

- Gagnon, J., Katyk-Longtin, N., de Groot, J. A., and Barbeau, A. (1961). Double trisomie autosomique à 48 chromosomes (21 + 18). *Union Médicale du Canada*, **90**, 1220-1226.
- Garson, O. M., Baikie, A. G., Ferguson, J., and Greer, C. H. (1969). Double autosomal trisomy and mosaicism for three cell lines in man. *Journal of Medical Genetics*, **6**, 209-215.
- Glogowska, I. (1969). Mosaicism 47/48 in a patient with Down's syndrome. *Neurologia i Neurochirurgia Polska*, **19**, 263-266.
- Gustavson, K.-H., Ivemark, B. I., Zetterqvist, P., and Böök, J. A. (1962). Post-mortem diagnosis of a new double-trisomy associated with cardiovascular and other anomalies. *Acta Paediatrica*, **51**, 686-697.
- Hamerton, J. L. (1971). Autosomal abnormalities—Group G. In *Human Cytogenetics*, vol. 2, chap. 5, pp. 253-257. Academic Press, New York and London.
- Hsu, L. Y. F., Schwager, A. J., Nemhauser, I., and Sobel, E. H. (1965). A case of double autosomal trisomy with mosaicism: 48/XX (trisomy 18 + 21) and 46/XX. *Journal of Pediatrics*, **66**, 1055-1060.
- Koch, F., Santamouris, C., and Ulbrich, F. (1967). D + G Trisomie bei einem Patienten mit Rothmund-Syndrom. *Zeitschrift für Kinderheilkunde*, **99**, 1-13.
- Marks, J. F., Wiggins, K. M., and Spector, B. J. (1967). Trisomy 21-trisomy 18 mosaicism in a boy with clinical Down's syndrome. *Journal of Pediatrics*, **71**, 126-128.
- Porter, I. H. Petersen, W., and Brown, C. D. (1969). Double autosomal trisomy (trisomy D + G) with mosaicism. *Journal of Medical Genetics*, **6**, 347-348.
- Reed, T. E., Borgaonkar, D. S., Conneally, P. M., Yu, P. L., Nance, W. E., and Christian, J. C. (1970). Dermatoglyphic nomogram for the diagnosis of Down's syndrome. *Journal of Pediatrics*, **77**, 1024-1032.
- Schmidt, G. W., Stibane, H., Ulbrich, F., and Griesse, H. (1967). Edwards-syndrome with double trisomy D and E (mosaicism). (Edwards-Syndrom mit Doppeltrisomie D and E [mosaik].) *Klinische Wochenschrift*, **45**, 634-638.
- Seabright, M. (1971). A rapid banding technique for human chromosomes. *Lancet*, **2**, 971-972.
- Seabright, M. (1972). The use of proteolytic enzymes for the mapping of structural rearrangements in the chromosomes of man. *Chromosoma*, **36**, 204-210.
- Smith, G. S., Tips, R. L., and Howard, H. (1965/1966). Autosomal mosaicism occurring in conjunction with Down's syndrome. *American Journal of Mental Deficiency*, **70**, 218-222.
- Tolksdorf, M., Lehmann, W., Hansen, H. G., and Wiedemann, H. R. (1965). Edwards-syndrom mit aussergewöhnlichem chromosomalem Befund. *Zeitschrift für Kinderheilkunde*, **93**, 55-63.
- Zellweger, H. and Abbo, G. (1967). Double trisomy and double trisomic mosaicism. *American Journal of Diseases of Children*, **113** 329-337.

## Turner Phenotype : Mosaic 45,X/47,XY,+18\*

**Summary.** A 14-year-old girl with Turner phenotype is described, whose lymphocyte and skin fibroblast cultures both revealed a 45,X/47,XY,+18 chromosomal mosaicism. In blood cultures one third and in fibroblasts 7% of the cells had 47 chromosomes. The identity of the Y and the supernumerary 18 were determined by fluorescence and Giemsa banding patterns. The patient is of normal intelligence and does not exhibit any signs of masculinization or stigmata of trisomy 18.

There are several instances of mosaicism with X-monosomic and 21-trisomic cell lines. Cohen and Davidson (1972) published one case of a mosaic 45,X/47,XX,+21, and Prieur *et al* (1972) one of 45,X/47,XY,+21. Several cases of mosaic 45,X/46,XX/47,XX,+21 (Pfeiffer, 1968) and one

case of mosaic 45,X/46,XY/47,XY,+21 (Edgren, de la Chapelle, and Kääriäinen, 1966) have been reported. To our knowledge the present case is the first one involving an extra autosome 18.

### Case Report

The proposita is the third daughter of healthy unrelated parents; the father was 38 years and the mother 41 years at her birth. All the family is of short stature, the father being 162 cm, the mother 152 cm, the 21-year-old sister 150 cm, and the 18-year-old sister 160 cm. The patient was born by Caesarean section at 36 weeks; birth weight was 2400 g. Swelling of the dorsum of both feet was noted at birth and persisted for more than one year. The patient was said to have been always smaller than her sisters at comparable ages, but otherwise her physical and mental development was normal.

At 12 years of age she was referred to this hospital because of short stature (length 117.7 cm, weight 25.2 kg, both below third centile) and absence of pubertal signs. She presented the following stigmata of Turner's syndrome: multiple pigmented naevi, prominent auricles, short broad neck with slight pterygium, broad chest with widely spaced hypoplastic nipples, relatively large clitoris, hyperextensibility of elbow joints, and short fourth fingers. Radiology of both hands revealed short fourth metacarpals, a coarse trabecular pattern of the bone, and a bone age of 9-10 years, giving a predicted adult height of only 139 cm.

Sex chromatin was studied in buccal smears and in hair root preparations (Schmid, 1967a and b). The chromosomes from blood cultures were studied in

Received 28 August 1973.

\* Reprint requests to: Professor W. Schmid, Abteilung für Medizinische Genetik; Kinderspital Zürich, Steinwiesstrasse 75, CH-8032 Zurich, Switzerland.

orcein-stained preparations, after staining with quinacrine mustard (Caspersson, Zech, and Johansson, 1970) and after trypsin digestion and Giemsa staining (Seabright, 1971). A fibroblast culture was set up from a skin biopsy of the patient. Dermatoglyphics from both hands of the *proposita* were analysed.

### Results

**X-Chromatin** was negative in 500 nuclei counted from both buccal smears and hair roots.

**Chromosome Studies.** The results from peripheral blood and a fibroblast culture are shown in Table I. Two cell lines were present, one with 45 chromosomes with a missing C and the other with 47 chromosomes including 15 of group C, seven of group E, and five of group G, respectively. The latter group contained one Y-like chromosome. This cell line was found in more than a third of lymphocytes but only in 7% of fibroblast mitoses. Cells with 46 chromosomes belonged to the 47,XY,+E cell line with random losses. The analysis of quinacrine-stained preparations showed a brightly fluorescent Y in the cells with 47 chromosomes. The supernumerary element in group E exhibited the characteristics of a No. 18 both in fluorescent preparations and in the Giemsa-stained preparations after trypsin digestion (Figs. 1 and 2).

TABLE I  
CHROMOSOME ANALYSIS

	Chromosome Count					Total
	43*	44*	45	46*	47	
Blood (11.8.1970)	2	2	60	2	34	100
Blood (3.10.1972)	—	3	52	5	40	100
Skin fibroblasts (3.10.1972)	—	—	93	—	7	100

\* Random losses.

**Dermatoglyphics.** There were loop loops on all 10 fingers. The total ridge count was 142 (father: 118, mother: 67). Digital triradii *a-d* were present on both sides in normal positions. Palmar axial triradii on both sides were in the *t* position. No thenar patterns were present; hypothelar patterns revealed ulnar loops on both sides. The *atd* angle was 45° on both sides.

After the finding of chromosomal mosaicism with a Y chromosome, laparotomy was performed. A hypoplastic uterus with oviducts and gonadal streaks in the position of ovaries was found.

Streaks and oviducts were resected and histologically examined. The streak gonads were found to contain neither primordial follicles nor did they give evidence of male gonadal elements; the oviducts were normal. A psychological examination at that time revealed average intelligence but emotional infantilism and clinical re-examination showed no signs of trisomy 18 in that the face was normal, micrognathia absent, and the position of fingers and toes not typical of that syndrome. Oestrogen therapy was given for a year, and subsequently the patient developed an induced regular menstruation and scanty pubic and axillary hair. The breasts measured 7 and 8 cm, respectively and had darkly pigmented nipples and areolae.

### Discussion

The most probable explanation for the origin of a 45,X/47,XY,+18 mosaic is that a 47,XY,+18 zygote was formed, which lost one Y and one 18 chromosome during the same early division. The age of the mother at birth (41 years) is in favour of this hypothesis. Abnormal cell division in a 46,XY zygote leading to an 18-trisomic and 18-monosomic cell line (the latter not being viable) and subsequent simultaneous loss of a Y and an 18 chromosome is more complicated and less likely. It is also rather unlikely, but not impossible, that the extra chromosome is a structurally rearranged element composed of other autosomal or X-chromosomal parts.

All the cases with double aneuploidy, X monosomy, and autosomal trisomy mentioned above exhibited some features of Down's syndrome. In Pfeiffer's case (1968) of a girl with signs of Down's syndrome and 45,X/46,XX/47,XX,+21 mosaicism, no information about the proportion of the three cell lines was given. In the typical Down's syndrome reported by Cohen and Davidson (1972), blood lymphocytes revealed a 45,X/47,XX,+21 mosaicism in a proportion of 86:101, whereas the skin fibroblasts were pure 47,XX,+21. One case of 45,X/46,XY/47,XY,+21 (Edgren *et al*, 1966) is male and a typical Down's syndrome with very pronounced psychomotor retardation; 33 out of 51 lymphocytes revealed a 21-trisomic cell line and 49 out of 96 were revealed in fibroblasts. On the other hand, the case of 45,X/47,XY,+21 (Prieur *et al*, 1972), also male, exhibited far fewer signs of Down's syndrome and moderate psychomotor retardation. Here, from a fibroblast culture, 14 out of 52 cells were trisomic, whereas in lymphocytes there were more trisomic cells (47 out of 82). In our patient over one third of the lymphocytes and 7% of the fibroblasts exhibited the karyotype 47,XY,+18; this girl

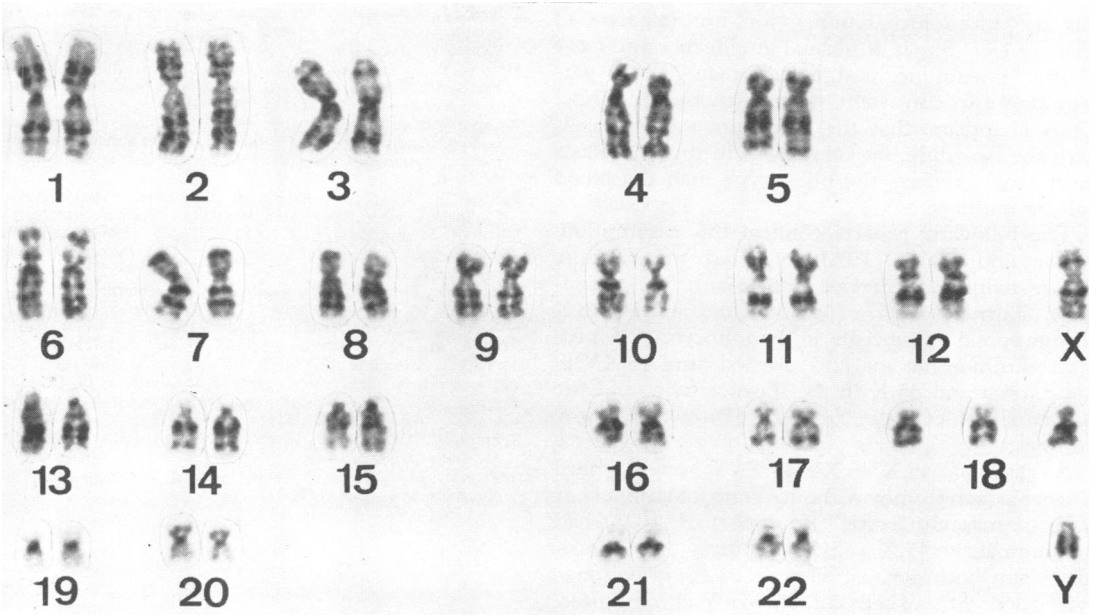


FIG. 1. Giemsa-stained karyotype containing 47 chromosomes, XY, with a supernumerary No. 18.

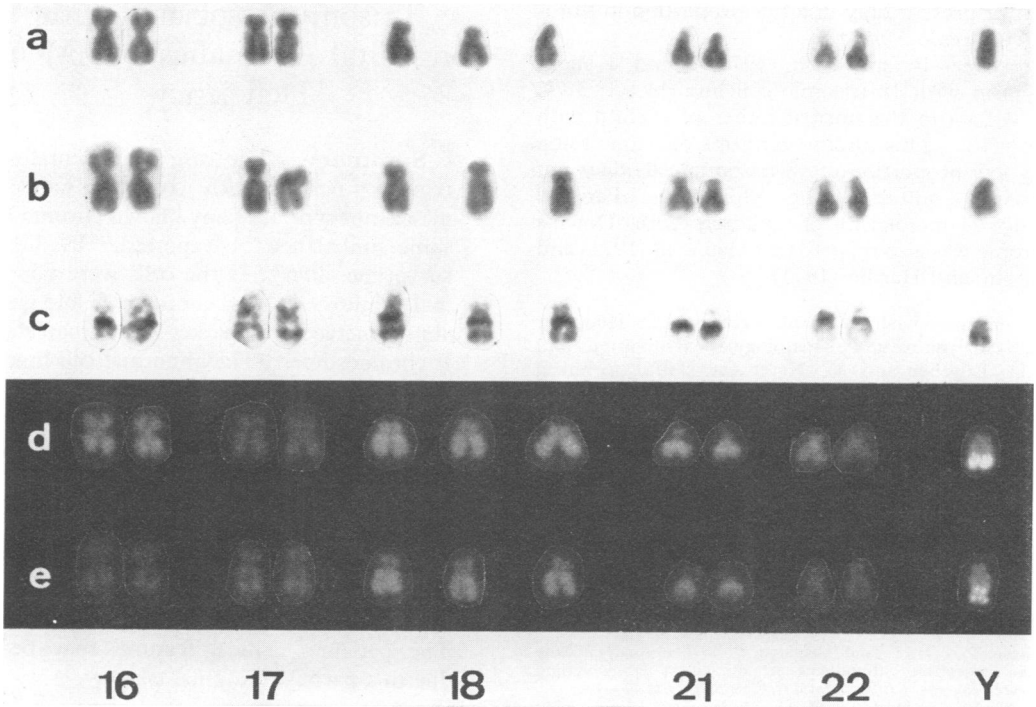


FIG. 2. Group E and G chromosomes from two orcein-stained (a and b), one Giemsa-stained (c), and two fluorescent (d and e) mitoses with a 47,XY,+18 karyotype.

has no trace of masculinization nor stigmata of trisomy 18. She is of normal intelligence and has a Turner phenotype, and her dermatoglyphic patterns are also consistent with Turner's syndrome. Thus it appears that the distribution of the cells with the two different karyotypes in the fibroblasts more truly reflects the phenotype than the blood culture findings.

The following reports confirm this assumption. Potter and Taitz (1972) reported monozygotic female twins, one normal female and one phenotypic Turner, both of whom had 45,X/46,XX chromosomal mosaicism in lymphocytes. Fibroblast chromosome analysis revealed pure 46,XX in the normal and 45,X in the Turner twin, and the dermatoglyphics were in accordance with those findings.

A case of 45,X/46,XY/47,XYY with typical Turner's syndrome without gonadoblastoma or trace of masculinization (Roubin *et al*, 1973) had predominantly 45,X cells in cultures from fibroblasts and both gonads, whereas in blood lymphocytes about 50% of cells contained a Y chromosome. This is additional evidence that an XY cell line in about half of lymphocytes does not have a phenotypic influence in X/XY mosaics, if the XY cell line is absent or present only in a low proportion in fibroblast cultures.

Moreover, Beratis *et al* (1972) found a slight mosaicism with 18-trisomic cell line (blood: 5/70, skin: 4/100) in the normal father of a child with trisomy 18. This finding confirms our conclusion that a low proportion of 18-trisomic cells does not necessarily influence the phenotype. Parental trisomy 21-mosaicism of children with Down's syndrome was also reported by Hsu *et al* (1971) and Krmptotic and Hardin (1971).

The authors wish to thank Professor C. Hedinger (Zurich) for the results of histological examinations and Mrs U. Lüscher and M. Nater for skilful technical assistance.

A. SCHINZEL, W. SCHMID, and A. PRADER  
Division of Medical Genetics, Department of  
Paediatrics and Department of Paediatrics,  
University of Zurich, Switzerland

#### REFERENCES

- Beratis, N. G., Kardon, N. B., Hsu, L. Y. F., Grossman, D., and Hirschhorn, K. (1972). Parental mosaicism in trisomy 18. *Pediatrics*, **50**, 908-911.
- Caspersson, T., Zech, L., and Johansson, C. (1970). Analysis of the human metaphase chromosome set by aid of DNA-binding fluorescent agents. *Experimental Cell Research*, **62**, 490-492.
- Cohen, M. M. and Davidson, R. G. (1972). Double aneuploidy (47,XX,21+/45,X) arising through simultaneous double nondisjunction. *Journal of Medical Genetics*, **9**, 242-244.

- Edgren, J., Chappelle, A., de la, and Kääriäinen, R. (1966). Cytogenetic study of seventy-three patients with Down's syndrome. *Journal of Mental Deficiency Research*, **10**, 47-62.
- Hsu, L. Y. F., Gertner, M., Leiter, E., and Hirschhorn, K. (1971). Parental trisomy 21 mosaicism and Down's syndrome. *American Journal of Human Genetics*, **23**, 592-601.
- Krmptotic, E. and Hardin, M. B. (1971). Secondary nondisjunction causing regular trisomy 21 in the offspring of a mosaic trisomy 21 mother. *American Journal of Obstetrics and Gynecology*, **110**, 589-590.
- Pfeiffer, R. A. (1968). *Karyotyp und Phänotyp der autosomalen Chromosomenaberrationen beim Menschen*. Fischer, Stuttgart.
- Potter, A. M. and Taitz, L. S. (1972). Turner's syndrome in one of monozygotic twins with mosaicism. *Acta Paediatrica Scandinavica*, **61**, 473-476.
- Prieur, M., Dutrillaux, B., Carpentier, S., Berger, R., Raoul, O., Rethoré, M.-O., and Lejeune, J. (1972). Mosaïque 45,X/47,XY+21. *Annales de Génétique*, **15**, 195-196.
- Roubin, M., de Grouchy, J., Josso, N., and de Menibus, C. H. (1973). Mosaïque 45,X/46,XY/47,XYY chez un sujet atteint d'un syndrome de Turner. *Annales de Génétique*, **16**, 123-125.
- Schmid, W. (1967a). Sexchromatinbestimmung aus der Haarwurzel. *Experientia*, **23**, 319.
- Schmid, W. (1967b). Sex chromatin in hair roots. *Cytogenetics*, **6**, 342-349.
- Seabright, M. (1971). A rapid banding technique for human chromosomes. *Lancet*, **2**, 971-972.

## Presumptive Mosaic Partial Trisomy Associated with Congenital Anomalies and Mental Deficiency

**Summary.** The case of a mentally retarded patient with congenital anomalies not typical of any known chromosome unbalance is reported. In his karyotype, 40-6% of the cells were normal, while 59-4% had a missing G and an almost metacentric marker longer than an F chromosome. The abnormal cell line was interpreted as resulting from a chromatid translocation involving the short arm of a No. 22 and a segment from an unidentified chromosome. The translocation probably took place after the first cell division and was followed by segregation of the translocated chromatids. Other obvious hypotheses were excluded by the study of fluorescence patterns. The patient's clinical features may be due to a partial autosomal trisomy.

Received 30 May 1973.