1111 URINARY EXCRETION OF γ-CARBOXYGLUTAMIC ACID (GLA) IN X-LINKED HYPOPHOSPHATEMIA (XLH) AND AUTOSOMAL RECESSIVE VITAMIN D DEPENDENCY (ARVDD). David E.C. Cole, Theresa Reade, Jane B. Lian and Caren Gundberg. (Spon. by Charles R. Scriver). MRC Genetics Group, McGill Univ.-Montreal Children's Hosp. Res. Inst., Montreal, Quebec, Canada and Depts. of Orthopedic Surgery and Biological Chemistry, Harvard Medical School, Children's Hospital Medical Centre, Boston, Mass.

The mineralization defect in vitamin D deficiency (animal model) results in decreased turnover of osteocalcin, a unique vitamin K-dependent calcium-binding protein of bone matrix. GLA is the modified glutamate residue that is excreted quantitatively after osteocalcin degradation. To determine whether a similar effect occurs in mendelian rachitic disorders of man, we assayed urinary content of GLA. We studied 11 XLH patients (5M, 6F) treated with calcitriol (1,25-$(OH)_2D_3$) and phosphate. Urinary GLA excretion (50±15(SD) μmol/g creat) was not different from normal (44±11 μmol/g creat, n=63). We compared GLA excretion in 5 ARVDD patients in a vitamin D-depleted state with 7 ARVDD patients receiving a therapeutic dose of 1,25-$(OH)_2D_3$ (1.0-1.5 μg/day). GLA excretion in the D-depleted ARVDD group was significantly lower than normal (31±6 μmol/g creat, p=.006). GLA excretion was higher in the 1,25-$(OH)_2D_3$ treated group (44±4 μmol/g creat, $p < .001$) and not different from controls. These observations suggest that osteocalcin turnover is decreased in untreated individuals with impaired mineral metabolism. GLA excretion appears to be a useful marker for turnover of bone matrix in disorders of mineralization.

● 1112 DECREASED ENDOGENOUS GLUCOSE PRODUCTION (EGP) IN LOW BIRTHWEIGHT (LBW) INFANTS. Richard M. Cowett, John B. Susa, William Oh, and Robert Schwartz; Brown Univ. Prog. in Med., Women & Infants Hosp., Dept. of Ped., Providence RI

Since hypoglycemia occurs in LBW infants, glucose production rates were measured in 6 SGA infants (1959±142 gms B.W. and 37.7 ±0.6 wks. G.A., M±SEM) who received glucose to treat hypoglycemia and 7 AGA LBW infants (2071±126 gms; 34.1±0.6 wks) who received glucose to supplement feedings. Both were studied at 35.5±8.6 hrs. and compared to 5 AGA infants (3250±116 gms; 39.2±0.4 wks) studied at 6 hrs. After 3 hrs. NPO, baseline glucose and insulin were obtained and a prime plus constant infusion of 4 μg/kg/min D-{U-^{13}C}glucose was given. At equilibrium, pl. glucose, insulin, glucagon and ^{13}C glucose were analyzed and EGP rates were derived during the turnover period.

		BASELINE (Plasma)		TURNOVER		
	Gluc. Inf.	Gluc.	Ins.	Gluc.	Ins.	EGP
Group	mg/kg/min	mg/dl	μU/ml	mg/dl	μU/ml	mg/kg/min
SGA	6.1±1.3	73±12	16±4	94±19	25±7	0.2(0-0.6)
AGA(LBW)	5.1±0.2	82±5	14±2	97±6	14±2	1.6(0-4.4)
AGA(term)	0	71±5	18±5	70±7	19±5	3.8(3.7-4.2)

Pl. glucose in the term AGA was lower than in the AGA-LBW group during the turnover period ($p<.01$). No differences were noted in pl. insulin or glucagon concentration. The SGA group had a consistent suppression of EGP in comparison to the term AGA infants ($p<.01$). Suppression of EGP could not be correlated with changes in insulin or glucagon. We speculate that less substrate may be available to the SGA group for glucose production.

1113 FACTORS AFFECTING METABOLIC CONTROL IN CHILDREN WITH INSULIN-DEPENDENT DIABETES(IDD). Denis Daneman, David Wolfson, Dorothy J. Becker, Allan L. Drash, University of Pittsburgh, Children's Hospital of Pgh., Dept. of Pediatrics

In 477 children with IDD treated conventionally, glycosylated hemoglobin(GHb),blood glucose(BG)& C-peptide(CP)were measured 2-3 hr.postprandially over a 1yr period as indicators of metabolic control to assess the effects of pt. age,sex,disease duration, & in a subgroup of 273,no. of daily injections & dose of insulin. The mean±SEM %GHb over this period was 11.8±.2% & BG 237±9 mg/dl. Only 13(2.7%)had a normal %GHb(≤7.5%).There was a highly significant correlation($p<0.001$)between %GHb &both age & BG,but not with sex or duration >1yr.In 321 IDD children evaluated more than once %GHbremained within ±.5% of the initial value in 17%,decreased in 53%,& increased in 30%.There was no relationship between %GHb & no.of daily injections or dose of insulin.There was no seasonal variation.In 150,GHb was measured in RBCs both without(routine)& with incubation 1:10 in normal saline to assess the labile&stable forms of GHb respectively.%GHb was 11.6±.2% &10.1±.1%respectively ($r=.91, p<0.001$).Correlation to BGremained significant in both, though less in the saline-incubated specimens(r=.54&.37respectively).CP levels did not correlate with %GHb in either the remission or later stages.Because of the closer correlation of %GHb to age than to other factors such as disease duration,we suggest that hormonal&compliance factors during puberty may be more important determinants than residual β-cell function in achieving good metabolic control.Our ability to improve control over the short term has been quite limited.This study may help target those IDD children requiring more aggressive therapy.

1114 AN ACUTE MODEL OF THE FETUS (F) OF DIABETIC PREGNANCY (DP). S. Devaskar, S. Ganguli, U. Devaskar, P. Harris and M. Sperling, Dept. of Peds. Univ. of Cincinnati.

To gain insight into mechanisms responsible for disturbed CHO metabolism in DP, we acutely simulated F hyperglycemia and hyperinsulinemia in sheep (n=5) late in gestation (129 ± 1D; term ~ 150D). Labeled glucose was simultaneously infused to steady state in M (2-^{3}H) and F (U-^{14}C) before infusing F with glucose (G) 10 mg/kg/min plus insulin (I) 0.05 U/kg/hr for 3 hrs. Glucose turnover (GT), production (Ra), utilization (Rd) and the bidirectional placental transfer (T) were analyzed kinetically in M and F, before and after the G+I infusion. F pH, pO_2, pCO_2 and Hb did not change throughout. M Glucose kinetics and I levels were unaltered. F G rose from 11 ± 1 mg/dl to 21 ± 2 by 15 min and to 28 ± 2 by 3 hrs. Fetal I increased from 7 ± 1 uU/ml to 15 ± 3 at 15 min and was ~100 by 90 min, remaining constant thereafter. The M→F T of G, fetal GT and Ra dropped in the first 15 min from 34 ± 2 mg/min to 7 ± 3 (correcting for infused G). Despite ongoing G+I infusion, all variables returned to their original values by 60 min and then remained constant. Fetal Rd increased from 34 ± 2 mg/min to 82 ± 17 by 90 min, but T of G from F→M remained constant throughout. I alone at 0.05 U/kg/hr (n=10) did not cause similar changes in F Rd. Conclusions: (i) Infusions of I+G to F produce only a transient decrease in F GT, Ra and M→F transfer of G; all are rapidly compensated. (ii) In contrast, this procedure causes a sustained 2-3 fold increase in Rd but F→M transfer remains constant. (iii) Our data may explain the CHO changes seen in the F of DP, in which enhanced glucose uptake predominates.

1115 LIPID CLEARING IN PRETERM INFANTS: RELATIONSHIP OF LIPOLYTIC ACTIVITY TO GESTATIONAL AGE AND LIPID LOAD. Ramasubbareddy Dhanireddy, Margit Hamosh, Kolinjavadi N. Sivasubramanian, Parveen Chowdhry, John W. Scanlon and Paul Hamosh. Georgetown University Medical Center, Washington, D.C.

To determine the development of the lipid clearing mechanism, we have measured serum postheparin lipolytic activity (PHLA), triglyceride (TG) and free fatty acid (FFA) levels in 18 preterm infants, gestational age (G.A.) 25-32 wks, aged 16±1.5 days. Intralipid (I), 0.5 g/kg, was infused without or (after 1-4 days) with heparin (H), 10 U/kg for 4 h and blood was collected at 0, 10, 30, 120 and 240 min of infusion. PHLA (1 unit (U)=1 μmol FFA released from tri-^{3}H olein/ml/h), TG and FFA were measured in all serum specimens. The data show:

G.A.	PHLA*		I infusion-min			I+H infusion-min		
wks	U	(range)	0	30	240	0	30	240
25-26	3.3±0.8	(0.2-6.2)	137†	201	215	103†	136	215
27-28	10±4	(2.8-21)	43	126	203	42	83	195
29-32	9.6±2	(5-15)	50	78	155	54	80	129

*peak PHLA 10 min after H. †TG (mg/dl)

1. TG clearing develops at 27-28 wks G.A.: PHLA is low <27 wks, highly variable at 27-28 wks and adequate >29 wks. 2. A single bolus of H has only a transient effect on I clearance. 3. PHLA may be depleted by prolonged I infusion-correlation between PHLA and cumulative I infused was $r=-0.53$, $p<0.02$ (n=18). We conclude that infants <28 wks G.A. are most susceptible to hepatic and pulmonary complications following prolonged I infusion. (Support NIH grant HL-19056)

1116 GLUCOSE TURNOVER IN ADOLESCENTS: EFFECT OF OBESITY AND DIET ON RATES OF GLUCOSE PRODUCTION (Ra), CLEARANCE (Cl) AND OXIDATION (Ox). William H. Dietz, and Robert R. Wolfe (Spon. by R.J. Grand). Children's Hospital Medical Center, Department of GI-Nutrition, Boston, and Massachusetts General Hospital, Department of Surgery, Boston.

To explore abnormalities of carbohydrate metabolism in obesity, we studied Ra and Cl in 11 obese male and female adolescents under basal conditions. Eight of the same patients were also studied in a crossover fashion on a diet containing 1.5 gm meat protein/kg IBW/d and 1.0 gm glucose/kg IBW/d (P+G) or an isocaloric, isonitrogenous, carbohydrate-free diet (P+F). Glucose (G) kinetics were studied using a primed constant infusion of U-^{13}C-glucose after an overnight fast.

Basal Ra was 2.63 ± .50 mg/kg IBW, was unaffected by short term weight reduction and was readily suppressed by the infusion of 1 mg unlabelled glucose/kg IBW. In the basal state Ra did not correlate with insulin (I) or free fatty acid (FFA) levels. During hypocaloric dietary therapy Ra fell to 77% of baseline; the decrease was similar for both diets. Cl and % CO_2 from G were significantly lower on P+F than on P+G. Under all conditions, Cl did not correlate with FFA or I. Percent CO_2 from G was inversely correlated with FFA only with P+G, but did not correlate with I on either diet.

Caloric intake rather than energy source appears to be the primary determinant of Ra. Contrary to previous hypotheses, our kinetic data suggest that Ra, Cl, and Ox are generally unrelated to levels of I and FFA during hypocaloric dietary therapy.