaches the terminal airways of the lung. (Supported by Canadian Cystic Fibrosis Foundation.)

- 168 *Re-evaluation of Mist Therapy in Children with Cystic Fibrosis Using Maximum Expiratory Flow-volume Curves*. ETSURO K. MOTOYAMA, LEWIS E. GIBSON, CHARLENE J. ZIGAS and CHARLES D. COOK, Yale Univ. Sch. of Med., Depts. of Ped. and Anesth., New Haven, Conn.

The measurement of maximum expiratory flow rates ($\dot{V}_{max}$) on MEFV curves is a simple yet sensitive method for detecting peripheral airway obstruction. In order to re-examine the efficacy of mist therapy (MT) in cystic fibrosis, MEFV curves as well as vital capacity (VC) and timed vital capacity (FEV_{1.0}) were measured in 16 patients every two weeks for a period of 4 to 5 months. In half of the patients, all of whom had been in mist tents at night for at least 6 months, the studies were done during an initial 8 to 12 week period out of mist and then a similar period in mist; in the other half the test conditions were reversed. The results were expressed as percent of predicted values.

	$\dot{V}_{max}$ (25% VC)	$\dot{V}_{max}$ (50% VC)
In mist (% pred. $\pm$ S.E.)	43.3 $\pm$ 6.2	60.3 $\pm$ 6.9
Out of mist	45.9 $\pm$ 6.7	63.9 $\pm$ 6.4
Significance	n.s.	n.s.
	VC	FEV _{1.0}
In mist (% pred. $\pm$ S.E.)	86.6 $\pm$ 4.5	71.0 $\pm$ 4.5
Out of mist	89.9 $\pm$ 5.3	74.5 $\pm$ 4.7
Significance	n.s.	p < 0.025

During the period without MT, 4 patients improved and 2 worsened as indicated by changes in all 4 parameters studied. As a group, FEV_{1.0} was significantly (p < 0.025) better when they were without MT. VC and $\dot{V}_{max}$ at 25% VC and 50% VC were also closer to normal without MT but the difference was not significant. Thus, these studies failed to show any beneficial effect of mist therapy in cystic fibrosis. (Supported by PHS HD00989, NCFRF and the State of Conn.)

- 169 *Physiological Mechanisms Underlying Periodic Breathing in Low Birth Weight Infants*. HENRIQUE RIGATTO, JUNE BRADY, WARREN TICKNOR and FE DUMPTRE, Dept. of Ped. and Cardiovascular Res. Inst., Univ. of California, San Francisco, CA.

Twenty babies (b.w. 1-2 kg) were studied 106 times in the first 34 days of life. In 11 babies breathing periodically and 9 breathing regularly, we compared minute

ventilation, alveolar PO_2 and PCO_2 , arterial pH, PCO_2 and PO_2 , CO_2 respiratory response curves, and sensitivity to O_2 . We measured ventilation with a nose piece and a screen flowmeter, using a constant flow-through to eliminate dead space and valves. Analyses were made from 3 to 5 min after the baby began breathing air, 2% or 4% CO_2 in air or 100% O_2 . Sensitivity to O_2 was assessed by the change in ventilation when 100% O_2 was substituted for air.

Results:

	V_E L/min/kg	$PaCO_2$	$PACO_2$	PaO_2
P^1	0.230 ± 0.008	41 ± 2	39 ± 1	57 ± 3
R^1	0.273 ± 0.011	38 ± 2	35 ± 2	66 ± 4
	$p < 0.001$	$p < 0.025$	$p < 0.005$	$p < 0.001$
		PAO_2	pH	
P^1		102 ± 2	7.34 ± 0.01	
R^1		108 ± 2	7.33 ± 0.01	
		$p < 0.001$	$p > 0.5$	
	CO_2^2		% ΔV_E	
	Slope	Position ³	Air . . O_2	
P^1	0.030 ± 0.007	42.7 ± 2.2	-37 ± 11	
R^1	0.035 ± 0.007	36.0 ± 2.7	-20 ± 9	
	$p > 0.2$	$p < 0.001$	$p < 0.025$	

All values: mean $\pm$ 0.2 S.E.

¹ P = periodic; R = regular.

² Response curve in L/min/kg/mm Hg.

³ $PACO_2$ at 0.300 L/min/kg.

These findings show that periodic breathing in low birth weight infants is associated with hypoventilation, shift of the CO_2 response curve to the right and marked sensitivity to O_2 . We suggest that low birth weight infants have increased O_2 chemoreceptor activity, but breathe periodically because of relative central depression.

170 *Ventilatory Disturbance and Arterial-Alveolar N_2 Differences During Recovery from Hyaline Membrane Disease.* A. PATHAK, L. MORRISON, L. M. PRUDENT, R. B. CHERRY and N. M. NELSON, Harvard Med. Sch. and Boston Hosp. for Women, Boston, Mass.

In infants recovering from hyaline membrane disease (HMD) persistent hypoxemia has been identified which seems not to result from venoarterial shunting [ADAMSON *et al.*, *Pediatrics* 44: 168, 1969] but which could be due either to pulmonary diffusing defect or to ventilation/perfusion imbalance. Since the arterial-alveolar N_2 difference ($aADN_2$) and venous-alveolar N_2 difference ($vADN_2$) are unaffected by diffusion defect or by venoarterial shunting but are increased by impairment of ventilation with respect to perfusion, we have measured $vADN_2$ in a group of 10 normal low birth weight infants and in 4 infants convalescing from HMD. (Simultaneous comparison of $vADN_2$ and $aADN_2$ in seven infants revealed no significant difference.) In another 4 infants convalescing from HMD the alveolar-arterial O_2 difference ($AaDO_2$) and arterial-alveolar CO_2 difference ($aADCO_2$) were also examined.

Number of infants	Age (days)	Birth weight (g)	Dx
10	18.5 ± 11.2	1713.6 ± 331.5	normal
4	7 to 16	1644 to 2892	HMD
4	10 to 33	1276 to 2395	HMD

Number of infants	$AaDO_2$ mm Hg	$aADCO_2$ mm Hg	$aADN_2$ mm Hg	$vADN_2$ mm Hg
				14.1 ± 18.6
				77.0 ± 36.8
	59 ± 7.5	9.5 ± 5.5	44.8 ± 4.9	42.8 ± 7.4

Unlike the hypoxemia seen in infants with early and developing HMD (which is due to an inequality of perfusion and a persistence of venoarterial shunting), the present findings suggest that it is inequality of ventilation which is mainly responsible for persistent hypoxemia during convalescence from HMD.

171 *Adjustment of Ventilation in the Newborn.* PETER A. M. AULD, ALFRED N. KRAUSS and JANE SOODALTER, Dept. of Ped., Cornell Univ. Med. Center, New York, NY.

In adapting to extrauterine life, ventilation and perfusion must soon become well-matched. The time course of this process can be assessed by measurement of the urinary-alveolar nitrogen gradient ($uADN_2$). An elevated $uADN_2$ is an indication of the maldistribution of VA/Q , specifically the presence of areas of low VA/Q . Seventeen healthy full-term neonates were studied serially from the first day of life. Values of $uADN_2$ within the range for normal adults were found (less than 10 mm Hg). Serial studies on 3 infants with evidence of aspiration pneumonia revealed $uADN_2$ consistently elevated above the normal. Children and adults with obstructive pulmonary disease were tested as a validation of the method and the expected elevation of $uADN_2$ was found. The studies indicate that (1) ventilation is uniformly distributed in the first days of life in normal infants; (2) maldistribution of ventilation is an important cause of arterial unsaturation in aspiration pneumonia. These results will be considered in the context of other studies of extrauterine pulmonary adaptation.

172 *Immaturity and Enhanced Susceptibility to Acute Hemodynamic Pulmonary Edema.* ELIHU P. REES, DORA A. STINSON, PAUL M. TAYLOR and DORIS W. WATSON, Dept. of Ped., Univ. of Pittsburgh Sch. of Med. and Magee-Women's Hosp.

The hypothesis that the immature lung is more susceptible than the mature lung to the development of acute pulmonary edema (PE), was tested by determining the transmural hydrostatic pressure in excess of whole blood colloid osmotic pressure (COP) necessary to produce PE in pups and adult dogs. Ten pups and ten adults were anesthetized with pentobarbital, paralyzed with succinylcholine, and artificially ventilated. Transmural pulmonary artery wedge pressure (TPAWP) (as a reflection of vascular filtration pressure) was monitored continuously and whole blood COP intermittently. A balloon catheter in the thoracic aorta was inflated to produce an elevation of TPAWP in relation to COP that was maintained for 30 min by infusion of isosmotic dog blood to maintain a constant differential pressure (TPAWP-COP). Lungs were then removed and the degree of PE assessed by gross and microscopic appearance and determination of water content.

Interstitial edema first appeared with the following range of values:

	TPAWP mm Hg	Total protein g%	COP mm Hg	TPAWP-COP mm Hg
Adult dogs	24-30	5.6-7.0	19-22	6 to 8
Pups	10-15	4.2-5.6	12-17	-2 to +1