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A Mosaic Mongol with Normal Leucocyte Chromosomes

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The finding of chromosomal mosaicism in mongolism (Clarke *et al.*, 1961) has added a new dimension to the problem of mongolism which has helped to answer some questions, but which has also created some new ones. It has been suggested that mosaicism may explain some of the microsymptoms of mongolism found in the siblings, parents and relatives of mongols. This has particular application to the increased atd angles on the palms of some mothers of mongols (Penrose, 1963).

Mosaicism may occur with different frequency in various tissues (Lindsten *et al.*, 1962; Nichols *et al.*, 1962). In general, cell lines containing 46 and 47 chromosomes are found, but mosaic mongols with more than two cell lines have been reported (Gustavson and Ek, 1961; Fitzgerald and Lycette, 1961; Valencia *et al.*, 1963). An example of extreme mosaicism occurred in monozygotic twins, one of whom was normal with 46 chromosomes and the other was a mongol with 47 chromosomes (de Wolff *et al.*, 1962).

The present report deals with a special type of mosaicism which has both diagnostic importance as well as theoretical implications as to its derivation. Different cell lines were found in two different tissues. The leucocytes of the peripheral blood contained almost exclusively 46 chromosomes, while the fibroblast cultures from the skin contained a majority of cells with 47 chromosomes. The diagnostic significance of this case is that if only the blood chromosomes had been studied the cytological diagnosis of mongolism would have been missed, even though the clinical diagnosis was obvious.

Case History

The patient is a mongol, born in 1913 and admitted to Harperbury Hospital in 1946. He is the last born in a sibship of eight live births, 4 male and 4 female, there being two miscarriages between the birth of the 6th and 7th children. His mother was 45 years old and his ather 46 years old at his birth. A male sibling, 7th in birth order, was apparently normal when born, but developed convulsions at 3 years and was admitted to Harperbury Hospital in 1936. He was said to be an imbecile and suffered from severe epilepsy. He died in 1937, the causes of death being registered as bronchopneumonia, influenza and carcinoma of the kidney. Apart from the propositus and his brother, there is no record of chronic illness in the family and no evidence of mental or neurological illness. The patient is short (148·9 cm.) and the shape of his skull is brachycephalic with a cephalic index of 80. He has upward and outward slanting palpebral apertures, but no epicanthic folds. There is marked internal strabismus of the left eye, but no speckling of the irides. The hard palate is highly arched and the teeth are poorly shaped and irregular. The tongue is fissured. His fingers are short with bilateral incurving of the little fingers: there is a single palmar crease on each hand and an increased space between the first and second toes. Details of the dermatoglyphic patterns are given in Figure 1. His mental age was assessed at about 3 years 3 months on the "Draw a man test" and the "Peabody picture vocabulary test". He was too low grade for his I.Q. on the Wechsler Adult Intelligence Scale to be of any significance.

Laboratory Investigations:

Haemoglobin, 13·5 g./100 ml.; erythrocytes, 5·6 million/c.mm.; leucocytes, 8,400/c.mm.; polymorphs, 66 per cent.; lymphocytes, 23 per cent.; monocytes, 7 per cent.; eosinophils, 4 per cent.

Arneth Count:	Lobes/Cell	1	2	3	4	5
	Per cent.	16	29	40	13	2
	Mean Lobes/Cell	2·56				

Cytology: buccal smears and leucocytes; chromatin negative.

Chromosome analysis was performed on two independent blood cultures, two independent skin cultures and one sternal marrow. The results are given in Table I. The second skin culture was divided into two and grown for different lengths of time.

A testicular biopsy was performed which showed normal spermatogenesis in the seminiferous tubules and healthy interstitial cells. Numerous meiotic chromosomes were present.

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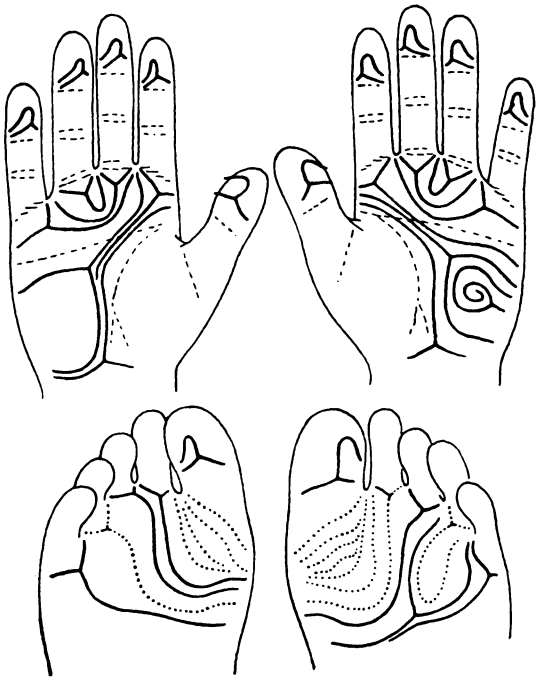


FIG. 1.—Dermal patterns, palms and soles. The finger-prints show 10 ulnar loops. A distal loop is present in the third interdigital areas on both palms. The sum of the atd angles on the hypothenar areas of the palms measure 160°. The hallucal areas of the soles have an open field arch tibial pattern. The dermal patterns are all quite characteristic and diagnostic of mongolism.

TABLE I

Type of Culture	Chromosome Count		Total Cells
	46	47	
Skin 21.1.63 ..	2	29	31
Skin 7.6.63:			
Culture I			
Grown 24 days	3	25	28
Culture II			
Grown 17-19 days	22	16	38
Blood I	14	0	14
Blood II	91	1	92
Sternal marrow ..	13	3	16

On analysis, the cells with 46 chromosomes were found to have a normal male karyotype and those with 47 to show an additional small acrocentric chromosome. The sternal marrow culture gave preparations that were adequate for counting but were unsuitable for analysis.

DISCUSSION

Even though there have been only a small number of mosaic mongols reported so far, some interesting and important findings have come to light. In general, mosaic mongols tend to be more intelligent, as a group, than non-mosaic mongols and their dermatoglyphic patterns tend to be midway between those of normal individuals and non-mosaic mongols (Penrose, 1963). Based on measurements of atd angles in a large group of mothers of mongols, Penrose has estimated that about 10 per cent. of such mothers are themselves mosaic mongols. So far, four cases of mosaicism in the mothers of mongols have been recorded (Blank *et al.*, 1962; Smith *et al.*, 1963; Weinstein and Warkany, 1963; Verresen *et al.*, 1964).

In the case of mosaic mongols reported there has been a higher percentage of cells with 47 chromosomes in the skin fibroblast cells than in the peripheral blood (Penrose, 1963). The only exception has been the case reported by Lindsten *et al.* (1962), in which the blood leucocytes contained 63 per cent. of the cells with 47 chromosomes, while the skin contained only 29 per cent. of cells with 47 chromosomes.

The mosaicism in the present case could have arisen in two ways. First, the original zygote might have been normal and, after a number of cell divisions, non-disjunction of chromosome 21 occurred in some of the cells before tissue differentiation took place. However, a more likely explanation is that the original zygote was trisomic for chromosome 21 and that a chromosome 21 was lost in the cells which were the precursors of the haemopoietic system. The advanced age of the patient's mother at the time of his birth tends to support the possibility of maternal non-disjunction, causing a zygote trisomic for chromosome 21. The method of cell selection in embryonic tissue is poorly understood, so that whether or not normal cells would be favoured in growth over trisomic cells is uncertain.

In our case the second skin culture showed a marked difference in the relative proportion of cells containing 46 and 47 chromosomes, depending on the length of time that the culture was grown (see Table 1). The 24-day

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culture contained predominantly cells with 47 chromosomes, whereas the 17-day culture had nearly an equal number of cells with 46 and 47 chromosomes. These cultures were derived from the same skin biopsy sample and the differences cannot be explained by a variation in mosaicism in different areas of the skin. The explanation for these findings is obscure but does raise the question of selection in a culture which contains more than one cell line. If there is a growth selective process in *in vitro* cultures containing more than one cell line, such cultures may not be an accurate reflection of the *in vivo* condition. It is of interest that the peripheral leucocytes contained, almost exclusively, cells with 46 chromosomes and that the Arneth count did not show the shift to the left usually found in mongolism.

This patient showed classical physical, mental and dermatoglyphic signs of mongolism, which is at variance with some of the previous observations made on mosaic mongols. However, very little is known about the physical features in mosaic mongolism in relation to the proportion of normal and trisomic cells found in the various tissues. The type of mosaicism found in this case emphasizes the importance of examining more than one tissue when looking for mosaic mongols. If the patient had been a newly-born infant and only the leucocyte chromosomes were tested, it is possible that the diagnosis might have been missed.

Summary

An unusual case of mosaic mongolism is reported. The patient had a typical mongol phenotype. Skin cultures showed predominantly trisomic cells, whereas leucocyte cultures showed a normal karyotype.

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