1129 RICKETS WITH ELEVATED 1,25-(OH)₂ VITAMIN D (1,25-(OH)₂) AND NORMAL 25-OH VITAMIN D (25 OHD) IN PREMATURE FED HUMAN MILK EXCLUSIVELY: INCREASING BONE MINERAL CONTENT (BMC) WITH CA AND P SUPPLEMENT. F.R. Greer, R.C. Tsang, J.J. Steichen, M. Ho, G. Hug, U. Cincinnati, Dept. of Pediatrics

Rickets in premature fed human milk may be related to decreased Ca and P intake rather than deficiency in vitamin D (D). In a 27 wk, 970 g infant expressed mother's milk and vit D 250 IU/d were begun on d 7. By 2 wks, milk intake averaged 165ml/kg/d; D intake was 400 IU/d after 9 wks. During lactation, breast milk Ca was 22.4-28.8 and Mg 3.1-4.8mg/dl; P decreased from 19.6 at 10 d to plateau of 7.1mg/dl by 8 wks. Physical signs, x-rays, serum P (3.6 mg/dl) and alk phosphatase (630 IU) showed rickets at 16 wks; serum Ca was 8.8mg/dl, 25-OHD 40ng/dl (N 11-68) 1,25-(OH)₂ vit D 129 pg/ml (N 17-44) parathyroid 27uEq/ml (N<57) and calcitonin 12pg/ml (N<107). BMC was 36-33mg/cm at 8-16 wks (term infants 90). Calcium gluconate (60mg Ca/kg/d) and potassium phosphate (P 30mg/kg/d) was supplemented. Rickets resolved, P rose, phosphatase fell, 170IU/L. BMC increased to 49, 61 and 109mg/cm by 9 mos, and serum 1,25(OH)₂D fell to 111 and 100pg/ml. Very low birth weight infants fed human milk with D supplements may develop rickets with elevated 1,25(OH)₂D: Ca and P supplements are effective in treatment; we speculate that rickets in premature on human milk feeding is secondary to inadequate Ca and P intake and not related to D deficiency.

1130 HbA_{1c} AND NEWBORN SKINFOLD THICKNESS: REFLECTION OF MATERNAL DIABETIC CONTROL. David O. Hakanson and Shirazali G. Sunderji, Depts. of Pediatrics and Obs. & Gyn., SUNY, Upstate Med. Ctr., Syracuse, NY. (Spon. by F.A.Oski).

Recent studies have shown a correlation between the size of offspring and levels of glycohemoglobin (HbA_{1c}) in gestational diabetes, and levels of HbA_{1c} have been shown to reflect the degree of diabetic control. Newborn skinfold thickness (ST) also has been shown to reflect maternal diabetic control, showing a significant correlation with maternal fasting blood glucose values during the last trimester of pregnancy.

To determine if maternal HbA_{1c} levels also correlate with ST of the offspring, 50 maternal/infant pairs were analyzed. Maternal HbA_{1c} levels were determined within one week prior to delivery. ST of the offspring was measured and compared to reference means for gestational ages 35-40 weeks.

In only 1 of 14 instances was ST found to be in the normal range when maternal HbA_{1c} was elevated. In 13 pairs both maternal HbA_{1c} and ST of the offspring were elevated. In an additional 13 pairs, elevation of ST was associated with a normal maternal HbA_{1c}. When these two groups with contrasting levels of HbA_{1c} were compared utilizing the ratio ST/birthweight(BW) a difference was found; in those mothers with increased HbA_{1c}, ST/BW was significantly higher than for infants of mothers with normal HbA_{1c} (p<.001).

HbA_{1c} levels reflect the status of diabetic control. Offspring of pregnant diabetics whose HbA_{1c} levels are elevated are significantly fatter than those of diabetic women with normal HbA_{1c}.

1131 EVALUATION OF THERAPY IN DIABETES MELLITUS: USE OF FREE INSULIN. Alberto Hayek, Ellen Kaufman, and Robert E. Greenberg, University of New Mexico School of Medicine, Department of Pediatrics, Albuquerque

Diabetic therapy is traditionally evaluated using measurements of blood glucose regulation. The ability to measure free (unbound) insulin enables a more direct study of the relationship between insulin dose and the concentration of free insulin and metabolic parameters in blood.

Eight insulin-dependent, C-peptide negative diabetics, 7 to 22 years, were given their usual dose of NPH and regular insulin, and blood samples were serially obtained for levels of free and total insulin, glucose, FFA and ketone bodies. Twenty-four hours later, a standard four hour low dose constant infusion of crystalline insulin was given. Data were analyzed using individual and integrated concentrations of hormones and substrates.

In all patients, NPH insulin led to minimal increases in blood insulin (< 15 µU/ml). Low insulin concentrations were associated with elevated parameters of metabolic control. Insulin infusion led to insulin levels between 35 and 50 µU/ml at steady state, and with normalization of glucose, FFA and ketone bodies. A significant reduction in serum [K⁺] occurred during insulin infusion.

These data suggest that: 1) long-acting insulin produces minimal increases in serum insulin; 2) measurement of free insulin can be used to distinguish inadequate insulin dose or aberrant absorption from insulin resistance; 3) conventional NPH therapy cannot lead to adequate metabolic control; 4) hypokalemia may be a marker for states of excess insulin administration.

1132 FURTHER EVIDENCE FOR TWO CLASSES OF INSULIN RECEPTORS ON HUMAN ERYTHROCYTES. Donald E. Hill, J. Mark Boughter, Thomas J. Szisak, and Linda G. Szisak.

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We previously reported evidence for two classes of insulin receptors on erythrocytes based on the interaction with concanavalin A (Nature 28:279, 1980). Further evidence for this hypothesis is provided here when proinsulin is used as a competitive inhibitor of insulin binding to human and rabbit erythrocytes. Proinsulin in a molar ratio of 33:1 to insulin (Endocr. 107:195, 1980) binds to the low affinity, high capacity site in a preferential manner allowing the high affinity, low capacity site to be expressed. When insulin binding data are analyzed using a computer model (Ligand, NIH) the values obtained for affinity (K₁) and maximum (R₁) are nearly identified for site I as shown for a typical experiment.

	SITE I		SITE II	
	(K ₁) x10 ⁹ M ⁻¹	(R ₁) x10 ⁻¹⁰ M/L	(K ₂) x10 ⁸ M ⁻¹	(R ₂) x10 ⁻¹⁰ M/L
Std. insulin inhibition curve	4.45±1.13	0.25±0.06	1.41±0.09	1.17±0.33
Proinsulin: Insulin (33:IM)	3.69±0.47	0.28±0.02	No computable Site II	

We conclude that these findings are further evidence supporting the concept of two classes of insulin receptors on erythrocytes. If only the linear site I affinity and capacity are used this may simplify insulin binding data interpretation.

1133 SERUM VITAMIN D BINDING PROTEIN (DBP) IN PRETERM INFANTS. Laura S. Hillman and John G. Haddad, Wash. Univ. Med. Sch., St. Louis Children's Hosp., Dept. of Ped., St. Louis, MO, and Univ. of Penn., Dept. Med., Philadelphia.

DBP is low in the cord blood of preterm infants (359±24µg/ml) while term infants (558±78µg/ml) have adult concentrations (525±24 µg/ml). To see when preterm infants develop normal concentrations of DBP and to look for any relationship to DBP's major ligand, 25-hydroxyvitamin D (25-OHD), DBP was measured by radial immunodiffusion using a rabbit antiserum in serial serum samples from 28 preterm infants, gestation 29.7±2.5wks and birthweight 1162±344gms. DBP remained low until there was a significant increase at 12wks of age (p<.01 by paired t-test). 25-OHD also increased (p<.025) at 12wks and was then correlated with serum calcium (r=.44, p<.05) and phosphorus (r=.48, p<.05). At 12wks only there were positive correlations of DBP with 25-OHD (r=.69, p<.01) and phosphorus (r=.49, p<.05). There was no correlation with gestational age or birthweight. In very preterm infants, serum albumin, ceruloplasmin and somatomedin follow a similar pattern. In 11 study infants, Lowry proteins on the same samples increased at 12wks so that DBP/gm protein remained stable. In 10 other study patients, albumin similarly increased. The changes in DBP probably reflect a maturation in the liver's ability to synthesize many proteins. The correlation with 25-OHD may represent a concurrent maturation in the liver's ability to hydroxylate vitamin D and is probably without physiological significance.

Age(N)	Cord(17)	1w(16)	3w(21)	6w(18)	9w(13)	12w(19)
DBPµg/ml	375±97	396±82	382±67	393±78	372±120	490±130
25-OHDng/ml	16±8	17±8	21±8	20±7	21±7	27±13

1134 HEPATIC NET GLUCOSE PRODUCTION AND O₂ UPTAKE BEFORE AND AFTER FEEDING IN CONSCIOUS NEWBORN LAMBS. Ian R. Holzman and Daniel I. Edelstone (Spon. by Paul M. Taylor).

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We determined hepatic arterial (Q_{HA}) and portal venous (Q_{PV}) blood flows and calculated, utilizing the Fick principle, net hepatic glucose production (P_{GLUC}), O₂ delivery (DO₂), O₂ consumption (VO₂), and O₂ extraction (VO₂/DO₂), in 7 chronically catheterized lambs (9-15 d). Studies were done with the lambs fasted and at 1, 2, 3, 4, and 6 hr postprandially. We measured O₂ contents (Lex-O₂-Con), blood flows (radioactive microspheres), and glucose (glucose oxidase). The table indicates mean results. (* = significantly different from fasting)

	Fasting	1 hr	2 hr	3 hr	4 hr	6 hr
P _{GLUC} (µmoles/kg/min)	23	19	41*	31	27	21
DO ₂ (ml O ₂ /min/kg)	5.8	6.0	5.7	5.3	5.4	5.3
VO ₂ (ml O ₂ /min/kg)	2.3	2.4	1.9	1.5*	2.0	2.2
O ₂ extraction (%)	40	40	33	29*	37	42
Q _{PV} (ml/min/kg)	66	81*	71	65	62	65
Q _{HA} (ml/min/kg)	6	7	7	6	6	8

Our results show that the VO₂ of the neonatal liver decreases postprandially. This decreased VO₂ is associated with a decreased O₂ extraction rather than a decrease in DO₂ or hepatic blood flow. Since glucose production is increasing at a time when hepatic oxygen consumption is decreasing, these data indicate that hepatic metabolism shifts postprandially to less oxygen-dependent processes.