aemia and sickling genes but were not anaemic. The incidence of the haemoglobinopathy among the Eti-Turks is equalled only in Sicily.

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A STUDY OF THE SURVIVAL RATE OF CASES OF SICKLE-CELL ANAEMIA

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It is now generally accepted that the phenomenon of the sickling of red cells at reduced oxygen tensions is due to the presence of greater or lesser amounts of an abnormal haemoglobin within the cells. The production of this haemoglobin is controlled by a gene which is allelic to the gene controlling normal haemoglobin production. The heterozygous inheritance of this sickle-cell gene produces the harmless sickle-cell trait, while the homozygote is manifest as sickle-cell anaemia. This anaemia is characterized by haemolysis with intermittent crises and is usually fatal in childhood. This death in childhood of the homozygotes must remove abnormal genes from the population, and the immediate question arises of how, in the face of this recurrent gene loss, the gene frequency can be maintained at the high levels at which it is found in many African tribes.

The answer seems to lie in the interaction of three main factors. Firstly, recurrent mutations must play some part, though it is highly improbable that they could provide the sole replacement of all the genes lost by childhood deaths. Secondly, it is now well established that the heterozygote sickler enjoys some advantage over the normal in respect of falciparum malaria, though the magnitude and exact mechanism of this effect are not yet clear. Thirdly, there is the fact that while most subjects with sickle-cell anaemia die in childhood, some few do survive to adult life and contribute abnormal genes to the next generation. This paper presents some evidence on this third factor as found in a single African tribe in Uganda.

The older literature on the natural history of sickle-cell anaemia has become largely invalidated by the recent discovery of other genetically controlled abnormal haemoglobins and by the description of microdrepanocytic disease. Both this latter disease and the anaemia often resulting from the double inheritance of two abnormal haemoglobins may produce a clinical picture closely similar to sickle-cell anaemia. In East Africa, however, other abnormal haemoglobins have not been found among the African tribes (Jacob, 1955 ; Roberts and Lehmann, 1955) and thalassaemia has never been detected. The same situation appears to obtain in the Belgian Congo. A high degree of validity can therefore be attached both to clinical reports in children and to simple electrophoretic surveys in adults directed towards defining the survival rate of cases of sickle-cell anaemia in these two areas. Nevertheless, published work has produced somewhat variable estimates of survival rates.

In Kenya, Allison (1954) examined 70 adult sicklers of the Luo tribe by paper electrophoresis and found two cases with the pattern of sickle-cell anaemia. He calculated that these two represented a 35% survival rate to adult life. He later suggested that the survival rate in Africa was more likely to be in the region of 20% on the basis of figures collected from the Musoma tribe of Tanganyika (Allison, 1956). In a survey of the Baamba tribe in Uganda, Lehmann and Raper (1956) found no case showing the electrophoretic pattern of sickle-cell anaemia in a random sample of 478 adults. They conclude "that the survival of sickle-cell homozygotes plays no significant part in the maintenance of the high sickling rate in the Baamba." Workers in the Belgian Congo have expressed the same opinion on the basis of clinical observations in children. The Lambotte-Legrands (1955) state that the great majority of patients die in childhood, and Vandepitte (1955) estimates that only about 1% survive to adult life. It was therefore decided to undertake an electrophoretic survey of adults of the Baganda tribe in an attempt to obtain a more exact figure for the survival rate to reproductive age.

Method

Blood samples were obtained from specimens which had been sent in to the laboratory for routine Kahn tests from the antenatal clinic and from the male V.D. clinic of Mulago Hospital. A few samples were also obtained from mothers bringing their children to the paediatric clinics. Specimens from the Baganda tribe only were examined. In all cases a sickling test was done by the *E. coli* method, and all which were positive were subject to paper electrophoresis by the method already described (Jacob, 1955). An attempt was made to see all cases showing the pattern of sickle-cell anaemia at their next clinic attendance.

Results

Altogether 3,362 specimens were examined, of which 545 were from sicklers and were subjected to electrophoresis. The source of the specimens can be seen from the Table.

Cases 291, 316, and 543 of this series of 545 sicklers showed the pattern of sickle-cell anaemia. These samples were all from the antenatal clinic, and further details are as follows.

Sources of Blood Specimens

Source of Blood	Non-sicklers	Sicklers	% Sickling
Antenatal clinic	2,090	396	15·9
Male V.D. ,, ...	651	126	16·2
Mothers in paediatric clinic ..	76	23	23·2
Total	2,817	545	16·2

Case Reports

Case 291.—A woman aged 18, who had had one abortion and was three months pregnant when seen, gave a history of recurrent fevers throughout childhood which had gradually decreased in severity. The attacks occurred about once a month, and she stated that during them she ached all over, her fingers and toes often swelled, and her eyes often became yellow. She never felt really well between the attacks. It was not possible to obtain a proper family history from her. On examination there was no bossing of the skull, and the spleen was impalpable. Her conjunctivae were slightly yellow and the mucous membranes a little pale. There were no joint swellings. The haemoglobin was 8.1 g. per 100 ml. (M.R.C. grey-wedge photometer); red blood cells, 3,400,000 per c.mm.; P.C.V., 32%; white blood cells, 9,400 per c.mm. Stained blood film: the differential white count was within normal limits and the polymorphs showed no shift to the left; the red cells showed some hypochromia and moderate polychromasia; occasional irreversible sickle cells were seen. There were no normoblasts and no malaria parasites. The bilirubin was 2 mg. per 100 ml. Alkali-resistant haemoglobin (Singer *et al.*, 1951), 13.0%. The solubility of haemoglobin was 0.79 g. per litre of 2.24 phosphate buffer (Itano, 1953).

Case 316.—This patient, aged 28, was 34 weeks advanced with her first pregnancy when seen. She did not return to the clinic for the result of her Kahn test, and only clotted blood was available. A film made from the clotted blood showed considerable polychromasia. The bilirubin was 2.8 mg. per 100 ml.; alkali-resistant haemoglobin, 12.0%.

Case 543.—A woman aged 30, who was 28 weeks advanced with her first pregnancy when seen, gave a vague history, but it appeared that she had had recurrent fevers throughout childhood, occurring about once every two months, and accompanied by pains in the limbs and by yellow eyes. She was unable to give any family history. On examination her skull showed slight bossing, her mucous membranes were pale, and the conjunctivae slightly yellow. There were no joint swellings and the spleen was impalpable. The haemoglobin was 6.5 g. per 100 ml.; red blood cells, 2,200,000; P.C.V., 24%; white blood cells, 4,300; normoblasts, 15,600 per c.mm. A blood film showed large numbers of normoblasts in varying stages of maturity. There was very marked polychromasia, and irreversible sickle cells were present. The polymorphs showed a shift to the left and occasional myelocytes were seen. The bilirubin was 2.3 mg. per 100 ml.; alkali-resistant haemoglobin, 8.0%. The urine had a considerable excess of urobilinogen. This woman had a stillbirth at home at 36 weeks. She was subsequently admitted to Mulago Hospital with peritonitis. She refused to allow any further blood examinations, and on her death, a few days later, her relatives refused permission for a post-mortem examination.

Discussion

All three women showed the pattern of sickle-cell anaemia on paper electrophoresis and had evidence of a haemolytic process. It could be maintained, however, that they were not true cases of sickle-cell anaemia—in other words, homozygotes for the sickle-cell gene—since it was not possible to prove that they had inherited a single sickle-cell gene from each parent. This proof is theoretically necessary, as both microdrepanocytic disease and sickle-cell haemoglobin D disease produce an electrophoretic haemoglobin pattern on paper indistinguishable from the true case of sickle-cell anaemia. Nevertheless, as in other published reports from East Africa, a high degree of validity can be attached to the diagnosis in the absence of other abnormal haemoglobins and of thalassaemia. Collateral evidence in favour of accepting these as true cases is obtained from the Mulago Hospital records, which show that other young adults with sickle-cell anaemia have been seen in whom the diagnosis has been firmly established by the finding of sickling in both parents.

In order to determine what proportion of the expected number these three cases represent it is assumed that the sickling rate is static. It is further assumed that a system of random mating occurs. It can then be calculated from the sickling rate of 16.2% that this population at birth should have included 22 cases of sickle-cell anaemia. Since only three of these cases were seen in adult life it can be presumed that approximately 86% have died in childhood.

This figure of 14% survival rate lies between the estimates made by Allison (1956), on the one hand, and by Lehmann and Raper (1956) and the workers in the Belgian Congo on the other. The difference might be explained on the basis of the smaller samples of Allison and of Lehmann and Raper; and the Congo workers, relying on clinical diagnosis, might have missed just those mild cases which might be expected to survive to adult life. It seems possible, however, that the different estimates represent a true variation in survival rate. A subject with sickle-cell anaemia may die of the disease *per se* in a crisis, but he may die from many other diseases, such as pneumonia and typhoid, to which he is likely to be less resistant owing to persistent anaemia. The prevalence of these other diseases are therefore likely to affect the survival rate in any one area. The Bwamba forest, in which Lehmann and Raper worked, is certainly more unhealthy than the conditions under which the Baganda live in and around Kampala, and, though accurate vital statistics for these areas are not available, it is certainly clear that the general childhood death rate is by far the higher in the Bwamba forest.

The fact that the heterozygote (sickle-cell trait) is in some degree protected from falciparum malaria has already been referred to. Allison (1956) has stated: "It will be clear that the main factor determining the frequency of the gene in any population is environmental—that is, mortality from falciparum malaria." If the survival rate of the homozygote is truly variable in different areas, and if this variability is due to the relative prevalence of other diseases, then malaria is only one of the many environmental factors concerned in the maintenance of the sickle-cell gene. A study of the maintenance of the sickle-cell gene in any area must include both a study of the childhood mortality from malaria and of the survival rate of the homozygote to reproductive life; only general qualitative inferences may be drawn from such a study, and quantitative inferences are likely to be invalid.

Summary

A study of 3,362 adults of the Baganda tribe has been made. Paper electrophoresis of the haemoglobin solutions revealed three cases of sickle-cell anaemia.

The sickling rate of the whole series was 16.2%, and it is calculated that these three cases of sickle-cell anaemia represent a 14% survival to adult life.

It is suggested that the survival rates of subjects with sickle-cell anaemia may vary in different parts of Africa.

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The Central Council for Health Education has produced a pegboard triptych screen display unit for use by local authority health departments. Printed displays in colour are available, with supporting leaflets and posters, for making a compact exhibition of a size to fit an ordinary table. The council hopes also to produce a series of "Make It Yourself" displays on various topics for the triptych screens. Further details and prices will be provided on application to the medical director, Central Council for Health Education, Tavistock House, Tavistock Square, London, W.C.1.