Histidinaemia in a consanguineous marriage*

Summary. Support to the autosomal recessive inheritance for histidinaemia is given by the finding of an affected product from a first-cousin marriage. The histidine loading test done on the parents confirms previous reports that female heterozygous metabolize the amino acid at a slower rate than male heterozygous.

Histidinaemia is a rare disorder which equally, affects both sexes. A case from a first-cousin marriage is reported.

Case report

The propositus, a caucasian male, was born of a primiparous mother on 16 March 1971 at term by Caesarean section because of breech presentation after an uncomplicated pregnancy. The father was 36 years old and the mother 33 years old. The parents are first cousins. Birth weight was 4500 g with spontaneous crying and breathing immediately after delivery. His development was normal up to the age of 4 months when it was noticed that he was not able to hold his head.

At the age of 8 months he was fully examined. He had decreased muscular tone, IQ of 35, and a flat EEG record. Radiology showed slight generalized osteoporosis, and the bone age was normal. A pneumoencephalogram revealed moderate diffuse cortical atrophy. Sex chromatin were negative and the karyotype was normal, 46,XY.

Metabolic studies

Two-dimensional paper chromatography done on a 24-hour urine collection detected histidine, alanine, lysine, and tyrosine. The plasma amino-gram on a fasting sample with the Beckman Amino-acid Analyzer showed elevation of the following amino acids: histidine, threonine, glycine, and alanine (Table I). Assay of skin histidase was planned but the parents refused further studies and

agreed only a study of their histidine loading. After a 12-hour fast a single oral dose of 5 g of L-histidine (Merck) was administered. Blood samples were taken at hourly intervals over 6 hours. In both parents the amino acid was metabolized more slowly than in adult controls as shown in Figure 1.

TABLE I
FREE AMINO ACIDS ELEVATED
IN PLASMA*

	Index Case	Infant Controls †
Histidine	2.06	0.46-0.86
Threonine	1.75	0.39-1.16
Glycine	1.41	0.58-1.26
Alanine	2.36	0.96-2.00

* All values expressed in mg/100 ml.

† Range of values of 10 normal children from 1 to 18 months.

FIG. 1. Plasma levels of histidine after a 5-g load given orally.

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Discussion

The fasting plasma histidine level (2.06 mg/100 ml) in our case is lower than that (above 5 mg/100 ml) reported by Neville *et al* (1972). Yet it is almost three times higher than our control values.

The presence in plasma of greater amounts of other amino acids has been previously reported with no satisfactory explanation, and the urinary excretion of other amino acids may be explained by a physiological saturation of the transport enzymes by histidine (Ghadimi, Partington, and Hunter, 1962).

The oral histidine loading test for detecting heterozygotes has given contradictory results (Hague and Holton, 1971; Neville *et al*, 1972). An interesting finding is that normal or heterozygous females metabolize histidine at a slower rate than normal or heterozygous males (Ghadimi *et al*, 1962; La Du *et al*, 1963; Holton, Lewis, and Moore, 1964; Cain and Holton, 1968; Rosenblatt, Mohyuddin, and Scriver, 1970). The parents of family 2 in Neville *et al*'s study (1972) are an exception. Further research is necessary into this apparent sex difference, especially in infants when histidine is considered an essential amino acid (Stifel and Herman, 1972).

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A 21/21 tandem translocation with satellites on both long and short arms

Summary. We report a case of 21/21 tandem translocation resulting in a chromosome with satellites on both the long and short arms, in a patient with relatively few stigmata of Down's syndrome.

Eight cases have been reported of Down's syndrome associated with an increase in the length of the long arms of a G-group chromosome. Familial translocations have been reported by Soudek, Laxová, and Adánek (1968) and Cohen and Davidson (1967). A few reports of non-familial G/G tandem translocations have also appeared (Warkany and Soukup, 1963; Zellweger, Mikamo, and Abbo, 1963; Lejeune *et al*, 1965). Sachdeva, Wodnicki, and Smith (1971) and Vogel (1972) found a G/G tandem translocation chromosome with satellites on both the long and short arms, and identified it as a 21/21 translocation by differential staining. The present report deals with the finding of a chromosome similar to those described by Sachdeva *et al* (1971) and Vogel (1972). However, our patient shows relatively few signs of Down's syndrome in contrast to the numerous stigmata reported in the majority of the other cases.

Case report

The proposita was born on 18 December 1963. Her mother died shortly after the patient's birth and the father is unknown. No further information about either parent or family could be obtained.

She was referred for chromosome studies following a report of slow progress at school and was seen by us at the age of 9.5 years. She was alert and responsive and her words were well articulated. She was in a special class at that time and seemed to be doing fairly well. Her IQ was reported to be 56.

On physical examination she found to be below the 3rd centile in both height and weight. Her bone age was retarded by 1 year 8 months. The only stigmata of Down's syndrome noted were a slight mongoloid slant, flattened nasal bridge, high arched palate, and a furrowed tongue. The creases on the palms and fingers were normal. The palmar dermatoglyphics, however, were typical of Down's syndrome and arch tibials were found bilaterally in the hallux areas.

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