87. Chromosome Studies in Thirty-one Cases of Congenital Diseases^{*)}

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In the development of the new human cytogenetics started since 1956, many surprising discoveries have been made included among which are abnormalities of chromosome number and/or structure in a variety of abnormal individuals and in some normal ones, as well as apparently normal complements in patients diagnosed as congenital syndromes or sex anomalies. The senior author has contributed since 1959 to a chromosome survey of normal and abnormal human subjects in joint work with his colleagues; to date more than 250 cases with various clinical abnormalities have been examined in relation to chromosomal abnormalities.

As a link in the above project, the present paper was prepared to report the results of chromosomal analyses in 31 cases of congenital diseases. The subjects under consideration are as follows; 16 cases of Down's syndrome, 2 cases of *syringomyelia, 2 cases of Wilson's disease, 2 cases of mental retardation, 2 cases of microcephaly, 2 cases of *suspected cerebral palsy, each one of *Recklinghausen's disease, *myasthenia gravis, *cerebral edema with spinal hernia, *retinodialysis and *congenital ptosis. Those marked with asterisks are subjected to chromosome study for the first time.

Mitotic chromosomes were obtained by leucocyte cultivation of peripheral blood derived from each patient (for details, see Makino and Kikuchi 1962, Makino *et al.* 1962 a-f). The leucocytes in 3-day-old cultures were squashed on slide after exposure to colchicine solution and use of the water-pretreatment acetic dahlia method. Karyotype analyses were made according to the standard system of nomenclature (Denver system) for the classification of human chromosomes. Diagnostic and clinical findings for each patient are tabulated in Tables I and II. The results of chromosome counts in those patients are

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Table I. Diagnostic features of sixteen Down's syndrome cases under study

Diag. notes \ Case no.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Sex	♀	♂	♂	♀	♂	♂	♂	♂	♂	♀	♀	♂	♂	♀	♂	♂
Birth order	1	1	6	4	2	6	4	4	2	3	3	2	1	1	2	3
Brachycephaly	-	+	-	+	-	-	+	+	-	-	-	-	-	-	+	+
Slanting eye	-	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+
Epicanthus	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	-
Strabismus	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-
Flat nose bridge	+	+	+	-	+	+	+	+	+	-	-	+	+	+	+	+
Small or absent lobule of ear	+	+	-	+	+	-	+	+	-	+	-	-	-	+	-	-
Furrowed tongue	+	-	-	+	+	-	-	+	+	+	+	+	-	-	-	-
High arched palate	-	-	-	+	+	-	-	-	+	-	+	+	-	+	-	-
Marcus line	-	-	+	+	+	+	-	+	-	-	-	+	+	+	+	-
Short fingers	-	+	+	-	-	+	+	+	+	+	-	-	-	+	-	-
Crooked 5th finger	+	-	-	+	+	+	+	+	+	+	-	-	+	-	-	-
Hyperextensible joints	-	-	-	-	-	-	-	-	+	+	-	-	+	-	-	-
Heart defects	-	-	-	-	-	-	+	-	-	+	-	-	-	-	-	-

Table II. Diagnostic features of patients under study, those of Down's syndrome being excluded

Case no.	Age and sex	Diagnosis	Clinical findings
17	30 yr. ♂	Syringomyelia	Lateral curvature, hard to walk, cervico-thorax dissociated anesthesia, Morvan's disease, Charcot's anhrthis.
18	65 yr. ♀	"	Hard to walk, lingual atrophy and facial palsy due to injury of medulla oblongata, cervico-thorax dissociated anesthesia, Morvan's disease, Charcot's arthritis.
19	21 yr. ♂	Wilson's disease	Muscular rigidity, tremoring fingers, hard to walk, Kayser-Fleischer ring.
20	13 yr. ♀	"	Idiocy, muscular rigidity, tremoring fingers, impediment in speech, Kayser-Fleischer ring.
21	24 yr. ♀	Recklinghausen's disease	Multiple neurofibroma, pigmentation of skin, lateral curvature.
22	3 yr. ♂	Mental retardation	Xeroderma pigmentosum, sensitive to ultra-violet light, speech retardation.
23	6 yr. ♀	"	
24	♂	Myasthenia gravis	Fatigue and exhaustion of muscles of eye, mouth, throat and limbs, hard to take foods and to work standing, frequent occurrence of respiratory deficiency.
25	4 m. ♀	Cerebral edema and spinal hernia	
26	43 yr. ♀	Retinodialysis	Blind right eye, left eye with myopia gravis.
27	23 yr. ♀	Congenital ptosis	Epicanthus, myopia gravis, a daughter of the patient no. 26.
28	1 yr. ♂	Microcephaly	Internal strabismus on the right side, protruded tongue, transverse palmar creases on both sides.
29	♀	"	
30	7 yr. ♂	Cerebral palsy	Mental retardation, slight speech retardation, impossible to walk, flat nasal bridge.
31	2 yr. ♂	"	Normal mental development, slightly spastic extremities, small penis, red cheeks, omphalocele, abnormal shadow of the lung in X-ray examination.

presented in Table III together with additional remarks.

As given in Table III, cytological findings showed that the majority of cells derived from all 16 cases of Down's syndrome here considered, 11 males and 5 females, possessed 47 chromosomes. Karyotype analyses made in several 47-cells for each patient revealed that they consisted of a normal complement of 46 chromosomes plus one extra element almost certainly identical with the 21st satellited autosomes in size and shape (Fig. 1). In the light of the above findings, it is evident that all of the 16 Down's syndrome cases studied are standard no. 21 trisomic cases. The situation concurs with the features found in a number of cases of this syndrome so far reported to date.

Examination was made of chromosomes by blood-culture technique in the following 15 cases of congenital diseases: syringomyelia,

Table III. Chromosome conditions in thirty-one patients under study

Case No.	Chromosome counts						No. of cells observed	Chromosome constitution
	44	45	46	47	48	92		
1				27			27	47, trisomy 21
2	2		2	18	1		23	"
3	1			5			6	"
4			2	20	1		23	"
5		1	3	16			20	"
6			1	5	1		7	"
7			2	12	2		16	"
8		1		8	1		10	"
9			2	14	2		18	"
10			1	10	1		12	"
11		1		6			7	"
12		2	2	12			16	"
13			2	11	1		14	"
14			3	13			16	"
15	2		3	18			23	"
16				15	1		16	"
17			16				16	46, XY
18			15				15	46, XX
19			16		1		17	46, XY
20			36	4		1	41	46, XX
21			6				6	46, XX
22			25				25	46, XY
23			29	1			30	46, XX
24		2	12				14	46, XY
25		1	22				23	46, XX
26			19			4	23	46, XX
27			23			1	24	46, XX
28	2		13	1			16	46, XY
29		2	16				18	46, XX
30			27				27	46, XY
31		1	13				14	46, XY

Wilson's disease, mental retardation, microcephaly, Recklinghausen's disease, myasthenia gravis, cerebral edema with spinal hernia, retinodialysis, congenital ptosis and suspected cerebral palsy (Table II). Demonstrated in most cells derived from each case was a consistent count of 46 chromosomes (Table III). In morphological analyses all cells under study showed a normal chromosome complement of man:

Figs. 1-5. Karyotype analyses in patients with congenital diseases. 1, Down's syndrome (case no. 1, female), 47 chromosomes. 2, Mental retardation (case no. 22, male), 46 chromosomes. 3, Mental retardation (case no. 23, female), 46 chromosomes. 4, Wilson's disease (case no. 20, female), 46 chromosomes. 5, Microcephaly (case no. 28, male), 46 chromosomes.

there were in every case 22 pairs of autosomes and a couple of sex-elements, being XY-chromosomes in males and XX in females. Some representatives of karyotypes shown in Figures 2 to 5 were derived from patients with mental retardation, Wilson's disease and microcephaly, respectively. It is apparent from the above findings that the chromosome complement of each of the 15 patients is superficially identical with that of normal individuals.

Remarks: Since the first report of Lejeune *et al.* (1959), a considerable amount of literature has been accumulated on the chromosomes of various kinds of congenital diseases published by many cytogeneticists. Among the chromosomal abnormalities reported to date, regular cases of Down's syndrome were characterized by 47 chromosomes with the standard trisomic condition for no. 21 (Carr 1962). The Down's syndrome cases considered in this study are fully regular cases of this syndrome.

Fifteen cases of congenital defects other than Down's syndrome dealt herewith were found to show a normal complement of chromosomes, being 46 in number, although cryptosstructural rearrangement of the chromosomes might be considered in every case. It should be commented that retinodialis and congenital ptosis presented no sign of mental deficiency. Blumel *et al.* (1961) in two children with cerebral palsy found a certain chromosomal anomaly which was characterized by a slightly long X chromosome. Detailed examinations were made in this respect in the cases of the authors' study, but resulted in failure to detect any abnormality in the X chromosome. Further precise diagnostic examination will be made on those patients.

In summary, 16 cases of Down's syndrome here studied were found to possess 47 chromosomes with the standard trisomy. In 2 cases of syringomyelia, 2 cases of Wilson's disease, 2 cases of mental retardation, 2 cases of microcephaly, 2 cases of suspected cerebral palsy, and one each of Recklinghausen's disease, myasthenia gravis, cerebral edema with spinal hernia, retinodialis and congenital ptosis there was found a normal chromosome constitution, so far as the morphological configurations observed on the basis of blood-cultures are concerned.

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