ureter (right), stenosis of ureteral ostia, lack of involution of fetal adrenal cortex, and accessory spleens.

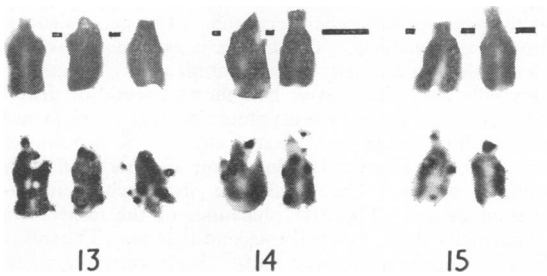

FIG. 2. Partial karyotype of the D-group (Nos. 13, 14, 15) chromosomes, with autoradiograph below showing three No. 13 chromosomes.

Cytogenetics

Chromosome analysis from the peripheral blood leukcocyte cultures revealed 47 chromosomes with an extra D-group chromosome (47,XX, + D) in all 52 metaphases examined. Autoradiographic studies with ^{3}H-thymidine added during the latter part of DNA synthetic period showed this extra D-group chromosome to have a late replicating nature as that of No. 13 chromosome (Fig. 2). Therefore, the diagnosis of trisomy 13 was confirmed.

Discussion

Our patient was initially diagnosed as having Rubinstein–Taybi syndrome mainly because she had the prominent nose, and broad thumbs and first toes characteristic of that syndrome. However, due to the presence of the multiple congenital anomalies and the suspicion of trisomy 13, chromosome studies were carried out. The cytogenetic diagnosis of trisomy 13 was then confirmed. Our patient did have some of the clinical features of trisomy 13 namely, malformed, low-set ears, antimongoloid slant of the eyes, colobomata of the iris, and cleft palate.

There are at least five known cases (including this case) of trisomy 13 associated with broad thumbs and first toes (Wilson, 1968; H. Fox, personal communication). Since an initial diagnosis of Rubinstein–Taybi syndrome was made in four of these infants, it is important for clinicians to be aware that trisomy 13 syndrome may mimic Rubinstein–Taybi syndrome. It is possible that both syndromes may coexist in the same individual. However, since the prognosis of trisomy 13 is so much worse than that of Rubinstein–Taybi syndrome, the diagnosis of trisomy 13 must not be missed. Therefore, cytogenetic studies should be considered in all patients with clinical diagnosis of Rubinstein–Taybi syndrome.

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Partial 12p deletion: a cause for a mental retardation, multiple congenital abnormality syndrome

Summary. A severely mentally retarded man displayed the following main symptoms: short stature, microcephaly, antimongoloid slant of palpebral fissures, big ears with hyperplastic helices, imperfect dental enamel, short and webbed neck, short arms, short hands, brachymetaphalangy, short second fingers, broad thumbs, short metatarsal bones, and unusually big first toes. It seems almost certain that the syndrome was caused by a chromosome deletion involving about half of 12p which was present in all of the lymphocytes examined.

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The present patient was found in the Madison Blind Study IV (Magnelli, 1975) amongst 50 mentally retarded patients with at least three other anomalies and 50 normal subjects. In addition to the propositus, four other patients showed major chromosome anomalies and one low-grade mosaicism; three patients had an innocuous chromosome anomaly, as had two normal subjects.

The propositus displayed a deletion of 12p and is —at least to our knowledge—the only case of its kind verified with banding techniques.

Case history

The patient (EB 130133), a Caucasian male, was born, when his father was 41 and his mother 34 years of age, after an uneventful pregnancy as the youngest of four children; the three brothers were normal and healthy, until the youngest died of polio at the age of 21.

At the time of the investigation the patient (Fig. 1) was 35 years old; his height was 145·5 cm and weight 45·6 kg. He is microcephalic, and shows an antimongoloid slant of the palpebral fissures especially at right. The ears are very large with hyperplastic helices. Several teeth have never appeared; the enamel is hypoplastic, the gingiva hyperplastic. The hairline is normally masculine, and the face and the thorax display acneiform lesions with increased sebaceous secretion. The neck is short, broad, and webbed. The thorax is asymmetric with a depression on the left. The umbilicus is situated abnormally low. The pubic hair shows a feminine distribution. The patient has cryptorchidism at the right and an inguinal hernia on the same side. The extremities are especially abnormal. Both arms are short and show cubitus valgus. The hands are short with brachymetaphalangy. The first phalanges of the fingers are abnormally short, as are the second fingers. The finger tips are square with broad nails. Both thumbs are unusually broad. The lower extremities display valgus knees. The metatarsal bones are short. Both big toes are unusually long and broad. The toe nails are hypoplastic; the toes have a tendency to overlap. The legs have normal hair distribution, whereas the arms and the chest are bare. The patient is mildly spastic, the upper limbs and the muscles of the shoulder girdle are hypertrophic.

His IQ is estimated to be 20.

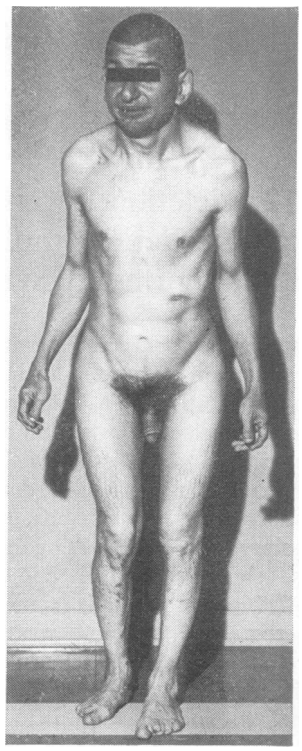

FIG. 1. Propositus (35 years) with 12p− syndrome.

Cytogenetic studies

The methodology of the Blind Study has been described elsewhere (Summitt, 1969).

The chromosomes were analysed in lymphocytes cultured according to a modification of the usual Moorhead technique. The slides were stained with Azur A. Fluorescence microscopy was done on atebrin-stained slides.

The modal chromosome number in the patient's lymphocytes was 46. Initially 17 cells were analysed; later numerous photomicrographs both in the light and in the fluorescence microscope were taken. In all cells, one C-chromosome had a partially deleted short arm. This was identified as No. 12 with Q-banding (Fig. 2) from which about half of the short arm was missing. One No. 22 had an unusually bright short arm. This chromosome was inherited from the mother (Fig. 2).

The lymphocytes of both parents and of a brother showed normal chromosomes.

Discussion

A number of substantial autosomal deletions have been found compatible with life in man. As apparently pure deletions not involved in translocations the following have been described repeatedly: 4p−, 5p−, 13q−, 18p−, 18q−, and possibly monosomy for No. 21. At least a small deletion in both arms must be present in all ring chromosomes.

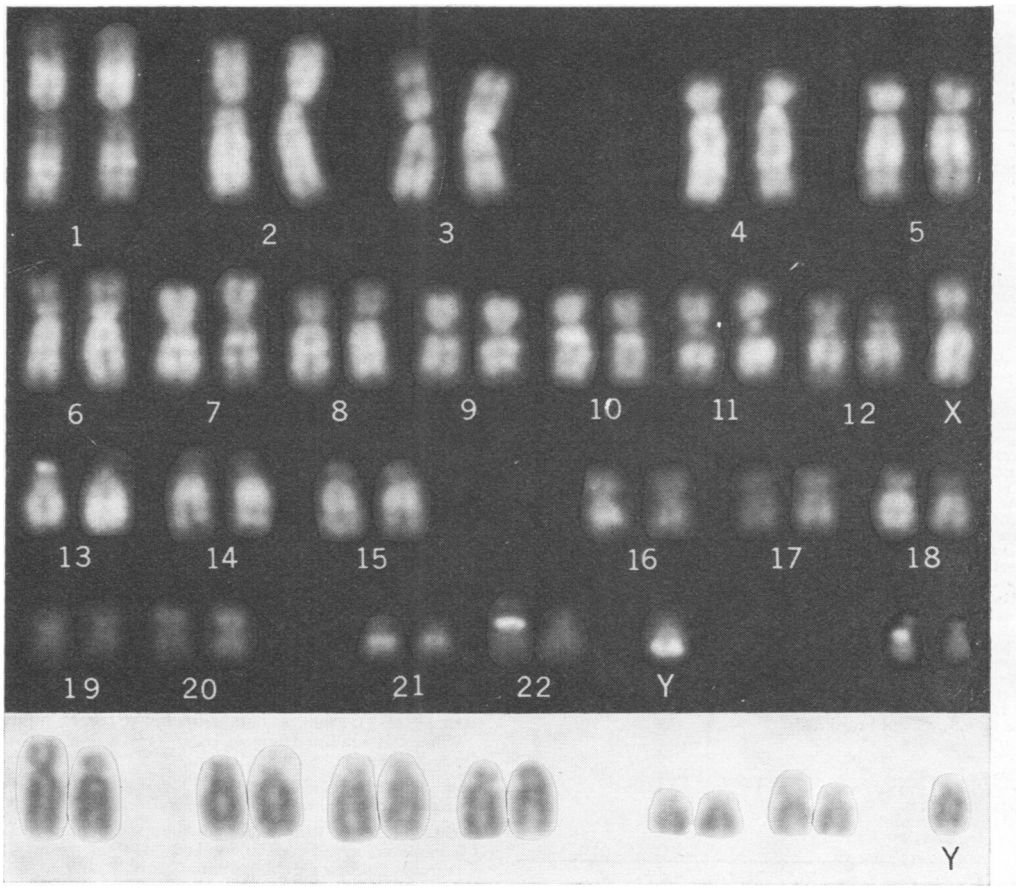

FIG. 2. Fluorescent karyotype of the patient: 46 chromosomes including a 12p−, and the mother's No. 22 chromosomes. Note the bright 22p in mother and son. The bottom line shows chromosomes 12, 12p−, the D and G groups, and the Y (restained with Azur A).

The pattern of anomalies displayed by the present patient with a partial 12p deletion is so strikingly similar to that described elsewhere (Laurent *et al*, 1968) for a patient with a short-arm deletion of an undetermined C chromosome (Table I) that it appears almost certain that the latter was also chromosome 12. The new deletion syndrome appears remarkably well-defined especially if one takes into account the age difference of the two patients and the incomplete penetrance, characteristic of most anomalies in any chromosomal syndrome.

Deletions not involved in recognizable translocations pose the problem whether single breaks in human chromosomes (or in the chromosomes of other organisms) are able to heal. In other words, can a broken end be stabilized and act as a telomere (*cf*, Patau, 1965)? A number of observations speak for healing occurring at least in some chromosome regions. After X radiation of human cells in early G_1, sister chromatids in the broken chromosome never seem to join (Bochkov, Patau, and Therman, 1969; K. Patau, unpublished observations). A

TABLE I

COMPARISON OF TWO MALE PATIENTS WITH A PARTIAL 12p DELETION. (IDENTITY OF THE CHROMOSOME VERIFIED IN THE PRESENT CASE, PRESUMED IN THE CASE OF LAURENT *et al* (1968))

Symptoms	Patients	
	Present Case	Laurent *et al*
Age (yr)	35	8
Mental retardation	+	+
Shortness of stature	+	+
Microcephaly	+	+
Antimongoloid slant of palpebral fissures	+	+
Big nose	+	+
Receding chin	+	+
Small mouth	−	+
High palate	−	+
Agenesis of some teeth	+	+
Imperfect enamel	+	−
Big ears	+	+
Low-set ears	−	+
Hyperplasia of helix	+	+
Preauricular tubercles	−	+
Short and webbed neck	+	−
Narrow thorax	−	+
Asymmetric thorax	+	−
Low-set umbilicus	+	−
Umbilical hernia	+	−
Inguinal hernia	+	−
Cryptorchidism	+	−
Feminine pubic hair	+*	−
Short arms	+	+
Cubitus valgus	+	−
Short hands	+	+
Brachymetaphalangy	+	−
Clinodactyly of the 5th fingers	+	+
Broad thumbs	+	+
Short 2nd fingers	+	−
Square finger tips and broad nails	+	+
Metacarpal dimples	−	+
Valgus knees	+	+
Short feet	−	+
Big first toes	+	+
Overlapping of toes	+	+
Muscular hypertrophy	+*	−
Unusual dermatoglyphics	−	+

Symptoms: present +; absent −; age dependent *.

ring may break up into a rod in a number of cells (Cooke and Gordon, 1965; Hecht, 1969; Summitt, 1969). In an overwhelming majority of cri-du-chat cases, 5p has broken within a very limited region. If a translocation were involved, the length of the 5p− ought to vary much more. In addition the broken end of 5p seems to be different from the normal B ends: in fibroblast metaphases, it sometimes is fuzzy (Patau, 1965).

The cri-du-chat syndrome and most of the other deletion syndromes mentioned above seem to occur much more frequently than 12p−. Different explanations are possible: certain chromosome regions may break more often than others, and/or the break may heal in certain regions, but not in others (*cf*, Hsu, 1963). In contradistinction to trisomy syndromes, the manifestation of a deletion syndrome may in part depend on the presence of different recessive genes on the homologue so that a mutant on the homologue may render an ordinarily lethal deletion viable. A possible illustration of such genetic variation in the homologue is provided by the family described by Uchida *et al* (1965) in which two children with 18p− displayed very different severity of symptoms.

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