A HERITABLE FRAGILE SITE AT 5q31 IN MAN

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A LARGE number of fragile sites have been observed distributed on various autosomes as well as on the X-chromosome[1] of man. Broadly they may be classified into (a) heritable and (b) "common" fragile sites in which heritability has not been established. To establish heritability in the latter is difficult because of the low frequency at which some of the "common" fragile sites are expressed[2]. A "common" fragile site has been described [3] at 5q31. In the present paper we report heritability of fra(5q31) in a mother and son.

The study concerned a 10-year-old male attending the Hyderabad Special School for mentally retarded. His IQ was 50 with a mental age of 4 years. The propositus was a product of consanguineous (first cousin) marriage born after full term and normal delivery. He had delayed milestones of development, low-set ears squint in the right eye and abnormal teeth. He had two sisters and a brother. His parents and sibs appeared to be normal.

Whole blood (heparinized) cultures were initiated in McCoy's 5A medium (without folic acid, supplied by Hindustan Dehydrated Media, Bombay). The medium was supplemented with 5% human AB serum and its pH adjusted to 7.3–7.5. The cultures were maintained at 37°C for 72 hr. Colchicine was added 2 hr prior to harvest. Slides were dried in an oven maintained at 40°C, stained in 4% giemsa solution, and scanned for the presence of fragile sites; the same slides were destained and processed for G-banding after Seabright[4] with some modifications.

A total of 200 well-spread lymphocyte metaphases were scanned in the propositus and 100 metaphases each in the rest of his family members. A fragile site was observed on the long arm of chromosome number 5 in 6% of the cells from the propositus (figure 1). Family studies revealed the mother to be the carrier of this site with 10% expression in her cultured lymphocytes. The other sibs and the father did not show the presence of this fragile site. In our study the lesion always appeared as an isochromatid gap. Banding studies demonstrated the site to be at 5q31 (figure 2).

The induction of heritable fragile site at 5q31 appears to be sensitive to folic acid since it was observed by us in a folic acid deficient medium.

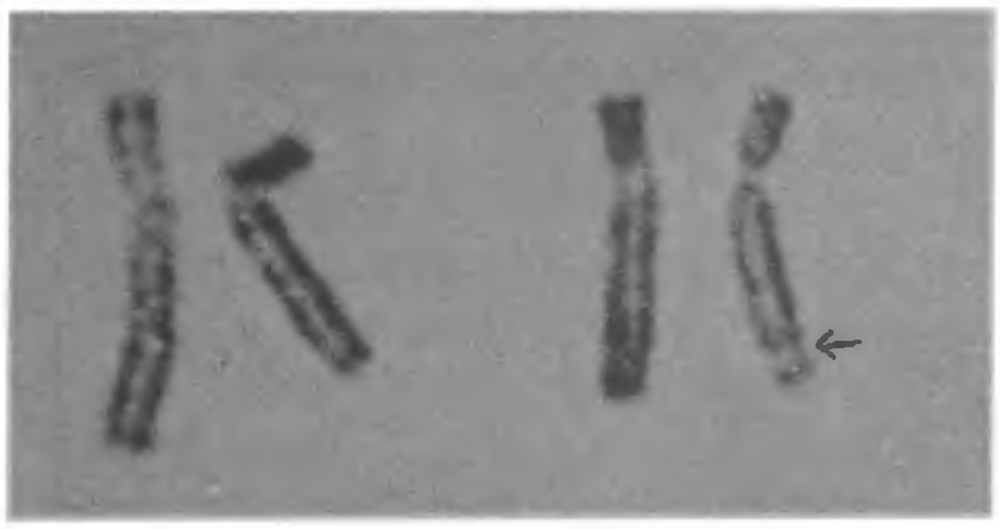

Figure 1. Cutout B-group chromosomes from a metaphase plate from the propositus showing a fragile site on the long arm of one of its chromosomes.

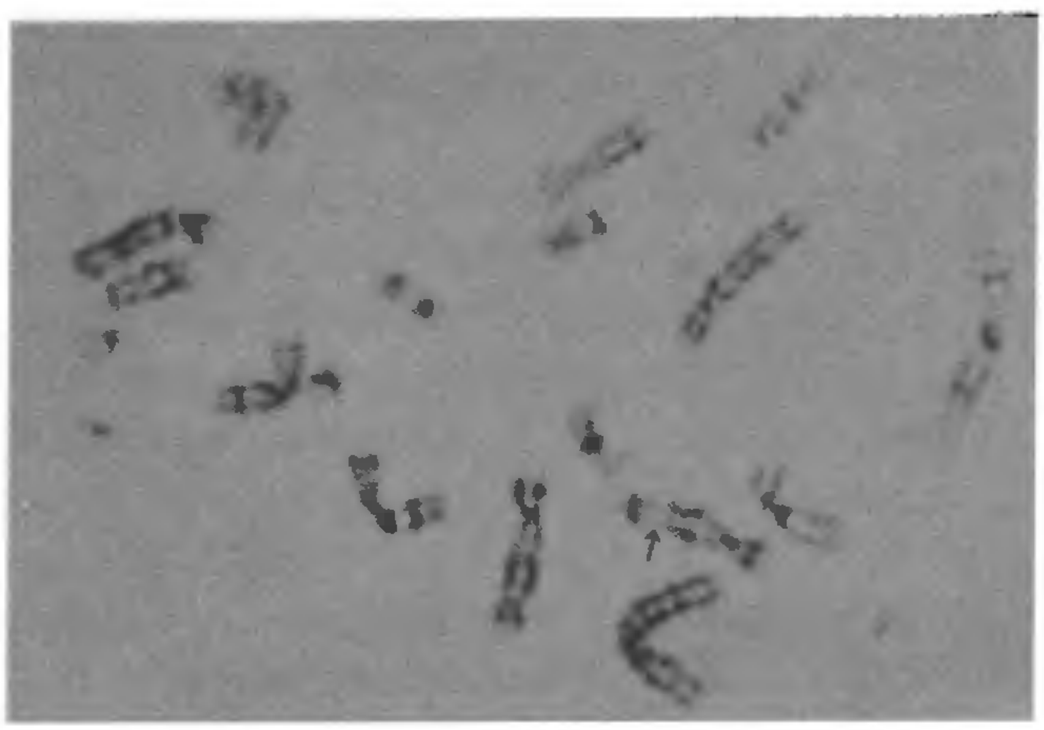

Figure 2. Partial G-banded metaphase plate from the propositus showing a fragile site at 5q31.

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