883 FRUCTOSE 1:6 DIPHOSPHATASE DEFICIENCY: ? A DIAGNOSTIC PITFALL. Andrew J. Macnab. (Spon. by S. Israels) University of British Columbia, Department of Paediatrics, Vancouver, B.C.

Clinically, a girl aged 6 months with hepatomegaly, fasting hypoglycaemia and lactic acidosis closely resembled Type 1 glycogenosis (GSD I). However, hepatic biopsy revealed normal glycogen pathway enzymes. Further assays revealed complete absence of Fructose 1:6 diphosphatase (FDPase), but atypically she had shown no glycaemic response to oral galactose and an insignificant response following glucagon injection. A bleeding diathesis was present and abnormal platelet function with reduced platelet adenine nucleotide levels was demonstrated. The 7 children previously reported with absent hepatic FDPase were reviewed; also 8 of their siblings who had similar physical or biochemical abnormalities but died prior to positive diagnosis. There is a high morbidity and mortality during prolonged biochemical diagnostic studies and a marked individual variation in response. Liver biopsy provides optimal definitive diagnosis in spite of the platelet defect described and high overall incidence of abnormal bleeding in the group as a whole (43%). Administration of glucose 0.5 mg/kg & hour by continuous nasogastric infusion corrected the coagulation defect and improved clinical and biochemical parameters, but when the same dose of glucose was given as 3 hourly oral supplements significant hypoglycaemia and bleeding reoccurred intermitently. Many cases described of "atypical GSD I" may represent undiagnosed FDPase deficiency. With attention to the coagulation defect, prompt diagnosis and treatment, prognosis is excellent.

884 NORMOTRIGLYCERIDEMIC ABETALIPOPROTEINEMIA - CLINICAL AND BIOCHEMICAL FEATURES OF A NEW SYNDROME. Mary J. Malloy and John P. Kane. (Sponsored by Arthur J. Ammann), Univ. of Calif., School of Medicine, Dept. of Pediatrics and Cardiovascular Research Institute, San Francisco, Calif.

Electrophoresis of serum from a 8 yr old girl whose fasting cholesterol (C) and triglyceride (TG) levels both range from 25 to 30 mg/dl, shows prebeta and alpha, but not beta lipoprotein (LP). The patient is obese, has moderate ataxia, developmental retardation, and mild stomatocytosis of RBCs but no steatorrhea. Intestinal mucosa was normal 24h after a fat load. Retinoscopy and electroretinograms were normal. Electron microscopy of the d<1.006 g/cm^3 ultracentrifugal fraction of fasting serum showed spherical particles of 390 to 2000 Å resembling very low density LP (VLDL). In the low density LP (LDL) interval (d 1.006-1.063) which contained only 0.2 mg/dl of protein, spheres of ∿350 Å with electron-lucent cores, resembling "remnant" particles, and cuboidal particles of ∿220Å were seen. The d 1.21 - 1.063 fraction contained spheres of ∿100 Å, consistent with high density LP. After a fat meal serum TG and C rose to 155 and 36 mg/dl, but there was no increase in LDL. Serum TG rose with carbohydrate feeding also. Although immunoreactivity of the patient's serum with anti-apolipoprotein B (apo-B) is very low (0.2 mg/dl), 35% of VLDL protein is precipitable by tetramethylurea (a property of apo-B). The apparent molecular weight of this protein is ∿60% that of normal apo-B on SDS gel electrophoresis. These data suggest a partial deletion mutation or absent subunit of apo-B. This abnormal apo-B permits secretion of chylomicrons and VLDL which are not converted to normal LDL.

885 DEVELOPMENT OF MICROVASCULAR DISEASE IN CHILDREN WITH DIABETES, Malone, J.I., Van Cader, T.C. and Steinberg, M.P., University of South Florida, College of Medicine, Depts. of Pediatrics and Ophthalmology, Tampa, Florida. Spon. by Lewis A. Barness.

Flourescein angiography (FA) was performed on 80 children with diabetes one year after an initial evaluation with FA. The grading system: Stage 0 no microaneurysms (MA), Stage 1<10 MA, Stage 2>10 MA, Stage 3>10 MA plus neovascularization. 2-3 DPG was measured as an indicator of vascular compromise and compared with FA. The levels in non-diabetics is 14.4 ± 1.0mM/gmHb, Stage 0 is 15.6 ± .2 and Stage 1-3 is 16.7 ± .5. The difference between controls and Stages 1-3 is significant at p<.02 and suggests that the abnormalities noted on FA indicate functional vascular abnormalities. The Stage was unchanged in 71/80, 9/71 remained Stage 0, 3 improved and 6 increased in severity. The percent of hemoglobin A_1 (HbA1) and the concentration of sorbitol (S) in packed red blood cells (PRBC), indicators of glycemic control, were not significantly different in children with Stage 0 when compared to those with Stage 1,2 and 3. Three of 4 children with chemical diabetes (CD) had MA. A 12 yr. old child with diabetes of 3 mos. duration had Stage 3 retinopathy. The demonstration of MA early in the clinical course of diabetes (CD) plus the lack of apparent difference in the degree of glycemic control between those with progressive vascular abnormalities and those with none or stable retinopathy suggest that factors other than glycemic control are important in the prevention of the vascular complications of childhood diabetes.

886 RED CELL SORBITOL AN INDICATOR OF GLYCEMIC CONTROL, Malone, J.I. and Steinberg, M.P., University of South Florida, College of Medicine, Dept. of Pediatrics, Tampa, Florida. Spon. by Lewis A. Barness.

Blood glucose concentrations may change from physiologic to pathologic levels and vice versa within a few minutes. This is particularly true of insulin deficient diabetes and therefore the evaluation of glycemic control in children with diabetes is difficult. A less volatile indicator of hyperglycemia is the fraction of hemoglobin A (HbA) that is glycosylated (HbA1). HbA1 was determined chromatographically in 30 children with diabetes (13.9 ± 2.1%) and 10 non-diabetics (6.8 ± 1.4%). Incubation of washed red cells from diabetic patients in Krebs bicarbonate buffer with 5mM glucose for 3 hrs. results in no change in the % of HbA1. Sorbitol, a polyol of glucose, accumulates in red blood cells (RBC) in concentrations that corrolate directly with the blood glucose concentration (r=.84). RBC sorbitol concentration in 30 ambulatory diabetics was 33nM/ccPRBC ± 13.7 while 10 non-diabetics had sorbitol levels of 5.3 ± 2.1. Incubation of non-diabetic RBC's in 50mM glucose produced an hourly linear increase in sorbitol concentration throughout the 3 hr. incubation reaching diabetic levels in one hour. Reduction of the glucose concentration to 5mM resulted in decreasing but still elevated sorbitol concentrations at one hour with a return to non-diabetic levels by 3 hours.

Thus RBC sorbitol concentration may be a more useful indicator of glycemic control in diabetes than either the blood glucose or HbA1.

887 THE ENZYMIC BASIS FOR THE PHENOTYPIC VARIATION OF HURLER AND SCHEIE SYNDROMES. Reuben Matalon, and Minerva Deanching. (Spon: by Ira M. Rosenthal) Abraham Lincoln Sch. of Med. Dept. Ped., Univ. of Ill. Chicago.

The Hurler and Scheie syndromes are autosomal recessive mucopolysaccharidoses, characterized by mucopolysacchariduria and profound deficiency of α-L-iduronidase when assayed with α-L-phenyliduronide as substrate. Phenotypically, Hurler patients are severely retarded while Scheie patients have normal intelligence. In order to study the substrate specificity of α-L-iduronidase toward natural substrates, tissue culture techniques were utilized. Skin fibroblasts from patients with Hurler and Scheie syndromes and normal controls were grown to confluency in modified Eagle's medium, washed X 3 with cold NaCl 0.15 M and suspended in 0.05 M acetate in 0.1M NaCl buffer pH 3.8. Cells were sonicated then centrifuged at 10,000 X g for 10 min. The supernatant solution was used for α-L-iduronidase activity with substrates prepared from the chemical desulfation of dermatan sulfate and heparin. Following 16 h. of incubation the released iduronic acid was isolated using ion exchange chromatography, and the iduronolactone was identified by paper chromatography. The Hurler cell extracts failed to release iduronic acid from either desulfated heparin or dermatan sulfate while the Scheie extracts released iduronic acid from heparin. Both Hurler and Scheie extracts had α-L-iduronidase deficiency when assayed with phenyliduronide. These findings indicate difference in the α-L-iduronidase specificity toward iduronic acid residues in heparan sulfate, which offers an explanation for the clinical differences between these syndromes.

888 GLUCOSE-6-PHOSPHATASE IN HUMAN PLACENTA: A NEW METHOD FOR THE STUDY OF GLYCOGEN STORAGE DISEASE TYPE I. POSSIBLE IDENTIFICATION OF A HETEROZYGOTE. Reuben Matalon, Parvin Justice, and Kimberlee Michals. Abraham Lincoln Sch. of Med. Dept. Ped., Univ. of Ill. Chicago, Ill.

Glycogen storage disease type I (Von Gierke's disease) is an autosomal recessive disorder characterized by growth retardation hepatomegaly, recurrent episodes of hypoglycemia and acidosis. The enzyme deficiency in this disease has been shown to be glucose 6-phosphatase, which its activity has been reported mainly in liver and kidneys. In order to find a tissue that may exhibit glucose-6-phosphatase activity, full term human placentas were utilized. Placental slices were washed X3 with cold 0.15 M NaCl, then sonicated in 0.1M cacodylate buffer pH 6.5 and centrifuged for 10 min at 10,000 Xg. The supernatant fractions were assayed for glucose 6-phosphatase with glucose 6-phophate. The liberated glucose was determined by glucose oxidase. Normal human term placentas hydrolyze 33.0-80.0 ug glucose/mg/protein/h. 0-1- ^{14}C-glucose-6-phosphate was used as an additional substrate and ^{14}C-glucose was identified by thin layer chromatography. Extracts of normal term human placentas release 50%-86% of the label/mg protein/h. A pregnancy at risk for glycogen storage disease type I was followed and the full term placenta was assayed for glucose 6-phosphatase. The values obtained from the extracts of the placenta at risk released 16.5 ug glucose/mg protein/h. while a normal control placenta released 34.0 ug glucose/mg protein/h. This finding suggests heterozygous state of the newborn. These data offer a new source for the study of glucose-6-phosphatase and for possible prenatal detection.