effect on Ca^{++}. The clinical significance of this observation requires further evaluation.

Controlled clinical trial of phenobarbital (PB) and light for management of neonatal hyperbilirubinemia in a predominant Negro population. O. S. VALDES, H. M. MAURER, C. N. SHUMWAY, D. DRAPER, and A. HOSSAINI. *Med. Coll. of Virginia, Richmond, Va.* (Intr. by W. E. Laupus).

Low birth weight infants, less than 24 hrs of age, were randomly assigned to receive either oral PB, 5 mg/kg/day for 5 days, blue light (200–300 footcandles) continuously for 4 days, a combination of PB and light, or no treatment. 90% or more of the infants in each group were Negroes. Infants with a positive Coomb's test were excluded.

	No.	Total serum bilirubin concentration, mg% (mean ± S.E.)					
		day 1	day 2	day 3	day 4	day 5	day 6
Control	15	2.4±0.5	5.0±0.7	8.0±0.8	8.2±0.8	8.0±1.0	6.7±1.2
PB	23	2.4±0.4	4.0±0.5	5.1±0.6	5.5±0.7	5.6±0.7	4.7±0.8
Light	19	1.9±0.5	3.1±0.6	3.4±0.7	3.0±0.7	3.4±0.8	2.9±1.0
PB + light	18	2.0±0.5	3.3±0.6	3.6±0.7	3.7±0.8	3.4±0.9	3.2±0.9

By the 3rd day, infants receiving PB, light, and PB and light had significantly lower mean bilirubin concentrations than the controls. Those receiving light had the lowest values. Combining PB with light did not have an additive effect. Bilirubin concentrations of 10 mg% or higher were found in 66% of the controls, 26% of the PB group and in none of the other 2 groups. Mild lethargy occurred in 5 infants receiving PB and mild diarrhea occurred in 2 receiving light. The findings indicate that in Negroes continuous phototherapy is more effective than PB in lowering the serum bilirubin concentration. Results are not improved by combined therapy. PB may be useful when phototherapy is not available.

Hepatic metabolism and transport of bilirubin during physiologic jaundice in the newborn rhesus monkey. LAWRENCE M. GARTNER and DONNA LANE. *Albert Einstein Coll. of Med., N. Y., N. Y.*

Maximal hepatic uptake, conjugation and excretion of bilirubin was studied simultaneously in 12 newborn rhesus monkeys ranging in age from 4 hours to 19 days. In this model of human physiologic jaundice, maximum serum bilirubin concentrations prior to infusion of bilirubin were 4.5 mg/100 ml between 12 and 36 hours of life and less than 1.0 mg/100 ml by 48 hours. Endogenous bilirubin excretion in bile in monkeys 12 hours to 19 days of age was 2 to 10 times greater than in normal adult rhesus monkeys. During the first 36 hours of life maximal cumulative hepatic uptake of bilirubin was 35% of adult capacity; hepatic conjugation of bilirubin *in vitro* and *in vivo* was 5% of adult capacity; and hepatic excretory capacity was 10% of adult capacity. Each of these functions increased rapidly to adult levels by the fourth day of life. The rate-limiting step in the transfer of bilirubin from blood to bile at 12 to 36 hours of age is the capacity to conjugate bilirubin with glucuronic acid. In the period immediately following this, significant accumulation of direct-reacting bilirubin occurs in liver and sera during infusion of unconjugated bilirubin, indicating that excretion is the rate-limiting process after 36 hours of age. These studies suggest that physiologic jaundice results from a markedly increased load of bilirubin presented to the liver either from increased bilirubin synthesis or enhanced intestinal reabsorbtion and marked limitation in the capacity to conjugate.

Studies performed at 4 hours of age in a monky born 2 weeks post-maturely revealed that hepatic transport and conjugation of bilirubin was fully mature, indicating that maturation of each of these functions may occur in utero.

A controlled study of intravenous fibrin hydrolysate supplement in prematures <1.3 kg. M. HEATHER BRYAN, PATRICK WEI, RICHARD HAMILTON, SANFORD H. JACKSON, INGEBORG C. RADDE, GRAHAM W. CHANCE, and PAUL R. SWYER. *Univ. of Toronto and The Research Inst., The Hosp. for Sick Children, Toronto, Ont. Canada.*

We have compared the effect of early supplemental intravenous 3.5% fibrin hydrolysate plus 10% dextrose to 10% dextrose alone on the mortality, morbidity, weight gain and biochemical changes in 2 equal groups of 15 low birth weight infants of appropriate gestation. The initial alimentation was intravenous with gradual replacement by oral formula over the first 2 weeks of life. Total fluid intake of 200 ml/kg/day was maintained. Total caloric intake and urinary output did not differ between groups. The amino acid infants received twice the amount of protein (g/kg/day) as the controls. Mortality did not differ between groups when infants were assessed by body weight. In the survivors apnoea was significantly less frequent in those receiving amino acid and regain of birth weight more rapid. Total protein and BUN were higher in those on amino acid reflecting increased N_2 intake, and serum PO_4 lower. Serum electrolytes, sugar, osmolality, HCO_3 did not differ. Fatal cases in the amino acid group, many <1.0 kg, exhibited an excessive rise in BUN, and high plasma osmolality within 3 days of infusion.

	Cals/kg/day		Mortality		Regain of birthweight in survivors
	oral	IV	1.0–1.3 kg	<1.0 kg	
Amino acid	79	30	2/8	5/7	14 days
Control	84	21	2/12	2/3	22

Fetal-maternal metabolic fuel adaptations to caloric deprivation in human pregnancy. YOUNG J. KIM, VINCENT LYNCH, and PHILIP FELIG. *Yale Univ. Sch. of Med., New Haven, Conn.* (Intr. by Charles D. Cook).

Although glucose is considered the sole metabolic fuel utilized by the fetus to meet its energy requirements, induction of ketone-oxidizing enzymes in fetal brain tissue has recently been demonstrated in experimental animals fasted during pregnancy. The significance of such enzyme induction to fetal fuel economy is dependent ultimately on substrate availability. To examine the latter during caloric deprivation in human pregnancy, 14 physically healthy pregnant women (PW) undergoing theraputic abortion for pychiatric reasons during week 16–22 of gestation and 6 non-pregnant women (NP) were fasted for 84 hours. In PW, blood β-OH-butyrate and acetoacetate rose to 4.2 and 0.9 mM/L respectively, and were 2–3 fold higher than in NP for the first 60 hours of the fast. Throughout the fast plasma glucose was significantly lower ($P < .005$) in PW falling to 47 ± 1 mg%, 25% below NP levels. Maternal

ketonemia and hypoglycemia influenced fetal substrate levels as reflected in amniotic fluid obtained at termination of the fast and from 11 additional non-fasted PW. Ketone acid levels in amniotic fluid increased 30–40 fold in fasted PW to levels comparable to maternal blood (4–5 mM/L); glucose levels in amniotic fluid in fasted PW (21 ± 1 mg%) were 40% below those in non-fasted PW ($P < .001$). In contrast, free fatty acid levels in amniotic fluid were not consistently increased by starvation though markedly elevated in maternal plasma. Conclusions: Pregnancy accelerates and exaggerates the ketogenic and hypoglycemic response to starvation. Increased ketone availability to the conceptus suggests that ketones become an important metabolic fuel for the fetus during maternal caloric deprivation.

Hyperammonemia complicating parenteral nutrition in infants. J. JOHNSON, W. L. ALBRITTON, and P. SUNSHINE. *Stanford Univ., Stanford, Calif.*

The parenteral administration of protein hydrolysate-glucose mixtures is being used increasingly to prevent tissue catabolism and promote growth in infants with various conditions which preclude adequate ingestion or absorption of calories. Although nitrogen retention can be regularly attained, several complications have been reported.

We have found elevated blood ammonia levels in 5 of 6 infants receiving parenteral nutrition. In 4 of these infants, blood ammonia was >200μ g%. All 3 low-birth weight infants in the series developed hyperammonemia. Elevations of blood ammonia were seen during the infusion of either casein or fibrin hydrolysates. In 2 infants receiving long term infusions the level of blood ammonia correlated directly with the rate of infusion of protein hydrolysate whereas blood urea nitrogen levels did not change significantly. Elevations of serum transaminases and bilirubin accompanied hyperammonemia in 3 patients.

These data show that hyperammonemia is a common biochemical abnormality in newborn infants receiving parenteral nutrition with casein or fibrin hydrolysates at commonly employed infusion rates. Liver cell damage may accompany this mode of nutrition. The cause of hyperammonemia is unknown, but may be the result of an amino acid imbalance in the infusate.

The association of hypocalcemia with recurrent apnea of prematurity. JUAN J. GERSHANIK, ABNER H. LEVKOFF, and ROBERT DUNCAN. *Med. Univ. of South Carolina, Charleston, S. C.* (Intr. by Warren E. Wheeler).

Serum calcium, phosphorus, magnesium and total proteins were determined at 8 hour intervals during the first 48 hours of life in 27 neonates weighing under 1750 grams at birth, who were monitored for apnea. 14 babies developed recurrent apnea during the first 72 hours of life. The remaining 13 neonates had no distress. None of the 27 babies received calcium during the period of sampling. Calcium values were grouped into 9 consecutive 5 hour intervals and the mean value of the calcium levels in each interval was plotted using the mid-point of the 5 hour interval for time. Using the standard polynomial regression for a quadratic response, the apneic subjects showed a decrease in calcium values to a level of 5.9 mgm./100 ml. at 32 hours of age. The minimum mean calcium value for the non-apneic babies was 8.3 mgm./100 ml. at 32 hours of age. Apneic babies had higher phosphorus values and lower total serum proteins than the non-apneic babies. Recurrent apnea was associated with an increased maternal age and a higher incidence of previous abortion. Apneic babies had higher incidence of 1 min. Apgar below 5 (75% vs. 30%). Apneic spells developed in most of the cases during the first 24 hours of life (22.1 hours average). Thus, for the most part the onset of apnea precedes the development of hypocalcemia. Calcium urinary losses were similar in both groups. Calcium therapy appeared to reduce the number of apneic spells in 6 out of the 14 infants.

Low arterial oxygen tension: A primary event leading to periodic breathing and apnea in preterm infants. HENRIQUE RIGATTO, JUNE BRADY, FE DUMPIT, and WARREN TICKNOR. *Univ. of Calif., San Francisco, Calif.*

Nine babies (b.w. 1-2kg) were studied 38 times in the first 35 days of life. They were given 21, 19, 17 and 15% O_2 to breathe for 5 min each, then 21, 15 and 21% O_2 for 5 min each. We determined the incidence of periodic breathing, ventilation/apnea (V/A) time ratio, respiratory minute volume and frequency, heart rate, P_{AO_2} and P_{ACO_2}, and the P_{CO_2}, P_{C_2} and pH of arterialized blood. With 15% O_2 the incidence of periodic breathing was substantially increased (see Table); with 17% O_2 the incidence was less pronounced but significant ($P < .005$).

	Periodic breathing	V/A ratio	VE L/min/kg	Resp. Rate	Heart Rate	$PaCO_2$	$PACO_2$	PaO_2	PAO_2	pH
21% O_2	13%	2.0 ± .2*	.231 ± .017	36 ± 2	146 ± 2	42 ± 1	35 ± 1	68 ± 1	107 ± 2	7.319 ± .008
15% O_2	71%	1.4 ± .1	.192 ± .015	30 ± 2	151 ± 2	44 ± 1	35 ± 1	56 ± 1	69 ± 2	7.332 ± .008
P	<.005	<.005	<.025	<.005	<.005	<.001	>.05	<.001	<.001	>.05

Means ± SE.

* At onset of periodicity (baby breathing 21, 19 or 17% O_2).

In 3 babies the oscillations in oxygen saturation (ear oximeter) increased from 4% during 21% O_2 to 12% during 15% O_2. One baby became apneic (>20 sec) after prolonged periodic breathing with marked hypoventilation and low V/A ratio. These findings suggest that decreased P_{aO_2} may be a primary event leading to hypoventilation, periodic breathing and apnea in the preterm infant.

Visual estimation of body temperature in neonates. THOMAS K. OLIVER, JR. and ROBERT T. HALL. *Univ. of Pittsburg Sch. of Med., Pittsburgh, Pa., and Univ. of Missouri Sch. of Med., Columbia, Mo.*

Abdominal skin temperature of human neonates who are dressed and blanketed closely approximates core temperature. Although valuable in the detection of such illnesses as sepsis and hypoglycemia, the low yield of detecting abnormalities in term infants has resulted in temperature being measured at widely spaced intervals in most nurseries. This report describes a way of visually estimating body temperature using the cholesteric phenomenon. A mixture of cholesteric crystals was formulated