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A CYTOGENETIC SURVEY OF CONSECUTIVE LIVEBORN INFANTS-INCIDENCE AND TYPE OF CHROMOSOME ABNORMALITIES

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Summary Cytogenetic investigations have been carried out with particular concern to the frequency of chromosome abnormalities in newborn infants, and this is a preliminary report of data derived from 2,626 consecutive liveborns (1,393 males and 1,233 females) which were collected in one hospital. Of these, 18 infants (0.69%) were found to have a major chromosome abnormality. Eight infants (0.30%) showed sex-chromosome abnormalities: two with 47, XYY, one with 47,XXX, one with 45,X/47,XXX mosaicism, one with 46,XY/47,XYY mosaicism, one with 45,X/46,XX mosaicism, and a pair of twins with 45,X/46,XY/47,XYY mosaicism. Ten infants (0.38%) were carriers of autosomal abnormalities: three with 21-trisomy, one with 13-trisomy by translocation, three with a balanced 13/14 translocation, two with a balanced 14/22 translocation and one with an extra small marker chromosome. Of chromosomally abnormal infants, 14 were phyiscally normal.

INTRODUCTION

Recently chromosome surveys of newborn infants have been undertaken in considerably large scale in various countries (Sergovich *et al.*, 1969; Gerald and Walzer, 1970; Lubs and Ruddle, 1970; Bochkov *et al.*, 1974; Jacobs *et al.*, 1974; Hamerton *et al.*, 1975; Nielsen and Sillesen, 1975). They have provided incidence figures for chromosome aberrations among the newborn populations necessary for genetic counseling. This report presents preliminary data on the frequency and type of major chromosome abnormalities in a newborn population observed in one hospital. Further detailed accounts particularly of clinical

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findings of abnormal infants will be reported elsewhere. This is the first contribution to the cytogenetic survey of the newborn population in Japan.

MATERIALS AND METHODS

A total of 2,795 infants were born alive in the Kitasato University Hospital during a period from 1 December 1975 to 30 November 1977. Out of 2,672 infants available for blood cultures, a successful cytogenetic analysis was possible in 2,626 infants consisting of 1,393 males and 1,233 females. Since 14,020 infants were delivered in Sagamihara during the period of the present study, and since 1,221 (46.5%) of the 2,626 infants karyotyped in the Kitasato University Hospital were born to mothers resident in Sagamihara, this survey thus covered 8.7% of livebirths in Sagamihara.

Umbilical cord blood samples were collected in the delivery room immediately after birth and cell cultures were set up within 24 hours (48 hours at weekend). 0.3 ml of whole blood were inoculated into a plastic culture tube containing 3 ml of Eagle's Minimum Essential Medium supplemented with 15% of fetal calf serum and 0.1 ml of phytohaemagglutinin. The containers were placed in a humidified gasflow incubator at 37°C for 3 days. Colchicinization, hypotonic treatment, fixation and preparation of slides were carried out according to standard procedures. Two slides were prepared from each baby, one of them was stained with conventional Giemsa and the other was stored for further special staining when requested. Repeat cultures were made with peripheral blood samples from cases with a chromosome abnormality, and at the same time blood samples were collected from the parents when needed. At least 5 cells were chromosomally analysed for each baby and one well-spread metaphase plate was photographed in each. When any doubtful finding was obtained about the chromosome, the cell-number for examination was increased. Special staining methods including Q-banding (Caspersson *et al.*, 1970) and/or G-banding (Seabright, 1972) were applied to identify the abnormal chromosomes.

RESULTS

Some anamnestic and clinical data of the present population are given in Table 1. Of the 2,626 infants successfully karyotyped, 18 infants (0.69%) were carriers of a major chromosome abnormality. In addition, 7 infants with a pericentric inversion of a chromosome 9 and one with a pericentric inversion of the Y chromosome were found in this series, but they were not included in the above 18 abnormal infants.

1. Sex-chromosome abnormalities in phenotypic males

Out of 1,393 male infants successfully karyotyped, 4 infants (0.29%) showed sex-chromosome abnormalities: they were two (6/77 and 203/77) having a 47,XYY karyotype, one (394/76) showing a 46,XY/47,XYY (clone ratio 27:73) mosaicism and one (389/76) carrying a 45,X/46,XY/47,XYY (clone ratio 45:49:6) mosaicism.

Table 1. Some anamnestic and clinical data of the study population.
(December 1, 1975 to November 30, 1977)

Total livebirths	2,795
No. of blood samples obtained	2,672
No. of unsuccessful cultures	46
No. of babies successfully karyotyped	2,626
Male	1,393
Female	1,233
Sex ratio	1.13
Mean maternal age (years)	28.9±3.6
Mean gestational age (weeks)	38.1±1.2
Mean birthweight (g)	
Male	3,024.4±385.5
Female	2,905.0±351.0
Mean birthlength (cm)	
Male	48.8±1.9
Female	48.1±1.8
Mean head circumference (cm)	
Male	33.5±1.4
Female	32.9±1.4

All the infants were physically normal at birth. Q-banding identification of the Y chromosome was made in each of these infants.

2. Sex-chromosome abnormalities in phenotypic females

In 1,233 females karyotyped successfully, 4 infants (0.32%) were those of sex-chromosome abnormalities: they consisted of one case (1224/76) of a 47,XXX karyotype, one (327/76) showing a 45,X/47,XXX (clone ratio 50:50) mosaicism, one (388/76) having a 45,X/46,XY/47,XYY (clone ratio 38:57:5) mosaicism and one (1415/76) carrying a 45,X/46,XX (clone ratio 76:24) mosaicism. Case 388/76 and 389/76 were twins with an apparent opposite sex. All of the above 4 infants were physically normal at birth. In case 388/76, the Y chromosome was identified by the Q-banding method, and G-banding analyses were made for case 327/76, 1224/76 and 1415/76. Cytogenetic data of infants with sex-chromosome abnormality are presented in Table 2 and their clinical data in Table 4.

3. Autosomal trisomics

Three (316/77, 699/77 and 1243/77) were characterized by 21-trisomy with clinical features of Down's syndrome. The extra 21 chromosome was identified by the G-banding method in each.

4. Unbalanced autosomal rearrangement and supernumerary chromosome

One (346/76) had a 13-trisomy by translocation. The baby showed the clinical features characteristic of Patau's syndrome and expired soon after birth. The father of this baby was a carrier of a balanced 13/14 translocation. Another case (700/76)

Table 2. Cytogenetic data of the 8 infants with sex chromosome abnormalities.

Case No.	Tissue	Chromosome count					Karyotype	Karyotype	
		<45	45	46	47	Total		Mother	Father
327/76	Cord blood	—	4	—	9	13	45, X/47, XXX	46, XX	46, XY
	Peripheral blood	1	54	3	42	100			
388/76	Cord blood	2	17	27	1	47	45, X/46, XY/47, XYY	—	—
	Peripheral blood	—	23	33	4	60			
389/76	Cord blood	2	42	51	5	100	45, X/46, XY/47, XYY	—	—
	Peripheral blood	—	38	36	6	80			
394/76	Cord blood	—	1	4	11	16	46, XY/47, XYY	—	—
	Peripheral blood	—	—	27	73	100			
1224/76	Cord blood	—	—	2	18	20	47, XXX	46, XX	—
1415/76	Cord blood	1	39	10	—	50	45, X/46, XX	—	—
	Peripheral blood	—	36	14	—	50			
6/77	Cord blood	—	—	2	18	20	47, XYY	—	46, XY
	Peripheral blood	—	—	3	17	20			
203/77	Cord blood	—	—	—	10	10	47, XYY	—	—
	Peripheral blood	—	—	3	17	20			

had 47 chromosomes with an additional chromosome smaller than a member of G chromosomes (47,XY,+mar). G- and Q-banding methods were not useful for the identification of this marker chromosome. The mother of this baby had 47 chromosomes with an additional chromosome which was similar in shape and size to that found in the baby. This baby and the mother were physically normal.

5. Balanced autosomal rearrangements

Among 2,626 infants successfully karyotyped, there were 5 infants (0.19%) who had a balanced Robertsonian translocation. Three (1034/76, 1039/76 and 281/77) showed 13/14 translocation and two (737/76 and 1242/77) 14/22. Two (737/76 and 1034/76) were inherited from the father and three (1039/76, 281/77 and 1242/77) from the mother. The abnormal chromosomes were identified by the G-banding method in them. In case 737/76, a chromosome examination had been undertaken in amniotic fluid cells at the 18th week of gestation, since the mother had previously an abortion with trisomy 22 and the father had been known to be a balanced 14/22 translocation carrier. Cytogenetic data for the above cases are presented in Table 3 and their clinical data in Table 4.

DISCUSSION

The current literature refers to at least seven cytogenetic studies of unselected newborn infants populations (Sergovich *et al.*, 1969; Gerald and Walzer, 1970; Lubs and Ruddle, 1970; Bochkov *et al.*, 1974; Jacobs *et al.*, 1974; Hamerton *et al.*, 1975; Nielsen and Sillesen, 1975). Their data are summerized in Table 5 along with the

Table 3. Cytogenetic data of the 10 infants with autosomal abnormalities.

Case no.	Tissue	Chromosome count					Karyotype	Parental karyotype	
		45	45	46	47	Total		Mother	Father
346/76	Cord blood	—	—	5	—	5	46, XX, −14, +t(13q14q)	46, XX	45, XY, t(13q14q)
	Peripheral blood	1	—	10	—	11			
700/76	Cord blood	—	—	2	8	10	47, XY, +mar	47, XX, +mar	46, XY
	Peripheral blood	—	1	2	17	20			
737/76	Cord blood	—	5	—	—	5	45, XX, t(14q22q)	46, XX	45, XY, t, (14q22q)
	Peripheral blood	—	15	—	—	15			
1034/76	Cord blood	—	10	—	—	10	45, XY, t(13q14q)	46, XX	45, XY, t(13q14q)
	Peripheral blood	2	18	—	—	20			
1039/76	Cord blood	2	8	—	—	10	45, XY, t(13q14q)	45, XX, t(13q14q)	46, XY
	Peripheral blood	—	20	—	—	20			
281/77	Cord blood	—	10	—	—	10	45, XX, t(13q14q)	45, XX, t(13q14q)	46, XY
	Peripheral blood	—	20	—	—	20			
316/77	Cord blood	—	—	—	10	10	47, XY, +21	46, XX	46, XY
	Peripheral blood	—	—	3	27	30			
699/77	Cord blood	—	—	1	19	20	47, XX, +21	—	—
1242/77	Cord blood	—	20	—	—	20	45, XX, t(14q22q)	45, XX, t(14q22q)	46, XY
1243/77	Cord blood	—	—	—	10	10	47, XX, +21	—	—
	Peripheral blood	—	—	—	20	20			

Table 4. Clinical data of the 18 infants with major chromosome abnormalities.

Case No.	Phenotypic sex	Gestation (weeks)	Birth weight (g)	Birth length (cm)	Parental age		Comments
					Mother	Father	
Sex chromosome abnormalities							
327/76	Female	38	2,634	47.0	28	37	No congenital malformation
388/76	Female	38	2,761	48.0	32	35	A pair of twins with opposite sex, zygosity unknown
389/76	Male	38	2,761	47.5	32	35	
394/76	Male	38	2,927	48.0	29	29	No congenital malformation
1224/76	Female	39	2,363	45.5	25	25	No congenital malformation
1415/76	Female	39	3,130	47.0	27	31	No congenital malformation
6/77	Male	38	2,682	48.0	37	36	No congenital malformation
203/77	Male	?	2,417	45.0	39	37	No congenital malformation
Autosomal abnormalities							
346/76	Female	32	1,280	—	28	29	Patau's syndrome
700/76	Male	37	3,050	48.5	38	40	No congenital malformation
737/76	Female	38	2,820	49.0	32	36	No congenital malformation
1034/76	Male	39	2,900	49.0	26	35	No congenital malformation
1039/76	Male	38	2,900	49.0	31	33	No congenital malformation
281/77	Female	38	2,963	49.0	26	30	No congenital malformation
316/77	Male	38	2,650	44.0	27	27	Down's syndrome
699/77	Female	39	2,147	45.5	25	27	Down's syndrome
1242/77	Female	39	3,778	50.5	26	28	No congenital malformation
1243/77	Female	39	1,945	45.0	21	32	Down's syndrome

Table 5. Incidence of major chromosome abnormalities among newborn infants.

Type of chromosome abnormalities	Present study		Previous 7 studies*	
	Total	Per cent	Total	Per cent
Sex-chromosome abnormalities				
Nonmosaics	3	0. 11	88	0. 18
Mosaics	5	0. 19	22	0. 04
Autosomal abnormalities				
Trisomics	3	0. 11	78	0. 16
Balanced structural	5	0. 19	99	0. 20
Unbalanced structural	2	0. 08	18	0. 04
Total	18	0. 69	305	0. 62
Total babies tested	2, 626		49, 244	

* Sergovich *et al.* (1969); Gerald and Walzer (1970); Lubs and Ruddle (1970); Bochkov *et al.* (1974); Jacobs *et al.* (1974); Hamerton *et al.* (1975); Nielsen and Sillesen (1975).

present ones. The seven infant populations involve approximately 50,000 infants and the incidence of major chromosome abnormalities was shown as 0.62%. There is a wide variation in the percentage of chromosomally abnormal neonates among them, the lowest at 0.46% (Hamerton *et al.*, 1975) and the highest at 0.83% (Nielsen and Sillesen, 1975). The incidence of newborns with major chromosome abnormalities was 0.69% in the present study, though the sample size is still small for any assessment. Sex-chromosome abnormality occcurred in 8 infants (0.30%), 4 in phenotypic males and 4 in phenotypic females. Among the 8 sex-chromosome abnormalities, 5 were mosaics. While the incidence of sex-chromosome abnormalities found in our series was rather close to the averaged incidence of the seven reports, a marked difference occurs between them regarding mosaicism. The difference may be caused by the number of cells examined. Generally the diagnosis of mosaicism requires the analysis of a large number of cells. According to Bochkov *et al.* (1974), the probability of finding mosaics in 25% cells with the abnormal chromosome count was 76.1% in the initial 5-cell analysis. Nielsen (1975) reported that the first cell with the chromosome abnormality was found among the first 5 cells in 40 of the 44 cases with mosaicism. The incidence of female infants with abnormal sex-chromosome constitutions in our series was almost identical to that of male infants. All infants with sex chromosome abnormalities in our series showed no physical abnormality. Of 10 infants with autosomal abnormalities, 6 were of the Robertsonian translocation type, one being unbalanced 13/14, three with balanced 13/14 and two showing balanced 14/22 type. The incidence of the balanced translocation was 0.19% in our series, which was comparable well to those in the seven other surveys. In a survey of 64 cases with D/D translocation, Cohen (1971) found that 77% were of 13/14 type. The excess of 13/14 type among D/D translocation was also observed in newborn surveys (Jacobs *et al.*, 1974; Hamerton *et al.*, 1975; Nielsen and Sillesen, 1975) and in our series. In contrast, 14/22 translocation was very rare,

only one (Jacobs *et al.*, 1974) having been reported in the seven newborn surveys. An unbalanced 13/14 translocation or 13-trisomy by translocation was also rare, only two (Sergovich *et al.*, 1969; Jacobs *et al.*, 1974) having been detected in the seven newborn surveys. It is of clinical importance to study the phenotypic effects of sex-chromosome abnormalities through follow-up studies of the infants with those abnormalities. Amniocentesis may be efficiently applied for familial members having a balanced Robertsonian translocation in preventing the birth of unbalanced zygotes in future pregnancies.

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