Chromosome Studies in 14 Cases of Down's Syndrome and in One Suspected Case[1)]

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(With 2 Text-figures and 2 Tables)

Beginning with the work of Lejeune, Gautier and Turpin in 1959 reporting an extra autosome in several cases of Down's syndrome, generally referred to as mongolism, a number of papers have been contributed by many authors in the world, confirming their reports with supplementary data or with new findings additional to the standard 21-trisomy. They were excellently reviewed by several authors (Penrose 1961, Hamerton 1961, 1962, Carr 1962, and others). It has been shown that chromosome mosaicism, the association of abnormal sex chromosomes or autosomes, translocation of chromosome 21, and so on, occur in cases of Down's syndrome.

The present authors have had an opportunity to observe the chromosomes in 14 cases of Down's syndrome and in 1 suspected case, the results of which are described in the present paper.

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Materials and Methods

Chromosome observations were carried out on cells from short-term cultures of leucocytes from peripheral blood. Leucocytes of 3 or 4 days in culture were exposed to colchicine for 90 minutes in order to accumulate metaphase cells. After hypotonic treatment, cells were fixed with Carnoy's fixative and air-dried on slides (Moorhead *et al.* 1960). Chromosomes were stained with Giemsa. Chromosome analyses were performed according to the Denver system of nomenclature for the classification of individual chromosomes.

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Results

Diagnostic and clinical features of 15 patients under study are shown in Table 1. The results of chromosome observations are presented in Table 2. It was revealed that 14 cases of Down's syndrome had 47 chromosomes irrespective of sex. Karyotype analyses showed that the 47 chromosomes consisted of 46 normal chromosomes and an extra chromosome which was almost certainly identical with the 21st element in shape and size. It is interesting to note that an unusually long Y chromosome was found in a boy (case 1) in addition to no. 21 trisomy. The measurement revealed that the abnormal Y corresponded in length to chromsomes of group 16–18 (Fig. 1).

Chromosome counts in one suspected Down's case (case 15) showed that the patient had a normal complement of 46 chromosomes, consisting of 44 autosomes and a pair of sex chromosomes. There was no evidence for translocation or mosaicism.

Discussion

Although recent cytogenetic information has pointed out that the vast majority of cases of Down's syndrome are characterized by 47 chromosomes being

Table 1. Clincial features of fifteen patients under study

Case no.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Sex	M	F	M	F	M	M	F	F	M	M	M	M	M	M	M
Age (year)	7	7	10	14	13	9	8	6	4m*	3	10m*	5	2	7m*	5m*
Brachycephaly	+	+	+	+	+	+	−	+		+	+	+	+		−
Facial configuration															
Slanting eye	+	±	+	+	+	+	+	±		±	+	+	+		+
Epicanthic eyefolds	+	−	+	+	+	+	+	+	+	+	+	+	+	+	−
Strabismus	+	−	−	−	±	−	−	−	+	−	+	−	−		−
Flat nose	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+
Malformed ear	+	+	+	+	+	+	+	+	+	+	−	−	+	+	−
Wrinkled forehead	+	−	±	+	+	+	−	−	+						
Red cheek	−	−	+	−	±	+	−	−	+						
High arched palate	+	+	+	+	+	+	+	+		+	−	−	−		−
Fissured tongue	+	+	+	+	+	+	+	+	−	+	−	+	+		−
Protruding tongue	+	+	+	+	+	+	+	+	+	+	+	+	+		−
Open mouth	+	+	+	−	+	+	+	+	+						
Widely spaced teeth	+	+	+	+	+	+	+	+		−		+	+		−
Curved 5th fingers	−	−	+	−	+	+	+	+	+	−	−	−	−		−
Short 5th fingers	+	−	+	+	−	+	−	+	+	−	+	+	−		−
Horizontal palmar crease	−	+	−	−	+	+	+	−	−	+	−	+	+		−
Dry skin	−	−	−	+	−	−	−	−				+	+		
Hypotonic muscle	−	±	±	+	−	±	±	±	+			+	−		
Short & broad neck	+	−	+	+	+	±	−	+	+						
Low voice	+	−	+	+	+	+	+	+							
Heart defect	+	−	−	−	−	−	−	−		−	−	+	−		

m* : month

trisomic for chromosome 21, the simple 21-trisomy is not an only abnormality in this syndrome. The literature refers to a minority of cases of Down's syndrome in which the extra chromosome is not present freely but attached to another chromosome (13–15, 21–22, or 17–18) (Carr 1962, Shaw 1962). It has been known that Down's syndrome with cell-mosaicism is not generally uncommon (Zellweger and Abbo 1963, Blank *et al.* 1963).

Table 2. Chromsome conditions in 15 patients under study

Case no.	Chromosome counts					No. of cells obs.	Chromosome constitution
	44	45	46	47	48		
1			3	55		58	47/21 trisomy, longY.
2			1	71		72	47/21 trisomy
3			2	32	1	35	47/21 trisomy
4			2	21		23	47/21 trisomy
5			2	62		64	47/21 trisomy
6			1	45		46	47/21 trisomy
7			1	45		46	47/21 trisomy
8			3	26		29	47/21 trisomy
9		1	1	21		23	47/21 trisomy
10		2	1	21		24	47/21 trisomy
11		1	1	11		13	47/21 trisomy
12		2	2	45		49	47/21 trisomy
13	2		3	36		41	47/21 trisomy
14		2	2	28		32	47/21 trisomy
15	1		34			35	46/normal

Several cases have been reported in which 21-trisomy is associated with other chromosome aberrations such as XXY sex-mechanism (Ford *et al.* 1959), XXX sex-mechanism (Yunis *et al.* 1964), XO/XX mosaicism (van Wijck *et al.* 1964), XO/XX/XXX mosaicism (Zergollern and Hoefnagel 1964), partial deletion of chromosome 16 (Sasaki *et al.* 1963), the long Y chromosome, and so on. In the present study was found a male patient (case 1) having a long Y chromosome corresponding in length to chromosomes of group 16–18. The remaining 13 Down's syndrome patients here studied were standard trisomic cases for chromosome 21 without any other abnormality.

It must be mentioned here that, although the majority of Down's syndrome cases are known to be responsible for trisomic condition of chromosome 21, there are a few cases in which no chromosome abnormality was detected (Makino *et al.* 1962, Hall 1963, 1964). G-trisomy, on the other hand, has been reported in individuals showing features other than those of Down's syndrome. Opie *et al.* (1963) found 21-trisomy in a 53-year-old mentally retarded woman without mongolian traits, Hayward and Bower (1960) in Sturge-Weber syndrome, Fitzgerald (1962) in dystrophia myotonica, and Gustavson *et al.* (1962) in multiple malformations.

In patients suspected of being Down's syndrome, several kinds of chromosome conditions have been reported. Most of such cases are known to be chromosomally normal. Some of them are, however, mosaic of cells with 46 and 47 chromosome complements (Zellweger and Abbo 1963). Further in a few cases, partial trisomy

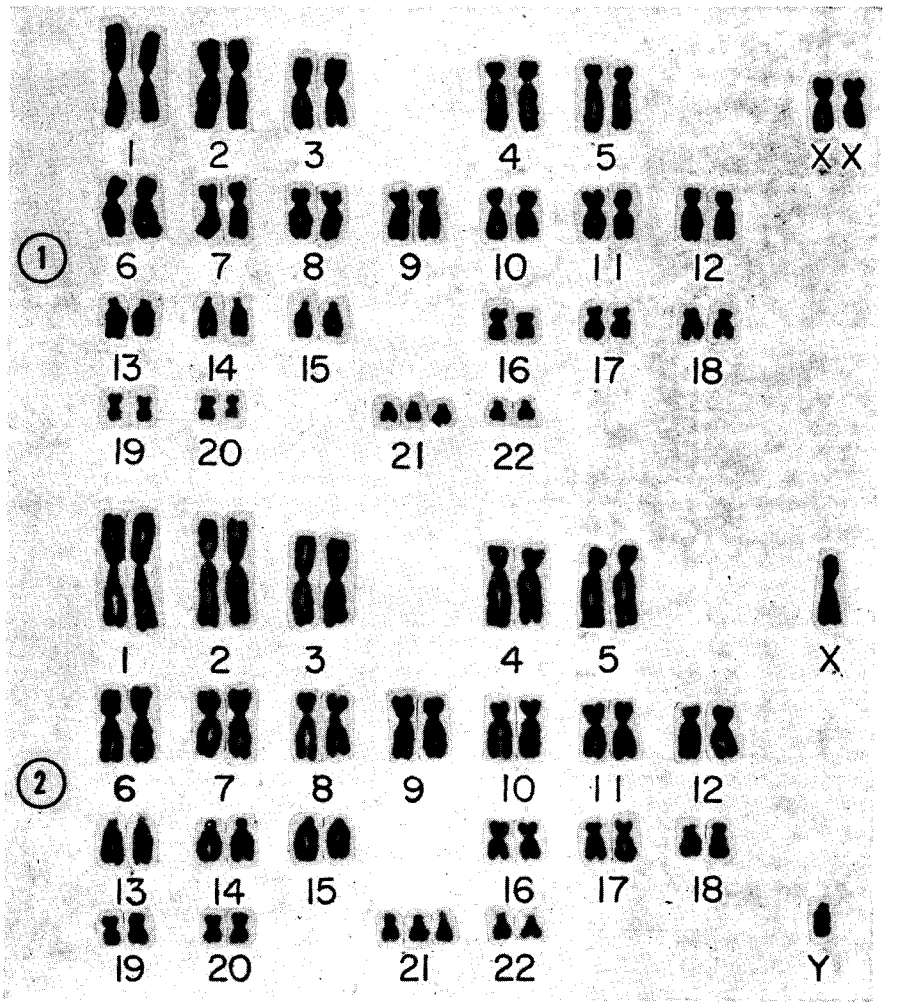

Fig. 1. Karyotype of a girl with Down's syndrome (case 2) showing trisomy for chromosome 21.

Fig. 2. Karyotpye of a boy with Down's syndrome (case 1) showing trisomy for chromosome 21 and a long Y chromosome.

for chromosome 21 has been postulated (Ilbery *et al.* cited from Carr 1962). A suspected Down's syndrome case reported in this paper was found to have a normal complement of 46 chromosomes showing no abnormality, so far as cultured leucocytes are concerned. Chromosome study in patients with incomplete manifestation of Down's syndrome, however, seems to be prospective to solve the role of the extra chromosome in cause or rise of the syndrome.

Summary

Fourteen cases diagnosed as Down's syndrome showed a standard trisomy for chromosome 21 in each. One of them (case 1) had an unusually long Y chromosome in addition to no. 21 trisomy. One suspected Down's syndrome case (♂) possessed a normal chromosome complement with an XY sex-mechanism.

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