565 A BRUSH BORDER MEMBRANE DEFECT IN PHOSPHATE TRANSPORT IN X-LINKED HYPOPHOSPHATEMIA. H.S. Tenenhouse and C.R. Scriver. MRC Genetics Group, McGill Univ.-Montreal Children's Hosp. Res. Inst., Montreal, Quebec.

Stability of genes on the X chromosome during evolution and homologous mutant phenotypes in human X-linked hypophosphatemia (XLH), and Hyp mouse convinced us to study phosphate (Pi) transport in the latter to delineate the mutant gene product. Net reabsorption of Pi in the Hyp/Y (hemizygous) mouse is impaired in vivo. The defect in transepithelial transport of anion is not dependent on PTH. Hyp/Y cortex slices which expose the basolateral membrane take up and efflux Pi and incorporate anion into cellular pools normally. Accordingly neither "transport run out" nor "metabolic run out" of Pi, from the cytosol pool in equilibrium with luminal Pi across the brush border membrane, are affected in the mutant phenotype. Brush-border membrane vesicles (BBMV) purified ten fold from normal renal cortex transport Pi against an electrochemical gradient by an Na^+-dependent, arsenate-inhibited process; an Na^+-independent diffusional process is also present. Hyp/Y BBMVs have a partial deletion of the Na^+-dependent Pi transport process (Hyp/Y, 227 pmoles/mg protein at 60s; +/Y littermate control, 408 pmoles/mg; $p < 0.001$). Time-course studies confirm a significant loss of Na^+-dependent Pi transport in Hyp/Y at 30 and 60s, 2 min, 10 and 30 min. Simultaneous transport of D-glucose is normal in Hyp/Y BBMV. We conclude that the mutant gene product which impairs transepithelial transport of Pi in XLH is a Pi carrier located in the brush border membrane.

566 PROPIONICACIDEMIA PRESENTING AS HYPERAMMONEMIA. Jess G. Thoene and Lawrence Sweetman (Spon. by Roy D. Schmickel) Univ. of Mich., Dept. Peds., Ann Arbor and Univ. of Calif. at San Diego, Dept. Peds., La Jolla.

A male infant, with an apparent urea cycle defect, with hyperammonemia and absent ketoacidosis, was proven to have propionicacidemia. It is important to consider defects of organic acid metabolism in patients with hyperammonemia. The patient was admitted at 9 days of age because of persistent vomiting followed by coma. There were no gestational ills, and no family history of neonatal deaths. The coma, responsive only to deep pain, and moderate hepatomegaly, were the only abnormal physical findings. Initial laboratory investigations included: hemoglobin 16.7, WBC 3600, platelets 57,000, normal electrolytes including a serum bicarbonate concentration of 22 mEq/l, normal Ca^{++} and $PO_4^{=}$ and normal liver function. The urine was negative for ketones. The concentration of NH_3 in the blood was 660 µg/dl, the glycine concentration was 12.3 mg/dl (nl < 2.3). The plasma propionate concentration was 86.6 µM (nl < 10), and the urinary methyl citrate excretion was 53.5 µEquiv/mg creatinine (nl < .03). Other abnormal metabolites of propionate detected in the patient's urine included: propionylglycine, 3-OH propionate, and 3-OH valerate. Three new metabolites, 2-methylbutyrylglycine, 2-methyl-3-oxovalerate and 2-methyl-3-hydroxyvalerate were additionally detected. Propionyl-CoA carboxylase activity in cultured fibroblasts was less than 5% of normal. The patient responded well to peritoneal dialysis with return of ammonia, glycine, WBC, and platelets to normal. He is gaining weight and making developmental progress on dilute Isomil supplying 1g/kg/day of protein.

567 THE CHERRY RED SPOT-MYOCLONUS SYNDROME DUE TO NEURAMINIDASE DEFICIENCY. Robert E. Tipton, George H. Thomas, Lawrence T. Ch'ien, L. W. Reynolds and C.S. Miller (Spon. by Robert L. Summitt). Depts. of Pediatrics and the Child Development Center, Univ. of Tenn. Center for the Health Sciences, Memphis, Tenn., and The John F. Kennedy Institute, Dept. of Pediatrics, the Johns Hopkins University School of Medicine, Baltimore, Maryland.

The cherry red spotmyoclonus syndrome has been reported in at least 11 individuals in the past 20 years. The symptoms usually have their onset in the second decade of life and include macular cherry-red spots, myoclonus and increased deep tendon reflexes and no dementia. Recently neuraminidase deficiency has been documented in some of these patients. This report is of a 31 year old male with macular cherry-red spots, hyperreflexia and myoclonus (tremors and sudden quick jerks of both hands) without dementia. An older brother who had progressive myoclonus died at age 33 with myoclonic seizures. Homogenates of cultured fibroblasts from the proband exhibited a marked deficiency of neuraminidase activity. The neuraminidase activities in fibroblasts from the proband's parents and in two children of the proband were in the intermediate range. The cherry red spot-myoclonus syndrome is clinically distinct from Mucolipidosis I in which neuraminidase deficiency has also been reported.

568 PATTERN AND ASYNCHRONY OF LATE X REPLICATION IN CASES OF MULTIPLE X. Daniel L. Van Dyke, Lester Weiss, Mary Poel. Henry Ford Hospital, Departments of Pediatrics & Pathology, Detroit.

The replication patterns of human chromosomes can be visualised using the RBG technique. Five to six hours prior to termination of lymphocyte culture, BudR is added to a concentration of 75 mcg/ml. Prepared slides are exposed to 33258 Hoechst and sunlight concurrently, and subsequently stained with Giemsa. The BudR-incorporated (late replicating) regions are stained pale, and the resultant pattern is similar to R-banding. We have been examining the fine details of X chromosome replication in subjects with structural or numerical X abnormalities. In early metaphase cells of children with multiple X chromosomes the late-replicating X's do not replicate synchronously. The degree of asynchrony varies from cell to cell. However, the late-replicating X chromosomes follow a single sequence of replication. Xp22, p11, and q13 replicate first (98%), followed by q26 (95%), q24 and q28 (80%), and q22 (60%). (Percentage indicates the probability of replication prior to addition of BudR). The late replicating major bands are q12 (10%), q23 and q27 (5%), q25 (2%), q21 and p21 (0%). Late replicating sub-bands are seen in p22 (60% of X's), p11 (30% of X's), and q13 (10% of X's). Very early metaphase chromosomes are still under examination and are likely to reveal other late-replicating sub-bands. Exceptions to the above sequence of replication include late replication of Xq13 (4% of X's) and fusion of q22, q24, or q26 possibly due to early replication of q23 or q25 (7% of X's).

569 BETA-GLUCOSIDASE ACTIVITY IN CULTURED SKIN FIBROBLASTS FROM CONTROLS AND PATIENTS WITH GAUCHER'S DISEASE. David A. Wenger and Grant Olson. University of Colorado Medical Center, Department of Pediatrics, Denver, Colorado 80262.

Gaucher's disease is a group of autosomal recessive disorders involving the storage of glucosylceramide because of a deficiency of glucosylceramide β-glucosidase activity. The clinical pictures range from the non-neuronopathic form with variable symptoms ranging from mild to severe (Type 1), acute neuronopathic form with severe visceral and CNS involvement (Type 2) and subacute neuronopathic form with less severe visceral and CNS involvement (Type 3). A study of β-glucosidase activity has been aimed at defining a method for predicting the clinical type before symptoms are obvious. This is especially true of samples received from 2-4 year old patients who are still free of neurological symptoms. Beta-glucosidase activity has been measured in cultured skin fibroblasts using 4-methylumbelliferyl-β-D-glucopyranoside and ^{14}C-glucose-labeled glucosylceramide. Kinetic studies using ^{14}C-glucosylceramide and pure sodium taurocholate of varying concentrations have provided evidence for two β-glucosidases. Using either 5-7 nmoles or 60-65 nmoles of glucosylceramide, controls and patients with all clinical types of Gaucher's disease were studied. Type 2 patients had less residual activity when the higher substrate concentration was used than when the lower concentration was used. The Type 1 patients did not show this difference. This effect was not observed with the fluorogenic substrate.

570 PLACENTAL LIPIDS, FATTY ACID COMPOSITION, AND ENZYMES J.W.Whitsett, P.Russell, C.J.Glueck, R.C.Tsang, C.McLain, T. Joyce, K.Bove, M.J.Mellies, and P.M.Steiner. Gen.Clin.Res Center, Cincinnati General Hospital, U. Cincinnati, Coll. of Medicine.

In a subject homozygous for familial hypercholesterolemia (FHC) placental lipids (PL), enzymes (E), and insulin receptors (IR) were studied to determine if changes in PL were associated with change in E or IR. Levels of FHC placental phospholipids, free fatty acids, triglycerides, cholesterol esters, and cholesterol were respectively .031, .106, .045, .149, and .044 mg/g placenta, with ($\bar{X}$+SD) values in 6 normal placentas being .11±.02, .07±.01, .09±.004, .15±.04, and .13±.03. The FHC placenta had much less phospholipid, triglyceride, and cholesterol and more free fatty acids than normals. Placental palmitic acid in all lipid classes of the FHC was twice that of normals, while FHC placental linoleic acid was increased and arachidonic acid decreased. Marker E content and localization in the FHC placenta was normal. FHC placental alkaline phosphatase, 5' nucleotidase, Ca++ and Mg++ ATPase, and IR concentrations were normal when compared to 6 normal term placentas. Microvillus brush border membranes were enriched 10-12 fold with marker E, as compared to activities in the whole placental homogenate in FHC and normals. The IR concentration at 12×10^{-10}M I-125 insulin in the FHC and normal placentas was 33.7 vs. 37±8.2 $\times 10^{-6}$ nmoles/mg protein respectively, an insignificant difference. Despite changes in placental membrane lipids in the FHC, there were no changes in marker E or IR concentration, implying normal placental function as measured (indirectly) by these parameters, and by the successful outcome of this pregnancy and birth of a healthy obligate heterozygote male neonate.