mortality of the non-sickling homozygote in these peoples to raise the frequency of the gene if introduced—that is, there may be other genetic factors besides sickling which protect against death through malaria. Alternatively, the gene may never have been introduced (by mutation or intermarriage with individuals from populations possessing the sickle-cell) among the northern Nilotes. Had they received it, then selection would have increased its frequency to that at which equilibrium occurred, its diffusion among these peoples being broadened by their mating systems: the increase in gene frequency would have been rapid at first, since its introduction would presumably be in the heterozygous condition, matings between heterozygotes would occur much more rarely than between heterozygote and non-sickling homozygote, and the sickling homozygote would therefore in the initial stages very rarely be produced; loss of the gene in appreciable quantities would only occur after its frequency had reached such a level that heterozygotes were mating.

The finding by Foy *et al.* (1954) of the sickle-cell trait in one or two individuals among the southernmost groups of the northern Nilotes suggests that the gene is only now beginning to enter this region from the south. Certainly such Shilluk as migrated to their present territory from the south could not have brought the gene and subsequently lost it. Nor could the southward-moving Lwo groups, who according to Crazzolar's reconstruction of traditions subsequently became the peoples known to-day as the central and southern Nilotes, have taken the gene with them when they diverged from the northern Nilotic peoples. Since the southern Nilotes now possess the trait in appreciable frequencies (Lehmann and Raper, 1949; Foy *et al.*, 1954; Allison, 1954b), they must have received it at a date later than that at which they diverged from the northern groups.

If, on the other hand, the postulated selective advantage under malarial conditions of the sickle-cell trait should prove to be more apparent than real, then the presence of the trait among the southern Nilotes would seem to be due to hybridization with peoples of high sickling frequency in the areas to which they wandered. On this hypothesis, the alternative explanation for the difference in sickling between northern and southern Nilotic groups—that a northward-moving Shilluk group possessing the gene interbred with non-sickling groups in their new territory, with subsequent dilution of the gene frequency—seems less feasible, since in this instance the gene would be expected to occur at low frequency among the northern Nilotes, which the data do not show.

The above discussion shows clearly the increase in anthropological interest that may accompany increased knowledge of a particular gene. Whatever the explanation, the sickle-cell trait to-day is a physical criterion distinguishing between the northern and southern Nilotic groups, being absent in the former and present at medium frequency in the latter. Some degree of genetic divergence is thereby implied—less if the trait is selectively advantageous, greater if it is not.

Summary

No abnormal haemoglobin was discovered by paper electrophoresis of 75 blood specimens from northern Nilotes of the Southern Sudan. In 739 specimens examined no sickling was found. These findings suggest that the association between malaria and sickling is more complex than might at first appear; their anthropological significance is discussed.

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A SURVEY FOR HAEMOGLOBINS C AND D IN UGANDA

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The sickle-cell trait and sickle-cell anaemia, which have long been known, are associated with an abnormal shape of the red cell at reduced oxygen tensions. In 1949, Pauling *et al.* demonstrated that the potentiality for sickling is associated with a variety of haemoglobin which differs from the normal in its electrophoretic mobility.

This sickle-cell haemoglobin was at first called haemoglobin B (the normal being haemoglobin A), but it is now generally known as haemoglobin S. In the sickle-cell trait haemoglobin S usually forms from 25 to 45% of the total haemoglobin, and in sickle-cell anaemia from 85 to 100%. The former state is regarded as characterizing persons who are heterozygous for the sickle-cell gene, and the latter those who are homozygous (Neel, 1951).

Incidence

During the course of family studies of cases of haemolytic anaemia associated with sickling, Itano and Neel (1950) found a further abnormal haemoglobin, since designated haemoglobin C. This differs in electrophoretic mobility from both haemoglobins A and S. It is not associated with anaemia in the heterozygous C/A combination. The C/S combination, however, produces a haemolytic anaemia which is in many ways similar to sickle-cell anaemia though milder in degree (Kaplan *et al.*, 1953).

The incidence of haemoglobin C in the negro population of Detroit was estimated by Lawrence *et al.* (1952) to be about 0.3%; Smith and Conley (1953) found an incidence of 1.8% in 500 unselected negroes in Baltimore, while Edington and Lehmann (1954) found it to be as high as 12% in Gold Coast Africans. A further abnormal haemoglobin has been described by Itano (1953) which has the same mobility as haemoglobin S but differs in its solubility and in that it does not cause sickling. Like haemoglobin C this haemoglobin, now known as D, will cause a haemolytic

anaemia when in combination with S. Its incidence in American negroes is not known, but it must be much rarer than C. Apart from the studies of Edington and Lehmann on haemoglobin C in persons from the Gold Coast, haemoglobins C and D have so far been described only as occurring in American negroes. The combination of the single gene for sickling and the single gene for thalassaemia can also produce a haemolytic anaemia (Powell *et al.*, 1950). Thus, of all the cases of a haemolytic anaemia with sickling that are seen in America, most are true sickle-cell anaemia, but a proportion are due to the combination of the sickling gene with some other inherited abnormality of haemoglobin synthesis.

Thalassaemia, which is readily recognizable, is not known to occur in the Africans of tropical Africa, and hence it is unlikely that there are in Uganda any cases of anaemia due to the combination of the sickle-cell gene and the thalassaemia gene. It, however, appeared possible that some of the cases of apparent sickle-cell anaemia were due to the coexistence of haemoglobin S with C or D. In order to determine this, it seemed easiest to examine only non-sickling bloods—in other words, to screen the population for possible haemoglobins C and D in combination with A rather than S and to preserve any of these bloods showing a double haemoglobin for identification elsewhere.

Method

Bloods sent in to the laboratory for routine Khan tests were used. A sickling test was done, using a 24-hour *Bact. coli* culture and reading the unsealed preparation in two hours. All sicklers were discarded except one out of each batch, which was used as a control. As much serum as possible was drawn from the clot and discarded, and, after shaking, a drop of concentrated red cell suspension was withdrawn. To this was added a drop of 0.5% saponin in watery solution to cause lysis. Paper strip electrophoresis was performed in the Shandon apparatus with the apex height adjusted to 4½ in. (11.4 cm.) instead of the standard 7½ in. (19 cm.). A barbituric acid/sodium barbitone buffer of pH 8.6 and ionic strength 0.06 was used, and, with eight strips of Whatman No. 3, each 1½ in. (3.8 cm.) wide, electrophoresis was allowed to proceed at a voltage of 90–110, giving a current of 1.5–2 mA, for 12 to 18 hours. A sickling control was included in each run. The position of the haemoglobin could readily be seen without further staining provided the solutions were concentrated enough. If there was any doubt a washed and cleared preparation was made from the original clot and the procedure repeated.

Results

Of 500 bloods examined, 250 were male and 250 female. They were almost entirely adults. The tribal composition is not accurately known but is largely Bantu, of which the majority are Baganda. There were probably some 40 to 50 Nilotics. No case was found with a double haemoglobin, and all the haemoglobins migrated with the same speed as normal adult haemoglobin.

Conclusion

In a series of 500 non-sickling bloods examined in Kampala no example of haemoglobins C or D has been found. Since, on the other hand, there is known to be a considerable amount of haemoglobin C in West Africa, it is probable that this area is the source of the genes for haemoglobin C found in American negroes. This is, in any case, the most likely source, since the slaves largely came from this area. Most, if not all, of the haemolytic anaemias in Uganda, in which sickling appears to play a part, may therefore prove to be true cases of homozygosity for the sickling gene. There remains, however, the possibility that other modifying haemoglobins exist here which could be distinguished by properties other than electrophoretic mobility at alkaline pH.

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Medical Memoranda

Death from Hexamethonium Ileus

In view of the increasing use of ganglion-blocking drugs in the treatment of patients with severe hypertension, this report of an avoidable death caused by one of these drugs may be of interest.

CASE RECORD

A carpenter, aged 54, was admitted to another hospital in April, 1953, in congestive cardiac failure, due to hypertension. He was discharged, improved by orthodox treatment, after three weeks.

In August, 1953, he was admitted to this hospital in a further attack of congestive cardiac failure with a blood pressure of 250/180 mm. Hg. He had now developed bilateral papilloedema with retinal haemorrhages and exudates. In view of the severe retinopathy it was decided to begin treatment with hexamethonium bromide in addition to full doses of digitalis and mersalyl.

On discharge, five weeks later, he was giving himself 280 mg. of hexamethonium subcutaneously three times daily. His blood pressure was fluctuating between 180/110 and 140/95 mm. Hg, whilst the papilloedema was beginning to regress.

At follow-up his dose was reduced to 200 mg. thrice daily, and he was advised to take 7½ mg. of neostigmine orally for his alimentary dysfunction. He took this dose for three days, when both eructation and diarrhoea ceased. However, on the fourth day he became obstructed and began to vomit, and on the fifth day he developed colicky abdominal pain. He continued to inject full doses of hexamethonium in spite of having been told to reduce the dosage if the diarrhoea or constipation should become severe. Only on the sixth day did he permit his wife to arrange for urgent readmission to hospital. He was found to be very dehydrated, with a thready, regular pulse and a blood pressure of 110/90 mm. Hg. The abdomen was greatly distended, particularly over the upper quadrants. There was some lower abdominal tenderness and guarding, and almost complete absence of bowel sounds. A radiograph of the abdomen showed gaseous distension of the small gut with fluid levels. Small amounts of gas and faeces were present as far as the hepatic flexure.

Ileus due to hexamethonium was provisionally diagnosed, and treatment was started with gastric suction and intravenous glucose-saline. A total of four pints of black fluid was aspirated from the stomach within the next four hours, during which time the patient's condition improved greatly. Further improvement seemed to justify continuation of conservative treatment, but 16 hours after admission the pulse rate rose to 120 a minute over the space of an hour, and his condition gravely deteriorated. Immediate operation was decided upon, as it was now thought likely that a perforation had taken place. The patient died before he could be got to the theatre.

Post-mortem examination within 3½ hours of death showed that operative intervention would have been valueless. The stomach and 5 to 6 ft. (1.5 to 1.8 metres) of small intestine were dilated and filled with foul faecal fluid. No perforation was found, but throughout the small intestine there were areas showing thinning of the bowel wall.