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Abstract

Cytogenetic and dermatoglyphic studies were performed on a group of 197 institutionalized patients with severe mental and physical handicaps in order to evaluate the contribution of chromosomal aberrations on the etiology of the condition, and to determine whether any association exists between the dermatoglyphics and the severe handicaps. There were 4 patients with trisomy 21 and 2 patients with a de novo balanced reciprocal translocation. In addition, 9 patients were found to have a pericentric inversion of chromosome 9 (inv (9) (p11q13)). Other chromosome variations identified included inv (1) (p11q11) (one case), elongation of 1 qh (one case), and telocentric chromosome 13 (two cases). Dermatoglyphics from the patients excluding cases with Down syndrome were compared with those from 500 normal controls. Significant differences were observed in several dermatoglyphic characteristics, including simian crease, fingertip pattern, mean a-b ridge count, thenar/first interdigital pattern, hypothenar pattern, and hallucal pattern. The present study indicated that de novo balanced translocation as well as chromosome duplication or deficiency is causally related to the severe combined handicaps. This study also showed that the incidence of inv (9) (p11q13) in the patients was 4.2 times higher than that in the general Japanese population. If a real association exists between the inv (9) (p11q13) and severe handicaps, the increase of inv (9) (p11q13) in the patients may be explained by the concept of a risk factor. Moreover, the dermatoglyphic deviations found in patients may be evidence that pathological factors had been operating during early embryonic life in some of them.

KEYWORDS: chromosomes, banding techniques, dermatoglyphics, severely handicapped patients

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CYTOGENETIC AND DERMATOGLYPHIC STUDIES ON SEVERELY HANDICAPPED PATIENTS IN AN INSTITUTION

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Abstract. Cytogenetic and dermatoglyphic studies were performed on a group of 197 institutionalized patients with severe mental and physical handicaps in order to evaluate the contribution of chromosomal aberrations on the etiology of the condition, and to determine whether any association exists between the dermatoglyphics and the severe handicaps. There were 4 patients with trisomy 21 and 2 patients with a *de novo* balanced reciprocal translocation. In addition, 9 patients were found to have a pericentric inversion of chromosome 9 (inv (9) (p11q13)). Other chromosome variations identified included inv (1) (p11q11) (one case), elongation of 1qh (one case), and telocentric chromosome 13 (two cases). Dermatoglyphics from the patients excluding cases with Down syndrome were compared with those from 500 normal controls. Significant differences were observed in several dermatoglyphic characteristics, including simian crease, fingertip pattern, mean a-b ridge count, thenar/first interdigital pattern, hypothenar pattern, and hallucal pattern. The present study indicated that *de novo* balanced translocation as well as chromosome duplication or deficiency is causally related to the severe combined handicaps. This study also showed that the incidence of inv (9) (p11q13) in the patients was 4.2 times higher than that in the general Japanese population. If a real association exists between the inv (9) (p11q13) and severe handicaps, the increase of inv (9) (p11q13) in the patients may be explained by the concept of a risk factor. Moreover, the dermatoglyphic deviations found in patients may be evidence that pathological factors had been operating during early embryonic life in some of them.

Key words : chromosomes, banding techniques, dermatoglyphics, severely handicapped patients.

In Japan, the term “severely handicapped children or individuals” is applied to those who have serious impairments of motor and mental functions, for which training is usually unrewarding. Health statistical data in 1970 from the Ministry of Health and Welfare of Japan showed 2790 institutionalized patients and at least 11200 patients cared for in their own homes. The existence of such a large number of patients has raised increasing medical as well as social concern, and a full elucidation of causes of the condition is mandatory.

Previous studies concerning the etiology were based mainly on patient his-

tory and physical examinations (1-3). They revealed that various diseases and malformations, especially those involving the central nervous system, are associated with the condition. In a considerable proportion of the patients, however, no obvious cause could be elicited. In view of the excessive physical stigmata, Morooka (1971) stressed the importance of prenatal factors in a group of patients with obscure cause (3). The use of more specific and diagnostic approaches will lead to better clarification of the etiology. Dermatoglyphic analysis appears to be most useful in evaluating the pathological factors in early embryonic life, since dermal ridges and palmar creases develop between the second and fifth month of gestation and once completed they remain unchanged for life, and since various pathological processes during that time are known to exert an influence on their configurations. Furthermore, although chromosome aberrations have been implicated as a cause of the above-mentioned condition, there have been no systematic cytogenetic studies.

The present paper describes cytogenetic and dermatoglyphic data from a group of 197 institutionalized patients with severe combined handicaps.

MATERIALS AND METHODS

Subjects. The subjects were 197 patients consisting of 104 males and 93 females, who were being admitted to Asahigawa Jidoin, Okayama, a residential institution for the severely handicapped. The study was performed from May, 1979, to June, 1980. Their ages at the start of the investigation ranged from 4 to 46 years (Table 1). The great majority of

TABLE 1. AGE DISTRIBUTION OF THE PATIENTS

Age	Male	Female	Total
4 - 5 y	3	5	8
6 - 10 y	11	16	27
11 - 15 y	15	15	30
16 - 20 y	26	29	55
21 - 25 y	21	16	37
26 - 30 y	21	9	30
31 - 35 y	5	2	7
36 - 46 y	2	1	3
Total	104	93	197

them (182 patients) came from Okayama prefecture, and the remaining 15 came from neighboring prefectures. A wide variety of clinical diagnosis was given to the patients, and approximately a half of them were diagnosed as having cerebral palsy due to perinatal origins such as neonatal asphyxia, kernicterus and low birth weight (Table 2). In 53 cases (27 %), however, there was no diagnosis. According to the classification for the degrees of mental and physical handicaps reported by the Ministry of Education Research Group, Japan (1967), 87 % of them (172 patients) were consistent with the category of "severely hand-

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TABLE 2. CLINICAL DIAGNOSES OF THE PATIENTS

Prenatal origin	
Phenylketonuria	1
Tuberous sclerosis	1
Arthroglyposis multiplex	2
Congenital hydrocephalus	4
Congenital rubella syndrome	1
Progressive degenerative disease of CNS	7
Multiple congenital malformations	6
Down syndrome	4
Microcephalic idiot	2
Perinatal origin	
Cerebral palsy due to perinatal origin	84
Postnatal origin	
Meningitis or Encephalitis	17
Intracranial bleeding	5
Encephalopathy	7
Sequelae of convulsive disorders	3
Unknown	53
Total	197

TABLE 3. THE DEGREES OF THE HANDICAPS IN THE PATIENTS ACCORDING TO THE CLASSIFICATION OF THE MINISTRY OF EDUCATION RESEARCH GROUP FOR SEVERELY HANDICAPPED CHILDREN (1967).

Mental handicaps Physical handicaps (IQ)	> 85	85—75	75—50	50—25	25>
	1	2	3	4	5
No handicaps					
Slight handicaps	6	7	8	9	10 1
Moderate handicaps	11	12	13	14 7	15 10 15+X 29
Severe handicaps	16	17	18	19 6	20 60 24 25
Profound handicaps	21	22	23 1	24 18	25 65

15+X: Motor disturbances are moderate, but associated with behavioral disorder, blindness or deafness.

The dark area (15+X, 20, 24 and 25) corresponds to the category of severe mental and physical handicaps.

icapped individuals" (areas 15 + X, 20, 24 and 25 in Table 3). Most of the remaining patients had the possibility in the future of falling into this category.

Chromosome analysis. Whole blood was cultured by a modification of the method described by Hungerford (1965) (4), using Eagle's MEM medium supplemented with 15 % bovine calf serum, phytohemagglutinin and antibiotics. Cultures were set up at 37°C for 72 h, and colchicine was added two hours before harvest. Hypotonic treatment was done with 0.075 M KCl for 10 min. The cells then were fixed in Carnoy's solution. Air-dried slides were prepared for conventional staining and G-banding studies (Seabright, 1971, with minor modifications (5)). Where necessary, the C-banding method was applied (6). A minimum of 20 cells per patient was counted, and at least 5 banded metaphases from each patient were photographed and karyotyped.

Dermatoglyphic analysis. Dermatoglyphics were recorded using the fingerprinter method, and analyzed according to the Memorandum on Dermatoglyphic Nomenclature (7). The characteristics studied were fingertip patterns, total finger ridge count, mean a-b ridge count, patterns in the second, third and fourth interdigital areas on palms, axial triradii, thenar/first interdigital pattern, hypothenar pattern, simian crease, and hallucal pattern on soles. Positions of axial triradii were measured with Walker's method (1957), (8). According to Uchida and Soltan (1969), (9) and Dar *et al.* (1971), (10), typical and transitional forms of simian creases were regarded as equivalents. The control group consisted of 250 male and 250 female adults, ranging from 20 to 51 years in age. They were all unrelated, of Japanese origin and apparently healthy. The χ -square test and Student's 't' test were used for statistical analyses.

RESULTS

Cytogenetic Findings

Chromosome analysis was successful in all patients but one. Chromosome abnormalities were found in 6 (3.0 %), and variations in 12 (6.1 %) patients (Table 4). There were 4 patients with trisomy 21 (cases 1-4) and 2 patients with a *de novo* balanced reciprocal translocation: one with 46, XX, t(18;19) (q22.2;q13.3) (Case 5) and the other with 46, XY, t(3;6) (q13.2;p23) (Case 6) (Fig. 1).

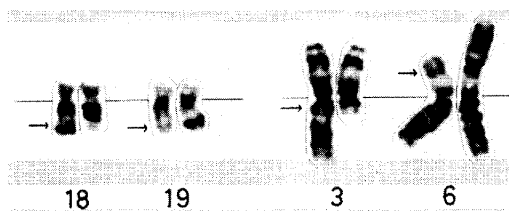


Fig. 1. Partial G-banded karyotypes of Case 5 (left) and Case 6 (right). Arrows indicate the breakpoints.

Of 12 patients with chromosome variations, nine (Cases 7-15) had pericentric inversion of chromosome 9 (inv (9) (qh)). In all of those cases the breakpoints were identical (p11 and q13), and the inversion involved only constitutive heterochromatin of the long arm of chromosome 9 (9 qh) which is genetically inactive

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TABLE 4. SUMMARY OF CYTOGENETIC FINDINGS IN THE PATIENTS WITH CHROMOSOME ABNORMALITIES AND VARIATIONS

Case no.	Sex	Age	Karyotype	Clinical diagnosis
1	F	7 y	47,XX,+21	Down syndrome
2	F	17 y	47,XX,+21	Down syndrome
3	M	15 y	47,XY,+21	Down syndrome
4	M	11 y	46,XY,-14,+der(14),t(14;21)(p11;q11)	Down syndrome
5	F	17 y	46,XX,t(18;19)(q22.2;q13.3)	Multiple malformations
6	M	10 y	46,XY,t(3;6)(q13.2;p23)	Cerebral palsy of unknown origin
7	M	17 y	46,XY,inv(9)(p11q13)	Cerebral palsy due to asphyxia
8	M	25 y	46,XY,inv(9)(p11q13)	Cerebral palsy due to asphyxia
9	F	16 y	46,XX,inv(9)(p11q13),inv(1)(p11q11)	Cerebral palsy due to asphyxia
10	F	18 y	46,XX,inv(9)(p11q13)	Cerebral palsy of unknown origin
11	M	31 y	46,XY,inv(9)(p11q13)	Cerebral palsy of unknown origin
12	M	18 y	46,XY,inv(9)(p11q13)	Cerebral palsy of unknown origin
13	F	8 y	46,XX,inv(9)(p11q13)	Acute encephalopathy
14	F	20 y	46,XX,inv(9)(p11q13)	Acute encephalopathy
15	M	26 y	46,XY,inv(9)(p11q13)	Phenylketonuria
16	F	24 y	46,XX,lqh+	Degenerative disease of CNS
17	F	32 y	46,XX,13p-	Cerebral palsy of unknown origin
18	F	20 y	46,XX,13p-	Cerebral palsy of unknown origin

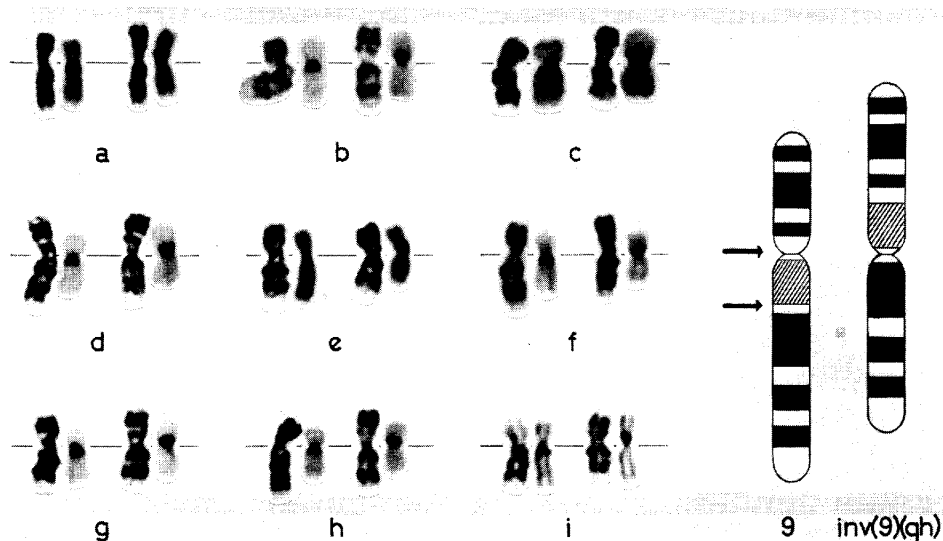


Fig. 2. Partial G- and C-banded karyotypes of Cases 7-15 (a to i), and diagrammatic representation of pericentric inversion of chromosome 9 (Arrows indicate the breakpoints). In each of the 9 cases, normal chromosome 9 is on the left, and inverted chromosome 9 is on the right.

(Fig. 2). Other chromosome variations identified included partial pericentric inversion of constitutive heterochromatin of chromosome 1 (inv (1) (qh)) (Case 9), elongation of 1 qh (Case 16), and telocentric chromosome 13 (13p—) (Cases 17 and 18) (Fig. 3). No apparent congenital malformations or dermatoglyphic

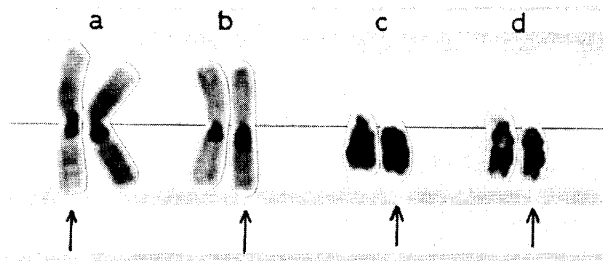


Fig. 3. Chromosome variants. a: inv (1) (qh) in Case 9 (C-band), b: 1qh+ in Case 16 (C-band), c: 13p— in Case 17 (G-band), d: 13p— in Case 18 (G-band). Arrows indicate variant chromosomes.

abnormalities were present in any of the cases with chromosome variants except for Case 9, in which a right simian crease was noted.

Dermatoglyphic Findings

Four patients with Down syndrome were excluded from the dermatoglyphic study. Dermatoglyphics were obtained from 185 out of the remaining 193 patients. Of the 8 patients whose dermatoglyphics were not available, one moved to other institution during the study and 7 had severe contractures of the hands and feet.

Fingertip patterns. The frequencies of arches, ulnar and radial loops, and whorls on all observable digits in the patients and the controls are shown in Table 5a. There was a significant difference in the fingertip patterns between the two groups ($0.01 < P < 0.05$). This difference was due to the increased

TABLE 5. a. FINGERTIP PATTERNS IN THE PATIENTS AND THE CONTROLS

	A	L ^u	L ^r	W
Patients (N=1832 digits)	49 (2.7%)	934 (51.0%)	54 (2.9%)	795 (43.4%)
Controls (N=5000 digits)	91 (1.8%)	2618 (52.4%)	113 (2.3%)	2178 (43.6%)

A: arch, L^u: ulnar loop, L^r: radial loop, W: whorl

$\chi^2 = 7.87$, $df = 3$, $0.01 < P < 0.05$

TABLE 5. b. FREQUENCY OF INDIVIDUALS WITH 3 OR MORE ARCHES ON 10 FINGERTIPS

	3 or more	2 or less
Patients (N=175)	9 (5.1%)	166 (94.9%)
Controls (N=500)	10 (2.0%)	490 (98.9%)

$\chi^2 = 4.68$, $df = 1$, $0.01 < P < 0.05$

frequency of arches in the patient group. The frequency of an individual with 3 or more arches on 10 digits in the patients was also significantly higher than in the controls ($0.01 < P < 0.05$) (Table 5b).

Total finger ridge count (TFRC). There was no significant difference in the TFRC between the patients and the controls ($P > 0.1$) (Table 6).

Mean a-b ridge count. The mean a-b ridge count of the patients were significantly reduced as compared to the controls (Male: $0.01 < P < 0.025$, Female: $0.01 < P < 0.025$) (Table 7).

Thenar/first interdigital pattern. The thenar/first interdigital patterns were observed in 7.8% of the patients on the left palm and 3.9% on the right palm, while in the controls the frequencies were 2.2% and 0.8%, respectively. The frequencies of thenar/first interdigital patterns on both palms of the patients were significantly increased (left; $P < 0.001$, right; $0.001 < P < 0.01$) (Table 8).

Hypothenar pattern. True hypothenar patterns were noted in 12.2% of the patients on the right palm and 9.9% on the left palm, while in the controls the frequencies were 21.6% and 21.8% respectively. The frequencies of hypothenar patterns on both palms of the patients were significantly lower than in the

TABLE 6. TOTAL FINGER RIDGE COUNT (TFRC) OF THE PATIENTS AND THE CONTROLS

		Mean	SD
Male	Patients (N=83)	136.3	37.4
	Controls (N=250)	139.7	40.3
Female	Patients (N=65)	128.5	48.1
	Controls (N=250)	132.8	46.0

Male: $t=0.678$, $df=331$, $P > 0.1$ Female: $t=0.665$, $df=314$, $P > 0.1$

TABLE 7. MEAN a-b RIDGE COUNT OF THE PATIENTS AND THE CONTROLS

		Mean	SD
Male	Patients (N=84)	35.88	4.88
	Controls (N=250)	37.14	4.55
Female	Patients (N=72)	35.78	4.39
	Controls (N=250)	37.04	4.84

Male: $t=2.156$, $df=332$, $0.01 < P < 0.025$ Female: $t=1.986$, $df=320$, $0.01 < P < 0.025$

TABLE 8. THENAR/FIRST INTERDIGITAL PATTERNS IN THE PATIENTS AND THE CONTROLS

		Left palms		Right palms	
		True patterns*	No patterns	True patterns*	No patterns
Patients	(N=180)	14 (7.8 %)	166 (92.2 %)	(N=181)	7 (3.9 %)
Controls	(N=500)	11 (2.2 %)	489 (97.8 %)	(N=500)	4 (0.8 %)

* True patterns include distal loop, proximal loop, and whorl.

Left palms: $X^2=11.63$, $df=1$, $P < 0.001$. Right palms: $X^2=7.87$, $df=1$, $0.001 < P < 0.01$

controls (left; $0.001 < P < 0.01$, right; $P < 0.001$) (Table 9).

Interdigital patterns. There were no significant differences in the frequencies of the second, third and fourth interdigital patterns on both palms between the patients and the controls ($P > 0.1$) (Table 10).

Axial triradii. There were no significant differences in the positions of axial triradii on both palms between the patients and the controls ($P > 0.05$) (Table 11).

TABLE 9. HYPOTHENAR PATTERNS IN THE PATIENTS AND THE CONTROLS

		Left palms		Right palms	
		True patterns*	No patterns	True patterns*	No patterns
Patients	(N=181)	22 (12.2 %)	159 (87.8 %)	(N=182)	18 (9.9 %)
Controls	(N=500)	108 (21.6 %)	392 (78.4 %)	(N=500)	109 (21.8 %)
					391 (78.2 %)

* True patterns include radial loop, ulnar loop, radial loop/ulnar loop, and whorl.
Left palms: $X^2=7.68$, $df=1$, $0.001 < P < 0.01$. Right palms: $X^2=12.49$, $df=1$, $P < 0.001$

TABLE 10. FREQUENCIES OF SECOND, THIRD AND FOURTH INTERDIGITAL PATTERNS IN THE PATIENTS AND THE CONTROLS

	L^d in second interdigital area	L^d in third interdigital area	L^d or W in fourth interdigital area
Left palms			
Patients (N=181)	2 (1.1 %)	14 (7.7 %)	142 (78.5 %)
Controls (N=500)	2 (0.4 %)	59 (11.8 %)	383 (76.6 %)
Right palms			
Patients (N=182)	2 (1.1 %)	50 (27.5 %)	116 (63.7 %)
Controls (N=500)	4 (0.8 %)	161 (32.2 %)	312 (62.3 %)

L^d : distal loop, W: whorl
Second interdigital patterns Left palms : $X^2=0.25$, $df=1$, $P > 0.1$
Right palms: $X^2=0.01$, $df=1$, $P > 0.1$
Third interdigital patterns Left palms : $X^2=2.29$, $df=1$, $P > 0.1$
Right palms: $X^2=1.40$, $df=1$, $P > 0.1$
Fourth interdigital patterns Left palms : $X^2=0.26$, $df=1$, $P > 0.1$
Right palms: $X^2=0.10$, $df=1$, $P > 0.1$

TABLE 11. POSITION OF AXIAL TRIRADII IN THE PATIENTS AND THE CONTROLS

	Left palms				Right palms			
	t	t'	t''	t ^b	t	t'	t''	t ^b
Patients (N=181)	85 (47.0 %)	94 (51.9 %)	2 (1.1 %)	0	98 (54.1 %)	78 (43.1 %)	3 (1.7 %)	2 (1.1 %)
Controls (N=500)	282 (56.4 %)	214 (42.8 %)	2 (0.4 %)	2 (0.4 %)	302 (60.4 %)	193 (38.6 %)	4 (0.8 %)	1 (0.2 %)

Left palms: $X^2=6.50$, $df=3$, $P > 0.05$ Right palms: $X^2=4.98$, $df=3$, $P > 0.05$

Simian crease. Simian creases were found in both palms in 5.4 % of the patients, and in one or the other palm in 14.1 % of the patients, while in the controls the frequencies were 2.4 % and 6.6 %, respectively. The frequency of simian creases in the patients was considerably higher than in the controls ($P < 0.001$) (Table 12).

Hallucal pattern. Frequencies of various types of patterns in the right and left hallucal areas of the patients and the controls are shown in Table 13. There was a significant difference in the left hallucal patterns between the two groups ($P < 0.001$). This difference was due to the increased frequency of arch tibial in the patients (9.4 % vs. 1.2 % in the controls) ($X^2 = 27.52$, $df = 1$, $P < 0.001$). In the right hallucal patterns, no significant difference exists between the two groups ($P > 0.1$), although the frequency of arch tibial in the patients (5.1 %) was about 3 times higher than that in the controls (1.8 %).

TABLE 12. SIMIAN CREASES IN THE PATIENTS AND THE CONTROLS

	Both palms	Either palm	Not present
Patients (N=185)	10(5.4 %)	26(14.1 %)	149(80.5 %)
Controls (N=500)	12(2.4 %)	33(6.6 %)	455(91.0 %)

$X^2 = 14.17$, $df = 2$, $P < 0.001$

TABLE 13. HALLUCAL PATTERNS IN THE PATIENTS AND THE CONTROLS

	L ^d	L ^t	L ^f	W	A ^t	V/A ^t	A ^p	Others*
Left soles								
Patients (N=180)	92 (51.1 %)	17 (9.4 %)	2 (1.1 %)	38 (21.1 %)	17 (9.4 %)	9 (5.0 %)	2 (1.1 %)	3 (1.7 %)
Controls (N=500)	275 (55.0 %)	41 (8.2 %)	3 (0.6 %)	121 (24.2 %)	6 (1.2 %)	32 (6.4 %)	9 (1.8 %)	13 (2.6 %)
Right soles								
Patients (N=178)	94 (52.8 %)	19 (10.7 %)	2 (1.1 %)	41 (23.0 %)	9 (5.1 %)	5 (2.8 %)	5 (2.8 %)	3 (1.7 %)
Controls (N=500)	282 (56.4 %)	48 (9.6 %)	1 (0.2 %)	130 (26.0 %)	9 (1.8 %)	8 (1.6 %)	10 (2.0 %)	12 (2.4 %)

L^d: loop distal, L^t: loop tibial, L^f: loop fibular, W: whorl,

A^t: arch tibial, V/A^t: vestige/arch tibial, A^p: arch proximal

* including arch fibular, arch distal, and tented arch.

Left soles: $X^2 = 29.53$, $df = 7$, $P < 0.001$

Right soles: $X^2 = 10.38$, $df = 7$, $P > 0.1$

DISCUSSION

In the present study, chromosomes from all patients were investigated using

banding techniques routinely. Besides four cases with Down syndrome only two cases could be shown to have a major chromosome abnormality. Cytogenetic surveys in institutions for the mentally retarded disclosed that the overall incidence of major chromosome abnormalities is 6.8 to 15.3% (Table 14), (11).

TABLE 14. SUMMARY OF CYTOGENETIC SURVEYS CONCERNING MENTALLY RETARDED PATIENTS.*

References	Total examined	Down syndrome		Sex Ch. Ab.		Autosomal abnormalities				Total	
		No.	%	No.	%	Unbalanced No.	%	Balanced No.	%	No.	%
Sutherland and Wiener (1971)	159	17	10.7	0	0	3	1.9	0	0.	20	12.6
Newton <i>et al.</i> (1972)	1255	103	8.2	10	0.8	10	0.8	5	0.4	128	10.1
Fujita and Fujita (1974)	59	1	1.7	2	3.4	1	1.7	0	0	4	6.8
Cassiman <i>et al.</i> (1975)	857	111	12.9	3	0.3	11	1.3	4	0.5	129	15.0
Sutherland <i>et al.</i> (1976)	588	73	12.4	4	0.7	10	1.7	3	0.5	90	15.3
Speed <i>et al.</i> (1976)	2770	250	9.0	31	1.1	16	0.6	0	0	297	10.7
Jacobs <i>et al.</i> (1978)	475	40	8.4	3	0.6	9	1.8	5	1.0	57	12.0
Kondo <i>et al.</i> (1980)	449	33	7.3	1	0.2	2	0.4	1	0.2	37	8.2
Total	6612	628	9.5	54	0.8	62	0.9	18	0.3	762	11.5

* Modified from the paper of Kondo *et al.* (1980) (11).

The comparatively lower incidence in the present study (3.0%) is due in large part to the decreased frequency of patients with Down syndrome (2.0%). The lack of ascertainment of unbalanced autosomal abnormalities excluding trisomy 21 and sex chromosome abnormalities is another finding in this study. Since patients with sex chromosome abnormalities are concentrated among the mildly retarded (12), the absence of this type of abnormality would not be unexpected in the severely handicapped. The lack of unbalanced autosomal abnormalities, on the other hand, suggests that most of the serious autosomal abnormalities result in early mortality while less serious abnormalities are rarely associated with severe motor handicaps, and accordingly patients with those abnormalities are mainly cared for in institutions for the mentally retarded.

The frequency of balanced reciprocal translocation in this study was 1.0%, a figure much higher than that of the combined data from consecutive newborn surveys (0.08%) (13). Although it is theoretically expected that a balanced reciprocal translocation have no phenotypic effects, an increased frequency of this rearrangement is noted in patients with mental retardation (14-18) or mul-

tiple congenital malformations (19-21). Jacobs (1974) indicated that it was *de novo* or mutant balanced reciprocal translocations which were found in excess in the mentally retarded (22). In our cases with a *de novo* balanced translocation there is no other obvious cause for the handicaps, and it seems likely that the rearrangement is causally related to the condition. As suggested by Jacobs (1974), (22), deleterious phenotypic effects of a *de novo* balanced translocation may arise through the following mechanisms: (1) a small deletion or duplication below the level of microscopic detectability, (2) a gene mutation at the site of chromosome breaks, or (3) a position effect. It is also possible that an agent causing the chromosome rearrangement has exerted a detrimental effect pre-conceptionally on the gametes as well (17).

The most remarkable finding in the present study is the demonstration of 9 cases with a pericentric inversion of 9qh. The total incidence of inv (9) (qh) in the severely handicapped patients (4.6%) is 4.2 times as many as in the general population in Japan (1.1%), (23), and the increase is highly significant ($X^2 = 13.39$, $df = 1$, $p < 0.001$). If a sampling bias is excluded, this would suggest an association between the inv (9) (qh) and severe handicaps. Chromosome inversions are essentially euploid structural rearrangements, and their phenotypic effects are similar to those of balanced reciprocal translocations. As for the clinical significance of inv (9) (qh), however, there has been much controversy. It is generally believed that this is a heteromorphic variant without any detrimental phenotypic effect (24-26). According to de la Chapelle *et al.* (25), the relatively higher incidence of inv (9) (qh) in the general population as compared with other chromosome inversions might not be due to its frequent occurrence but to the lack of deleterious effects, most probably because of the absence of crossing over within the inverted segment and subsequent production of duplication-deficiency gametes. On the other hand, Ford and Lester (1978) have shown a significant increase of aneuploidy in cells with inv (9) (qh) on peripheral blood cultures, suggesting that this chromosome inversion may cause mitotic nondisjunction *in vitro* (27). If a real association exists between the inv (9) (qh) and severe handicaps, a concept of a risk factor may explain the increased frequency of inv (9) (qh) in the severely handicapped. It would be tempting to suppose that the mitotic instability of cells with inv (9) (qh) as suggested by Ford and Lester (27) make the carrier's developing brain more susceptible to severe damage.

Other heteromorphic variants observed in the present study were a partial inversion of 1qh (one case), an elongation of 1qh (one case) and a telocentric chromosome 13 (two cases). The incidences of inv (1) (qh) and 1qh+ in the Japanese general population are 0.6% and 0.8%, respectively (23). The detection of the two variants in this study is explained more simply by chance coincidence, although there have been several reports of the increased frequency of 1qh+ in patients with congenital malformations or mental retardation (28-

30). The clinical significance of telocentric 13 was studied by Nielsen *et al.* (1974), who concluded that telocentric 13 is associated with neither abnormal phenotypes nor reproductive failures (31). Since the frequency of telocentric chromosome 13 in the Japanese general population is unknown, it cannot be concluded yet whether any association exists between this chromosome variant and severe handicaps.

Finally, the present study has shown that the severely handicapped patients differ distinctly from the healthy controls in dermatoglyphic patterns on the fingers, palms and soles. The unusual dermatoglyphic traits noted in the patients include an increased frequency of arches on the fingertips, a decreased mean a-b ridge count, an excess of true patterns on the thenar/first interdigital areas, a reduction of true patterns on the hypothenar areas, an excess of simian creases on the palms, and an increased frequency of arch tibial patterns on the hallucal areas.

It is well established that dermal ridges and palmar creases are formed in the early intrauterine life (32). The configuration of dermatoglyphics can be altered by various genetic and environmental factors acting early in pregnancy (33). Various clinical disorders have been known to be associated with dermatoglyphic abnormalities, including nearly all kinds of chromosome aberrations, congenital rubella syndrome (34), Thalidomide embryopathy (35), single gene defects such as phenylketonuria (36), Coeliac disease (37) and Wilson's disease (38), and certain malformation syndromes with undetermined genetic transmission such as de Lange syndrome (39), Holt-Oram syndrome (40) and Rubinstein-Taybi syndrome (41). In the present study, there were only two patients with chromosome aberrations, one patient with phenylketonuria and one with congenital rubella syndrome, and the number of such cases was too small to make any substantial contribution to the dermatoglyphic deviations. Hence, it is likely that the dermatoglyphic deviations in this study represent nonspecific pathological influences during the early embryonic life at least in some of the severely handicapped patients.

The dermatoglyphic deviations have also been described in individuals with conditions such as low birth weight (10), maternal gestational complications (42, 43) and mental retardation (44). There is a paucity of knowledge concerning the mechanisms whereby pathological factors can change dermatoglyphics. If more were known about such mechanisms, this would lead to a better understanding of the dermatoglyphic deviations in this study.

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