The examination of "pre-Dravidian" people is being continued with the hope of further defining the distribution of the sickle-cell trait in Southern India. However, the main purpose of the investigation has been achieved since the results lend support to the possibility of a link between prehistoric Africa and India.

Summary

The sickle-cell trait was found to be present in a number of individuals belonging to three aboriginal communities of Southern India. There was a low incidence of the Rh chromosome R_0 (cDe).

No sickle-cell-trait carrier was discovered among a control group of the non-aboriginal or "Dravidian" population.

The possible anthropological significance of these findings is discussed.

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THE SICKLE-CELL TRAIT IN WESTERN NIGERIA

A SURVEY OF 1,881 CASES IN THE YORUBA

BY

D. B. JELLIFFE, M.D., M.R.C.P., D.C.H. D.T.M.&H.

AND

JOHN HUMPHREYS, M.B., Ch.B.

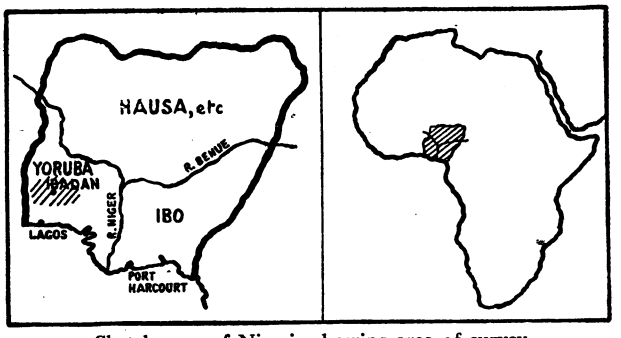
(From the Department of Medicine, University College, Ibadan, Nigeria)

Yorubaland occupies the greater portion of Western Nigeria, lying between the Lagos lagoon in the south, the River Niger in the north, the Dahomey frontier in the west, and the Benin country in the east. Ibadan itself is a huge sprawling city of mud-brick buildings. The population, which is mainly Yoruba, is in the region of half a million. Ibadan's present importance is due to the fact that it lies at the centre of the cocoa-growing area of Nigeria, although it has been the site of a considerable town for over a hundred years.

The Yoruba are for the most part peasant farmers and petty traders. Their diet is largely vegetarian, the staple farinaceous foods being yams, maize, and cassava. Animal protein is deficient in the food of the majority, as cattle cannot be reared locally but have to be brought for slaughtering from northern Nigeria.

Groups Examined

In this survey 1,881 Yoruba were examined. The majority were from Ibadan, although some came from all parts of Yorubaland. Sickling was looked for by the method of Scriver and Waugh (1930), although no preliminary congestion was used. The finger was pricked and a drop of blood transferred to a coverslip. This was inverted and placed face downwards on a clean slide. The coverslip was ringed with petroleum jelly and the preparation examined for sickling after 72 hours. In a few, the enclosed blood became either haemolysed or dried. These cases were not included in the series.



Sketch map of Nigeria showing area of survey

It is felt that the cases reviewed here represent a fair cross-section of the Yoruba population of Ibadan. The newborn babies were examined in the maternity wards and the other infants while attending welfare clinics. The older pre-school children and the elderly were difficult to test in large numbers. The few that were examined were in-patients, out-patients. or visitors at hospital. The three groups of schoolchildren were tested at several schools serving a wide area of the town. The young adult male group was the least balanced, as the majority were either policemen or Army recruits, and were probably of more than average physical development.

Results of the Survey

The results are shown in Table I. The average incidence in the whole series of 1,881 was 23.7%. As can be seen, no case of sickling was observed in any of the 51 newborn babies examined. The possible significance of this is discussed later. In the other groups the incidence of sicklaemia varied from 19.2% in young adult males to 28.3% in children between the ages of 1 and 4 years. If the first group containing babies up to 2 weeks old is omitted from analysis, a χ^2 test shows that the proportions of positive cases in the other age groups do not vary more than would be expected by chance ($\chi^2=8.83$). For 7 degrees of freedom P lies between 0.3 and 0.2. In other words, the sickle-cell trait would appear to occur with equal frequency at all ages, with the exception of the newborn.

TABLE I.—*Results of Survey for the Sickle-cell Trait in 1,881 Yoruba*

Age	No. Examined	No. Positive	% Positive
1st 2 weeks	51	None	—
Over 2 weeks to 1 year	120	30	25·0
,, 1 year to 4 years	60	17	28·3
,, 4 years ,, 8 ,, ...	301	84	27·9
,, 8 ,, ,,15 ,, ...	512	133	25·0
,, 15 ,, ,,18 ,, ...	144	30	20·9
Young adult males	302	58	19·2
,, ,, females	339	80	23·6
Older adults (males and females)	52	14	26·9
Total	1,881	446	23·7

Discussion

Comparatively few surveys for the sickle-cell trait have been undertaken in tropical Africa, and results in different countries vary. Thus, 45% of the pygmoid Baamba show sickling (Lehmann and Raper, 1949), while Sarmento (1944) found only 8% positive in a survey of adult males in

Angola. It is, however, correct to say that most investigators have found from 15 to 30% to show sicklaemia, so that the findings in the present series are in rough accord with observations made elsewhere.

As has been stressed by several authors (Raper, 1950), the sickle-cell trait is common in tropical Africa, while sickle-cell anaemia is rarely recorded. This is in contradistinction to findings in American negroes, in whom the sickle-cell trait is much less common (6–9%), but in whom sickle-cell anaemia is frequently seen. It has been estimated that in America the ratio of sickle-cell anaemia to trait is 1:50, while Raper (1950) estimates that the ratio in Africa must be below 1:1,000. The explanation of this undoubted fact is unknown. Raper suggests that it may be connected with genetic modification produced by intermarriage with Caucasians in the case of the American negro. However, as has been pointed out elsewhere (Jelliffe, 1952), it must be realized that a partial explanation for the rare reports of sickle-cell anaemia in Africa lies in the comparatively few doctors and laboratories in these regions, together with a lack of awareness of the disease entity and the difficulty of making a rapid and certain diagnosis, especially in view of the numerous other forms of anaemia which occur so commonly in indigenous Africans. The possibility that sickle-cell anaemia may be more frequent than has hitherto been suspected is suggested by Jelliffe and by a recent report from Kenya (Foy, Kondi, and Brass, 1951).

At the present state of knowledge, it nevertheless seems certain that sickle-cell anaemia is relatively rare in tropical Africa, despite the presence of an enormous population showing the sickle-cell trait. This is confirmed by the present survey. Of the 1,881 cases examined, none were observed to have an obvious haemolytic anaemia, although this cannot be regarded as scientific evidence, as neither careful clinical examinations nor full haematological investigations were undertaken. However, it is significant that, during the past nine months in Ibadan, where there must be over 100,000 persons with the sickle-cell trait, only 12 cases of sickle-cell anaemia have been seen.

The mode of inheritance of sickle-cell anaemia and its relation to the sickle-cell trait is still far from certain. The most recent suggestion (Neel, 1949) is that sickle-cell disease may be due to a gene which in a homozygous condition produces sickle-cell anaemia and in the heterozygous condition sicklaemia (sickle-cell trait). As Lehmann (1951) has noted, if this theory is correct, sickle-cell anaemia would be expected to occur more frequently in Africa than in America. As he remarks, "One possible explanation for this discrepancy could be that the gene is lethal and that homozygotes die earlier than the rest of the population." If this were the case the incidence of sickling would be expected to fall in the older age groups, whereas the frequency was found to be the same at all ages in three tribes examined in Uganda.

As has been noted previously, in the present series no variation in incidence could be found in the different age groups, with the exception of the newborn babies. This can be interpreted as supporting Lehmann's view that the simple homozygous-heterozygous theory does not appear to fit the facts as seen in tropical Africa. The most interesting feature of this survey was the apparent absence of sickling in newborn children examined in the first two weeks of life. In no instance were sickle-cells seen after 72 hours' observation; and, in order to follow up this type of case more carefully, blood from the last 18 newborn babies was examined again after 216 hours. The results are recorded in Table II. As can be seen, 12 showed no sickling even after this interval, 5 specimens were haemolysed, while 1 case showed the presence of less than 5% sickle cells.

It has recently been shown that the haemoglobin of sickle-cell anaemia and normal haemoglobin differ physicochemically, and that the haemoglobin of a subject with the sickle-cell trait is a mixture of the two (Pauling *et al.*, 1949). A possible explanation for the absence of sickling in these newborn infants is that sickle-cell haemoglobin is not present in foetal blood but develops after birth. Unfortunately, it was not possible to follow up this series of cases. In addition, in the normal subject, foetal haemoglobin has different biophysical properties from adult haemoglobin, although exact differences in chemical structure are still far from clear-cut. However, it is well recognized that foetal haemoglobin has an increased affinity for oxygen and that, conversely, it reduces more slowly. It has been shown by various workers that foetal haemoglobin persists, to a diminishing degree, in the blood of newborn infants, although the length of time it can be detected is uncertain. Periods varying from days to a few months have been described by different investigators (Smith, 1945).

TABLE II.—*The Sickle-cell Trait in the Newborn*

Case No.	Age in Days	Result at 72 Hours	Result at 216 Hours
1	5	Negative	Negative
2	8	,,	,,
3	7	,,	,,
4	2	,,	Haemolysed
5	4	,,	,,
6	10	,,	Negative
7	3	,,	,,
8	5	,,	,,
9	3	,,	,,
10	4	,,	Haemolysed
11	6	,,	Under 5% positive
12	3	,,	Negative
13	1	,,	Haemolysed
14	5	,,	,,
15	7	,,	Negative
16	4	,,	,,
17	4	,,	,,
18	6	,,	,,

Sickling of red blood corpuscles probably occurs only when haemoglobin is in a reduced state, at least in subjects showing the sickle-cell trait. It seems possible, therefore, that the apparent absence of sickling in the first two weeks of extrauterine life may be due to this persistence of foetal haemoglobin, and that sickling cannot be demonstrated because of the extreme difficulty of causing this type of haemoglobin to become reduced.

In this context it may be mentioned that recent work by Liquori (1951) has shown that in Cooley's anaemia, a disease with many points of similarity to sickle-cell anaemia, 40–60% of the haemoglobin may still be foetal at the age of 8 years. Although this is in contrast to the hypothesis suggested here, nevertheless both findings would seem to indicate that further work on the relation of foetal haemoglobin to sickle-cell haemoglobin is required.

Summary

A survey for the sickle-cell trait was undertaken in 1,881 Yoruba in Ibadan, Western Nigeria. The average incidence was 23.7%. The incidence showed no real variation with age, although no cases of sickling were noted in 51 newborn babies. The latter was thought to be related to a persistence of foetal haemoglobin into the first weeks of extrauterine life. The results of the survey are discussed, with especial reference to the homozygous-heterozygous theory of inheritance of the sickle-cell trait.

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