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THALASSAEMIA-HAEMOGLOBIN E DISEASE IN A CAPE COLOURED FAMILY

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In 1952 Budtz-Olsen and Woolf[1] described a Cape Coloured family whom they thought to be suffering from thalassaemia (Cooley's anaemia). With the knowledge then available the authors found it difficult to give a genetically satisfactory explanation of the varying severity of the disease in different members of the family. Blood from members of this family has now been re-examined with the help of paper electrophoresis, and it has been shown that the more severely affected children are suffering from thalassaemia-haemoglobin E disease. This was first described in 1954 by Chernoff *et al.*[2] and later by Sturgeon *et al.*[3]

MATERIAL

Fig. 1 shows the pedigree, with the electrophoretic patterns added. The mother, No. 1, was of Cape Coloured stock. This is a mixed people descended from Europeans, Hottentots, Bushmen and Asians, with very little negro admixture. Her mother, since dead, was examined by Budtz-Olsen and Woolf and correctly regared as having thalassaemia minor. The father of the family (No. 2) was a Cape Malay; these Malays are descended from Eastern slaves, not necessarily from Malaya. He died of heart disease some years ago, but it is clear from the findings that he must have been the bearer of the haemoglobin E trait; his relations could not be traced. Blood was taken from No. 3, the eldest child, only after she had received a large transfusion, which added haemoglobin A to the electrophoretic pattern.

Electrophoresis of haemoglobin was carried out as described by Brain.[4] The presence of alkali-resistant (F) haemoglobin was confirmed by denaturation (Singer *et al.*[5]). The other findings are from the paper of Budtz-Olsen and Woolf. The identity of the haemoglobin E was confirmed by Dr. H. Lehmann of St. Bartholomew's Hospital, and by the late Dr. Karl Singer of Chicago.

RESULTS

Fig. 1 and Table I show the pertinent findings, and illustrations will be found in the paper of Budtz-Olsen and Woolf.[1]

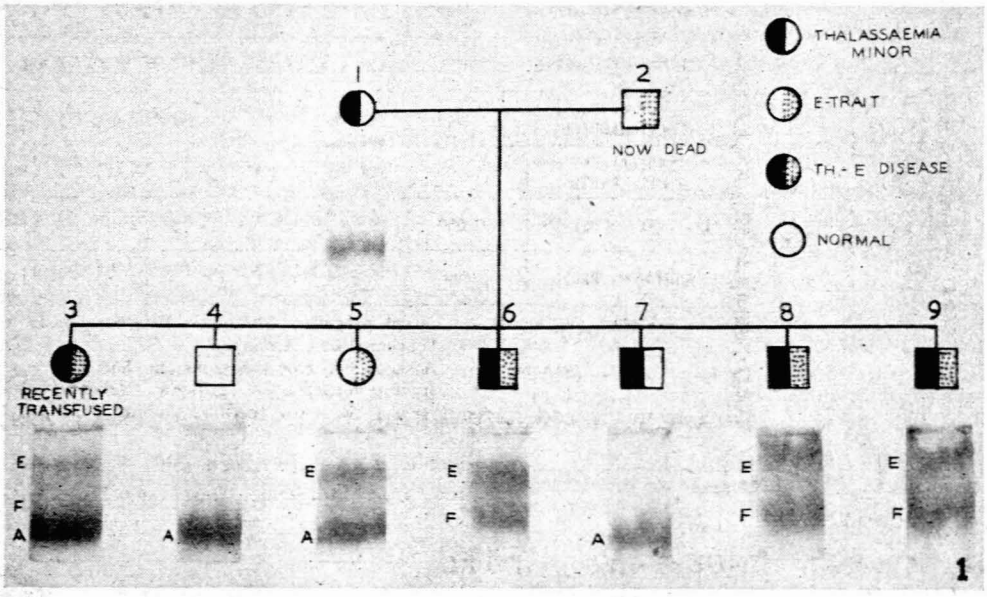

Fig. 1. Pedigree with electrophoretic patterns. The haemoglobin has been applied at the top of each strip and migration has taken place downwards towards the anode.

In this family, a mating between a woman with thalassaemia minor and a man with the haemoglobin E trait has produced in the 7 children every possible genetic combination—normal (No. 4), thalassaemia minor (No. 7), E-trait (No. 5), and thalassaemia-haemoglobin E disease (Nos. 3, 6, 8 and 9). The clinical manifestations of thalassaemia-haemoglobin E disease are much the same in the 4 cases, and agree closely with those described by Chernoff *et al.*[2] All 4 were of stunted growth with mongoloid features. The spleens were enlarged and hard, in one case (No. 3) reaching down to the anterior superior iliac spine. None showed obvious jaundice, but urobilin was occasionally found in the urine of No. 3. This girl, who in 1954 was 24 years old and had needed transfusions 2-3 times a year for the preceding 4 years, also had a persistent granulating ulcer over the lower part of the left tibia. X-ray examination showed generalized osteoporosis in the three subjects examined, but none had the 'hair-on-end' appearance of the skull. The picture of the peripheral blood was indistinguishable from that in thalassaemia major. The bone marrow of No. 3 was examined and showed a considerable increase in erythropoiesis with a preponderence of normoblasts. All the subjects were negative for sickling.

TABLE I. FINDINGS IN THE AFFECTED FAMILY

Subject No.	*Haemoglobin g.%*	*Hypochromia*	*Microcytosis*	*Anisocytosis*	*Target cells*	*Nucleated red cells*	*Reduced osmotic fragility*	*X-ray signs*	*Haemoglobins on electrophoresis*	*Diagnosis*
1.	11·8	+	+	+	+	—	+		A	Thalassaemia minor
3.	2·8	++	++	+++	++	++	+	+	EFA	Th.–Hb.E disease after transfusion
4.	12·2	—	—	—	—	—			A	Normal
5.	13·9	—	—	—	—	—			AE	E-trait
6.	9·3	+	+	++	++	+		+	EF	Th.–Hb.E disease
7.	9·6	—	+	++	+	—		+	A	Thalassaemia minor
8.	5·9	++	+	++	++	++			EF	Th.–Hb.E disease
9.	7·8	++	+	++	++	++			EF	Th.–Hb.E disease

Thalassaemia-haemoglobin E disease is thus clinically and haematologically (unless the haemoglobin is examined) indistinguishable from thalassaemia major, though perhaps rather less severe. Whereas in thalassaemia major the haemoglobin consists principally of F (foetal) with some A (adult) and no E, in thalassaemia-haemoglobin E disease it is made up of E and F components. The difference in electrophoretic mobility between haemoglobins F and A is well shown in the adjacent strips 5 and 6, representing the symptomless E-trait (haemoglobins E and A) and thalassaemia-haemoglobin E disease (E and F).

DISCUSSION

Haemoglobin E is relatively common in some oriental peoples, such as Thailanders,[2] Burmese[6] and Indonesians.[7] Thalassaemia also is common, at least in Thailand. The Coloured population of Cape Town contains a considerable oriental 'Malay' element, and the father of the family here described was in fact of 'Malay' extraction. Haemoglobin E, however, is not often found among the Coloured population. No example of it was seen in an electrophoretic study of 430 subjects, including 'Malays' (Brain[4] with additions). Thalassaemia, in its major form at any rate, is very rare in this population. Thalassaemia-haemoglobin E disease is therefore certainly very uncommon in South Africa.

Although in Fig. 1, for the convenience of drawing, the genes for thalassaemia and for haemoglobin E are shown as if allelomorphs, this is not so.[8, 9] The subjects with thalassaemia-haemoglobin E disease described here are in fact double heterozygotes. The combination of thalassaemia with homozygous haemoglobin E has recently been described from Thailand.[9]

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