Notes on the Chromosomes of Seven Patients with Congenital Diseases and of Their Parents[1)]

By

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(With 4 Text-figures and 2 Tables)

The present paper is one of continuous series of a chromosome survey in Japanese people, and deals with the chromosomal conditions in seven patients with congenital diseases and in their parents. In the previous reports (Makino *et al.* 1962a, b), chromosome studies of seventeen patients with congential disorders which were obtained at the Aiiku Hospital, Tokyo, and of their parents have been described. Additional data on similar syndromes are to be reported in this paper.

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Materials and methods: Clinical diagnosis of the patients and sampling of the peripheral blood for the cultivation of leucocytes were done in the Department of Pediatrics, Aiiku Hospital, and all the cytological work in the Makino laboratory, Zoological Institute, Hokkaido University. The clincial data of the patients studied herein are summarized in Table I.

White blood cells, separated from peripheral blood of each patient, were cultivated by a short-term culture method for obtaining mitotic cells (Makino and Sasaki 1961). Chromosome preparations were made by means of the air-drying method or water-pretreatment squashining method, staining with giemsa or acetic dahlia.

Results and Discussion

The results of chromosome counts in three male patients with Down's syndrome and in their parents are shown in Table II.

Karyotype analyses made in 2 or 3 cells of each case except no. 3 exhibited a typical chromosome pattern that has been widely known in Down's syndrome. These cells showed a consistent count of 47 instead of 46, due to the presence of an

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Table I. Diagnostic features in seven cases under study.

Case no.	Age & sex	Diagnosis	Clinical findings
1.	1yr. 3m. ♂	Down's syndrome	A typical facial configuration, oblique palpebral fissures,depressed bridged nose, four finger line, curvature of little finger, poor muscle tone, small and short penis.
2.	4yr. 0m. ♂	Down's syndrome	A typical facial configuration, epicanthus, oblique palpebral fissures, depressed bridged nose, four finger line, poor muscle tone, curvature of little finger, gap between 1st and 2nd toes.
3.	0yr. 6m. ♂	Down's syndrome & heart defect	Retarded body growth, heart murmurs, typical facial configuration, oblique and small palpebral fissures, depressed bridged nose, curvature of little finger, gap between 1st and 2nd toes, poor muscle tone, brachycephaly.
4.	4yr. 3m. ♂	Mental deficiency & craniofacial dysostosis	Enlarged skull circumference, brachycephaly, hypertelorism, exophthalmos, strabismus, four finger line, teeth of poor formation.
5.	3yr. 9 m. ♂	Mental deficiency	Nutritional disorder, small eye fissures, nystagmus, cataract, deformity of the extra ears, micrognathia, hypogenitalism, four fingre line, mental retardation.
6.	0yr. 10m. ♂	Mental deficiency	Microcephalus, convulsions. deformity of the extra ears, infantile spasm, seizure attack, mental retardation.
7.	0yr. 9m. ♂	Mental deficiency & epilepsy	Mental retardation, seizure attack without any physical defect.

extra chromosome which was of trisomy for a small satellited autosome corresponding to the 21st element (Figures 1 and 2). This is a regular feature for many Down's syndrome cases so far reported in recent literature. In contrast to the children with Down's syndrome, the chromosomes of their parents were essentially normal in constitution, numbering 46 in all cases without any detectable abnormality (Table II). These results closely resemble those in the previous reports by Makino *et al.* (1962a, b, c).

The four cases with congenital mental deficiencies showed invariably 46 chromosomes. Karyotype analyses made in 2 or 3 cells of each case revealed no detectable change or variation of chromosomes either morphologically or numerically (Figures 3 and 4): each showed 44 autosomes superficially of the normal complex and sex chromosomes which were two X's in females, and an XY in

Table II. Chromosome counts based on leucocytes of seven patients with congenital diseases and their parents.

Case no.	Patient and parent	Age & sex	Chromosome counts					Chromosome constitution	No. of cells ana.	No. of cells obs.
			44	45	46	47	92			
1.	Patient	1yr. 3m. ♂				12		47, trisomy 21	3	12
	Father	34yr.			16			46, XY	2	16
	Mother	34yr.		1	24			46, XX	3	25
2.	P.	4yr. 0m. ♂				4		47, trisomy 21	2	4
	F.	30yr.			27			46, XY	2	27
	M.	30yr.			23			46, XX	3	23
3.	P.	6m. ♂				1		47, trisomy 21	1	1
	F.	40yr.		1	24			46, XY	2	25
	M.	37yr.			18			46, XX	2	18
4.	P.	4yr. 3m. ♂			10			46, XY	2	10
	F.	34yr.			16			46, XY	2	16
	M.	26yr.			30			46, XX	2	30
5.	P.	3yr. 9m. ♂			9			46, XY	2	9
	F.	35yr.			20			46, XY	2	20
	M.	29yr.			26		1	46, XX	2	27
6.	P.	10m. ♂			10			46, XY	2	10
	F.	25yr.			16			46, XY	2	16
	M.	24yr.			20			46, XX	3	20
7.	P.	9m. ♀			8			46, XX	3	8
	M.	28yr.			18			46, XX	2	18

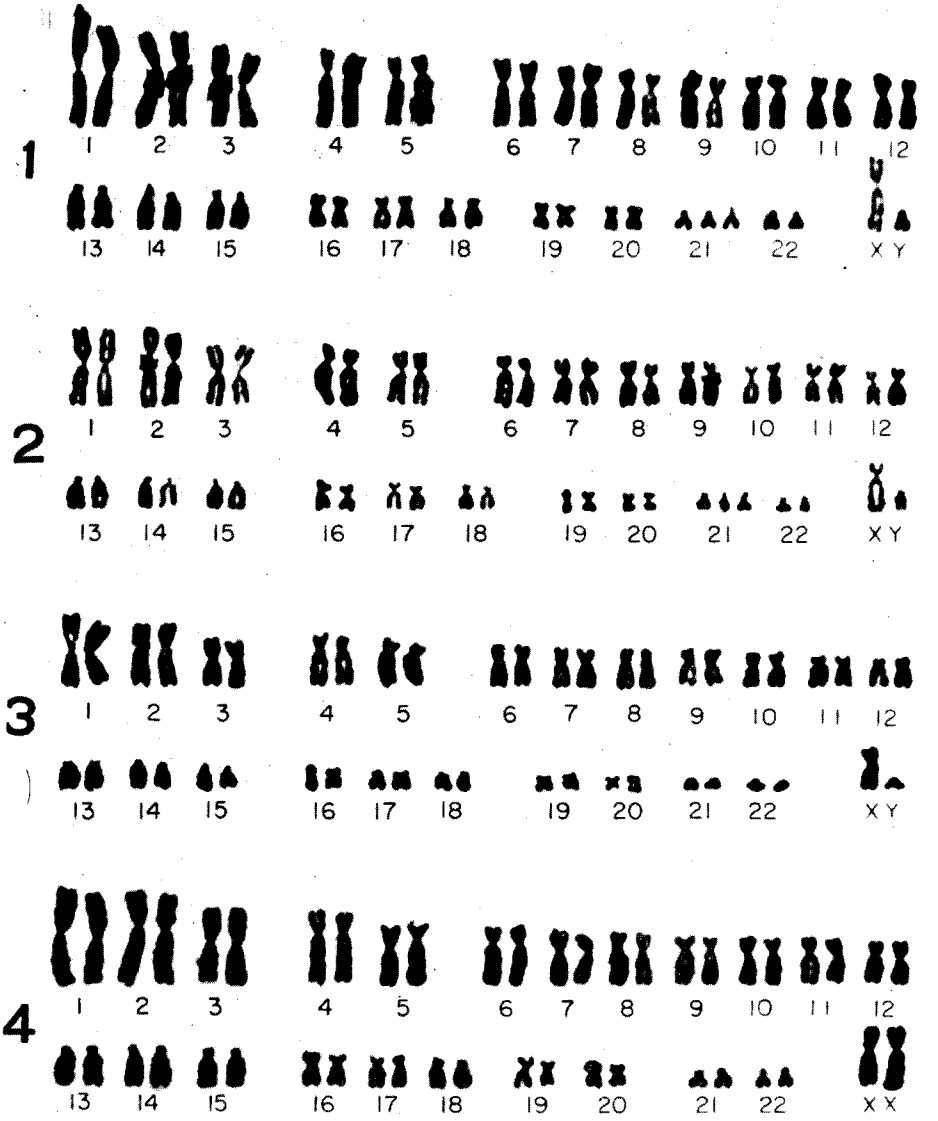
males. The parents of those four patients also showed a superficially normal chromosome complement both in number and morphology.

It has generally been accepted that nondisjunction during meiotic divisions is the most probable cause of trisomy. The present observations have made it clear that the parents of children with Down's syndrome have the normal complement. In reference to the above features, as Makino *et al.* (1962c) have inferred, nondisjunction might have occurred in either spermatogenesis or oogenesis of the parents in the present specimens, or, less likely, in the embryogenesis of the children.

Many cases of congenital diseases and developmental deficiencies have been reported in which no detectable change or visible variation of chromosomes occurs from a normal complement (c.f. Hamerton 1961, Ferguson-Smith 1961, Harnden 1961, Makino *et al.* 1963). Four cases of congenital mental retardation also exhibited no chromosomal variation from a normal somatic complement. It should be noted, however, that a morphologically normal chromosome complement found in a given patient with a certain syndrome does not always correspond to a normal genetic pattern.

Summary

Seven cases of congenital diseases and their parents were studied with respect to their chromosome constitutions. Three Down's syndrome cases were



Figures 1–4. Somatic chromosome complements of patients, based on leucocyte cultures. 1, from a Down's syndrome boy (Case 1). 2, from a Down's syndrome boy (Case 2). 3, from a boy with congenital mental deficiency (Case 5), 4, from a girl with mental deficiency (Case 7).

characterized by 47 chromosomes with trisomy for no. 21. The chromosomes of four cases with congenital mental retardation showed no change from a normal complement. The parents of all the above syndrome patients were found to possess a normal chromosome pattern.

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