877 FOLIC ACID IN THE PREVENTION OF FASTING-INDUCED HYPOGLYCEMIA. Fima Lifshitz, Susan A. Moak and Raul A. Wapnir. Dept. of Peds., North Shore Univ. Hosp., Manhasset, NY 11030 and Dept. of Peds., Cornell Univ. Med. Col., New York, NY 10021.

Since folic acid (FA) in pharmacological doses may affect gluconeogenesis in liver (Lv) and small intestinal mucosa (s.i.m.), we studied the effects of FA in preventing fasting-induced hypoglycemia (Hy). Three groups of male rats 70-90 g were fed diets containing either 18% protein (Pr) with 70% carbohydrate (CHO) (C); 4% Pr with 70% CHO (D); or 4% Pr with 45% CHO (M). Rats from each group were given a daily dose of 20 mg FA p.o. (FA^+), while other rats received no supplement (FA^-). Following 4 wks of treatment, they were either killed or fasted for 48 hr and then killed. FA^+ treatment was associated with higher blood glucose (Glc) after 48 hr of fasting in all groups. C,FA^+ rats maintained a normal blood Glc at the end of the fasting period (means ± SEM: FA^+=81.5±6.6 vs FA^-=47.0±1.8 mg/dl, $p<0.001$). Also, Hy was prevented in the malnourished rats (D,FA^+=47.3±4.9 vs D,FA^-=34.4±4.9, $p<0.05$ and M,FA^+=48.4±4.8 vs M,FA^-=33.9±1.8, $p<0.02$). C,FA^+ rats had a milder ketonemia than C,FA^- after fasting (16.8±2.8 vs 26.8±2.6 mg/dl, $p<0.02$). There were no differences under other conditions. FA^+ treatment induced higher Lv G6Pase and FDPase in all groups following fasting stress; differences being very marked in D and M rats. The G6Pase in s.i.m. also was enhanced by FA, but FDPase was not modified by it. These data suggest that FA affects gluconeogenesis through stimulation of key Lv and s.i.m. enzymes and thus prevents fasting-induced Hy in malnutrition.

878 DYNAMICS OF CALCIUM METABOLISM IN NEWBORNS (NB). Mary O. Lim and James W. Hansen (Spon. by Philip M. Farrell), NICHD, NIH, Bethesda, MD.

The dynamics of calcium (Ca) metabolism in NB are poorly defined although disorders are often encountered. We studied Ca dynamics in NB to improve our understanding of calcium physiology and provide a rational basis for therapy. An injection of radioactive Ca-47 was given to two NB monkeys and Ca-45 administered with each feeding; specific activities were determined in plasma, feces, and urine. Risks of radioisotopes led us to the analogous use of stable Ca-46 and Ca-48 in two low birth weight infants; these were measured by mass spectrometry. Analysis by computer modeling gave the following results in mg/kg/hr.

	Intake	Absorption	Endogenous feces	Urine	Bone Deposition	Bone Resorption	Turnover
Monkey	7.7	2.0(26%)	4.4	.31	3.1	5.8	7.8
Infant	7.0	2.7(38%)	2.6	.05	5.8	5.7	8.4
Adult	.50	.18(36%)	.07	.19	.33	.42	.59

The observed similarities between NB monkeys and humans in their calcium metabolism suggests this laboratory animal is an appropriate model. The exchangeable calcium turnover rate in NB is 14 times the adult rate, and bone calcium dynamics are likewise accelerated. Endogenous fecal Ca loss is also markedly increased in NB despite similarities to the adult in % absorption and urinary excretion. These studies demonstrate the value, safety, and potential of stable isotopes in defining Ca metabolism and disclosing related abnormalities in human infants. We are currently analyzing similar data from infants with short-gut syndrome and isolated dermal ossification.

879 A LONGITUDINAL STUDY OF THE EFFECTS OF VITAMIN D DEFICIENCY IN NEONATAL PIGS: E.T. LITTLEDIKE AND S.B. ARNAUD, NAT. ANIMAL DISEASE CENTER, AMES IA AND MAYO CLINIC, ROCHESTER MN (SPONS. BY G.B. STICKLER).

The effect of vitamin D on the sequential changes in serum calcium(Ca), phosphorus(P) and parathyroid hormone(iPTH) in the first weeks of life is unknown. Two groups of 6 2-3 day old pigs from 4 litters, raised in areas without ultraviolet light, were fed diet (Ca:P, 1.3:1) with (D) or without (-D) vitamin D. Weight, radiographic changes in the long bones and changes in Ca, P, iPTH and 25-hydroxyvitamin D (25-OH-D) were monitored weekly for 5 weeks and 2 weeks following treatment of the -D group with 1000 IU vitamin D_3 daily. Weight gain at 7 weeks was the same in D and -D pigs (3.3 vs 2.9 x baseline). In -D pigs, radiographic changes of rickets were present at 3 weeks, clinical signs at 4 weeks.

A pattern of decreasing values in Ca, P, and iPTH was observed in both groups to the 4th week. Thereafter, in D pigs, Ca and P returned to pre-diet values, and iPTH stabilized at values 50% lower. -D pigs showed greater changes* than D pigs (average mg/dl decrease from initial values): Ca at week 1 (1.05 vs .02); P at week 1 (2.43 vs .64), 2 (1.8 vs +.72), 3 (4.85 vs .98) and 4 (4.52 vs 1.18) and smaller decline in iPTH at week 4 (48 vs 65% of pre-diet values). Hypocalcemia, hypophosphatemia, and a two-fold increase in serum iPTH present in the -D group at 5 weeks were normalized after treatment; Ca remained slightly low. 25-OH-D, 78% lower than maternal values at the start of the study, was not less than 5 ng/ml regularly in -D pigs until the 4th week.

In neonatal pigs, the decrease in serum phosphorus before change in iPTH is an early feature of vitamin D deficiency, suggesting a direct role of vitamin D in the physiologic hyperphosphatemia in the very young. *p values range <.05 to <.001.

880 HYPERGLYCEMIA ASSOCIATED WITH HEMOLYTIC UREMIC SYNDROME. Sherry Loo, William Harmon, and Kenneth H. Gabbay, Children's Hospital Med. Ctr., Divisions of Endocr. and Nephr., Boston, MA. (Spon. by Warren E. Grupe).

Few reports have linked glucose intolerance to acute renal failure. We therefore evaluated hyperglycemia (hGlu) noted in a 3 yr. old white male with hemolytic uremic syndrome (HUS) after institution of peritoneal dialysis for oliguria and subsequent hemodialysis. Blood glucose (BG) values ≥ 1000 mg/dl and plasma glucagon levels of ≥ 1000 pg/ml were documented during the oliguric stage. Hyperglucagonemia (hGn) persisted but hGlu resolved with improvement in renal function. Insulin therapy was discontinued before discharge at which time blood glucose was normal, creatinine was 0.7, and total glycosylated hemoglobin (Hgb A_1) was 7.5% (nl= 5-9). Three days after discharge hGlu was again documented, but subsequent followup demonstrated normal random glucose levels and elevated glucagon values. Two months later a random BG was 302 mg/dl and Hgb A_1 was 11.3%. Fasting BG was 109 mg/dl, increased 1 hr p.c. to 240 mg/dl, and remained elevated for 10 hrs (191-385 mg/dl). Simultaneous insulin levels were ≤ 16 μU/ml. Intravenous tolbutamide and arginine each failed to stimulate insulin secretion. Glucagon levels also did not increase after arginine, whereas in diabetics an excess response is observed. While glucose intolerance and hGn have been documented in chronic uremia in adults, this patient clearly differs by showing both hypoinsulinemia, hGn, and persistent hGlu after return of normal renal function. The findings suggest a role for altered islet cell functions in the pathogenesis of hyperglycemia associated with HUS.

881 NEONATAL INTERVENTION IN TYPE I GLYCOGEN STORAGE DISEASE (GSD). S.L. Maby, M.L. Cowger, L. Howard, J.J. White, and H.L. Vallet, Birth Defects Inst., N.Y.S. Dept. of Health and Albany Med. Col., Dept. Ped. & Med., Albany, N.Y.

As the role of placental glucose-6-phosphatase is not known, children with this type of GSD may be severely affected at birth. If the diagnosis can be made at that time, treatment should be instituted prophylactically *before* growth is further affected. We studied one symptomatic GSD infant, *microcephalic at birth*, in whom the diagnosis was established by metabolic studies and liver biopsy (glucose-6-phosphatase activity < 5% of normal). Treatment, instituted at age 4½ months, consisted of a glucose and low fat formula (Vivonex, 20 cal/oz) given as a 12 hr continuous feeding with added calcium at night delivered via gastrostomy and infusion pump, and two hourly daytime formula feedings plus solids, with glucose as the only carbohydrate.

After one month of therapy, the initial hypoglycemia (< 25 mg/dl), hyperuricemia (7.9 mg/dl), lacticacidemia (136 ng/dl), acidosis (CO_2 17 mM/L) and elevated liver enzymes had reverted to normal. Triglycerides (2 hr pc) remained elevated. Correction of the microcephaly was noted within 6 weeks, and increase in weight velocity almost immediately after starting therapy. The child has been maintained on this feeding regime at home. Developmentally, at 37 weeks chronologic age, her adaptive behavior was at the 40 week level.

This case study implies that the placenta of this patient with Type I glycogen storage disease did not contain glucose-6-phosphatase and therefore did not protect the fetus from intrauterine metabolic derangement which affected brain growth. Prophylactic neonatal dietary intervention prevented further deterioration and induced significant catch-up growth and is therefore recommended for all future cases identified.

882 HYPOPHOSPHATEMIC BONE DISEASE (HBD) OF CHILDHOOD; A "NEW" ENTITY. W. MacDonald, C.R. Scriver, T. Reade, B. Nogrady, F.H. Glorieux and H.F. DeLuca, Dept. of Pediatrics, McGill Univ. and Shriners Hosp. Montreal, Que., Dept. of Biochemistry, Univ. Wisconsin, Madison, Wisc.

Four male probands presented with severe leg bowing after 1 yr of age. During 41 patient-yrs of observation, linear growth remained near the 3rd percentile (Tanner charts); bone X-rays show only coarse trabeculation and sclerosis in stress areas. Microradiography (R. Steendijk, Amsterdam) shows poor mineralization of forming osteones and perilacunar areas. Serum [Pi] is < 1 mM, as it is in X-linked hypophosphatemia (XLH); TRPi is significantly higher (76±7.3 μmoles/100 ml GF) in HBD than in XLH (31±2.8 μmoles/100 ml GF, $p < 0.01$) at the equivalent serum [Pi]. Tubular responses to bovine PTH and TmPi are abnormal (depressed) in HBD but different from XLH. Serum iPTH and 25-OHD are normal in HBD. 1α-OHD_3 by mouth (3-4 μg/d x 8 wk) does not restore TRPi or serum [Pi] to normal. The equivalent hypophosphatemias are clearly the result of different Pi transport defects in HBD and XLH; the more severe, rachitic bone disease in XLH points to an additional defect involving Pi access to bone in that disease. Pedigree studies indicate that HBD is not X-linked; otherwise the inheritance of the condition remains unclear.