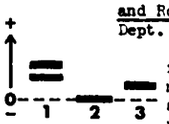
493 GAUCHER'S DISEASE: AN ELECTROPHORETIC TECHNIQUE FOR VISUALIZATION OF ß-GLUCOSIDASE ISOZYMES FROM LEUKOCYTES AND CULTURED FIBROBLASTS. Francis Y.H. Choy and Ronald G. Davidson, McMaster Univ. Med. Ctr., Dept. of Pediatrics, Hamilton, Canada.



Although an artificial fluorescent substrate for assay of ß-glucosidase activity is available, no electrophoretic technique has been described, since the enzyme cannot be solubilized with the usual techniques. Data from intact leukocytes showing 2 pH optima (4.0 and 5.3) suggested the existence of isozymes and prompted this study. We found that when a leukocyte or fibroblast suspension from normal individuals was freeze-thawed x 10, up to 30% of total enzyme activity remained in the 48,000 x g supernate and the enzyme would migrate in various gel systems. The diagram depicts fluorescent bands of ß-glucosidase activity after electrophoresis in cellulose acetate gel, followed by incubation in 4-methylumbelliferyl-ß-D-glucopyranoside and visualization under long wave UV light: lane 1, the expected 2 bands from leukocytes; lane 3, the single band from a fibroblast extract. Leukocyte extracts from 3 patients with juvenile onset Gaucher's Disease yielded a single band which remained at the origin (0), as shown in lane 2. Thus, the mutant enzyme may be bound to the lysosomal membrane in such a way as to interfere with its activity towards the natural substrate. The electrophoretic technique may be of value in the diagnosis of variants of Gaucher's Disease and in elucidation of the basic enzymatic defect.

494 EVALUATION OF ANEMIA IN CYSTINOSIS. Elfrid Cifuentes, Frances M. Gill, and Karl Roth. (Spon. by Elias Schwartz) Univ. of Pa. Sch. Med., The Children's Hosp. of Phila., Dept. of Ped.

Cystinosis is a metabolic disorder with deposition of cystine in various organs, including kidneys and bone marrow (BM). Slowly progressive renal failure is due to renal tubular dysfunction and glomerulosclerosis. Normocytic, normochromic anemia is usually present in later stages. We have studied 2 brothers, ages 8 and 5 years, with cystinosis and anemia with ^{59}Fe to measure the amount and effectiveness of erythropoiesis. The 8-year-old had a Hb of 5.5 g/dl with 4% reticulocytes, mildly decreased plasma iron clearance (PIC), normal iron utilization (FeU), and plasma iron turnover (PIT) at the lower limits of normal. There was delayed appearance of ^{59}Fe on BM scan, but normal distribution of marrow reticulo-endothelial elements, measured by ^{99m}technetium. Serum and urine erythropoietin levels were inappropriately low for the degree of anemia. Renal function values were BUN 59 mg%, creatinine (C) 6.9 mg%, and creatinine clearance (CC) 10.7 ml/min/1.73M^2. The 5-year-old had Hb of 9 g/dl with 0.6% reticulocytes, and normal PIC, PIT, and FeU. Renal function values were BUN 41 mg%, C 1.8 Mg%, and CC 43.7 ml/min/1.73M^2. The normal FeU and normal or nearly normal PIC indicate that the BM is capable of utilizing iron to produce red cells which survive to circulate. In the older patient, however, the PIT is at the lower limit of normal despite marked anemia, suggesting no compensatory increase in red cell production. These findings are similar to those in other renal disease and do not indicate a defect specific to cystinosis.

495 LYSOSOMAL ACID LIPASE ACTIVITY IN HUMAN LYMPHOCYTES: POPULATION STUDIES. Paul M. Coates and Jean A. Cortner. The Children's Hospital of Philadelphia, Joseph Stokes, Jr. Research Institute, Phila.

Lysosomal acid lipase (LAL) activity, measured with 4-methylumbelliferyl oleate as substrate, is present in high concentration in lymphocytes and monocytes, but not in polymorphonuclear leukocytes. Lymphocytes were isolated from whole blood samples by modification of the Ficoll-Isopaque method of Böyum (Scand. J. Clin. Lab. Invest. Suppl. 97, 1968). More than 300 random samples were obtained; LAL and acid ß-galactosidase (GAL) were assayed and their specific activities, as well as the LAL/GAL ratio, were determined. There was an approximately continuous unimodal distribution of LAL, GAL and LAL/GAL among males and females, blacks and whites. There were no significant sex differences for any of the measurements, nor was there a significant difference in GAL activity between blacks and whites. However, blacks appeared to have higher lymphocyte LAL activity than whites. This difference was most readily seen in the first decade of life. In this age group, the LAL/GAL ratio among blacks was nearly twice that for whites. Studies of LAL activity among families are underway. (Supported in part by NIH grant HL 18723-01; National Foundation grant 6-80 and AHA grant 76-768).

496 "MONOSOMY" RE-EVALUATED. Karen K. David, Lillian Y. F. Hsu, Steluta Cristian and Kurt Hirschhorn, Dept. of Peds., Mt. Sinai Sch. Med.,City Univ. of New York.

The chromosome constitution of a 4 year old retarded girl was recently re-evaluated using banding methods. Initial chromosome analysis performed at another institution using the conventional method was interpreted as 45,XX,-G. The patient was the full term 5 lb 14 oz product of a second pregnancy to a 23 year old mother. There was no history of fetal wastage. The positive physical findings included failure to thrive, moderate psychomotor retardation, mildly dysmorphic facies with a prominent nasal bridge and large ears, low set nipples, systolic ejection murmur, hypoplastic labia majora, generalized spasticity with limited hip abduction, knee extension, and distally located palmar triradii (t"). With the combination of Q, G and R banding methods, it is evident that the patient has an unbalanced insertion type of translocation, 45,XX,-17,-21,+ins(17;21)(17pter→17q23::21q11→21q22::17q23→17qter). The distal portion of 21q22 has been deleted. Apparently the absence of a portion of the euchromatic region of 21q22 is responsible for the patient's abnormal phenotype. The patient shows some features of 21 deletion syndrome. Both parents have normal chromosomes. Since complete autosomal monosomy is extremely rare, even in studies of early spontaneous abortion material, all liveborns with apparent monosomy must be re-evaluated with a combination of banding methods to search for an unbalanced translocation resulting in a partial deletion. If such a structural aberration is not found, multiple tissues should be studied to search for 45/46 mosaicism.

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Abstract withdrawn

498 IDENTIFICATION OF PARTIAL TRISOMY 13 SYNDROME BY DNA REPLICATION STUDIES. Beverly S. Emanuel, Elaine H. Zackai, William J. Mellman. The University of Pennsylvania School of Medicine, The Children's Hospital of Philadelphia. Department of Pediatrics, Genetics. Philadelphia

The Giemsa stainability of chromosomal regions containing late replicating DNA can be suppressed or enhanced by incorporation of BUdR into the DNA at the end or beginning of the S period. A terminal pulse of BUdR reveals a uniquely informative pattern of chromosomal bands coupled with specific decondensation of late replicating regions. These techniques provide new information for the clinician and cytogeneticist in precise identification of heretofore undecipherable "de novo" structural chromosomal rearrangements with partial aneuploidy.

Our patient was a one month old male with multiple congenital anomalies including postaxial polydactyly, heart defect and renal anomaly. Conventional chromosomal analysis revealed a 46,XY,Dq+ karyotype, while Trypsin G-banding suggested an inverted duplication of the distal long arm of chromosome 13 (i.e. 46,XY, inv dup (13q) (q14→q34). Chromosomes of both parents are normal. Bands q21 and q31 of chromosome 13 are late replicating and would be included in the presumed duplication. Employing a modified "33258 Hoechst" Giemsa procedure, and chromosomes prepared for enhancement and suppression of stainability of late replicating regions, we observed the predicted four bands of late replication on the abnormal D group chromosome, thus allowing confirmation of the diagnosis of partial Trisomy 13 Syndrome.