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Chromosome Studies in 101 Mentally Handicapped Jamaican Children

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Sex chromatin surveys have shown that inmates of institutions for the mentally retarded show an excess of sex chromosome abnormalities over newborns (Court Brown and Smith, 1969). The frequency of chromosomal abnormalities depends on the selection of the patients and the severity of retardation, autosomal abnormalities being commoner in the more severely retarded and sex chromosomal abnormalities in the mildly retarded. In fact the incidence of sex chromosomal abnormalities in the severely retarded approaches that in newborn populations (Court Brown and Smith, 1969).

For these reasons, it was felt worth while to examine children at an institution for mentally retarded in Jamaica. Initially it was hoped that there might be a high yield of sex chromosomal abnormalities from such a survey.

The incidence of mental retardation in Jamaica is not known. As might be expected in a country where the infant mortality rate is still in the thirties, and where malnutrition and infection are still potent causes of death (Thorburn and Hayes, 1968), facilities for the mentally handicapped are extremely limited. Custodial care is provided by the government for the severely handicapped, and at the mental hospital for the more ambulant but disturbed patients. Recently a small school for children with multiple handicaps due to rubella was opened by the Salvation Army. These institutions house approximately 120 children. A voluntary organization, the Jamaica Association for Mentally Handicapped Children (JAMHC), provides a home for 35 boys and the only school in the island for retarded children. A survey was carried out on the children attending this institution.

Method

A physical examination, buccal smears, and chromosome studies were performed on 85 unselected children in the home and school, with the parent's permission. To this group have been added 16 children of 3 years and older who were referred from the paediatric clinics for chromosome study because of mental retardation. These cases are selected, as children in whom a definite non-chromosomal clinical diagnosis had been made were not referred and children affected by the 1965 epidemic of congenital rubella (Miller and Thorburn, 1966) are not included. There was also selection in favour of patients with physical anomalies suggestive of chromosomal abnormality. The patients reported here do not include children with the D and E trisomies or gonadal dysgenesis. In spite of the lack of psychological testing, an attempt was made with the assistance of the teachers and the matron to assess and divide the children into 3 main groups, (1) mildly retarded (approx. IQ 50–80), (2) moderately retarded (approx. IQ 35–50), and (3) severely retarded (IQ below 30), using the classification developed by the American Association on Mental Deficiency (1963).* There were no profoundly retarded children.

Peripheral blood was cultured by a microtechnique modified from that of Arakaki and Sparkes (1963) for 48 or 72 hours. Twenty-five cells were counted and analysed microscopically in each case except in regular mongols where 12 or 15 cells were examined. Karyotypes were made in 3 cells. Buccal smears were stained with thionine and at least 100 cells were scored. Unsatisfactory smears were repeated. Where possible, studies on families were performed if indicated.

Results

One hundred and one children were examined.

Race. The racial make-up was very mixed, and because of this was not specifically analysed. Most children were of negro or mixed extraction. The rest were of Chinese, East Indian, or combinations of these with Caucasian. There were no pure Caucasians. Eighty-five children were from the school of the JAMHC, and made up about 80% of the school's pupils.

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* The President's Panel on Mental Retardation, *Mental Retardation, A National Plan for a National Problem: Chart Book.* U.S. Department of Health, Education and Welfare, Washington, D.C., 1963, p. 15.

TABLE

RESULTS OF STUDY

	Males	Females
Total number	73	28
Total with chromosome abnormality	15	10
G trisomy	9	9
XYY	1	
XXY	1	
Balanced translocations	1	1
Dp+	1	
Gp−	1	
Fanconi's anaemia	1	

Sex. In total there were 73 males and 28 females. The results are set out in the Table.

Degree of retardation. Of the boys, 9 were classed as mildly retarded, and 6 were severely retarded. The rest were moderately affected. Of the girls, 4 were mildly retarded and the rest moderately. All but 2 of the children were ambulant. The age range was 3 to 40 years, but the majority were between 6 and 18 years.

Males without chromosomal abnormality. There were 58. In 11 it was possible to make a clinical diagnosis. Of these, 2 patients in their mid-teens were examples of 'Turner's syndrome in the male', 2 were typical of the Rubenstein-Taybi syndrome, and a further 2 were suspected of having this condition. Features strongly suggestive of the congenital rubella syndrome were found in 2. A history suggestive of infantile meningitis or encephalitis was obtained in 3.

Other aetiological factors. A history of incest was present in one case and was possible in a second case. There was a family history of mental retardation in the brother of one boy. Genetic histories were generally not available so the absence of such information is not significant. Two brothers from one family were attending the school. These are described in the next section.

Males with chromosomal abnormalities. There were 9 mongols all of whom had trisomy 21. The oldest, aged 27 years, had an older sister with mongolism. Unfortunately one parent had died and the other had emigrated and it was not possible to examine any other members of the family.

Three other boys had autosomal anomalies. The first (H.H.) was the second child of a family of 4, whose father and mother were aged 36 and 29 years, respectively, at his birth. Normal physical development (height 131 cm. at 8 years) was accompanied by minor anomalies of antimongoloid slant of the eyes, ptosis, mild pes cavus, and delayed acquisition of speech (hearing was normal) (Fig. 1): he was considered to be moderately retarded. Chromosome studies showed a complement of 46 (Fig. 2) with 8 large acrocentrics, and missing autosomes from the C group and pair 18 (46,XY, C−,D+,D+,18−). His parents and sibs all had normal phenotypes and chromosomes. He was therefore considered to have a *de novo* translocation between the short arm of an autosome of the C group and the long arm of a member of pair 18 [46,XY,t(Cp−;18q+)]. The question of whether this was a balanced translocation and therefore just a coincidence could not be answered.

The second child (M.H.) was also a moderately retarded well-developed boy of 9 years with mild microcephaly (head circumference 48 cm.) (Fig. 3). He was the first child of an unmarried woman. The first of twins, each weighing 1361 g. at birth, he was born when his mother was 26. The other twin died at 1 week of age. She had two other normal children by a different father. Both child and mother showed an anomaly of the short arm of a D chromosome (Fig. 4) which was found on autoradiography to be a member of pair 14. It was not possible to examine the other children so no conclusions as to the significance of this anomaly could be drawn.

The third autosomal anomaly was in the older of 2 brothers. These were members of a family of 4, which will be reported in greater detail elsewhere. The abnormality was a deletion of the short arm, centromeric region, and part of the long arm of a G autosome. The younger brother, who had sickle-cell anaemia, had a normal complement. The rest of the family, one of whom has sickle-cell anaemia, live in New York where they are being investigated. Both boys are physically well developed except for high arched palates, and both are moderately retarded.

Two boys had sex chromosomal abnormalities and were mildly retarded. One had 47,XXY. Though at a normal school, he had long been a behaviour problem. His abnormal physical features of very mild webbing of the neck and epicanthic folds had led the referring doctor to suspect partial mongolism. The other boy (C.P.) born in August 1964 was diagnosed in 1965 as having G trisomy, because of a peculiar facies, failure to thrive, and the presence of an extra small acrocentric chromosome thought to be a G. When he was brought to hospital at age 4 because of failure to talk and general slowness he was 114·5 cm. in height, and had no physical anomalies other than mild micrognathia and epicanthic folds (Fig. 5). Re-examination of

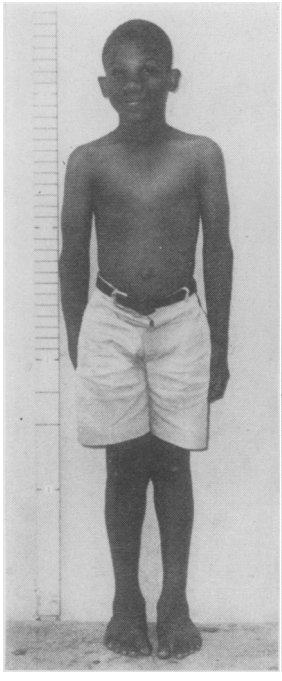

FIG. 1. Patient H.H. at 8 years.

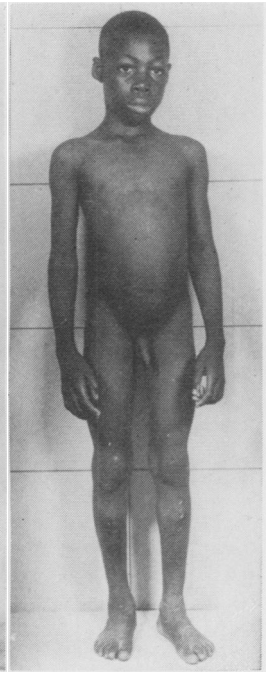

FIG. 3. Patient M.H. at 9 years.

his chromosomes and his old karyotypes showed that the extra chromosome was in fact a Y. The remaining boy who showed chromosomal abnormalities had Fanconi's syndrome of pancytopenia, radial anomalies, mild retardation, and probable renal anomalies, from which he subsequently died. One cell in 25 showed a quadriradial configuration.

Females with no chromosomal abnormalities. Eighteen girls had normal female complements. One was the daughter of a female mongol. One was considered to have the Rubenstein-Taybi syndrome. One had a history of meningitis in infancy. There were 2 sisters aged 13 and 9, both of whom showed features somewhat suggestive of phenotypic Turner's syndrome (Nora and Sinha, 1968). These were micrognathia, antimongoloid slant to the eyes, slightly low-set ears, a short neck with a low hairline, and a shield-shaped chest. Height was normal, however, and the older one had early pubertal changes. One other sib in the family was a normal boy.

Females with chromosomal abnormalities. There were 9 mongols all of whom had trisomy 21. The only other girl (P.B.) with a chromosomal

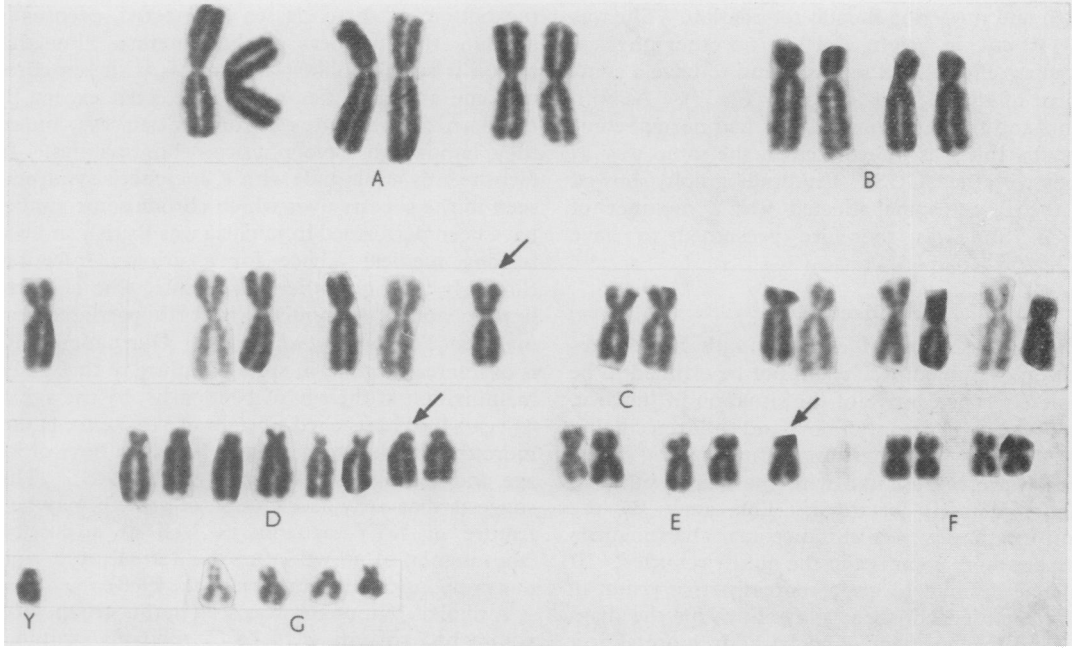

FIG. 2. Karyotype of H.H. showing 2 extra large acrocentric chromosomes and missing chromosomes in Group C and E.

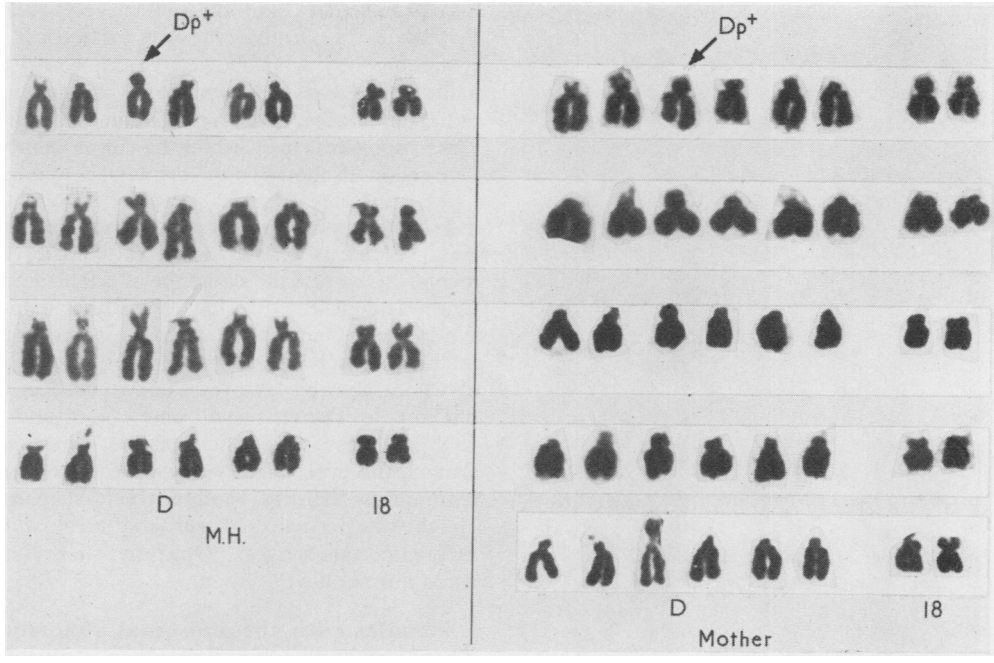

FIG. 4. Combined partial karyotypes of M.H. and his mother showing increase in length of the short arm of one of the D autosomes. Composite partial karyotypes of the D and No. 18 chromosomes of patient M.H. (left) and his mother (right) showing the Dp+ anomaly in chromosome 14.

abnormality was referred from a clinic because of mild microcephaly (head circumference 48·2 cm. at age 10) and moderate mental retardation. She was only 110 cm. in height and had no other physical anomalies (Fig. 6). She was found to have a complement of 46,XX,Bq+,F+,C− (Fig. 7). As both parents and the three normal sibs had normal complements, this was interpreted in the same way as the boy with the t(C;18). Autoradiography showed that the B autosome affected was a member of pair 5. She was therefore presumed to have 46,XX,t(5q+;Cq−).

Discussion

The cross-section of children with mental retardation examined here could not be claimed to be completely representive of the situation in Jamaica. There is a bias in favour of boys and children coming from the city of Kingston. Three levels of retardation are represented with the majority (82%) being moderately retarded. This may be the reason for the few sex chromosomal abnormalities which are more common in the mildly retarded. It would be difficult to get a representative group of mildly retarded children, as facilities for the diagnosis and management of such children are almost non-existent. In Government primary or junior secondary schools, classes of 70 or more are not uncommon; the mildly retarded presumably remain at the bottom of these classes undetected, eventually swelling the numbers of the illiterate. For this reason it seems unlikely that males with sex chromosome abnormalities will be detected except by newborn or school sex chromatin surveys, unless they happen to have physical abnormalities. In fact the only adult male with Klinefelter's syndrome seen in the 6 years over which chromosome studies have been performed in Jamaica was British and was seeking medical advice for a urinary infection. Similarly the only other XYY male, who also had hypogonadism, presented with orthopaedic abnormalities (Thorburn *et al.*, 1968). Our patient C.P. is of interest in that, in spite of failure to thrive and malnutrition at the age of 10 months, by the age of 4½ years he had reached a height of 114·5 cm., 11 cm. more than the mean height of Jamaican boys of his age and social class (Ashcroft *et al.*, 1965). This suggests that early acceleration of growth may be a feature of XYY patients as well as a possible continuation of growth after the normal time, as in our previous case (Thorburn *et al.*, 1968).

A total of 18 mongols was seen in this group, all of whom had trisomy 21. In 37 mongols examined over the past 5 years for reasons of maternal age

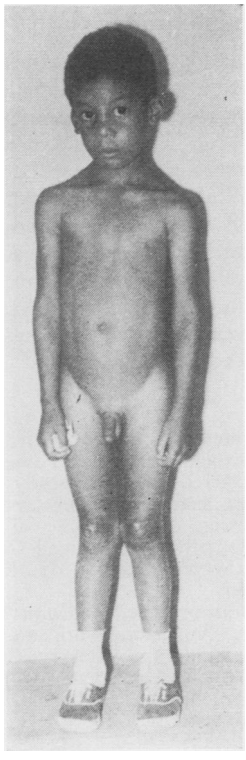

FIG. 5. Patient C.P. with XYY chromosomes at age 4 years.

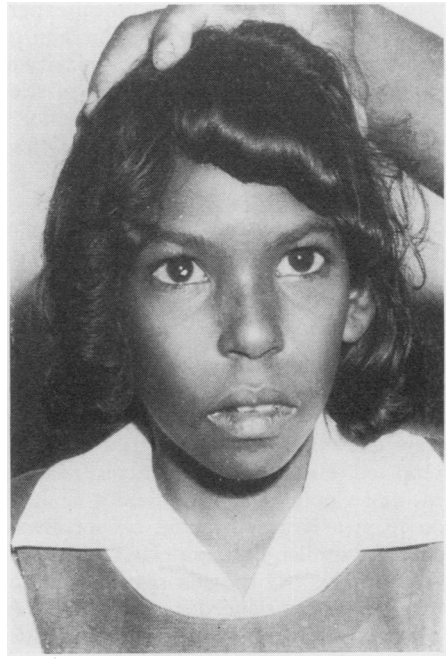

FIG. 6. Patient P.B. at age 10 years.

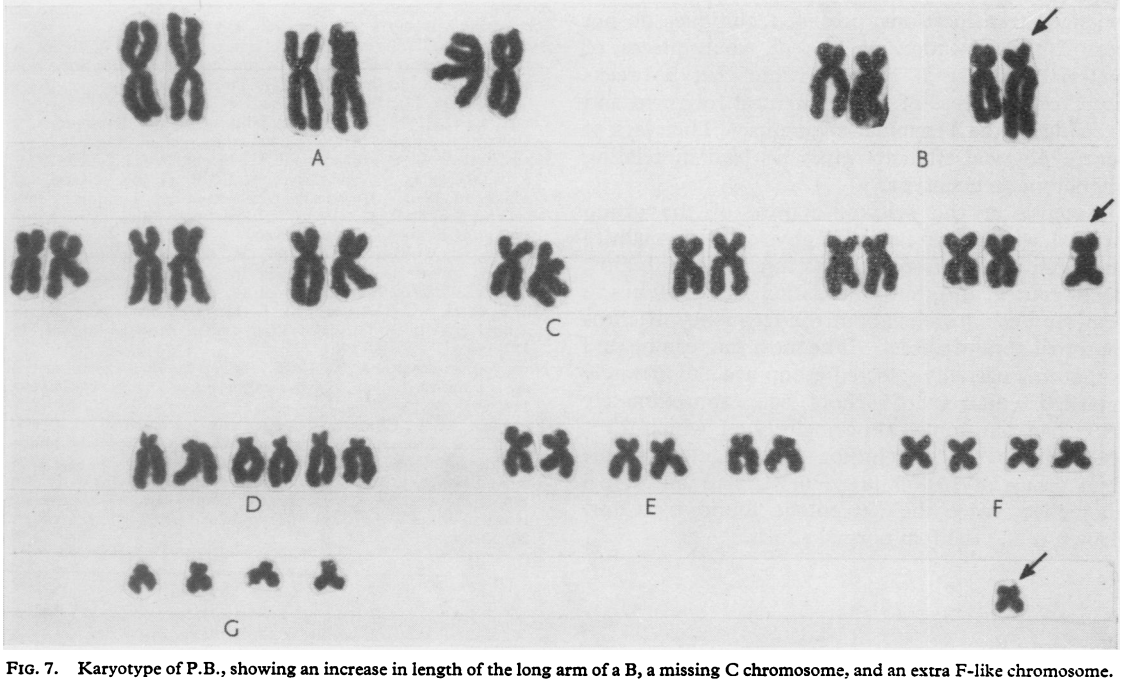

FIG. 7. Karyotype of P.B., showing an increase in length of the long arm of a B, a missing C chromosome, and an extra F-like chromosome.

below 30 at birth or to confirm a suspected diagnosis, one translocation t(GqGq) has been detected. No mosaics were found. The incidence of trisomy 21 in Jamaica is not known, but clinical experience suggests that it is probably as common as in Britain. Because of the racial heterogeneity of the children examined, one has to seriously question the significance of the finding of epicanthic folds. Generally speaking, however, the clinical diagnosis of mongolism was not made more difficult by the presence of features of the mongolian races.

The 4 cases with autosomal abnormalities other than the Fanconi syndrome were of interest because of their significance in relation to the presence of retardation. The Dp+ anomaly appears to be a controversial one. While studies on normal adults (Court Brown *et al.*, 1966) suggest that anomalies of the short arms of the acrocentric chromosomes are unrelated to developmental abnormality several phenotypically abnormal individuals with these have been reported (Carter, 1967; Francois, Matton-van Leuven, and Coppieters, 1968) and a small translocation from a large autosome cannot always be excluded. A similar situation exists with regard to a Gp− anomaly. This again may be due to a *de novo* balanced or unbalanced translocation. As the other retarded sib had no abnormality, one suspects that the anomaly may be coincidental.

Finally the two children with *de novo* translocations are interesting. Though they appear to have balanced translocations, present techniques do not permit the detection of loss of small pieces of material, and it is quite feasible that 3 breaks occurred with loss of a small central fragment and exchange of the 2 terminal fragments. Their lack of severe physical stigmata gives no lead in relating phenotype to genotype.

Because of the selected nature of the group studied, with bias in favour of physical abnormalities and against conditions such as infantile meningitis, birth trauma, and mild retardation, one hesitates to draw any conclusions about the frequency of chromosomal abnormalities. The most that can be said is that in a partially selected group of 82 moderately retarded children of school age, approximately 25% had autosomal abnormalities of which 22% were trisomy 21. Excluding the mongols from the total group of 101 children 6·3% had autosomal anomalies, twice the percentage found by Court Brown *et al.* (1966) in normal adults.

Summary

Buccal smears and chromosomal studies were performed on 101 mentally retarded Jamaican children. The initial aim of detecting sex chromosomal abnormalities was not fully realized, for, of the whole group, only 13 were mildly retarded; of these, 2 boys had 47,XXY and 47,XYY complements. Of the remaining 88 with moderate and severe retardation, 18 had trisomy 21, and 4 had other autosomal abnormalities. The significance of the latter 4 was not ascertained as 2 had anomalies of the short arms of the acrocentric chromosomes and 2 had apparently balanced translocations.

We are most grateful to Mr. and Mrs. Eric Dawson for the photographs and for technical assistance, and to colleagues who referred cases for study. This study could not have been performed without the help of Miss McNeill, the Matron of the home of the Jamaica Association for Mentally Handicapped Children; Miss C. Harding, the Secretary; and Mr. R. Eichstaedt, Peace Corps Worker.

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