Response appeared to depend on the ease of absorption of hydrocortisone, eroded and exuding eczema and dermatitis healing rapidly, while lichenified eczema showed little improvement.

Good results were obtained in acute contact dermatitis, nummular eczema, atopic eczema, and perianal dermatitis. Lichen simplex, lichenified atopic eczema, and lichenified cases of ano-genital pruritus responded poorly. Infection was spread by the ointment unless controlled before its use.

Relapse occurred in many chronic cases on stopping treatment, and could be prevented by using the ointment less frequently as maintenance therapy or by reverting to the use of tar applications.

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A SEARCH FOR ABNORMAL HAEMOGLOBINS IN SOME SOUTHERN SUDANESE PEOPLES

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Sickle-cell Tests

Nilotic peoples are found in two main areas—the southern Nilotes in Uganda and round the eastern shores of Lake Victoria, the northern Nilotes in the Southern Sudan. During the course of investigations among the northern Nilotes of Upper Nile Province, Sudan, the blood of a large number of individuals was examined for sickling. Some specimens were sent to laboratories for testing; in London, where positive specimens from West Africa could be used as controls, 344 specimens were tested, 83 by one of us (H.L.) and 261 by Dr. J. N. M. Chalmers, of St. George's Hospital; in Khartoum 215 were examined by Professor Dean Smith of the Kitchener School of Medicine.

These specimens were obtained from unrelated adult individuals; details of the sampling methods employed are given elsewhere (Roberts, Ikin, and Mourant, 1955). In the field, testing was largely restricted to specimens from children, 10 adults and 170 children of all ages being examined by D.F.R.; these children constituted the major part of the child population of one Dinka and two Shilluk villages, and the individuals from each village were therefore not all unrelated. As regards technique, in London and in the field, 2% solutions of potassium

metabisulphite were used, freshly made up on each occasion with distilled water; in Khartoum, each specimen was carefully enclosed bubble-free under a cover-slip ringed with petroleum jelly, and examined after 24, 48, and 72 hours.

Altogether specimens from 739 individuals were examined, representing the different indigenous peoples as follows:

People	Adults	Children
Northern Dinka	217	103
Shilluk	204	67
Nuer	100	
Mabaan	34	
Dinka/Shilluk/Nuer-hybrids ..	14	

Since in no individual of this large sample was the sickle-cell trait observed, it is concluded that the absence of the trait is a characteristic typical of the northern Nilotic peoples. This finding is similar to that of Foy *et al.* (1954).

Examination by Electrophoresis

Seventy-five specimens were further examined by paper electrophoresis according to the procedure described by Lehmann and Smith (1954). Of these, 64 specimens were from northern Dinka individuals, 4 were from Mabaan, 3 were from Dinka/Nuer hybrids, and 4 from Dinka/Shilluk hybrids.

All blood specimens contained nothing but normal adult haemoglobin. No haemoglobin S (or D), C, E, or G was found. The results of this survey are in striking contrast to those obtained in the Gold Coast (Edington and Lehmann, 1954a, 1954b), where out of 211 West Africans examined 41 were found to possess haemoglobin S, 29 haemoglobin C, and 1 haemoglobin G. On the other hand, in Tanganyika (Dar es Salaam) 100 out-patients of mixed tribal origin but mainly Bantu were recently examined by us through the kindness of Dr. Mackey; although 12 individuals with a haemoglobin showing the electrophoretic properties of S were noted, no haemoglobin C or any of the other known variants was found.

Discussion

In several recent publications the view has been advanced that the sickle-cell gene provides an example of balanced polymorphism in man. Neel (1953) discussed the possibility that the balance was attained through increased fertility on the part of the heterozygote. Allison's (1954a, 1954b, 1954c) experiment in Kampala, and his examination of the geographical distribution of the sickle-cell trait in East Africa, with high and low frequencies respectively confined to endemic and non-endemic malarious areas, provide some evidence, implementing that of Brain (1952), Mackey and Vivarelli (1952, 1954), and others, that possession of the trait confers selective advantage in malarious regions. He postulates a condition of balanced polymorphism, selection acting against the sickling homozygote through sickle-cell anaemia, against the non-sickling homozygote through malarial susceptibility, the heterozygote, however, being at an advantage over both homozygotes through the protection afforded by the sickle-cell trait against malaria, especially subtertian.

The role of malarial endemicity in determining sickle-cell frequency once the gene is introduced, however, should not be exaggerated. Many tribal areas are not sufficiently local in extent to be assigned to a single category of endemicity: the range of flight of the mosquito may admittedly be greater than the limit of several hundred yards generally quoted; but it is essentially local, and many "hyper-endemic" tribal territories must consist of intensely malarious and less malarious districts. Hence differences in selection pressure will occur within the territory, and if mating tends to be to any extent local differences in gene frequency will result. The actual value found for any sample will depend on a combination of social and ecological factors, the mating system of the people, the

length of time their economy requires individuals to spend in malarious areas, and the intensity of malarial infection in those areas. From these considerations it would seem that Allison's (1954b) attempt at a geographical analysis by means of a simple table is not sufficiently detailed to be convincing. Nor should the degree of selection pressure be overestimated. If, as is generally recognized (Taliaferro, 1949), malarial immunity is of two types, innate and acquired, then presumably the hypothetical immunity given by the sickle-cell trait falls into the former category. Is the non-sickling homozygote in endemic areas not protected to some extent by acquired immunity? Too little attention has been given to established work on malarial immunity during recent developments in this field.

Undoubtedly the functional approach to the problem of the sickle-cell trait represents a stimulating advance on the purely descriptive. The unequivocal establishment of this first example in man of balanced polymorphism would represent a considerable advance in anthropological theory. Hence the importance of clarifying the several points weighing against outright acceptance of the hypothesis in its present form.

As Edington (1953, 1954) and Lehmann (1954) have pointed out, the assumption that the simple homozygous theory of the inheritance of sickle-cell anaemia is correct remains difficult to accept completely. There are other factors to be considered; for example, those relating to the proportions of different haemoglobins such as are noted above, of which little is yet known. Certainly in areas where haemoglobin C exists, sickle-cell crises must occur in individuals heterozygous for S and C; and malarial infection, since it may precipitate such crises, may thereby adversely affect the proportion of heterozygotes. Some advantage of the non-sickling homozygote over sickling individuals could indeed be postulated to explain the several studies noted by Neel (1950), in which the sickle-cell frequency appeared to diminish with age, though other explanations can be advanced.

The assumption that malarial susceptibility is proportional to malarial mortality is not necessarily correct. As regards the demographic situation, Christophers (1949) concluded that in indigenous tropical populations "no obviously greater infant and child mortality rate accrues under hyperendemic conditions [of malaria] than is generally normal apart from malaria."

Neither Moore *et al.* (1954), in two samples, nor Edington (1954) in two samples, have been able to confirm any association between parasite rate and sickling such as is claimed by Allison (1954a) on a barely significant test of data relating to Baganda children; nor does either of Beet's (1946, 1947) investigations show any significant association; when the aggregate of the seven sets of data published by these authors is considered no significant relationship emerges. It should be pointed out that the χ^2 values given by Allison (1954a), if calculated by recognized procedures, are all incorrect; using Fisher's method with Yates's correction for continuity, χ^2 values of 1.64, 3.64, and 4.05, each with one degree of freedom, should replace those of 19.3, 4.1, and 5.1 calculated by Allison. In Raper's (1954) recent sample of 1,675 children, among those in the second year of life there was a significantly lower malarial rate in sicklers, but at no other age nor in the whole series was this association shown. It appears, then, that sickling has no effect on parasite rate in adults, though it may have an effect during a very limited period in early infancy. It is thus difficult to accept without further confirmation Allison's results on Luo adults, where in only 2 out of 15 adult sicklers, but in 14 out of 15 adult non-sicklers, malaria parasites were observed after repeated artificial inoculation. On each of the above points the evidence is unfortunately limited.

The findings reported here concerning the northern Nilotes, however, are not equivocal. Among the Shilluk, Dinka, and Nuer, by reason of their ways of life and the nature of their habitats, malaria is endemic. The Shilluk are a riverain people; they make more use of the rivers for

purposes of communication than do the Dinka: most of their villages are within a few hundred yards of the river, and a number are actually at the waterside. Most Dinka and Nuer spend the dry season by the rivers, and the wet season, when swamps abound, in inland villages. Malaria incidence would be expected to be at its lowest for the Dinka in the early dry season when the swamps inland have dried but immediately before the depletion of water in their wells, waterholes, and "hafirs" (waterholes of human construction) necessitates the movement of cattle and humans to the rivers. In a Dinka inland village, during the week before the move to the riverside cattle camp, out of a total village population estimated at 350, 11 individuals (3.1%) were seen to be suffering from a fever seemingly malaria, which responded to treatment with mepacrine; from only one of these individuals, unfortunately, could blood smears be obtained, in which instance M.T. rings were observed.

In the absence of published data concerning malaria in these peoples, the opinions of two authorities are quoted. Professor P. C. C. Garnham, of the London School of Hygiene and Tropical Medicine, states (personal communication) that "there is no doubt that the malaria incidence is very high in the Southern Sudan near Malakal." Dr. G. J. Clark, Province Medical Inspector, Malakal, states (personal communication) that new cases attending the out-patient department of Malakal Hospital for the year 1953-4 included 2,605 malarial cases, some 2% of the total, though many more were diagnosed as malaria which were either not proved or were probably relapses; that the majority of proved cases were *P. falciparum*, there being 2,488 positive M.T. slides; that malaria is endemic in the Malakal region; and that its incidence is reckoned to be greater than in the Nile region of Equatoria Province (where considerable frequencies of the sickle-cell trait occur).

Hospital figures are of course not representative of these primitive populations, since only a small proportion of individuals ever reach hospital; malarial cases are adequately treated at the outlying dispensaries, whereas more serious cases are sent to hospital; yet in the majority of many villages visited during the present investigation clinical malaria appeared to be the most frequent complaint. Thus all the evidence points to a high malarial endemicity in the region. This group of northern Nilotes, then, provides one exception to Allison's statement that "the world distribution of the trait is also in accordance with the view presented"—namely, the relationship of the sickle-cell trait to malarial endemicity. There are other exceptions. The sickle-cell trait is absent from aborigines of Malaya despite the high malarial incidence (Polunin, 1953); and the trait is virtually absent in the Union of South Africa. Budtz-Olsen and Burgers (1955) have tabulated surveys of nearly 6,000 Africans from that area, and have pointed out that at least in Zululand malaria has been present for generations.

Anthropological Interpretations

The differences noted here between West Africans and Nilotes in frequency of abnormal haemoglobins other than S suggest that further investigations may yield information of considerable anthropological interest. Haemoglobin E, for example, first found in a child of an Asian father (Itano *et al.*, 1954), has also been found in Siamese (Chernoff *et al.*, 1954) and in the Veddas of Ceylon (Graffe *et al.*, 1954), but not in the limited number of Africans so far examined.

As regards S haemoglobin, the present unresolved state of the hypothesis of marked association between sickling and malaria necessitates dual attempts at anthropological interpretation of the sickle-cell findings of the present survey.

If the hypothesis of balanced polymorphism associated with malaria is correct, then with this observed incidence of malaria the sickle-cell trait ought to be present among the northern Nilotes. To explain its absence, two suggestions may be offered. There may be insufficient malarial

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