889 SERUM LIPIDS VS SERUM APOLIPOPROTEINS IN CORD BLOOD

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In studies on the lipoprotein system of cord serum, we have determined the lipid and apolipoprotein (apo-LP) levels in various perinatal conditions. Infants of normal gestation and weight (>2500g) were characterized by the following lipid levels (mg/dl): TG=43.5 ± 18.3; TC=71.3 ± 20.9; FC=16.8 ± 6.2; PL=125.2 ± 36.7 (n=257). There were no distinct differences in the lipid levels between prematurity, postmaturity, caesarean section and miscellaneous abnormalities. Apolipoprotein concentrations in random cord sera were as follows: A-I=86.7; A-II=57.5; ApoB=26.9; C-I=5.9; C-II=3.1; C-III=6.6; ApoD=4.7; and ApoE=7.7 (mg/dl). All apo-LP concentrations were lower than those found in adult sera with ApoB levels representing the lowest one (25% of adult sera). The apo-LP levels of abnormal groups were similar to those of normals with the exception of reduced levels of A-I and A-II in prematures. Results of this study show that the lipid and apo-LP levels of cord sera are lower than those of adult sera and that perinatal problems have little effect on the cord serum lipoproteins. The availability of specific apolipoprotein assays will provide additional data necessary for evaluating dietary and other factors affecting the development of the lipid transport system in humans.

890 IMPAIRED MOVEMENT AND DEFORMABILITY OF NEUTROPHILS FROM PATIENTS WITH JUVENILE DIABETES MELLITUS. AN INSULIN INDUCED DEFECT? Shirley Murphy and Michael

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Data from several laboratories have demonstrated deficient chemotaxis of polymorphonuclear leukocytes (PMNS) from subjects with insulin dependent juvenile diabetes mellitus (JDM). We have also found deficient generation of antigen-antibody generated chemotactic activities from serums of patients with JDM. All patients previously studied were on insulin therapy at the time of study. In further exploring these relationships, we have added several new parameters: 1) We have studied, over the past three years, 8 children with JDM prior to and following the institution of insulin therapy; and, 2) studied deformability of PMNS from JDM by the technique of elastimetry, which measures rigidity of the PMN membrane. The data show: 1) Before insulin, no defect in JDM PMN movement or generation of chemotactic activity from JDM serums could be demonstrated; 2) Following insulin, sometimes within 12-24 hours, highly significant ($p < .001$) decreases were found in both cellular and humoral chemotaxis; 3) Deformability of JDM PMNS was markedly decreased when chemotaxis was diminished. The data, therefore, strongly suggest that a PMN membrane alteration occurs following insulin therapy in JDM. This is consistent with recent studies demonstrating decreased adherence of JDM PMNS and may explain the apparent chemotactic defect.

891 INSULIN-CARBOHYDRATE RELATIONSHIP IN THE SHEEP FETUS. Anthony F. Philipps, Bonita S. Carson, Giacomo Meschia, and Frederick C. Battaglia. University

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The relationship between plasma glucose [G], fructose [Fr] and immunoreactive insulin [IRI] in mother and fetus were studied in 7 pregnant ewes for periods up to 31 days, by means of chronically-placed arterial catheters. Maternal fasting (4 days) and re-feeding were used to alter [G]. For both maternal and fetal plasma, [IRI] was linearly related to [G] in each animal ($p < .001$). The fetal response curves were shifted to the left of the maternal (at 10 μ U/ml IRI, $\Delta G = 33.0 \pm 9.7$ mg/dl, $p < .001$) but had the same slope (sensitivity). Fetal infusion of G designed to create an instantaneous rise of [G] in fetal plasma to a new steady level caused a rise of [IRI] but failed to show the initial rapid response of adult animals to the same type of stimulus. Although [Fr] decreased with fasting ($\Delta[Fr] = -62 \pm 12$ mg/dl on the fourth day of fast) and rose promptly on re-feeding or glucose infusion, fetal Fr infusions failed to cause any major change in [IRI]. It appears that in a fed and fast cycle, fetal insulin secretion is related to [G] by a mechanism as sensitive as in the adult. However, the characteristics which are peculiar to the fetus are a relatively high [IRI]/[G] ratio and the absence of rapid [IRI] response to instantaneous changes of [G].

892 HYPERCHLOREMIA AND HYPERNATREMIA ASSOCIATED WITH CHOLESTYRAMINE THERAPY. William A. Primack, Lawrence M. Gartner, Harriet E. McGurk and Adrian

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Cholestyramine is recommended in the management of intractable diarrhea, cholestatic liver disease, and hypercholesterolemia. We observed an infant receiving cholestyramine because of neonatal hepatitis who developed severe hypernatremia (175 mEq/L) and hyperchloremia (145 mEq/L) during a period of increased gastrointestinal and insensible losses from intercurrent illness. We have since observed 2 infants on cholestyramine who developed similar, less severe biochemical abnormalities.

Cholestyramine is an anion exchange resin containing 4 mEq/gm of chloride. Bile acids and other anions are exchanged in the gut for the chloride, most of which is absorbed and excreted by the kidney. In addition, we have determined that about 5 ml of water are necessary per gram of powder (~440 mg of resin) to acquire the consistency of a normal infant's stool. Thus, unless extra water is provided to compensate for both the increase in solute load and the hydration of cholestyramine, the obligatory loss of fluid will lead to hyperchloremia and hypernatremia and a hyperosmolar state will develop. Newborns or infants with chronic disease who may not be able to concentrate the urine maximally are at highest risk. When cholestyramine therapy is indicated, it is therefore important to modify the diet such as to either decrease the solute load or provide additional water.

893 MATERNAL ENDOCRINE CONTROL OF FETAL SUBSTRATE AVAILABILITY: HUMAN PLACENTAL LACTOGEN. Peggy Rapoport, David Bolam, Yoshio Miyazaki, Hobart Wiltse, and

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Human Placental Lactogen (PL) has been proposed as the growth hormone of the last trimester of pregnancy. These studies were designed to determine the role of PL in the regulation of fetal substrate availability as reflected by changes in uterine and peripheral maternal carbohydrate metabolism. Six pregnant ewes of 90-126 days gestation were chronically prepared by placement of uterine and femoral artery electromagnetic flow transducers, bilateral uterine, jugular, and femoral vein, and unilateral femoral and cystic artery catheters. After a 4 day recovery period, baseline studies were obtained and PL was infused at a constant rate. Whole blood samples for glucose and lactate analysis were drawn at 1-4 hr. intervals. Peripheral maternal glucose uptake, and uterine lactate production were calculated by the Fick equation. A total of 34 glucose and 8 lactate studies were completed.

PL infusions did not alter maternal glucose concentrations or uterine and femoral blood flow. PL produced a 40% increase in uterine glucose uptake ($p < .005$), a 35% decrease in peripheral maternal glucose uptake ($p < .01$), but no significant change in uterine lactate production ($p > .10$). We conclude that PL enhances uterine glucose uptake without increased placental glucose conversion, and maternal glucose utilization is decreased. This supports the role of PL as a gestational growth hormone.

894 DIHYDROLIPOYL DEHYDROGENASE DEFICIENCY - A CAUSE OF CONGENITAL LACTIC ACIDOSIS. Brian H. Robinson, Jennifer Taylor and W. Geoffrey Sherwood (Spon. by

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A male infant born of consanguineous parents (8.Wt. 3 kg) presented acutely at 2 months of age (wt. 4.8 kg) with lethargy, hypertonemia, episodic irritability, optic atrophy, laryngeal stridor, irregular respirations and metabolic acidosis. He had elevated blood levels of pyruvate (0.38 mM, N<0.2 mM), lactate (5.3 mM, N<2 mM) and α -ketoglutarate (0.103 mM, N<0.054 mM). He also had elevated levels of branched chain amino acids (x2 upper limit of normal) and occasional alanine responsive hypoglycemia (30-35 mg%). A defect of oxidative decarboxylation was postulated. Neither high dose of thiamine therapy (1 g/day) nor a high fat diet, affected the persistent lactic acidosis (4-10 mM). He deteriorated neurologically and died at the age of 7 months. Autopsy revealed cavitation and demyelination in the basal ganglia, thalami, and brain stem. Key gluconeogenic enzyme activities were normal in liver, muscle, brain and kidney. Total pyruvate (PDH) and α -ketoglutarate (α KGDH) dehydrogenase complex activities were reduced in all tissues to 5-10% of control values. The pyruvate decarboxylase component of PDH (E_1) was normal but the dihydrolipoil dehydrogenase component (E_3) was reduced in activity (5% of control value). Deficiency of E_3 compromises both PDH and α KGDH activity. This compromises both entry into and activity of the tricarboxylic acid cycle. Normal growth and development indicates a greater reliance on glycolytic than oxidative metabolism in the early months of life.