maintained in a 'neutral' thermal environment from ages 4 to 140 hours. Infants were fasted till after the 12–20 hour sample when feedings were begun. Mean values ($\pm$ SD):

Age	pH	PaCO ₂	BE
4–6	7.32 (0.01)	38 (1.00)	–5.6 (0.6)
12–20	7.34 (0.10)	34 (1.60)	–6.1 (0.5)
24–30	7.37 (0.01)	32 (0.90)	–5.6 (0.4)
36–42	7.39 (0.02)	32 (1.67)	–5.1 (0.4)
Age	FFA	Ketones	Glucose
4–6	0.99 (0.16)	0.7 (0.23)	48.4 (4.1)
12–20	1.32 (0.12)	0.87 (0.12)	60.0 (5.3)
24–30	1.29 (0.12)	1.12 (0.21)	55.9 (9.3)
36–42	0.90 (0.08)	0.85 (0.15)	62.8 (3.4)

A significant increase in FFA ($p < 0.001$) and ketones ($p < 0.05$) occurred in fasting infants at age 12–18 h despite an increase in glucose ($p < 0.001$). Linear correlation existed between ketones and FFA ($y = 3.4 [\text{FFA}] + 0.7$; $r = 0.48$; $p < 0.01$). FFA varied independently of glucose. Acid-base parameters bore no correlation to the energy substrates. FFA and ketones fell to initial levels by 36–42 h; glucose remained at 62 to 67 mgms % to age 6 days. The data indicates that premature infants at neutral temperature and in a normal acid-base state rely on lipid substrates during the first 5 days of life despite adequate blood glucose concentration. (SPR)

- 77 *Ketotic Hypoglycemia: The Effect of Beta-Hydroxy Butyrate (β -OHB) Infusion and Heparin-induced Ketosis.* HENRY S. SAULS*, Univ. of Minn. Med. Sch., Minneapolis, Minn. (introduced by Robert A. Ulstrom).

Cause and effect are implied in the term 'ketotic hypoglycemia' used by COLLE and ULSTROM (J. Ped. 64: 632 [1964]) to describe a childhood syndrome of hypoglycemic convulsions associated with ketonuria. MADISON (J. clin. Invest. 43: 408 [1963]) showed a stimulatory effect of ketones on insulin secretion and postulated this as a feedback mechanism to prevent fatal ketosis. Two techniques to induce ketosis were used to study patients with ketotic hypoglycemia: 1. β -OHB was infused intravenously during a 2 to 6 hour period; 2. Heparin was injected intramuscularly to promote lipolysis. Patients fasted throughout the test period. The response of patients and control subjects was compared to a control day when no heparin was given. Blood sugar (BS), immunoreactive insulin (IRI), non-esterified fatty acids (NEFA) and ketones were measured. β -OHB caused a slow decline in BS at a rate more rapid than with starvation alone. Insignificant increases in IRI ($\bar{x} 9 \mu\text{U}$) within 60 minutes were seen in 3 patients whereas the values of a control subject rose $65 \mu\text{U}$ within 20 minutes. Patient's values remained low throughout the test period in spite of progressively increasing ketosis. After the initial rise and fall, IRI slowly increased in the control subject at the 4th, 5th and 6th hours of infusion.

A 16-hour fast did not cause hypoglycemia in patients or control subjects. With heparin, NEFA and ketones increased to high levels. Three of 4 patients became hypoglycemic by the 16th hour ($\bar{x}$ BS 21 mg %). Failure of two patients to respond to i.v. glucagon suggests depleted liver glycogen. IRI levels were low throughout the test periods. Hypoglycemia may be due to failure of ketone stimulation of insulin production with concomitant preservation of liver glycogen. (APS).

- 78 *Galactose-1-Phosphate Accumulation in Red Cells of a Neonate.* RUTH C. HARRIS and STANLEY V. ISBELL*, Columbia Univ., College of Physicians and Surgeons, New York, N.Y.

SCHWARTZ, HOLZEL and KOMROWER have demonstrated high levels of galactose-1-phosphate in tissues of newborns deficient in galactose-1-phosphate uridyl transferase activity. Following their recommendations to maintain a known heterozygotic pregnant mother on a galactose free diet, we examined the cord blood of a galactosemic infant. The levels of galactose-1-phosphate were found to be approximately four times normal. At age of ten days, the infant's red cell content of galactose-1-phosphate had increased to seven times normal, even though he was on a galactose free diet. Over the ensuing five weeks, the levels slightly decreased. Intravenous administration of galactose-1-phosphate uridyl transferase in 35 ml of packed normal red cells resulted in prompt disappearance of galactose-1-phosphate and decrease in liver size. Studies of maternal galactose levels in another pregnant woman as well as evaluation of maternal and newborn lactation are in process. (SPR)

- 79 *Prolonged Infusion of the Small Intestine of the Rat with Dilute Solutions of Lactic Acid.* J. RICHARD HAMILTON*, Dept. Ped., Univ. Toronto, Res. Institute, Hosp. for Sick Children, Toronto, Canada (introduced by Donald Fraser).

Using a new technique for the continual infusion of solutions into the jejunum of small animals, dilute solutions of lactic acid (2.0 g %–3.5 g %) were infused into the rat for 10 days and their effect on fat absorption and mucosal structure assessed. Thirty-five rats were studied in 5 groups. Control rats (water infused) ate well, gained weight, excreted normal amounts of fat (2.9 ± 1.9 %) and showed no abnormality of mucosal structure (villous length $465 \pm 35 \mu$). Although dilute acid (2.0 g %) produced no abnormality, groups infused with more concentrated acid did show significant increases in fat excretion (Lactic acid 2.5 %– 6.5 ± 2.1 %; 3.0 g %– 7.2 ± 2.1 %). Lesions of the mucosa were found localized to the site of infusion in both of these groups, characterized by shortened villi (2.5 g %– $276 \pm 95 \mu$, 3.0 g %– $266 \pm 56 \mu$) and some epithelial cell derangement at the villous tips. In some rats, fusiform extrusions of epithelial cells were seen at villous tips indicating abnormal turnover of these cells. Rats infused with 3.5 % lactic acid died within 72 hours from intestinal perforation at the infusion site. The findings suggest that the effects observed were due directly to the acid infusions and not secondary to factors such as undernutrition or altered intestinal microflora. The observations made may not be specific for lactic acid, but they do demonstrate that intraluminal factors may impair fat absorption and mucosal structure. In this experiment, the particular factor used is an organic acid that is present in the human intestinal lumen. The infusion technique may be a valuable experimental model for future studies of the malabsorptive state. (SPR)

- 80 *Stimulation of Active Intestinal Transport by Actinomycin D.* CONSTANTINE S. ANAST, LUCILLE F. ADAMSON* and JOAN A. FOLWELL*, Univ. of Mo. Sch. of Med., Columbia, Mo., and Harvard Med. Sch., Boston, Mass.

It is well known that actinomycin D, an inhibitor of DNA directed RNA synthesis, alters enzyme activity.

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 μ 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 New-born 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° 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% O₂ was only partially successful for animals exposed for 1 1/4 X 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° all of these changes took place at a slower rate than in warm littermates. In coenothermic animals (37°) 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).