1219 A TWENTY YEAR EVOLVING PROTOCOL TO PREVENT DEATH DURING STATUS ASTHMATICUS. Herbert C. Mansmann, Jr. and Stephen J. McGeady, Jefferson Medical College, Children's Heart Hospital, Philadelphia.

Therapeutic objectives, during all phases of illness, were employed to minimize progression to respiratory insufficiency. When status asthmaticus developed, the methods of medical management, with year initiated in ( ), were considered and if necessary, utilized to prevent respiratory failure. The techniques used could not have been possible without the aid of a cooperative and intellectually stimulating staff willing to comply with a rigid requirement for structured supervision of each level of care.

The useful modifications in regimen were aggressive patient and current protocol surveillance (1956), increased theophylline dose (1959), blood gas monitoring (1963), controlled ventilation (1964), correction of acidosis (1965), long-term hospitalization (1971), and serum theophylline monitoring (1976). Basic treatment was epinephrine, fluids, theophylline, sodium bicarbonate, oxygen, and corticosteroids. Neither bronchopulmonary lavage (1970), nor intravenous isoproterenol (1972) have been necessary.

The results from 1956 to 1968 have been summarized (J. Allergy 46:257, 1970). This service of seven physicians saw 3,624 outpatients last year, 80% with asthma. The daily in-patient census was 3-5 in the acute hospital and 25-30 intractable asthmatics in the chronic hospital. Controlled ventilation has not been required for eleven years. Death in hospitalized patients with status asthmaticus has not occurred in twenty years.

1220 FUROSEMIDE (FS) IN HYALINE MEMBRANE DISEASE (HMD). Keith H. Marks, William Berman Jr, Zvi Friedman, Victor Whitman, Susan Uhrmann, Cheryl Lee, M. Jeffrey Maisels (Spon by Nicholas M. Nelson). Penn State Univ Coll Med, M S Hershey Med Ctr, Dept Ped, Hershey, PA.

We conducted a random blind study to assess the effect of IV FS 2 mg/kg or 5% DW in 0.25 NaCl (control) on interstitial fluid mobilization and cardiorespiratory function in 7 infants with HMD. Criteria for entry into the trial were: peripheral edema and FiO_2>.4 to maintain PaO_2>50 torr. Echocardiogram and multiple gas analyses were performed in the 2 hours preceding and following the treatment. Results (mean ± SD):

		Urine Vol ml/kg/hr	PaO_2 torr	$PaCO_2$ torr	pH	LA/AO ratio	Eject Frac %
Control	before	1.8±1.8	57.3±6	42.0±7	7.33±0.6	1.1±0.3	36±6
n=4	after	3.6±1.1*	56.7±8	45.2±4	7.32±0.6	1.1±0.2	37±9
FS	before	1.8±0.8	52.1±5	42.0±8	7.31±0.5	1.1±0.1	34±5
n=3	after	8.9±1.7+	52.7±5	46.0±8	7.31±0.6	1.1±0.2	34±5

*p<0.01-control vs. FS. +p<0.01-before vs. after FS.

In spite of the diuresis, measurements of dynamic skinfold thickness did not confirm mobilization of subcutaneous interstitial water. We conclude that FS has a potent diuretic effect in infants with HMD but it does not improve cardiorespiratory function acutely. This may be due to failure to mobilize pulmonary interstitial fluid in the time period tested.

1221 EVIDENCE FOR A TONIC COMPONENT OF THE HERING-BREUER INFLATION REFLEX IN THE TERM NEONATE. R.J. Martin, A. Okken, P. Katona, M. Klaus. CWRU, Ped. Dept. Cleveland, O.

Animal studies have shown that an increase in FRC slows respiration, increases expiratory duration and is vagally mediated. To explore whether a similar response occurs in humans, we studied respiratory timing in 10 sleeping, healthy term neonates on days 1,2 and 3, before and after a change in lung volume accomplished by adding a continuous positive airway pressure(CPAP) of 3 and 6 cm H_2O. Using a mask and flowmeter with constant flow to reduce deadspace, we measured inspiratory time(Ti), expiratory time(Te), total respiratory cycle duration (Ttot), and tidal volume. Comparative movements of upper and lower rib cage were recorded via mercury strain gauges and transcutaneous(Tc) PO_2 monitored via a skin electrode. Increasing lung volume caused a significant prolongation of Te% (100xTe/Ttot) on all 3 days(mean data in table). As CPAP was raised from 0 to 6, respiratory rate fell from 47 to 42(NS), 58 to 42($p<.005$) and 50 to 36($p<.005$) on days 1,2, and 3 respectively. CPAP at 6 cm H_2O caused a mean increase in FRC of 19±7cc without significant change in tidal volume and there was no change in $TcPO_2$ when compared to the control period. The direction of paradoxical rib cage movement was unaltered by CPAP. These observations suggest that the significant rise in Te% at increased lung volume may be secondary to the stimulation of a tonic inflation reflex.

	Day 1		Day 2		Day 3	
CPAP	0	6	0	6	0	6
Te%	56.7	61.1	51.0	59.8	55.5	61.7
p	<.01(n=10)		<.005(n=10)		=.05(n=6)	

1222 PHOSPHATIDYL CHOLINE TRANSFERASE: PRE- AND POST-NATAL ACTIVITY IN RABBIT LUNG MICROSOMES AND LAMELLAR BODIES Cynthia H. Matsuyama, Ronald S. Bloom, and Alan K. Percy, Charles R. Drew Postgraduate Medical School, Los Angeles

Recent studies suggest that the lamellar bodies in lung tissue contain enzymes involved in the lecithin biosynthetic pathway. Phosphatidyl choline transferase (PCT), very possibly the rate-limiting enzyme in the lecithin biosynthetic pathway, has been described in fetal lung; however, the distinction has not been made between PCT activity in lamellar bodies and that in microsomes, a known site of lecithin biosynthesis. This study assessed lecithin biosynthesis by measuring the activity of PCT in these two subcellular fractions obtained from lung of New Zealand White rabbits of gestational age 25-31 days and postnatally to age 10 days. The lamellar and microsomal fractions were prepared by differential centrifugation, and their PCT activities were measured using the precursor, (^{14}C)-CDP-choline. In both subcellular fractions, PCT activity reached an initial peak on the 28th day of gestation after which the activity dropped dramatically at term, followed by a gradual rise beginning between the 5th and 8th postnatal day. At the 28 day peak, lamellar body PCT activity was double that in the microsomal fraction. The demonstration of high levels of PCT activity in the lamellar body fraction leads to the consideration of the lamellar bodies as a major site of lecithin biosynthesis as well as storage.

1223 SYNERGISTIC EFFECTS OF POLYCYTHEMIA (P) AND HYPOXIA (H) ON PULMONARY VASCULAR RESISTANCE IN DOGS. Robert L. McGrath and John V. Weil (Spon. by Frederick C. Battaglia). Dept. of Pediatrics and Cardiovascular Pulmonary Research Lab, Univ. of Colorado Sch. of Medicine, Denver, CO.

While P commonly occurs in patients with H most hemodynamic studies of P have been done with normoxia. This study examined the combined effects of P and H. In 11 splenectomized, anesthetized dogs hematocrit was increased-42.6±1.2 to 65.5±0.6 (SEM)% by isovolumic exchanges with fresh canine packed RBC's. Studies were done during normoxia (N) (P_aO_2 113.8±4.2 mmHg) and H (P_aO_2 40.5±1.6). P alone increased pulmonary vascular resistance (PVR) 112±5.4% ($p<.05$) and H alone increased PVR 90±6.2% ($p<.05$). Combined H and P increased PVR 300±8.2% ($p<.005$), an effect significantly greater than that of H or P alone ($p<.005$). In contrast, systemic vascular resistance (SVR) increased with P by 96±2.4% ($p<.05$) while H had no effect on SVR either separately or when combined with P. P decreased cardiac output 50±1.8% ($p<.05$) while H had no significant effect alone or when combined with P. Oxygen transport (O_2T) was decreased by P 29±0.8% ($p<.05$) due to decreased cardiac output. H decreased O_2T 28±0.9% ($p<.05$) due to a decrease in arterial oxygen content. Combined H and P decreased O_2T 50±2.6% ($p<.05$) an effect greater than that of H or P alone. In 4 control dogs, exchange with whole blood produced no change in the variables studied. Synergistic effects of H and P on PVR probably reflect combined influences of increased blood viscosity and hypoxic pulmonary vasoconstriction. Such a combination may contribute to the occurrence of cor pulmonale in patients with H and secondary P.

1224 MECHANISM OF EXERCISE INDUCED ASTHMA. C.M. Mellis, H. Levison, A. Mansell and A.C. Bryan. Research Institute, Hospital for Sick Children, Toronto, Ont.

There is uncertainty regarding the relative importance of chemical mediator release (humoral) and direct physical stimulation of epithelial irritant receptors (neurogenic) in producing exercise induced asthma (EIA). We have approached this question in light of the following: Disodium cromoglycate (DSCG) acts by interfering with the release of mediators from mast cells; histamine by inhalation acts predominantly by stimulating irritant receptors resulting in reflex bronchoconstriction and has only a minor direct effect on bronchial smooth muscle. DSCG effectively blocked EIA in 10/10 asthmatic children but failed to protect 8/8 from the effects of inhaled histamine. We also demonstrated that EIA can be prevented by breathing air at a temperature of 37°c and 100% relative humidity ("steam") in 8/8 asthmatic children. However, "steam" had no protective effect against inhaled histamine in 6/6 children. We conclude that EIA is due to the release of chemical mediators from bronchial mast cells, rather than by a direct physical effect on the irritant receptors. Moreover, the results with "steam" imply that the stimulus for this release is the cooling and/or drying effect of the inspired air as a result of the hyperventilation occurring during exercise. Once released these mediators, particularly histamine, then presumably induce bronchoconstriction by activating epithelial irritant receptors.