be observed. The parents and sibs of the present case are, like the proband, in the 75th centile for height. The retarded bone age of the proband suggests that his ultimate height may be greater than that of his normal sibs.

The mechanism by which this patient received his extra Y chromosomes is not clear. The most likely explanation appears to be the one originally proposed by Townes *et al* (1965), namely, non-disjunction in spermatogonial mitosis followed by a 2nd non-disjunction of one of the Y chromosomes in meiosis resulting in the formation of a sperm bearing 3 Y chromosomes.

The introduction of fluorescent and heterochromatin staining techniques has opened the door to further advances in the field of cytogenetics. The diagnosis of the present case was dependent upon these methods. Additional cases of 48,XXXX will almost certainly be recognized in the screening surveys utilizing fluorescent staining of blood smears, possibly among male patients with mild psychomotor retardation, simian creases, and evidence of retarded bone maturation.

Meanwhile the intention is to follow the growth, development, and personality pattern of this boy as he matures and later note gonadal function and meiotic chromosome morphology. Hopefully this will help increase understanding of the phenotypic expression and cytogenetics of the Y chromosome in man.

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Immunoglobulin Abnormality in a Girl with a Large Chromosome 18

Feingold *et al* (1968) first reported a case of IgA deficiency associated with partial deletion of the long arm of chromosome 18. Since then IgA deficiency has been reported in several patients with different abnormalities of chromosome 18, namely, partial deletion of the long arm, short arm deletion, and a ring 18 chromosome. Long arm deletion of chromosome 18 has been recognized as a clinical syndrome (de Grouchy, 1969). Chromosome 18 presumably has a locus for the production of IgA, and deletion of part of this chromosome results in deficiency in an immunoglobulin A. Hecht (1969), however, reported a case of 18 trisomy associated with a striking deficiency of serum IgA, and some reports had no IgA deficiency (Borgaonkar

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FIG. 1. Facial appearance of the patient.

et al, 1969; Haddad *et al*, 1969; Jensen *et al*, 1969; Christensen *et al*, 1970).

The patient reported here is a girl in whom an enlarged long arm of chromosome 18 is associated with deficiency in IgA. To our knowledge, this is the first example of a large chromosome 18 and abnormal IgA value. A preliminary note of cytogenetic findings on this case had been reported previously (Yanagisawa, 1971).

Case Report

The patient, who is now 13 years old, was first seen at 9 years of age because of mental and motor retardation. Her birth weight was 3200 g. She had coiling of the umbilical cord and asphyxia was recognized at the time of birth. There was an episode of convulsions in the neonatal period. Physical measurements at 13 years of age were 127.7 cm in length (below -3 SD), 28.0 kg in weight, head circumference 55.5 cm. Her non-consanguineous mother and father were both 23 years of age at the time of her birth, and there was no history of congenital defects or miscarriages in the immediate family.

Development of the patient was consistently delayed. She first walked alone at 3 years. She had severe mental and speech retardation.

Clinical features were as follows: short stature, prominent occiput, antimongoloid slant of the palpebral fissures, thick eyebrows, prominent nasal bridge, and low-set ears without abnormal helix. Her mouth was open and the tongue protruded (Fig. 1). There was a high arched palate but no mid-face aplasia. Joint involvements were recognized on wrist and ankle joints. Both 5th fingers were incurved. Finger and toe nails were hypoplastic. External genitalia were normally developed.

Immunological Studies. Serum immunoglobulins were quantified by immunoelectrophoresis. Immunoglobulin levels were as follows: IgG was 130 mg/dl, IgA 35 mg/dl, and IgM 195 mg/dl, respectively. There were deficiency of IgA and moderate elevation of IgM.

Dermatoglyphic Findings. Finger-tip patterns revealed 4 whorls, 5 ulnar loops, and a radial loop. Total ridge count was 112 (Table I; Figs. 2a and 2b). There was no simian crease on the palms.

TABLE I
DERMATOGLYPHIC PATTERNS OF THE PATIENT

	Finger-tip Patterns and Ridge Counts					Ridge Counts	a-b Ridge Counts	atd Angle	Hallucal Area
	I	II	III	IV	V				
Right	U 11	W 13, 3	U 8	W 16, 14	U 11	59	38	46°	L ^d
Left	W 6, 6	R 16	U 9	W 15, 16	U 6	53	50	55°	L ^d

Figs. 2a and 2b. Dermatoglyphic main lines of the patient.

FIG. 3. Karyotype of the patient showing an abnormal long chromosome 18 (indicated by arrow).

FIG. 4. Metaphase chromosomes stained with quinacrine dihydrochloride (A) and Giemsa (B). An abnormal chromosome is indicated by letters LE and a normal chromosome 18 by E. LE fluoresced more brightly than E.

Cytogenetic Studies. Chromosome analyses were performed on leucocytes cultured from peripheral blood. The modal chromosome number was 46 and sex chromosome constitution was XX, but one chromosome 18 had an enlarged long arm (Fig. 3).

Studies of fluorescence patterns on metaphase plates stained with quinacrine dihydrochloride (Borgaonkar and Hollander, 1970) were carried out. The abnormal chromosome 18 with the enlarged long arm fluoresced brightly. The other chromosome 18 appeared also brighter than chromosome 16 and 17 (Fig. 4).

Sex chromatin patterns in cells of the buccal mucosa were in agreement with her sex.

Chromosome analyses from the mother and two phenotypically normal sisters of the patient revealed normal karyotypes. The father is dead and therefore his karyotype was not available.

Discussion

Structural aberrations of chromosome 18 have been recognized as short arm deletion (18p-), long arm deletion (18q-), and ring formation (18r). Abnormal immunoglobulin values have been reported in patients with these structural aberrations. IgA deficiency associated with the long arm deletion of chromosome 18 has been reported by several authors (Feingold *et al*, 1969; Stewart *et al*, 1970; Wertelecki and Gerald, 1971). IgA deficiency has also been recognized in patients with short arm deletion (Ruvalcaba and Thuline, 1969; Jansch, May, and LaMarche, 1970) or with a ring formation (Feingold *et al*, 1969; Finley *et al*, 1969; Murken, Salzer, and Kunze, 1970; Michaels *et al*, 1971) of chromosome 18. Hecht (1969), however, reported a case of 19 trisomy syndrome associated with decreased serum IgA and IgM. Rudd and LaMarche (1971) described a high level of IgA in the partial trisomy of chromosome 18. Jensen *et al* (1969) described an increased IgM associated with a ring chromosome 18; on the other hand, Haddad *et al* (1969) reported a striking deficiency of IgM in a patient with partial deletion of the long arm of chromosome 18. In our patient IgM was moderately increased.

The 18q- syndrome is a clinically well defined syndrome characterized (de Grouchy, 1969; Wertelecki and Gerald, 1971) by the following features: mental retardation, microcephaly, mid-face aplasia, carp-shaped mouth, hypertrophy of the antihelix and antitragus, tapering fingers, and ophthalmic anomalies. Clinical findings of partial 18 trisomy syndrome can not be distinguished from those of complete 18 trisomy syndrome except for long survival in partial trisomy (Rohde, Lee, and Sapin, 1963; Rudd and LaMarche, 1971).

Quinacrine fluorescence patterns of chromosome

18 appeared brighter than chromosome 16 and 17 (Bobrow and Pearson, 1961; Červenka, Jacobson, and Gorlin, 1971). Therefore, there are 3 brightly fluorescent No. 18 chromosomes in trisomy 18 syndrome (S. Yanagisawa, unpublished data). However, the long arm of the abnormal chromosome 18 in this patient stained with quinacrine dihydrochloride fluoresced more brightly than the normal chromosome 18.

The phenotype of the patient appears to be closer to that of 18 trisomy syndrome rather than 18q- syndrome. However the result of quinacrine fluorescence study suggests that the abnormal chromosome could be the result of a reciprocal translocation between a chromosome 18 and an unknown chromosome resulting in partial monosomy of the long arm of chromosome 18 and a trisomic state of unknown material.

Immunoglobulin A deficiency in this case was interpreted as the result of the long arm deletion of chromosome 18 due to reciprocal translocation. Clinical features of the patient revealed few stigma of the 18q- syndrome and these could be interpreted as due to the trisomic state of a chromosome segment of unknown origin.

Summary

A 13-year-old girl with an enlarged long arm of chromosome 18 is described. Clinically she had short stature, mental retardation, thick eyebrows, low-set ears, prominent nasal bridge, and joint involvements. There is little stigma of 18q- syndrome but the serum IgA value was decreased.

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A Double Aneuploid Mosaic: Trisomy 13 and XXY*

We have examined a liveborn male who showed physical features of trisomy 13 syndrome and was

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found to have 47,XY,13+/48,XXY,13+ mosaicism. To our knowledge, this is the first report of trisomy 13 and an XXY sex chromosome complement coexisting in a liveborn individual.

Case Report

The patient, a Caucasian male, was born to a 17-year-old primigravida mother and a 19-year-old father. The father had a son by a prior union. The remainder of the pedigree was unremarkable. Both parents had taken lysergic acid diethylamide (LSD) 2 years before the pregnancy. The infant was the product of an apparently normal 36-week gestation and vertex delivery. Birth weight was 1480 g, length 42 cm, and head circumference 29 cm. The anterior fontanelle was large; the sagittal suture was 1 cm in each diameter. There was a bony defect 1.6 × 2 cm in the parieto-occipital region through which the meninges were seen (Fig. 1). The parietal bones overlapped the frontal and occipital bones. The face had an inverted triangular shape with a broad forehead and hypoplastic left eye (Fig. 2). The right eye was normal. The nose was large and prominent, the mouth was small and the ears were low set. The neck showed redundant skin folds. There was a ventral hernia 1.5 cm above the umbilicus. Except for an undescended left testis, the genitalia were normal for a male infant. Both hands had a simian crease and an extra ulnar digit. The feet were rocker bottom in shape and showed a wide space between the 1st and 2nd toes. The remainder of the physical examination was normal. The infant was alert, cried vigorously, and showed no abnormal neurological findings. Shortly after admission he became cyanotic and was given antibiotics for suspected

FIG. 1. Scalp view of the propositus.