by Johnson *et al*¹ and Wyandt *et al*.² Trisomy for the most distal part of 14q has been described only four times³⁻⁵ (Luzzatti, 1977, personal communication²). Of these cases that of Fryns *et al*³ is similar to our own both clinically and chromosomally, the only differences being the breakpoint at 14q23 and the parental translocation of paternal origin. The patient of Luzzatti (1977, personal communication²), on the other hand, has the same breakpoint as our case and although no great detail is given clinically, what is available compares favourably.

Until more reports appear it remains difficult to make specific karyotype-phenotype correlations.

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X chromosome replication patterns in a case of X;9 balanced translocation

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SUMMARY A case of X;9 balanced translocation in a female with amenorrhoea is reported. The X breakpoint was at Xq21, inside the 'critical region'. The normal X was consistently late replicating in blood lymphocytes and skin and ovary fibroblasts.

In somatic cells of mammalian females one X chromosome is randomly inactivated at the onset of embryonic development.¹ The inactivated X is late replicating and can be cytogenetically distinguished from the active one by means of ³H-thymidine or BUdR incorporation in late S period.^{2 3}

The analysis of balanced X;autosome translocations has revealed that in most cases the normal X is constantly late replicating.⁴ Hellkhul *et al*⁵ have recently reported in an X;3 balanced translocation that this general rule is restricted to blood lymphocytes; in skin fibroblasts the normal and the trans-

located X were alternatively inactivated. They have pointed out that in the majority of the reported cases only blood lymphocytes have been examined.

Our study concerns the X chromosome replication patterns in blood lymphocytes and skin and ovary fibroblasts in a case of X;9 balanced translocation.

Case report

The proband, aged 22, was referred because of secondary amenorrhoea. She was the third child of a family of five. Her mother was 28 and her father 33 when she was born and the delivery was uneventful. Both parents and the proband's brothers have normal karyotypes. At the age of 3 the proband underwent surgery for persistent ductus arteriosus. Menarche was at the age of 12, followed by three normal periods and then subsequently amenorrhoea. At the age of 18, she was treated with sequential oestrogestins and pseudo-menstruations ensued.

When seen by us the patient was 162 cm tall and was in apparent good health. Secondary sexual

characteristics were in accordance with her age and sex. Skull and sella turcica were normal. Laboratory data were as follows: FSH 114 mU/ml; LH >100 mU/ml; PRL 8.2 ng/ml; E2 <31 pg/ml; progesterone 0.68 ng/ml; testosterone 1.22 ng/ml. Laparoscopy showed a hypoplastic uterus (4.5 cm) and normal tubes with reduced diameter and small fimbriae. The ovaries were small with a smooth surface. A diagnosis of 'streak gonads' was made. Histological examination of the ovarian fragments revealed marked fibrosclerosis and absence of follicles.

PHA stimulated peripheral lymphocytes were cultured in RPMI-1640 medium supplemented with 16% FCS. Fibroblast cultures were set up from skin biopsy and ovary material. Cytogenetic studies were performed according to our standard methods.⁶ X chromosome replication patterns were analysed by using terminal BUdR pulse.³

Results and discussion

Cytogenetic analysis using QFQ and RBG banding techniques (figure) revealed a balanced translocation between chromosomes X and 9 with breakpoints located at Xq21 and 9p24. The karyotype can be expressed as follows: 46,X,t(X;9)(Xter→Xq21::9p24→9pter;9qter→9p24::Xq21→Xqter). The replication patterns of 50 metaphases for each of the three tissues examined (blood lymphocytes and skin and ovary fibroblasts) were investigated. The normal X chromosome was consistently late replicating.

In evaluating the X chromosome replication patterns in cases of balanced X;autosome translocation, it would be advisable to divide them into two groups: (1) those where, as in our case, the translocation produces two distinct portions of X chromosome; and (2) those where, as in the case

of Hellkhul *et al*,⁵ the X chromosome receives a portion of an autosome and is presumed to transfer only the telomeres.

Given the existence of a single inactivation centre on the X chromosome,⁷ one of two portions of the X chromosome, as far as the first group is concerned, cannot be inactivated. Thus, the sole inactivation of the normal X becomes obligatory for the balanced expression of the X linked genes. Our findings support these considerations. These limitations do not exist in the second translocation group and some authors have reported normal and translocated X alternative inactivation.^{8,9}

Therman and Patau¹⁰ and Summitt *et al*¹¹ suggested the existence of a 'critical region' on Xq, ranging from Xq13 to Xq26. Breakage in this region would result in gonadal dysgenesis. In our case the breakpoint is inside the 'critical region' and sterility is present.

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FIGURE Chromosome pairs 9 and X (a) QFQ banded, (b) RBG banded.

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