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HORMONAL VARIATION IN LBW INFANTS ON A CONSTANT GLUCOSE INFUSION. F. Ahmad, M.D., A.G. Beard, M.D., J.M. Boughter, R.H. Fiser, M.D., Dept. of Pediatrics,

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Baseline glucose (Gl), insulin (Ins), glucagon (Glucag), cortisol (Cor) and alanine (Ala) determinations were drawn between 0-1 hours in 16 LBW infants (BW 1040-1490 gms. GA 29-34 wks.) after which an I.V. electrolyte-glucose (6 mg/kg/min.) infusion was begun. Repeat evaluations were done at 24 and 48 hrs.

Mean Values for the 16 LBW Infants are Given Below

	Gl, mg%			Ins, uU/ml			Glucag, pg/ml			Ala, mgm/dl			Cor, ug/dl		
Hrs.	0-1	24	48	0-1	24	48	0-1	24	48	0-1	24	48	0-1	24	48
Mean	87	109	87	30	12	10	170	110	85	312	129	145	14	13	12
S.D.	62	63	36	34	8	6	112	53	59	100	54	52	5	7	5
No.	16	16	15	13	13	13	14	14	14	9	9	9	16	16	15

The data were analyzed according to B.W., gestational age, 5 minute apgar score and appropriateness for gestational age. Significant findings were: glucose was ↑ in the group <1200 gms. at 24 hrs. (p=.05) and 48 hrs. (p<.02). Insulin values in the apgar 1-5 group were ↑ (p<.05) at 24 hrs. coincident with a trend toward hyperglycemia. Alanine and glucagon levels were higher in all groups at 0-1 hrs. (p<.01).

No significant correlation between glycemia, insulin or cortisol levels could be found. Hyperglycemia was present in the groups <1200 gms. The presence of initially elevated glucagon and alanine levels in the immediate perinatal period suggest that the LBW infant is capable of active gluconeogenesis.

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NEONATAL HYPERLIPOPROTEINEMIA TYPE I. Carlos A. Ahumada, Moti L. Kashyap, Jeanne A. McCarthy, Roberto A. Sosa, Charles J. Glueck, Reginald C. Tsang, University of Cincinnati College of Medicine, Department of Pediatrics, Cincinnati; University of South Florida College of Medicine, All Children's Hospital, Department of Pediatrics, St. Petersburg, Florida.

At ten days of age a 2690 grams preterm female infant was studied because of weight loss while receiving Similac 120 kcal/kg/day. The serum was milky in appearance and had a creamy layer and clear infranate after refrigeration. No hepatosplenomegaly, xanthomata or lipemia retinalis were present. Triglycerides (TG) were 10,720 mg/dl; cholesterol 530 mg/dl. Lipoprotein electrophoresis (LPE) showed a chylomicron band. Maternal and paternal LPE showed a type IV pattern. Extrahepatic postheparin lipolytic activity was abnormally low: 1.6 μm free fatty acids/ml/60 min., confirming type I hyperlipoproteinemia (HLP). Plasma ApoCII was elevated: 33.2 mg/dl (Normal 5±2.3 M±SD); percent of ApoCII in very low density lipoproteins (VLDL) was low: 3.8 (Normal 9.9±5.8).

VLDL net lipoprotein lipase activator (LPL-A) was low: 54 units/mg (Normal: 145.6±47.5). After 15 days on skim milk TG: 1080 mg/dl; cholesterol 300 mg/dl. ApoCII activates extrahepatic lipoprotein lipase (LPL) which hydrolyses TG in VLDL. Deficiency of LPL results in severe hypertriglyceridemia. A deficiency of extrahepatic LPL in this infant was associated with markedly elevated plasma ApoCII, while ApoCII and LPL-A relative to VLDL were decreased. Overproduction of ApoCII in type I HLP is possibly a compensatory mechanism for the LPL deficiency.

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LONG TERM TREATMENT OF GLYCOGEN STORAGE DISEASE TYPE I (GSD I): CLINICAL IMPROVEMENT BUT PERSISTENT ABNORMALITIES OF LACTATE & TRIGLYCERIDE CONCENTRATION.

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Two patients, ages 5-6/12 & 8-10/12, with biopsy-proven glucose-6-phosphatase deficiency were restudied 2-3/12 & 2-8/12 yrs after starting nocturnal intragastric glucose infusion. Marked improvement in linear growth (velocities 11.3 & 7.5 cm/yr) was noted. Bone demineralization in both subjects was corrected and a pathological fracture healed in one. Hepatomegaly was reduced.

Mean pre-therapy levels obtained after the usual overnight fast were compared with mean pre-breakfast concentrations observed after 2+ yrs of nighttime glucose infusion:

	Patient 1		Patient 2	
	Pretreatment	Infusion	Pretreatment	Infusion
Glucose	25 mg/dl	82	30	91
Lactate	12.1 mM/L	7.2	12.9	5.4
Triglyceride	829 mgm/dl	570	4644	690
pH	---	7.36	7.27	7.36

These observations confirm that nocturnal intragastric glucose infusion is of significant benefit in the long term treatment of GSD I. Avoidance of hypoglycemia improved but did not totally correct the abnormalities of lactate and triglycerides. We speculate that the clinical improvement is due to correction of the chronic acidosis.

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HYPERGLUCAGONEMIA IN HYPOXIA. David Baum, Dan Porte Jr., John Ensink, Depts. of Peds. & Med. Stanford Univ., Stanford, CA and Univ. of Washington, Seattle, Wash.

We studied plasma glucagon (IRG) in hypoxia because other stressful states stimulate glucagon release. Two groups of paired experiments were performed in 12 puppies. In Group I, 8%O₂: 92%N₂ ventilation (PaO₂ 20-30 torr) for 45-min. produced a rise in plasma IRG (mean change +100.5 pg/ml) and glucose (+223.7 mg/dl) but no change in insulin (IRI) (-0.3 μu/ml). However, when Group I was air ventilated (PaO₂ >70 torr) and given 45-min. glucose infusions producing hyperglycemia of similar degree (+196 mg/dl), plasma IRG was unchanged (-7.8 pg/ml) while IRI (+32.8 μu/ml) rose. The IRG and IRI responses with 45-min. of hypoxia were different from those during a comparable period of air (p<.03). Because β adrenergic receptor stimulation mediates glucagon release in stressed dogs, its contribution to the IRG rise in hypoxia was examined by giving Group II the β adrenergic blocker, propranolol. Despite β blockade, 8%O₂: 92%N₂ ventilation caused a rise in plasma IRG (+394 pg/ml) and glucose (+71 mg/dl), but IRI was unchanged (+.8 μu/ml). With propranolol and air ventilation there were no significant changes in plasma IRG (+14.7 pg/ml) glucose (+9 mg/dl) or IRI (+6.7 μu/ml). These data suggest that a) glucagon release is caused by acute O₂ deficiency, but b) without β adrenergic receptor mediation. Since hepatic glycogenolysis, the primary glucose source in hypoxia, is stimulated by glucagon and retarded by insulin, we propose that increased glucagon and low insulin levels promote glucose mobilization and hyperglycemia at low O₂ tensions.

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A FREE FATTY ACID BINDING INDEX FOR SERUM

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We have developed a convenient spectrophotometric free fatty acid binding index (FFABI) for monitoring infants receiving intravenous lipid supplements, who may be at risk due to hyperbilirubinemia or the possible direct toxicity of FFAs. We use the conjugated tetraene fatty acid parinaric acid (9,11,13,15 octadecatetraenoic acid), which has a sharply resolved absorption spectrum. The position of the absorption peak shifts upon binding to albumin. By measuring parinaric acid absorbance at two wavelengths in the presence of a serum sample diluted into buffer, we quantitate binding by comparison with albumin/FFA standards. An equal aliquot of serum is added to the reference cuvette to eliminate interference due to bilirubin, hemolysis, or turbidity. The measurement requires 20 microliters of serum and knowledge of the serum albumin concentration. No complex instrumentation or extraction into organic solvents are required. The index is sensitive both to elevation in FFA levels and to reduction in the affinity of albumin for FFAs. Nine infants not receiving intravenous lipid had FFABI values ranging from 0.3 to 2.0 (mean 1.4). Four infants receiving intravenous lipid had FFABI values of 2.1, 2.6, 3.2, and 3.4, respectively. We believe that monitoring of FFA binding in serum will be an important part of the rational management of infants receiving intravenous lipid supplements.

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METHOTREXATE (MTX) EFFECTS ON CALCIUM TRANSPORT AND BONE MINERALIZATION IN ANIMALS. Turkan Dagoglu and William H. Bergstrom, Dept. of Peds., SUNY, Upstate Med. Ctr., Syracuse, N.Y.

The appearance of rickets in a 6 year old girl receiving MTX for acute lymphatic leukemia prompted a study of the effects of this compound on calcium transport and bone mineralization in animal models. Five days after a single MTX dose (15 mg/M² IP) rats showed a 75% decrease in TCa as measured in everted duodenal sacs. A second dose reduced TCa to 8% of the control value; it then increased gradually, reaching 78% 20 days after the second MTX dose.

Chicks were kept on a synthetic diet with just sufficient Ca and vitamin D (D) for normal growth in controls. After MTX (15 mg/M² IP x 2), growth retardation (6.7 gm/day vs. 10 gm/day), impaired gait, and radiographic evidence of rickets were seen at 20 days. Dietary Ca and D were then increased; growth rate, gait, and radiographs returned to normal in 8 days, though MTX was continued.

In the models described, MTX reduced TCa, Bone mineralization was compromised when Ca and D intake were just adequate; increased Ca and D permitted remineralization. These results suggest that MTX might cause bone disease in patients with low or borderline Ca and D intake; the ample quantities of both in the usual North American diet would be protective.