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HAEMOGLOBIN J TRAIT IN TWO INDIAN WOMEN

ASSOCIATED WITH THALASSAEMIA IN ONE

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Haemoglobin J was first discovered in an American Negro by Thorup, Itano, Wheby, and Leavell (1956). It has since been described in various parts of the world and in people of different racial stock. Raper (1957) found an example in a Gujerati Indian living in Uganda. This paper records the finding of haemoglobin J in two unrelated women belonging to the Gujerati-speaking Lohana. Of particular interest was that one of the two was also carrying a thalassaemia gene, and that it was therefore possible to observe the interaction of thalassaemia and of haemoglobin J.

Techniques

The haematological investigations were carried out by the accepted methods. Osmotic fragility was determined by measuring haemolysis in concentrations varying from 0.1 to 0.7% of Simmell's Tyrode solution, of which 0.4% was taken as a critical dilution for differentiation (Silvestroni and Bianco, 1945). In more than a hundred normal adults examined haemolysis was found to be 90–100%. Foetal haemoglobin was measured according to the method of Singer, Chernoff, and Singer (1951). Electrophoresis of the haemoglobin was performed with the same haemoglobin solutions that had been used for the determination of the foetal haemoglobin. Paper electrophoresis was carried out by the hanging-strip technique as described by Lehmann and Smith (1954), and starch electrophoresis according to the method of Kunkel (1954). Electrophoresis on agar was

performed according to the method described by Robinson, Robson, Harrison, and Zuelzer (1957). The plasma iron was measured after Walker (1938).

The identification of haemoglobin J was based on a comparison with known haemoglobin J samples kindly provided by Colonel W. H. Crosby, Dr. Lie-Injo Luan Eng, Dr. A. B. Raper, and Dr. F. Vella. On paper electrophoresis and starch electrophoresis at *p*H 8.6 haemoglobin J moves faster than haemoglobin K and more slowly than haemoglobin H (and the recently defined haemoglobin N). At *p*H 6.5 on paper and on agar electrophoresis haemoglobin J does not separate from haemoglobin A.

Haemoglobin A_2 was determined either by the elution of the separated haemoglobin fractions from starch or after paper electrophoresis by dyeing the dried paper strip with light green and by eluting the stain from the separated bands of haemoglobin.

The P. Family

This family was investigated after an infant had been examined because of severe jaundice 24 hours after birth. There was no haemoglobinopathy, and when the child was seen again nine months later no foetal haemoglobin was found and nothing haematologically abnormal could be demonstrated. It was, however, then noted that the infant was mentally retarded. In the routine investigation of the parents (Table I) it was found that the mother was a haemoglobin J trait carrier (Fig. 1). No other abnormality was found in either the parents or in the child.

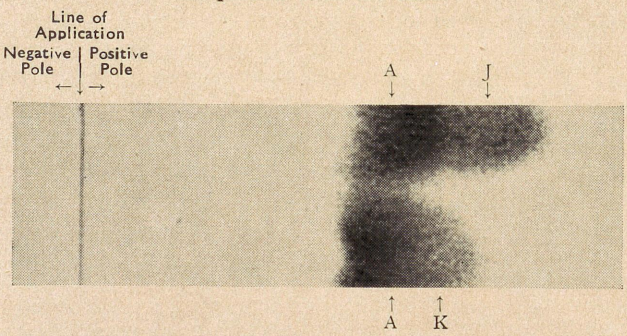

FIG. 1.—Comparison by paper electrophoresis at *p*H 8.6 of the haemoglobin of Mrs. P. (A+J) with a haemoglobin A+K control. At the end of the electrophoresis (hanging-strip technique) the paper was dried and the haemoglobin stained with light green.

The K. Family

This family came under investigation because of persistent anaemia in a male infant then 15 months old. He was said to have had diarrhoea from the age of 2½ to 3 months. From then on he had had fever off and on, and at the age

TABLE I.—*The P. Family*

	Age in Years	Red Cells per c.mm. $\times 10^6$	Haemoglobin g./100 ml.	P.C.V. %	M.C.V. cubic μ	M.C.H. $\gamma\gamma$	M.C.H.C. %	Osmotic Fragility % (0·4% Simmel's Tyrode Solution)	Foetal Haemoglobin %	Electrophoresis of Haemoglobin
Father	30	4·83	14·5	46	91	29	30	90·0	< 1·7	A
Mother	19	4·90	12·5	44	94	26	29	97·7	< 1·7	A + J (25%)
Baby	$\frac{3}{4}$	4·67	13·6	39	83	28	33	70·0	< 1·7	A

TABLE II.—*The K. Family*

	Age in Years	Red Cells per c.mm. $\times 10^6$	Haemoglobin g./100 ml.	P.C.V. %	M.C.V. cubic μ	M.C.H. $\gamma\gamma$	M.C.H.C. %	Reticulocytes %	Osmotic Fragility % (0·4% Simmel's Tyrode Solution)	Foetal Haemoglobin %	Electrophoresis of Haemoglobin
Father	32	6·15	12·5	39	63	20	32	1·6	34·6	< 1·7	A
Mother 20/5/57 ..	28	5·61	12	38	68	22	31·5	2·8	38·0	2·8	A + J (25%)
Mother 14/12/57 ..	—	5·58	12·5	39	69	23	32	2·2	49·0	2·0	A + J (25%)
Baby	$1\frac{1}{4}$	1·61	3	13	84	19	23	10·3	34·3	68·5	A + F

of 5 months it was first noted that he was unusually pale and inactive. He was then treated with iron by mouth and by injection, with folic acid and with cortisone. At the age of 9 months he had received three blood transfusions.

On examination he was found to be underdeveloped and very pale. The liver was palpable one fingerbreadth and the spleen three fingerbreadths below the costal margin. The haemoglobin level was 3 g. per 100 ml. of blood (Table II), and, although the age of the infant was 15 months, 68.5% of the pigment was foetal haemoglobin. This persistence of haemoglobin F at a high level and the resistance of the anaemia to treatment suggested the diagnosis of thalassaemia major. The appearance of the red cells was typical. There was marked hypochromia, anisocytosis, and poikilocytosis, and target cells were numerous. A striking feature was the nucleated red cells—66,500 per c.mm. of blood. The osmotic fragility of the erythrocytes was increased. When it was found that both parents had thalassaemia minor the diagnosis of thalassaemia major in their infant was made with confidence. A blood transfusion improved the clinical condition for the time being, but the patient succumbed to the disease six months later. The immediate cause of death is said to have been bronchitis.

The red cells of both parents were small, and numerous vacuolated and target cells were seen in the stained smear. Osmotic resistance was increased. As is often seen in thalassaemia minor as opposed to iron-deficiency anaemia the M.C.H. was much decreased whereas the M.C.H.C. was almost normal.

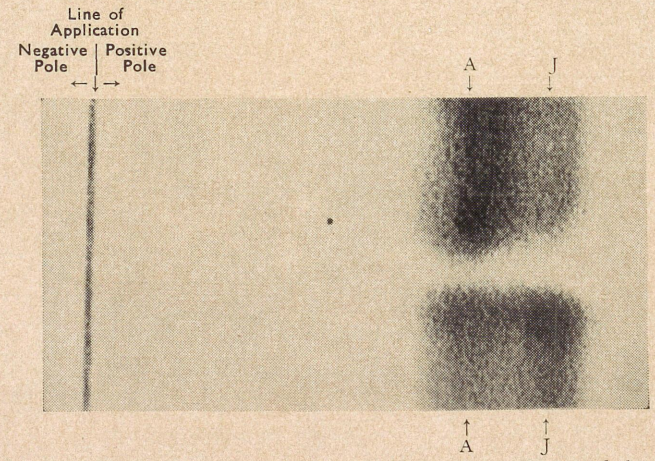

FIG. 2.—Comparison by paper electrophoresis at *p*H 8.6 of the haemoglobin of Mrs. K (above) with a haemoglobin A+J control. At the end of the electrophoresis (hanging-strip technique) the paper was dried and the haemoglobin bands were photographed unstained.

Electrophoresis of the parents' haemoglobin revealed the presence of haemoglobin J in the mother (Fig. 2). As this seemed to be the first occasion on which haemoglobin J had been found together with thalassaemia the mother was examined repeatedly. Though her red cells were hypochromic, her plasma iron level was 125 μg. per 100 ml. There was no evidence for an enhancing effect on the thalassaemia minor by the haemoglobin J, nor was the composition of the haemoglobin noticeably different in the thalassaemic haemoglobin J trait carrier from that which had been found in the non-thalassaemic Mrs. P. Evidence for the thalassaemia gene in Mrs. K. were: the appearance of the red cells; lowered osmotic resistance of the red cells; a low M.C.H. together with a normal or nearly normal M.C.H.C.: a low M.C.H. together with a normal plasma-iron level; the presence of a trace of haemoglobin F; and the family study showing thalassaemia minor in the husband and thalassaemia major in their child.

Haemoglobin A_2 was not increased and the concentration of this haemoglobin fraction was in fact the same in Mrs. K. and in Mrs. P. However, in our experience a rise of the haemoglobin A_2 level may be indicative of thalassaemia, but a normal haemoglobin A_2 level does not exclude this condition.

Summary

Haemoglobin J was seen in two unrelated women of Gujerati-speaking Lohana stock. In one of them the haemoglobin J trait was present together with thalassaemia minor. There was no evidence for a detrimental interaction between the genes for thalassaemia and for haemoglobin J—that is, for a hypothetical haemoglobin J thalassaemia disease.

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