

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 Adámek (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 hallucal areas.

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Cytogenetic findings

Chromosomal analysis of peripheral blood leucocytes revealed a modal count of 46 chromosomes. All chromosomes appeared normal, with the exception of the G group. Three morphological G-group chromosomes were found, along with an acrocentric chromosome about the size of a No. 18 which had satellites on both its long and short arms. Differential staining techniques (Caspersson *et al*, 1970; Seabright, 1971) identified the three morpho-

logical G-group chromosomes as being one No. 21 and two Nos. 22. The abnormal acrocentric exhibited a broad band on the proximal part of the long arm and an additional band, similar in size, on the distal part of the long arm (Fig. 1). These bands are comparable in size and staining intensity to the band seen on a normal No. 21. Satellite association, involving both ends of the abnormal chromosome was evident in numerous metaphases. Observation of the abnormal chromosome with interference contrast optics suggests that there may be a slightly raised structure midway between the two bands (Fig. 2).

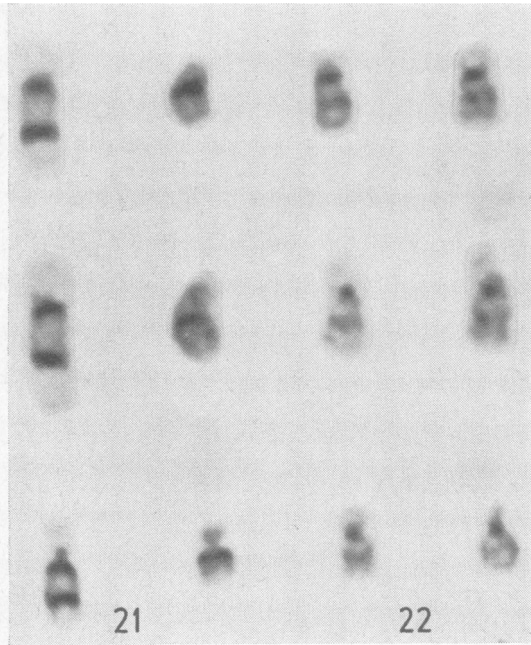


FIG. 1. Banding patterns of the G-group chromosomes.

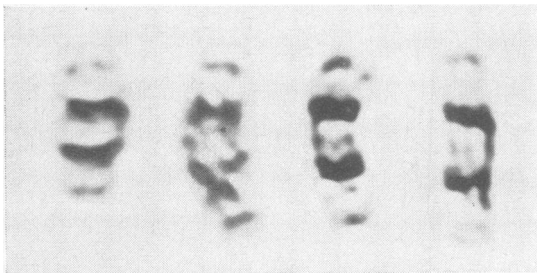


FIG. 2. The abnormal chromosome photographed through interference contrast optics, showing a raised area midway between the two bands.

Discussion

The origin of enlarged G-group chromosomes is clear in some instances. The case of Soudek *et al* (1968) was the result of a pericentric inversion of a familial G/G Robertsonian translocation chromosome. The case of Cohen and Davidson (1967) was also familial resulting from a balanced G/G translocation in the mother with subsequent trisomy in her children. As expected in cases of familial G/G translocation, random segregation of both translocated and normal G-group chromosomes leads to trisomy in some instances.

Warkany and Soukup (1963), Zellweger *et al* (1963), and Lejeune *et al* (1965) have reported cases of non-familial G/G tandem translocations which apparently resulted from break-rejoin events between two No. 21 chromosomes.

No simple mechanism, however, can explain the origin of the enlarged, bisatellited, G-group chromosomes described by Richards, Stewart, and Sylvester (1965), Vogel, Reinwein, and Engel (1970), Sachdeva *et al* (1971), and Vogel (1972). Vogel *et al* (1970) suggested that their abnormal chromosome was the result of a pericentric inversion that was followed by tandem translocation. In a later paper (Vogel, 1972) the suggestion was added that the abnormal chromosome could be the result of 'irregular' crossing over.

Our case presents a chromosome that is identical in morphology to those of Sachdeva and Vogel, except for the smaller size. We agree with the idea that it arose from a pericentric inversion and subsequent tandem translocation. No other mechanism, including a pericentric inversion with irregular crossing over, can explain the finding of a chromosome with this particular banding pattern and satellites on both the long and short arms. Fig. 3 illustrates how this type of rearrangement would result in a chromosome morphologically similar to the one found in our case.

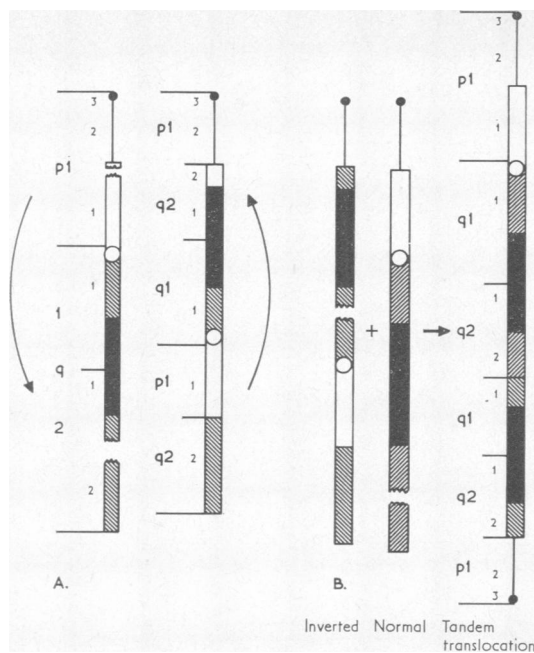


FIG. 3. **A:** Formation of the inverted No. 21 chromosome. A break between q21 and q22, and a break in the distal portion of p11, followed by a pericentric inversion would result in a satellite being attached to the long arm band.

B: Formation of the tandem translocation chromosome. A break, somewhere in q11 of the inverted chromosome, and translocation to the distal portion of the long arm of the normal No. 21 chromosome results in a tandem translocated chromosome.

Vogel *et al* (1970) noted a secondary constriction in the long arm of the abnormal chromosome and suggested that it represented the point of fusion between the two chromosomes participating in the tandem translocation. Similarly, it is interesting to speculate that the raised area visible in the euchromatic region of the present case also represents a point of fusion. If this is the case, a precise description of break points is possible. The translocation would be a result of a break near the centromere in q11 of the inverted chromosome, and one midway in q22 of a normal No. 21. This would result in a trisomy of the banded regions, most of the euchromatic region of q11 and a very small part of q22, along with monosomy for the distal half of q22.

The cases of Sachdeva and Vogel presented numerous features of Down's syndrome while our case shows relatively few. Excluding mosaicism, the smaller size of our marker chromosome relative to those of Sachdeva and Vogel may account for this. We feel that the size difference is due to the amount

of euchromatin present since all three cases appear to be completely trisomic for the banded regions.

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Partial trisomy 12 in a mentally retarded boy and translocation (12; 21) in his mother

Summary. Cytogenetic studies of an infant with malformations and a peculiar appearance showed a partial trisomy of chromosome 12. The mother carried a translocation of the distal part of chromosome 12 onto the short arm of chromosome 21, with breakpoints most likely at 12q24 and 21p11.