517 PHYSICAL CHARACTERISTICS OF 47,XXY BOYS AND 47,XXX GIRLS FOLLOWED FROM BIRTH. Michael J. Hudson, Arthur Robinson. University of Colorado School of Medicine and National Jewish Hospital and Research Center, Denver.

Identifying which children with sex chromosome abnormalities are at risk for aberrant development is important. To this end the following were identified at birth: 16 47,XXY (ages 2-12), and 11 47,XXX (ages 5-12) and are being followed with regular examinations. Sibs are intrafamily controls. 47,XXY Boys: a) Mean birth weight at 40 weeks gestation is 3.12 kg. (below the mean for the normal population). b) Heights fall within the normal range compared with siblings and general population. However there is a growth spurt between 3 and 7 years of age. c) Penile size is normal and testicular size in 60% is on the lower limits of normal. d) Head circumferences are within normal range but distribution is skewed to the left. e) The most common minor congenital malformation is clinodactyly (8). 47,XXX Girls: a) Mean birth weight at 40 weeks gestation is 3.09 kg. (below the mean for the normal population). b) Height is within normal limits. c) Head circumferences are all within normal limits with only two above the 50th percentile. d) Common minor congenital malformations are clinodactyly (8) and epicanthic folds (4). These 47,XXY boys have small but normal testes from infancy and an early growth spurt. Both groups have head circumferences less than the 50th percentile. The significance of these results in determining the future development of these children is not yet obvious.

518 LECTIN-MEDIATED UPTAKE OF LYSOSOMAL HYDROLASES BY HUMAN FIBROBLASTS. Rudy L.Juliano, Maureen R.Moore, Roy Gravel, John W.Callahan, and J.Alexander Lowden. The Hospital for Sick Children, Research Institute, Toronto, Ontario, Canada.

Although the enzyme defects in mucopolysaccharidoses are corrected with crude enzyme preparations from normal cells, those in sphingolipidoses are not. We tested the effect of several lectins on the uptake of β-hexosaminidase by Sandhoff fibroblasts and of β-galactosidase by fibroblasts from type 1 GM_1-gangliosidosis. The cells were incubated in phosphate-buffered saline in 2 cm^2 limbro wells for 16 hrs at 37° with various lectins and the specific purified human placental enzyme. Of the lectins tested Concanavalin A (Con A) was most effective. After incubation, the previously deficient cells had acquired enzyme activity. It was not removed by haptene treatment, suggesting an intracellular location. For example, when 2 x 10^5 GM_1 fibroblasts were treated with Con A followed by β-galactosidase, 10% of the enzyme remaining after incubation was associated with the cells. After treatment with mannose, 85% of this activity remained with the cells. In the absence of Con A only 0.5% of the enzyme was cell-associated. When the cells were incubated at 4°C, there was an increase in enzyme activity similar to that in the 37° cells but almost all activity was removed by the haptene. This technique should prove useful in manipulating the enzymatic complement of deficient cells.

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519 TAY-SACHS DISEASE (TSD): PRENATAL DIAGNOSIS AND HETEROZYGOTE SCREENING, 1969-1976. Michael M. Kaback, UCLA-Harbor General Hospital, Dept. of Peds., Torrance, Ca.

From 1969 (when the metabolic error in TSD was defined) to August 1976, the births of 115 infants with TSD have been prevented. This derives from prenatal monitoring of 461 pregnancies at-risk for TSD in centers from 12 reporting countries. Three hundred & seventy-one pregnancies were in couples with 1 or more previously affected children and 90 in couples identified "at-risk" thru heterozygote screening. All fetal TSD diagnoses were confirmed, where aborted tissue was available (103/115); 1 affected infant was missed by prenatal study; 4 TSD-identified fetuses were not electively aborted; and 340 unaffected children were born as predicted.

Sixty cities in 5 nations -- U.S., Canada, Israel, U.K., and S. Africa -- have initiated carrier screening programs. More than 150,000 adults have volunteered for the carrier detection serum Hex A test; over 6,000 heterozygotes identified; and 125 at-risk couples discovered (both parents: heterozygotes). An heterozygote frequency of 0.037 (1 in 27.3) is evident among the 101,000 American Jews screened (without known carriers or TSD infants in their families).

A quality control study in 13 N. American serum testing centers indicates nearly perfect accuracy in TSD heterozygote detection. Personal interviews with identified carriers suggest little, if any, psychological stigmatization. It is suggested from this experience that this approach to the control of TSD may serve as a model for future recessive genetic disease prevention efforts.

520 HETEROZYGOTE SCREENING IN TAY-SACHS DISEASE (TSD): A QUALITY CONTROL STUDY, 1976. Michael M. Kaback, Phyllis Hirsch, Chitra Roy, & Judy Anna. UCLA-Harbor General Hospital, Division of Medical Genetics, Torrance, California.

Thirteen centers in the U.S. and Canada, involved in TSD heterozygote screening, agreed to participate in a "blind" quality control study. Serum and WBC samples were prepared from 10 obligate TSD carriers (C) and 9 noncarriers (NC). Each lab received 4-6 C and 4-6 NC frozen serum aliquots and a similar number of WBC pellets (all samples: code-labelled). Raw data, methods used, and diagnosis for each sample was reported by each center.

Methods for quantification of serum Hex A varied, but did not appear to affect accuracy. Of 64C samples, 60 (94%) were diagnosed C; 3(4.7%) were designated inconclusive (I)-all in 1 lab; and 1(1.6%) was identified incorrectly as NC. A false positive frequency of 0.000 (with 75NC sera) and a false negative rate of 0.016 are evident with serum testing.

A serious problem (and its subsequent resolution) was uncovered by the WBC data. Although 81 of 81 NC pellets were correctly identified, 13 of 66C samples (19.7%) were called NC. Seven of 13 centers made no errors. The cause of this aberration has been shown to be high g centrifugation of WBC homogenates which preferentially reduces Hex B and results in an apparent increase in Hex A (making C → NC).

This study indicates a high, altho not perfect, level of accuracy, with serum screening. With appropriate modification, WBC analysis is also highly accurate. Surveillance of testing programs is critical for (a) monitoring testing accuracy (b) rapidly identifying and helping to correct technical problems, and (c) assuring that quality service is rendered the consumer.

521 ASSOCIATION OF 5q- AND REFRACTORY ANEMIA. Sara Kaffe, Lillian Y.F. Hsu, Ronald Hoffman and Kurt Hirschhorn. Depts. of Peds. and Med., Mt. Sinai Sch. Med., N.Y.

Specific chromosomal aberrations have begun to be recognized in hematologic disorders since the development of the current banding techniques. Within the last two years, six patients with refractory anemia have been reported from Belgium with a partial deletion of the long arm of one no. 5 chromosome (5q-). We have identified 5q- in another patient with refractory anemia. The patient is a 57 year old female with anemia for 3 years and headache for several months. Physical examination was within normal limits. There was no hepatosplenomegaly. The blood count revealed: Hb of 8.7; WBC 3200 with normal differential; platelets 689,000. There was poikilocytosis, anisocytosis and basophilic stippling. MCH, MCV, MCHC, Fe, Folate, B_{12}, haptoglobin and LAP were normal. Alkaline resistant Hb was 4.8%. The bone marrow aspirate showed normocellularity with a slight increase in megakaryocytes and erythroblasts, and 8% myeloblasts. Direct bone marrow preparation without PHA stimulation showed a 5q- in 60% of the cells analyzed. Banding studies showed that the partial deletion involves the terminal 2/3 of the long arm of one no. 5. del(5)(q14). Therefore, it appears that 5q- is specifically associated with refractory anemia. It remains to be seen whether patients with refractory anemia and 5q- tend to develop acute leukemia subsequently as has been implied recently in 5 patients with acute myelogenous leukemia.

522 ANDROGENIC ORIGIN OF HYDATIDIFORM MOLE. Tadashi Kajii and Koso Ohama. (Spon. by Lytt I. Gardner). Dept. of Peds., SUNY, Upstate Med. Ctr., Syracuse, New York, and Dept. of Obstetrics and Gynecology, Hiroshima Univ. School of Medicine, Hiroshima, Japan.

Hydatidiform mole (HM) is an abnormal pregnancy with grossly swollen chorionic villi, but without an embryo, cord, or amniotic membranes.

The origin of HM was studied in 7 cases of HM, all with a 46,XX karyotype, 2 of Caucasian and 5 of Japanese origin, and their parents, using fluorescent Q- and R- band chromosome polymorphisms as a marker. Homologous chromosome members in all the moles studied were homozygous for the polymorphisms. In 26 informative pairs, neither of the maternal homologues was inherited by the moles. In 20 of the 26 pairs, both the homologous members in a mole were derived from one of the paternal homologues. The findings indicate diploid androgenic origin of HM. Diploid androgenesis is the combination of failure of the female pronucleus in fertilization and the initiation of development with only a male component of chromosomes that have become diploid through fertilization either by a diploid sperm or a haploid sperm, followed by duplication of its chromosomes.