

Because of similarities in the kinetics of enzymatic reactions and of active intestinal transport, the effect of actinomycin D on the latter was investigated. Observations were made of the active transport of amino acids (L-leucine and cycloleucine), sugar (3-O-methyl-D-glucose) and inorganic sulfate in the small intestine of the rat utilizing the everted gut sac technique of WILSON and WISEMAN. Transport by intestinal segments obtained from actinomycin D treated animals (single injection of 66  $\mu\text{g}/100$  gms subcut.) was compared with transport by intestinal segments obtained from matched controls. Studies were carried out at time intervals ranging from 1 to 48 h following injection. No significant effect of actinomycin D on transport was noted before 24 h. However, active transport of each of the substances studied was markedly increased (2 to 4 fold increase in concentration gradients) in the animals who received actinomycin D 36 to 48 hours previously.

Although commonly used to inhibit enzyme activity, actinomycin D has been shown to induce several enzymes in rat liver 24 to 48 hours after the administration of a single dose (ROSEN: Science 146-661 [1964]). This delayed effect is similar to that observed in our study of intestinal transport and suggests a possible relationship between the two. The mechanism by which actinomycin D stimulates intestinal transport is unknown although it possibly acts by inhibiting a substance that normally limits the rate of transport. (SPR)

81 *Split Products of Fibrinogen in Cord Serum.* E. RICHARD STIEHM\*, Univ. Wisc. Med. Sch. Madison, Wisconsin (introduced by C.C. Lobeck).

The presence of split products of fibrinogen (SPF) in serum is an indicator of abnormal fibrinogen deposition or breakdown (e.g. intravascular coagulation). Normal serum (53 samples) does not have material reactive with antiserum to human fibrinogen. 66 umbilical cord serums were studied for SPF by a semi-quantitative precipitin tube technique using rabbit antiserum to human fibrinogen. 44 of 66 (67%) of cord serums had significant levels of SPF, including 26 (39%) with high levels (>2% of tube length). 13 of 32 (41%) maternal serums obtained immediately post partum had SPF. Serial determinations of SPF in several mothers and infants showed that these products generally disappear rapidly, usually by the second day after birth. No relationship existed between maternal and cord serum levels of SPF in 32 pairs specimens; the cord level exceeded the maternal level in 20 instances, the maternal level exceeded the cord level in 7 instances, and in 5 instances neither maternal nor cord serum had SPF. Since gel filtration on Sephadex G-200 indicated that the immunologically active material was a large molecule (MW > 160,000), it is unlikely that SPF in cord serum represents transplacental passage from the maternal circulation. Among randomly selected infants without SPF in their umbilical cord serum, 1 of 16 (6%) had a respiratory problem or illness during the first days of life. In contrast, 14 of 28 infants (50%) with SPF greater than 1.0% had a difficult birth or neonatal illness. This included 2 prematures, 2 neonatal deaths, 7 infants with Apgar scores below 7, 4 infants with respiratory problems and 2 infants with cephalo-hematomas. These data suggest that newborn infants with high and/or persistent levels of SPF may be a high risk group. (SPR)

82 *Temperature, THAM, Glucose and Asphyxia in Newborn Puppies.* JAMES A. MILLER, Jr.\*, MICKEY VIA\*,

EL SAYED H.H. HEGAB\* and FAITH S. MILLER\*, Tulane Univ. Sch. of Med., New Orleans, La. (introduced by Margaret H.D. Smith).

The time of last gasp (TLG) of asphyxiated neonatal puppies increases from 4.3 minutes at 42°C body temperature to 105 minutes at 15°C. Below 15°C survival times decrease. This is true protection; all 15°C animals recovered from exposures up to 1 hour (4X TLG of warm littermates) and 50% of those exposed 9X or 10X TLG recovered without assistance. In warm animals artificial respiration with 100% O<sub>2</sub> was only partially successful for animals exposed for 1 1/4X to 2X TLG and most showed behavioral deficits indicating brain damage. By contrast, cold animals which were exposed to 10X TLG of warm littermates and which recovered spontaneously showed no evidence of brain damage. During asphyxia, blood glucose, potassium, lactate and hydrogen ions increased and pyruvate decreased. In puppies at 15°C all of these changes took place at a slower rate than in warm littermates. In coenothermic animals (37°C) controlling pH by infusion of Trishydroxyaminomethane (THAM) increased survival times by 18%, infusion of glucose by 19%, and combining the two by 68%. Cooling to 15°C colonic temperature gave survivals of 655%. Combining THAM and glucose with hypothermia (15°C) gave an average of 1104%. THAM-glucose infusions also permitted recoveries from exposures which were lethal for non-infused animals at the same temperature. Thus, the combination has been the most effective of any tried to date. (SPR)

83 *Comparison of Rapid Versus Gradual Correction of Acidosis in RDS of Prematurity. A Sequential Study.* ROBERT USHER, Royal Victoria Hospital, McGill University, Montreal, Canada.

This therapeutic trial of rapid alkali therapy immediately after birth was initiated because of 1. the observation that prognosis in respiratory distress syndrome (RDS) is worse the longer that acidosis persists, as well as 2. the recently proposed hypothesis that the pathogenesis of RDS may be pulmonary hypoperfusion caused by hypoxemia and acidosis. From 1960-1964, and again in 1966, consecutively delivered infants with RDS were treated with slow drip infusions of sodium bicarbonate (5-15 mEq/100 ml 10% G/W, at 65 ml/kg/day until capillary pH rose to 7.35 (Pediat. Clin. N. Amer. 8: 525 [1961])). In 1965 a trial of rapid correction of acidosis was made in which pH was corrected up to 7.35 within 3 h of birth, using a solution of 20 mEq Na bicarb/100 ml 10% G/W. The rates of flow ranged from 10-50 ml/kg/3 h. Other than rapidity of alkali administration, therapy was similar to that used before and after.

	Mortality rate	
	Slow	Rapid
1001-1500 g	35/82-45%	7/13-54%
1501-2000	18/87-21%	6/16-38%
2001-2500	8/88-9%	3/12-25%

Mortality in RDS infants weighing 1001-2500 g was 61 out of 257 (23.7%) with slow correction, and 16 out of 41 infants (39.0%) with rapid correction (P < 0.05). (SPR)

84 *UDP-Glucuronyl Transferase.* ELIAS HALAC\* and PAMELA WEISS\*, New York Univ. Sch. of Med. New York, N.Y. (introduced by Joseph Dancis).

We have reevaluated the capacity of newborn rat livers to conjugate bilirubin and p-nitrophenol with glucuronic acid after activation of liver homogenates with EDTA and utilizing improved assaying conditions as previously reported.

We have found that the newborn liver conjugates p-nitrophenol at levels similar to adult male rats while bilirubin conjugation is not detected before the 12th hour of life. Phenobarbital injections to the mother during the last 8 days of pregnancy induced the prenatal development of this enzyme and 2-hour-old fetuses had about 1/3 of the adult level of bilirubin UDP-glucuronyltransferase activity. The capacity to conjugate p-nitrophenol was not significantly altered by phenobarbital.

The activation of UDP-glucuronyltransferase by EDTA has been studied by electron microscopy. We have found that EDTA induces the conversion of rough endoplasmic reticular membranes into smooth membranes. This finding correlates significantly with the increase of hepatic smooth membranes after birth and that induced by phenobarbital administration. (SPR)

85 *A Treatment for the Complications of Prolonged Artificial Ventilation of Small Infants.* PENELOPE CAVE\*, WILLIAM H. NORTHWAY, Jr.\*, MARSHALL KLAUS and GRANT FLETCHER\*, Stanford Univ. Sch. of Med., Palo Alto, Cal.

All infants in our center with severe respiratory distress syndrome who have required artificial ventilation with 80–100% O<sub>2</sub> for more than 5 days have shown abnormalities in the lungs with characteristic radiologic findings and prolonged hypercarbia following extubation. Microscopic examination of lung sections of 13 infants who died revealed hypertrophic bronchial mucosal glands and necrotic bronchial epithelium blocking some of the fine airways. The known tendency of the small airways of an infant to collapse and the microscopic appearance of the lung suggested that after extubation vigorous pulmonary drainage might be of value. To prevent this complication rapid graded weaning from the ventilator is now attempted and following extubation, postural drainage, chest percussion, vibration, and tracheal suction under direct vision are performed at first hourly, decreasing to daily intervals by the third day.

8 infants (1700–2020 g) maintained on a respirator for 5 to 17 days but not receiving intensive pulmonary physiotherapy, still had evidence of pulmonary disease 2–18 months after extubation. 3 infants (1700–2500 g) who received intensive pulmonary drainage after being on the respirator for 2 ½, 6 ½, 7 ½ days had no apparent pulmonary disease 18, 27, 30 days after extubation. 6 infants (860–4000 gm) with respiratory failure associated with other diseases who were maintained on a ventilator for 1–2 days and who were also treated with intensive suctioning following extubation, recovered promptly. These observations suggest that some of the complications of prolonged artificial ventilation with high O<sub>2</sub> concentrations may be preventable. (SPR)

86 *The Prevention of Prolonged Apnea as a Complication of Prematurity.* WILLIAM J. DAILY\*, H. BELTON P. MEYER\* and MARSHALL KLAUS, Stanford Univ. Sch. of Med., Palo Alto, Cal.

Hypoxia secondary to apnea has been suggested as one cause of neurological abnormalities in surviving premature infants. If hypoxia is, in part, responsible for brain damage, prevention by a simple and reliable

means would be important. Using an impedance plethysmograph incorporating an alarm system the respiratory patterns of 15 normal premature infants and 7 infants recovering from the respiratory distress syndrome (RDS) weighing 862–2552 gm have been continuously monitored for 5–16 days. In 7 infants we obtained simultaneous ECG tracings. The duration of apneic periods >30 s, ECG changes, and arterial blood gases were measured and the appearance of the infant and the nature of the stimulus required to re-initiate respiration was recorded.

A total of 217 apneic periods of >30 s were observed in the 22 infants. 6 infants (3 with healing RDS) had >10 apneic episodes. Apneic periods began at end expiration and were rare in infants weighing >1750 g. More frequent apneic periods at higher incubator temperatures were sometimes noted. When simultaneous ECG tracings were obtained marked cardiac slowing was noted within 10–15 s of the onset of apnea. Bradycardia (<100) ensued within 20–30 s. Prolonged apnea (>30 s) was associated with suggestive evidence of hypoxia (loss of muscle tone, cyanosis and mottling) whereas apnea of <20 s duration was not. This study suggests apnea is more frequent than previously noted and is poorly tolerated after 20 s. Utilizing an apnea alarm, hypoxia with resultant brain damage may be prevented. (SPR)

87 *Squamous Metaplasia and Necrosis of Trachea and Larynx after Nasotracheal Intubation of Premature Infants.* PAUL SYMCHYCH\*, MARCEL CADOTTE\*, RITA FOJACO\* and WILLIAM BLANC, Columbia Univ., and Babies Hosp., New York, N.Y.

Unrecognized hazards of intubation to laryngeal function have not been emphasized in the newborn and the cause of difficulties encountered at extubation are not clear. We examined at autopsy the trachea of 13 infants with respiratory distress, aged 14 to 98 days, who had been intubated for 9 to 44 days. Extensive diffuse necrosis of the mucosa, at times of cartilage rings, was seen in 4, multifocal squamous metaplasia in 2 and diffuse metaplasia in 6. These changes, related to decubital ulceration by a tightly fitted tube, and chronic irritation, explain the inability of the trachea to remove bronchial secretion after extubation. The spectrum of early and late changes was followed in 25 larynxes. Besides known alterations such as ulcers, metaplasia and granulomas, there were deep lesions attributed to compression of vessels between the tube and the cartilages. Most striking was the necrosis and atrophy of intrinsic laryngeal muscles, even with a relatively preserved mucosa. This might well lead to permanent laryngeal dysfunction. (SPR)

88 *Acetylcholine in the Treatment of Idiopathic Respiratory Distress Syndrome.* A.N. MOGHADAM\*, ESHAGH ESHAGHPOUR\*, LEONE MATTIOLI\* and MARGARET L. WILLIAMS\*, Department of Pediatrics, University of Pennsylvania School of Medicine and Philadelphia General Hospital, Philadelphia, Pa. (introduced by Lewis A. Barness).

In view of direct observations confirming low pulmonary blood flow in the idiopathic respiratory distress syndrome (IRDS) considerable interest in therapy directed toward relief of pulmonary hypoperfusion has been stimulated. Reports of the efficacy of infusin vasodilating agents have been conflicting to date. In the present study, infusions of acetylcholine (25–100 mg/