571 FAILURE OF FIBROBLAST ALLOGRAFT FOR ENZYME REPLACEMENT IN MUCOPOLYSACCHARIDOSIS, TYPE VI. Judith P. Willner, Reuben Matalon, Nicholas Beratis, Robert Ritch, Judith Rose, Kurt Hirschhorn, and Robert J. Desnick, Mt. Sinai School of Medicine, Department of Pediatrics, NYC.

Subcutaneous transplantation of histocompatible cultured human fibroblasts in a hemizygote with mucopolysaccharidosis Type II, reportedly resulted in both clinical and biochemical improvement, the latter supported by increased uronic acid excretion (Dean *et al.* Nature 261:323, 1976). Therefore, we evaluated the effectiveness of fibroblast transplantation for enzyme replacement in an 8-year-old girl with arylsulfatase (AS) B deficiency, MPS Type VI. A suspension of cultured skin fibroblasts (3×10^8 cells) obtained from a histocompatible sister with normal ASB activity was administered subcutaneously to the recipient, followed by immunosuppression with anti-thymocyte globulin. No rejection phenomena were observed. The activity of ASA and ASB in leukocytes, plasma, and urine, and the urinary excretion of total AMPS were determined pre- and post-transplantation. Clinical and pathological evaluation included assessment of changes in hepatosplenomegaly, long bone growth, and ultrastructural accumulation of conjunctival AMPS. These biochemical, ultrastructural, and clinical parameters were unaltered up to 9 months after transplantation. The failure of fibroblasts to synthesize sufficient ASB activity to effect a biochemical or clinical change may be due to insufficient cell dose, homograft rejection, or, more likely, the inability of the infused cells to produce and distribute active and stable enzyme for AMPS degradation.

572 THE MOLECULAR ANATOMY OF A HUMAN GENE. Golder N. Wilson, Barbara A. Hollar, Hilda Knoller, John R. Waterson, and Roy D. Schmickel, University of Michigan, C.S. Mott Children's Hospital, Department of Pediatrics, Ann Arbor, MI 48109.

The ability of bacterial restriction endonuclease to recognize specific sequences in DNA makes them a potent tool for dissection of the human genome. The organization of ribosomal genes in normal and neoplastic human tissues has been studied by the restriction of purified DNA. Fragments of DNA produced by the restriction endonucleases EcoRI and HindIII were separated according to size by agarose gel electrophoresis. DNA fragments which contained ribosomal genes were identified by hybridization to ^{125}I-labelled human ribosomal RNA and autoradiography. Analysis of these studies showed that EcoRI cleaves ribosomal DNA from human spleen into fragments of three sizes (molecular weights 12, 5, and 4.2×10^6). Digestion with HindIII yields fragments of two sizes (molecular weights 9.3, and 8.4×10^6). These data permit the construction of a single map for the human ribosomal gene of 17×10^6 daltons. A similar analysis of human DNA from several fibroblast and tumor cell lines shows variation only at a single EcoRI site. Despite marked alterations in karyotype, the organization of ribosomal genes has been strongly conserved in the neoplastic tissues so far examined.

573 HETEROZYGOTE EXPRESSION IN PROPIONYL CoA CARBOXYLASE (PCC) DEFICIENCY: DIFFERENCES BETWEEN THE MAJOR COMPLEMENTATION GROUPS. Barry Wolf and Leon E. Rosenberg Dept. Hum. Gen. and Peds., Yale Univ. Sch. Med., New Haven, CT

PCC deficiency, an autosomal recessively inherited disorder, constitutes at least two major genetic complementation groups (A and C) each characterized by the presence of structurally altered PCC. We now report studies of PCC activity in tissue extracts from controls and obligate heterozygotes from both complementation groups. PCC activity in fibroblast extracts from 6 group A heterozygotes was 43-64% of that in control extracts ($p<0.001$), while activity in 12 group C heterozygotes was indistinguishable from control values. Similar results were obtained using peripheral blood leukocytes. In none of 8 families (5 group C; 3 group A) in which PCC activity was studied in both parents of an affected child were significant differences observed between parents. Thermostability (45°C) of PCC activity in heterozygotes from both groups was identical to control. Activities of two other mitochondrial enzymes (β-methylcrotonyl CoA carboxylase and glutamate dehydrogenase) were comparable in controls and both groups of heterozygotes. Whereas the data from group A heterozygotes conforms to expected gene-dose effects, the results from group C heterozygotes are distinctly unusual. Since mammalian PCC is a tetramer, the latter results may reflect any of the following mechanisms: normal PCC activity in tetramers with at least one normal subunit; an increased proportion of normal subunits due to increased degradation of mutant subunits; or compensatory synthesis of normal subunits.

574 HEREDITARY FRUCTOSE INTOLERANCE: FATE OF PLASMA POTASSIUM DURING FRUCTOSE LOAD. Lawrence T.K. Wong, A. George F. Davidson, Kent Dooley, Derek A. Applegarth and Jim Dimmick, Dept. of Paediatrics, University of British Columbia, Vancouver, British Columbia. (Spon. by J.P. Skala).

A one year old North American Indian boy who presented with episodes of vomiting, lethargy and periodic hypoglycaemia was shown to have hereditary fructose intolerance. A liver biopsy showed typical histological changes and fructose-1-phosphate aldolase activity was greatly diminished.

Although blood fructose increased only slightly during an oral fructose tolerance test, he developed severe hypoglycaemia which did not respond to glucagon. Insulin levels remained low. Plasma lactic acid, uric acid, magnesium, methionine, valine, leucine, isoleucine and aspartate aminotransferase rose during the test while potassium and phosphate fell markedly. Continuous EEG monitoring showed no significant changes, but an ECG showed a slight cardiac arrhythmia when potassium was at its lowest level. Urinary excretion of uric acid and magnesium increased during the fructose load, but there was no rise in the excretion of potassium, phosphate, or bicarbonate.

Patients with hereditary fructose intolerance may exhibit a Fanconi syndrome and this has been blamed for the falling plasma potassium during a fructose load. The hypokalemic response to acute fructose loading in this patient has been demonstrated not to be due to renal losses. We speculate that potassium probably entered the intracellular space when fructose was administered.

575 GLYCINE THERAPY FOR THE ACUTE AND CHRONIC MANAGEMENT OF NEONATES WITH ISOVALERIC ACIDEMIA. M. Yudkoff, R. M. Cohn, B. Blazer-Yost, R. Rothman and S. Segal. Division of Biochemical Development and Molecular Diseases, Dept. Pediatrics, Univ. of Pa. and Children's Hospital of Philadelphia, Philadelphia, Pa. 19104

We have used glycine for the acute and chronic management of two newborn infants with isovaleric acidemia. Both infants presented with deep coma and serum isovaleric acid levels in excess of 50 mg/dl after several days of treatment with parenteral fluids and protein restriction. After administration of intravenous glycine (250 mg/kg/day) the serum isovaleric acid level declined to less than 1 mg/dl within 3 days. Restoration of normal clinical status occurred within 6 days. Unexpectedly, the sharp decline of the serum isovaleric acid level was not accompanied by an equally sharp rise of urinary isovalerylglycine excretion. This suggests that in neonates isovalerylglycine may be excreted by the GI tract or that the glycine effect is mediated through a mechanism other than the synthesis of isovalerylglycine. The infants have been treated prophylactically with a low protein diet and oral glycine for 3 and 8 months, respectively. Their psychomotor development has been entirely normal. Neither has suffered a relapse even though the older infant has had several intercurrent infections. Glycine treatment in neonates appears to have aided in the management of the acute toxicity of isovaleric acidemia and may have prevented the reaccumulation of isovaleric acid.

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576 URINARY IRON DOSE RESPONSE TO SUBCUTANEOUS (SQ) DESFERRIOXAMINE (DF) AND ORAL ASCORBIC ACID (VIT. C) IN CONGENITAL HYPOPLASTIC ANEMIA. Daniel R. Ambruso, Barry S. Mahony, John H. Githens, Richard D. Propper, Univ. of Colo. Med. Ctr., Denver, and Children's Hospital Med. Ctr., Boston, Departments of Pediatrics.

Urinary iron excretions with DF and vit. C were evaluated over 48-hour periods in an iron overloaded 9-year-old male with congenital hypoplastic anemia. SQ DF was 85% as effective as I.V. DF. A 12-hour SQ infusion produced the highest excretion during treatment but had a significant effect for 36 hours. Dose response curves were determined for each drug with continuous 12-hour SQ infusions. Using a constant vit. C dose of 500 mg p.o./d and increasing doses of DF, 36 hr. urinary iron increased from 22.5 mg with 1 gm DF to 56.2 mg with 4 gm DF (linear correlation coefficient 0.96, $p<0.01$). Increasing doses of vit. C (0.5 to 3 gm/d) with a constant DF dose of 2.9 gm were not associated with significant increases in iron excretion (from 44.2 to 49.9 mg) (linear correlation coefficient 0.66, $p>0.05$). Continuous EKG and frequent echocardiogram monitoring showed no arrythmias or other changes in cardiac function with doses up to 3 gm vit. C. Our data shows that increased iron excretion continues for 36 hours following 12-hour SQ infusions of DF. A linear increase in excretion occurred with SQ DF doses up to 4 gm. Raising the vit. C dose from 0.5 to 3 gm per day did not result in a significant increase in iron excretion.