542 BILIARY EXCRETION OF INTACT PROSTAGLANDIN $F_{2\alpha}$ AFTER GASTRIC ADMINISTRATION IN RATS: DEVELOPMENTAL DIFFERENCES. Alan D. Bedrick, Michael A. Wells, Debra L. Ford, Otakar Koldovský. Univ. of AZ, Depts. of Pediatrics, Biochemistry, Physiology, Tucson, Arizona 85724

Prostaglandins present in milk are absorbed from the gastrointestinal tract, and transported to the liver in an intact form in immature rats (Biol Neonate 48:351, 1985). To determine possible biliary excretion of $PGF_{2\alpha}$ and metabolites, we administered 2μCi of 3H-$PGF_{2\alpha}$ (PGF) via orogastric tube to suckling (SU- 12 days old) and weanling (WE- 33 days old) rats with bile cannulae. Animals were sacrificed 2 hours after PGF administration. Radioactivity present in bile (BL) was analyzed quantitatively by determining the percent of administered radioactivity recovered (ARR) and qualitatively by column and thin layer chromatography. Per 100 g body wt., BL from WE contained nearly 4 times as much ARR compared to SU (16.8 ± 4.1%, 6 (Mean ± SEM, N) vs 4.4 ± 0.5%, 5; $p < 0.01$). However, per unit volume of BL, SU contained more counts present as unmetabolized PGF (33.1 ± 2%) than WE (21.4 ± 1.5%, $p < 0.01$). The amount of intact PGF present in BL as a percent of the administered dose was 3.5 ± 0.9 in WE vs 1.4 ± 0.2, in SU ($p < 0.05$). SU had more radioactivity as polar metabolites, while WE had greater amounts as less polar compounds. WE BL contained more radioactivity as stable PGF metabolites than SU BL. Conclusions: This study establishes the enterohepatic circulation of intact, milk-derived prostaglandins. Additionally, developmental differences are present in the hepato-biliary excretion of PGF. The enterohepatic circulation of prostaglandins in bile may contribute to the overall content of cytoprotective prostaglandins in the small intestine.

543 VITAMIN E DEFICIENCY IN EARLY ONSET LIVER DISEASE AFFECTS MENTAL DEVELOPMENT. William Belknap, Sunita Stewart, Ricardo Uauy, Betsy Kennard, Margareta Benser, David Waller, and Walter Andrews (spon. by J. Warshaw). Univ. of Texas, Depts. of Pediatrics and Psychiatry, Dallas, Texas

We compared mental function and growth in 10 children (ages: 5-13 yrs) with end stage liver disease whose onset was in the first year of life ($\bar{x}$ age onset 0.3 yrs; range 1-12 months). Five children had chronic cholestasis: bilirubin 27±8 mg/dl, vitamin E 0.8±0.7 μg/ml, albumin 2.9±.5 g/dl; the other five were not cholestatic: bilirubin 1.5±.8 mg/dl, vitamin E 12.4±6.5 μg/ml, albumin 3.8±.4 g/dl. Mean age at onset, duration of symptoms, and age at testing were similar at both groups. Wechsler Scales of Intelligence provided Verbal (VIQ), Performance (PIQ) and Full Scale (FSIQ) IQs. Percent of median (NCHS standards) for weight (W) and height (H) for age (W/A, H/A) and W for H (W/H) were also obtained. RESULTS ($\bar{x}$±SD):

GROUPS	N	VIQ	PIQ	FSIQ	W/A	H/A	W/H
High Vit E	5	89±11	92±8	90±8	101±25	95±10	102±13
Low Vit E	5	74±15	74±14	72±15	68±17	78±10	121±30
p (t test)<		.10	.04	.05	.04	.03	.21

Patients with severe vitamin E deficiency scored significantly worse in PIQ and FSIQ; they exhibited stunted early growth but were of normal W/H at the time of study. We conclude that children with early onset liver disease with chronic cholestasis and severe vitamin E deficiency are more likely to have developmental delay and stunted growth.

544 ERYTHROCYTE TRANSKETOLASE ACTIVITY (RbcTK) IN THE OFFSPRING OF DIABETIC RATS. M. Berant, D. Berkowitz, H. Mandel, O. Zinder. Technion Fac Med, Haifa, Israel, sponsored by F. Lifshitz.

The enhanced glucose turnover in the fetus of a diabetic gestation may exhaust fetal thiamine (T) stores. We examined by RbcTK assay the T status in the offspring of streptozotocin-diabetic rats (D) and their controls (C). After mating, D rats were randomly assigned to have either daily SC Insulin Lente IU(DIn) or NS. Immediately after birth a pooled blood sample from each litter was examined for glucose, insulin, and RbcTK. Results (mean±SD):

	C (n=12)	D (n=10)	DIn (n=12)
glucose (mg/dl)	79±13	442±55	86±14
maternal	67±11	43±6	72±8
litter			
insulin (uU/ml)			
litter	4.8±1.2	11.2±3*	6.3±1.8
RbcTK (mU/l/min)			
maternal	66±8	60±4.7	59±12
litter	61.4±7.6	32±5**	52±7

*$p<0.05$ vs C and DIn; β-cell hyperplasia (histology)
**$p<0.001$ vs C and DIn; TPP-28±3.2%
Our study indicates that uncontrolled diabetic pregnancy can cause fetal thiamine deficiency, which may be responsible for some of the clinical features of the "infant of diabetic mother" syndrome.

● 545 IGA IS A BILE DUCT GROWTH FACTOR. Jeffrey Boscamp, Sheila Fallon-Friedlander, Marshall Horwitz, Rachel Morecki, Joy Glaser. Albert Einstein College of Medicine, Dept. of Pediatrics, Bronx, N.Y.

We have discovered a bile duct growth factor (BDGF) in serum which causes non-neoplastic proliferation of extrahepatic bile duct (EHBD) epithelium. BDGF activity was determined after 7 intraperitoneal injections of serum or serum fractions given every other day to BALB/c mice which were dissected for gross and microscopic study of the EHBD. The duct enlargement, up to seven times normal, occurred without luminal obstruction and without other tissue involvement. Early characterization demonstrated that the BDGF was a thermostable protein located in the 33-65% ammonium sulfate (AS) precipitate of serum and susceptible to proteases only after denaturation in 1% SDS. (Hepatology, in press).

The active 33-65% AS fraction was chromatographed on a G-75 sephadex column from which the BDGF eluted at a higher molecular mass than albumin. Affinity chromatography utilizing concanavalin A-sepharose or lentil-lectin demonstrated BDGF activity in the methyl mannoside elute, indicating it was a glycoprotein.

Since the BDGF was also present in bile as well as breast milk and had many of the properties of IgA, we tested chromatographically purified human IgA for BDGF activity. Isolated IgA (2mg/ml) was as active as whole serum while serum depleted of IgA by affinity chromatography produced no BDGF response. Calf serum was also positive for BDGF but fetal calf serum, naturally devoid of IgA, was negative. The only IgA-containing sera without BDGF activity was BALB/c mouse sera. We conclude, therefore, that heterologous IgA is a growth factor for the EHBD. The mechanism by which heterologous IgA enhances bile duct growth is being explored.

546 A ^{13}C-DEPLETED INFANT FORMULA USEFUL FOR METABOLIC STUDIES Thomas W. Boutton, Judy M. Hopkinson, Sara Sekely, Duane Benton, and Peter D. Klein (Spon. by Buford L. Nichols). USDA/ARS Children's Nutrition Research Center, Baylor College of Medicine, Dept of Pediatr, Houston, TX and Ross Laboratories, Columbus OH.

Studies of absorption and bioavailability of nutrients naturally enriched with ^{13}C require accurate measurements of small increases of ^{13}C in respiratory CO_2 and stool carbon. Sensitivity of these measurements would be increased by reducing the natural background of ^{13}C in these excreta. We have developed a ^{13}C depleted infant formula based on lactose, whey, and casein from New Zealand cows which consume only C_3 vegetation naturally low in ^{13}C. This formula, designated $CNRC_3$, was produced by Ross Laboratories and was comparable to a commercial 60/40 whey/casein product. To test the formula's ability to reduce baseline levels of ^{13}C in infant excreta, 10 formula-fed infants 28 to 56 days old and free of metabolic disorders were enrolled in the 9 day study. Two stool samples were collected daily and stored frozen. Infants received their usual formula on days 1 and 2 and were switched to $CNRC_3$ formula for days 3-9. On days 2 and 9, 7 breath samples were collected at 30-min intervals with a face mask. Breath and stool samples were analyzed for ^{13}C content by gas-isotope-ratio mass spectrometry. Infants consuming commercial formula had breath $\delta^{13}C$ values of -21.1 ± 0.6 °/oo over the 3-hr collection period; stool values were -21.6 ± 0.5 °/oo. After 7 days on the $CNRC_3$ formula, $\delta^{13}C$ values of breath declined by 5.6 °/oo to -26.7 ± 0.7 °/oo; stool values declined by 3.8 °/oo to -25.4 ± 0.4 °/oo. The reduced background of ^{13}C achieved in $CNRC_3$ formula can improve resolution of excess ^{13}C in infant excreta by approximately 50%.

547 LUMINAL DIGESTION OF TRANSFERRIN IN SUCKLING AND WEANLING RATS. John R. Britton and Otakar Koldovský, Univ. of Arizona Hlth. Sciences Ctr., Dept. of Pediatrics, Tucson, AZ.

Transferrins (TF) are major milk whey proteins which may function in iron absorption, protection against infection, and cell growth in the gastrointestinal tract. Their potential to perform such roles is dependent upon the degree to which they survive digestion within the gastrointestinal lumen. To evaluate the development of luminal digestion of TF, we measured the hydrolysis of ^{125}I-human TF incubated in vitro with fluid flushed from the stomach and small intestine of 12-day old suckling and 31-day old weanling rats, followed by analysis of radioactivity soluble in trichloroacetic acid. In the stomach, TF degradation at pH 3.2 was minimal in the suckling but increased greater than 20-fold by the time of weaning. In the small intestine at neutral pH, the rate of TF hydrolysis was 10-fold greater in the weanling than in the suckling; in both age groups peak degradative capacity was observed in the mid-jejunum. Corticosteroid administration to suckling rats increased TF hydrolysis in all gastrointestinal segments. We conclude that luminal TF digestion increases with weaning in the rat and that degradative capacity for this protein may be precociously increased by corticosteroids.