● **666** MECHANISM OF BILE ACID-INDUCED HEMOLYSIS. David G. Oelberg, Jeffrey W. Sackman, William P. Dubinsky, Eugene W. Adcock, and Roger Lester. Univ. of Tex. Med. Sch., Depts. of Int. Medicine, Pediatrics, and Physiology, Houston, Tx.

Hemolysis associated with liver disease may be partly induced by bile acids (BA). Since it occurs at concentrations below BA CMC's, it is probably not entirely due to RBC membrane solubilization. We studied the hemolytic effect of two cytotoxic (lithocholic acid sulfate and glucuronide (LCS, LCG)), and two non-cytotoxic (taurolithocholic acid sulfate and taurocholic acid (TLCS, TC)) BA's on human RBC's (0.75 μM BA, HEPES buffer, pH 7.4, 37°). LCS and LCG increased hemolysis over controls by 200-500%; TLCS and TC had no significant effect. Presence of calcium (Ca) chelator EDTA reduced hemolysis by LCS by one-half, and completely blocked LCG-induced hemolysis. ^{45}Ca uptake by RBC's exposed to LCS increased 40 x over controls, and further increased 3-fold by the addition of Stelazine, 1 μM, a known inhibitor of RBC Ca efflux. Neither TC nor Stelazine alone affected uptake. Conclusions: (1) LCS and LCG have a selective hemolytic effect not exhibited by TLCS and TC; (2) this hemolysis is prevented by EDTA and is associated with ^{45}Ca uptake. Working hypotheses: (1) In view of the known relations between cell toxicity and Ca uptake, BA-induced hemolysis may be Ca mediated; (2) cytotoxic BA's may generate Ca-permeating channels, as has been shown for BA-exposed black lipid films; (3) RBC's may prove a readily available and easily manipulated model for the study of BA-cell interactions.

† **667** FUNCTIONAL ENTERO-INSULAR AXIS IN THE NEWBORN. Anita Oliven and Katherine C. King, Case Western Reserve University at Cleve Metro Gen Hosp, Dept. of Peds, Cleveland, Ohio.

In adults, plasma immunoreactive insulin (IRI) response to oral glucose is enhanced by hormones of the enteroinsular axis, provided an increment plasma glucose (ΔPG) of >20 mg/dl occurs. Previously we failed to demonstrate a gastrointestinally (GI) enhanced insulin response in newborns (J. Peds 91:783) infused with glucose at 12 mg/kg.min. However, the PG rarely raised to levels above 100 mg/dl. The purpose of the present study is to re-evaluate the IRI response to orogastric (OG) vs intravenously (IV) infused glucose into newborn infants with infusion rates aiming to achieve comparable elevations of PG levels. At age 36-90 hrs, after 4 hr fast, 19 term infants, paired by birthweight categories of appropriate, small or large for gestational age, were infused with glucose at 16 mg/kg.min OG (n=10) or 8 mg/kg.min IV (n=9) for 2 hrs. Serial blood samples for PG and IRI were obtained at 15-30 min intervals for 3 hr. Peak PG were 107±21 mg/dl (M± S.D.) at 30-90 min of IV and 114±17 mg/dl at 60-120 min of OG infusion, while peak IRI were 18±9 μU/ml (IV) vs 42±17 μU/ml (OG)($p<0.001$) at 30-90 min and 90-150 min respectively. ΔPG were 50±19 mg/dl in the IV and 52±17 mg/dl in the OG infusion groups. Similar patterns of responses occurred in all weight categories. Concl: 1) The newborn has an enhanced insulin response to GI infused glucose, suggesting the presence of a functional entero-insular axis, 2) This enhanced insulin response will only occur with an adequate increment of plasma glucose.

668 ESOPHAGEAL STRICTURE DILATATION IN AWAKE CHILDREN. Susan R. Orenstein, Peter F. Whitington. University of Tennessee Center for the Health Sciences, LeBonheur Children's Medical Center, Department of Pediatrics, Memphis.

Dilatation of pediatric esophageal strictures has usually been performed in the hospital during general anesthesia. Over a four-year period, we performed 211 dilatations in 13 pediatric patients (ages 15mo-14yr, median 3yr) in the outpatient department without anesthesia; 72% were performed without any sedation. Strictures' etiologies were simple peptic (2), anastomotic after esophageal atresia repair (5), anastomotic after stricture resection or colon interposition (3), and undetermined (due to nasogastric tube, chronic vomiting, or chemotherapy, 2). Increases in esophageal lumen diameter (to at least 36Fr in 12 patients, 40Fr in 6) and in tolerance of food boluses occurred in all of the children. Growth accelerated in 5/10 who were below the 10%ile and remained parallel to the curve in 5/10. Six strictures are resolved (after 4-27 procedures over 4-24mo); four require dilatation twice-yearly (after 3-13 dilatations over 10-29mo); and three still undergo dilatation at intervals less than five months (after 11-62 visits over 2-33mo). Dilatation without anesthesia or sedation was preferred by all of the parents and by those children old enough to express a preference. Estimated reduction of medical costs by more than $100,000 were realized. No episode of perforation, significant hemorrhage, documentable aspiration, or neurologic complication occurred. Outpatient dilatation without anesthesia is an effective method of treating esophageal strictures in children.

669 HIGH DOSE SUPPLEMENTATION WITH BETA-CAROTENE: ITS EFFECT ON SERUM LEVEL OF VITAMIN A & LIVER FUNCTION IN RABBITS. Enrique M. Ostrea, Jr. and David Kroll. Wayne State University School of Medicine, Hutzel Hospital, Department of Pediatrics, Detroit.

Beta-carotene is an avid singlet oxygen radical quencher and hence a strong antioxidant. Its use has therefore been tried or suggested in conditions where oxygen toxicity is encountered, viz erythropoietic protoporphyria, pulmonary oxygen toxicity in newborns, etc. Because of the possible risk of Vit A and liver toxicity, with β-carotene supplementation, we studied the effects of prolonged (1 month) administration of high dose β-carotene on the serum level of Vit A and liver functions in rabbits. MATERIALS/METHODS: Beta-carotene (Roche) was given (through the water) to 3 fullgrown white rabbits at a daily dose of either 0.5, 1.0, or 1.5 mgs/kg body weight. Serum was drawn 2x weekly and analyzed for levels of β-carotene and Vit A and liver enzymes (SGOT and SGPT). RESULTS: Pre-treatment (control) serum values: β-carotene = 0.100 ± 0.041 mgs/dl; Vit A = 76 ± 42 μgs/dl; SGPT = 26 ± 4 units; SGOT = 21 ± 10.6 units. Within 1 week of treatment, β-carotene serum level attained steady state at concentrations > 10x control value (total mean = 1.36 ± 0.38 mgs/dl) with the mean concentrations in each animal at steady state (0.957 or 1.497 or 1.626 mgs/dl wherein 0.957 vs 1.497, $p < 0.005$; 1.497 vs 1.626, NS) directly related to the dose regimen. Likewise, the serum Vit A level attained steady state concentration at 2x control level (total mean = 137.8 ± 30.9 gs/dl, range = 66-175); however, the mean concentration in each animal at steady state was unrelated to the dose regimen. A slight rise in SGPT (33.9 ± 24.9 units) and SGOT (35 ± 37 units) occurred. After discontinuance of treatment, serum levels of Vit A and β-carotene approached control level after 1 and 2 weeks, respectively, and the liver enzymes, after 3 weeks. CONCLUSION: High dose treatment (optimum dose = 1.0 mg/kg) with β-carotene safely produces high serum levels of β-carotene (> 10x control) without the danger of hypervitaminosis A or liver injury. A return of the serum values to control level was noted within 1-3 weeks after the discontinuance of treatment.

670 INFANT FEEDING AND GROWTH, George M. Owen, Philip J. Garry, Elizabeth M. Hooper. Clinical Nutrition Laboratory, University of New Mexico, Albuquerque, and Bristol-Myers Company International Division, New York, N.Y. 10154.

This prospectively designed study was done to evaluate growth of 133 healthy full-term infants who received breast milk (B) or infant formula (F) as essentially the only source of calories during the first 6 months of life and who were followed through age 9 months. By analysis of variance, both sex and feeding had significant effect on gains in length and weight ($p < 0.01$). Weight-for-age centiles (WAC) and length-for-age centiles (LAC) were computed using NCHS reference data and are summarized for B and F infants by age (mos):

	Birth	3	6	9
WAC				
B	48.9	53.3	34.4	25.8
F	50.2	57.3	46.8	48.2
LAC				
B	43.1	47.9	38.7	34.4
F	45.6	54.4	50.3	49.3

NCHS reference data, based principally on formula-fed infants who received solid foods in the early weeks of life, may not be entirely appropriate to evaluate growth of today's infants breast-fed according to current recommendations.

671 IMMUNOLOGIC FUNCTIONS IN CHRONIC ACTIVE HEPATITIS (CAH) OF CHILDHOOD. S. Pahwa, L. Duffy, J. Fagin, F. Daum, M. Silverberg and R. Pahwa. Cornell University Medical College, North Shore University Hospital and Memorial Sloan Kettering Cancer Center, Depts. Of Peds., Manhasset and New York City.

Immunologic mechanisms are believed to play an important role in Hepatitis B surface antigen (HBsAg) negative CAH. We investigated immune functions in 5 females aged 10-15 years who had biopsy proven diagnosis of CAH with or without cirrhosis. At the time of study, all patients were on therapy consisting of Prednisone alone or in combination with 6 MP or Azathioprine. Enumeration of total T cells and T cell subsets using Ortho monoclonal antibodies OKT3, T4, T8 and T11 were within normal ranges in 4/4 patients tested. Proliferative responses of lymphocytes to mitogens phytohemagglutinin, concanavalin A and pokeweed were normal in all. Differentiation of B lymphocytes into immunoglobulin secreting cells in response to polyclonal stimuli pokeweed mitogen (T-dependent), Epstein Barr virus (T-independent) and to S. aureus Cowan 1 strain (SAC), a selective B cell mitogen which requires T cell help for B cell differentiation were severely depressed in 4/5 patients. Specific antibody responses in an antigen specific assay system were also depressed in these same patients. Dysfunction of B cells in vitro might result from a paucity of resting B cells in peripheral circulation consequent to hyperactivity of B cells in vivo which is manifested as hypergammaglobulinemia in this disorder. In CAH, functional assays of B cells might be more sensitive indicators of immune aberration than previously reported abnormalities of T cell subsets and function.