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Sickle Cell Anaemia in Nigerian Children*

BY

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In the light of knowledge of the sickling frequencies in African populations and the mode of inheritance of the sickle cell gene, it has been estimated that in every generation of Negroes born in Africa more than a million die of sickle cell anaemia (Vandepitte, 1955). Yet prior to 1950 so few cases of sickle cell anaemia had been reported in Africa that doubt was expressed as to whether the consequences of homozygous inheritance of the sickling gene were the same in indigenous Africans as in American Negroes (Raper, 1950).

Subsequently reports have shown that when the disease is sought for during infancy and childhood, the incidence is that expected in terms of the genetic theory advanced by Neel (1949, 1951) and Beet (1949). Most reports, however, have contributed little to knowledge of the clinical manifestations of the disease as seen against the African background with its closely interwoven themes of protein malnutrition, debilitation, tropical diseases and primitive social systems. Notable exceptions to the foregoing are the reports of the Lambotte-Legrandes (1951 and 1955) and Trowell *et al.* (1957). The former have described the natural history of sickle cell anaemia in the Belgian Congo and the latter in East Africa. Elsewhere in Africa, including West Africa, with its large pool of sicklaemics, the clinical manifestations of sickle cell anaemia have not been recorded on any large series of cases seen in the early years of life.

The object of this paper is to present the clinical features of sickle cell anaemia in Nigerian children and to compare our findings with those of workers elsewhere in Africa and in America.

Sickle cell anaemia is commonly encountered in the children's department at University College Hospital, Ibadan. This is hardly surprising, as Ibadan has a population of at least half a million, of whom approximately one-quarter show the sickling trait (Jelliffe and Humphries, 1952a; Garlick and Barnicot, 1957). In such a population the incidence of sickle cell anaemia can be estimated at 15.6 per 1,000 births (Vandepitte, 1955). Our experience is very different from that of Jelliffe and Humphries, who reported in 1952: "It has been our experience that in Ibadan examples of sickle cell anaemia are definitely uncommon, especially when considering the large pool of sicklaemias in the area" (Jelliffe and Humphries, 1952b). The likely explanation for the discrepancy between their findings and ours is that we have been more advantageously placed in respect of staff and laboratory services than they were. It should be noted that sickle cell anaemia accounts for only a relatively small percentage of the many severely anaemic children seen in Ibadan. As Jelliffe and Humphries themselves observed, the average haemoglobin level of children between four months and two years in Ibadan is probably between 50 and 60 per cent. Against such a background, in the absence of adequate facilities, sickle cell anaemia may understandably be overlooked.

This presentation is based on a detailed analysis of 75 cases of sickle cell anaemia seen prior to December, 1956. At the time of writing, well over 200 cases have been seen in the children's department at University College Hospital, Ibadan, and while the total number of cases is not reflected in *figures* quoted below, our continued experience accords with the general conclusions based on the study of the smaller series. Diagnosis in all cases was con-

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firmed by filter paper electrophoresis of the haemoglobin.

CLINICAL FEATURES OF SICKLE CELL ANAEMIA

Race, Sex, Age

All our patients are indigenous Nigerians; the majority belong to the Yoruba race, which predominates in Western Nigeria, but Ibos (Eastern Nigeria) and Hausas (Northern Nigeria) are also represented. The sex incidence is equal. The age distribution of our cases at diagnosis is shown in Table I. The average age at diagnosis was 3.8 years as compared with 1.4 years in the 300 cases in the Belgian Congo (J. and C. Lambotte-Legrande, 1955), and 4.7 years in 63 American Negroes (Scott *et al.*, 1955). Reports from the Belgian Congo are unique for the exceptionally high percentage of cases diagnosed during the first 18 months of life.

Table I

Years	0-2	3-4	5-6	7-8	9-10
No. of cases	29	19	9	10	7

Figure 1 compares the age at diagnosis in our cases with that recorded in the Belgian Congo (Fig. 1) (J. and C. Lambotte-Legrande, 1955). It will be seen that in the latter the disease is mainly a problem of infancy, while in our series, though infants are frequently involved, the emphasis is on early childhood.

SYMPTOMS

Sickle cell anaemia in Nigerian children is characterised by frequent episodes of fever, limb pain often associated with inflammatory swelling of the affected parts, and various gastro-intestinal complaints, including anorexia and vomiting, abdominal pain and distention. Some patients present with disorders referable to the central nervous system. These include drowsiness and irritability and convulsions, and occasionally evidence of focal cerebral damage. A few cases have presented with purulent meningitis. Other complaints met include "weakness" and tiredness, epistaxis and bleeding gums, jaundice and "dark urine" and various respiratory symptoms. Diarrhoea is common, especially among infants, but this may simply reflect the high incidence of diarrhoeal disorders locally rather than any special tendency to diarrhoea in sickle cell anaemia.

It will be seen that the mode of presentation is very variable. The symptom most helpful in arriving at the diagnosis is the episodes of limb pain. The intensity and distribution of pain vary from case to case and in the same patient from time to time. Sometimes it is little more than slight discomfort, while on other occasions it might completely incapacitate the patient. Pain may be generalised, but is more commonly

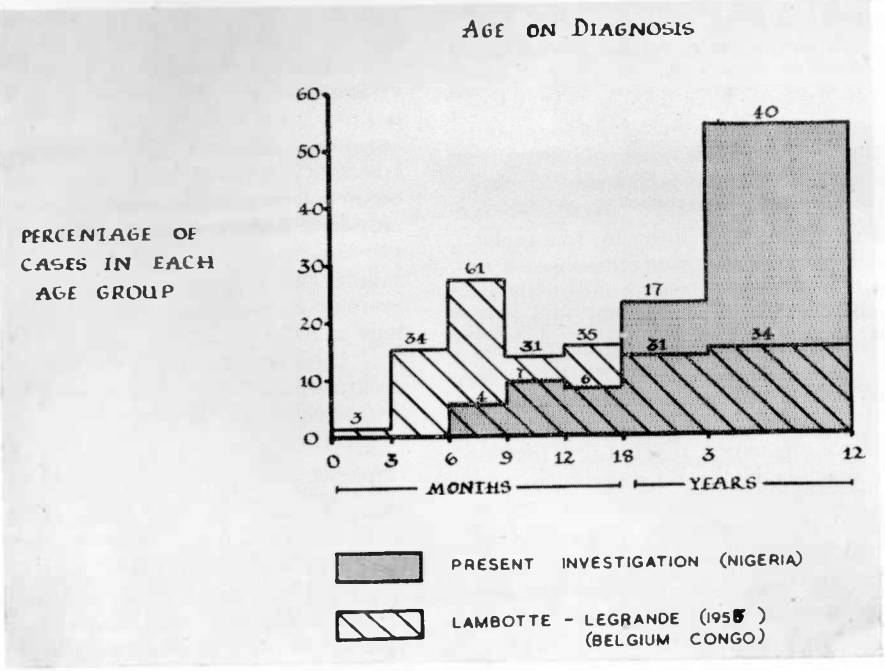

Fig. 1—Comparison of age on diagnosis of sickle cell anaemia in Nigeria and the Belgian Congo.

localised to particular limbs. In general, pain tends to be distributed in relation to bones rather than joints. In infants the hands and feet are commonly involved, but in older children the emphasis shifts to the legs and arms. "Inflammatory" swelling in association with limb pain is commonly met. This will be dealt with in more detail later.

Anorexia with or without vomiting is a common presenting complaint. Usually it occurs in association with crises of the disease and often it precedes the onset of other symptoms. Our experience is similar to that of Scott *et al.* (1955), who state: "We have observed that anorexia, even in the absence of demonstrable infection, is often the forerunner of crisis episodes and may precede by days or weeks the more dramatic onset of pain." Abdominal pain occurs most frequently between the ages of three and six years. The severity of the pain varies from vague discomfort to episodes simulating the surgical "acute abdomen." Sometimes pain is localised to the liver or spleen.

Occasionally cases are diagnosed during the investigation of some unrelated disease or disability. Recently a boy of seven years who was admitted for repair of an inguinal hernia was found to have sickle cell anaemia.

PHYSICAL FINDINGS

Anaemia is a constant feature, but, seen against the local background of generally low haemoglobin values, is often not striking and may on occasion be missed.

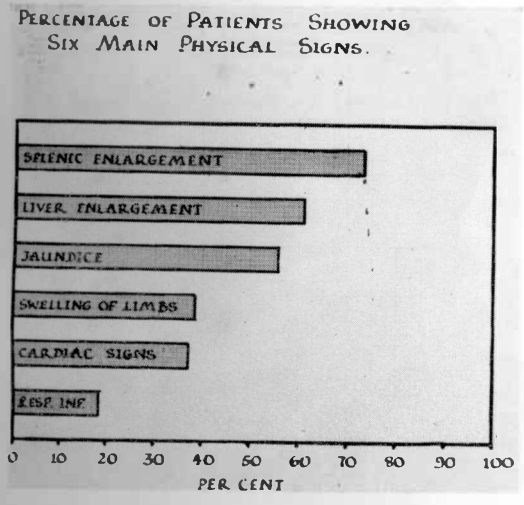

Fig. 2—Sickle cell anaemia in Nigerian children. Percentage of patients showing six main physical signs.

Our experience with six of the other main physical signs is shown in Figure 2, and the age relations of these findings is shown in Figure 3. Further comment will be confined to a few specific features (Figs. 2 and 3).

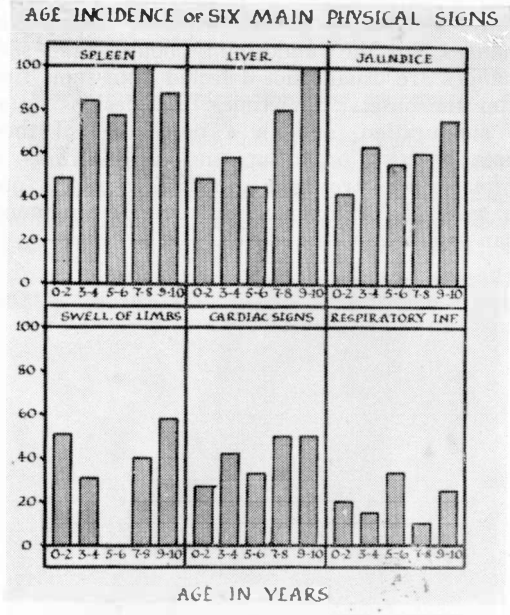

Fig. 3—Age incidence of six main physical signs in sickle cell anaemia in Nigerian children.

Splenomegaly

There is great variability in spleen size from case to case and in the same patient from time to time. Many patients present with massive spleens. Usually the organ is very firm in consistency and non-tender, but splenic pain and tenderness sometimes occur. Our experience is very different from that recorded in the United States of America, where it is found that the spleen is seldom palpable after the first few years of life and rarely if ever after ten years of age (Smith and Conley, 1954). It is probable that this difference is related to prevalence of malaria in West Africa, but other factors may be involved.

Limb Swellings

These include all peripheral manifestations of sickle cell anaemia associated with swelling except oedema from general causes. Approximately 40 per cent. of our cases show limb swellings of some type during the course of the disease. The characteristic lesions in infants are warm, tender, brawny swellings occurring over the middle and proximal phalanges of the fingers and the metacarpals, and on the dorsum

of the feet in relation to the shafts of the metatarsals. Our findings agree with those reported by authors elsewhere in Africa (J. and C. Lambotte-Legrande, 1951; and Trowell *et al.*, 1957). These swellings usually subside spontaneously after a variable period of days or weeks. In many, swelling is asssociated with radiological changes in the underlying bones, but such changes are usually not detected until some time after the onset. Sometimes these lesions go on to suppuration, and in a percentage of these cases specific organisms including strains of *Salmonellae* have been isolated from the pus. In general, swelling of the feet is commoner than swelling of the hands.

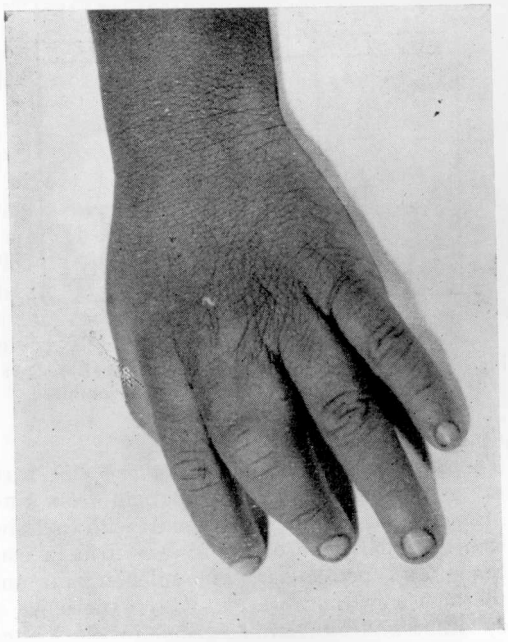

Fig. 4—Characteristic lesions of hands and feet in infants with sickle cell anaemia.

Figures 4 and 5 show typical appearances in hands and feet. In older patients findings are more variable and the long bones of the legs and arms are more frequently involved. Swelling sometimes occurs in relation to a joint, but usually the underlying mischief is located in the bones forming the joint. True arthritis is rare.

Cardiovascular System

The incidence of abnormal cardiac findings increases with age. The common findings are cardiomegaly and haemic murmurs, usually systolic in timing, but diastolic murmurs are sometimes heard. In long-standing cases, pul-

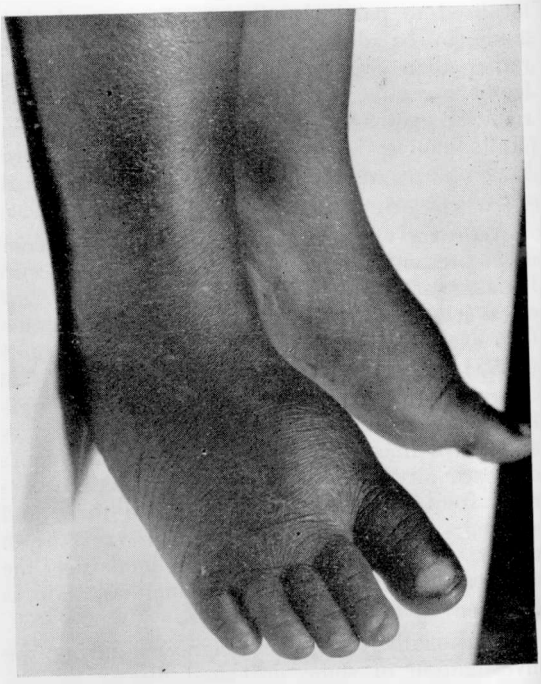

Fig. 5—Showing swelling of the dorsum of the foot over the first and second metatarsal bones

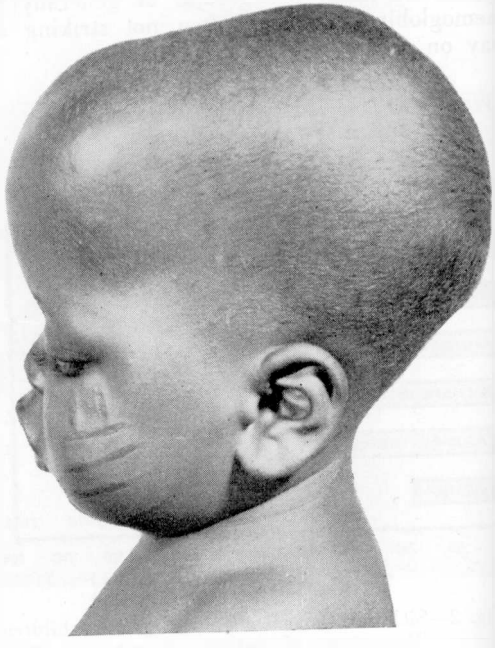

Fig. 6a—Bossing of skull in sickle cell anaemia.

monary hypertension tends to occur. Sometimes patients present in cardiac failure due to severe anaemia, but this occurs less frequently than one would expect. The radiological features of the heart are described below.

Central Nervous System

Reference has already been made to disturbances of consciousness and sleep in the section on symptomology. On the whole, severe central nervous system disturbances are infrequent. We have encountered meningism and meningitis, hemiplegia and psychotic behaviour. It is of interest to note that in the Belgian Congo, haemophilus meningitis is reported as a not uncommon terminal event in infants with sickle cell anaemia (J. and C. Lambotte-Legrande, 1951).

Shape of the Skull

In many patients the shape of the skull shows little or no abnormality. Some patients, however, show frontal or biparietal bossing, and very occasionally we see a typical "hot cross bun" head. Figures 6a and 6b show examples of bossing of the skull.

Habitus

Many authors have described a characteristic habitus in adults with sickle cell anaemia (Windsor and Burch, 1945; Margolies, 1951; Smith and Conley, 1954). Apart from abdominal protrusion, none of our cases below the age of seven show a noticeably abnormal habitus. Over this age patients begin to show some of the features of the abnormal habitus described in adults (Figs. 7a and 7b). The features most commonly seen are:—

(1) Abdominal distention.
(2) Increased anterior-posterior diameter of the chest (hoop chest).
(3) Thin, disproportionately long limbs.
(4) Exaggeration of the normal spinal curvatures.

Lymphadenopathy, reported as a prominent finding in children by American authors (Scott *et al.*, 1955), is not a feature in our cases.

None of our cases have had leg ulcers attributable to the disease. Our experience rein-

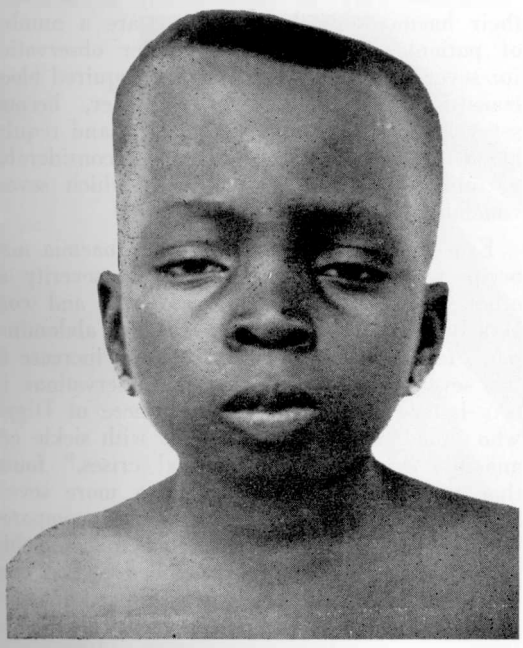

Fig. 6b—Bossing of the skull—one of the features of sickle cell anaemia. The asymmetry in this case is unusual.

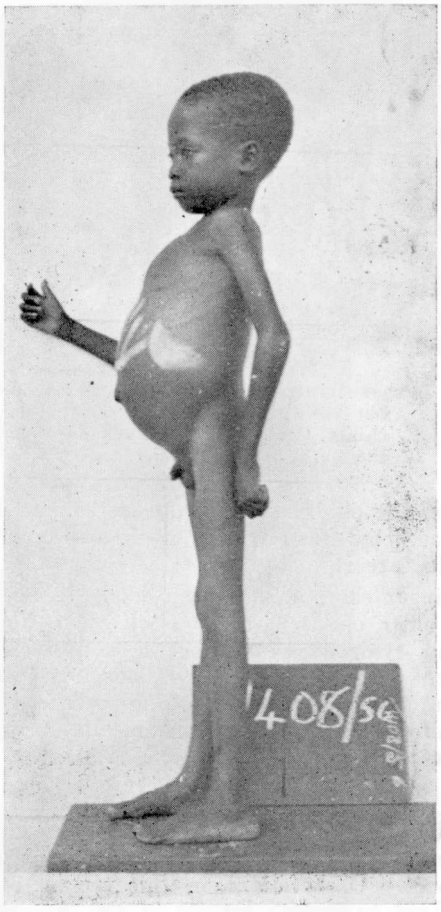

Fig. 7a shows abdominal distention associated with hepatosplenomegaly, increased antero-posterior diameter of chest and disproportionately long limbs.

Fig. 7b shows sisters. Both have sickle cell anaemia; but while the habitus is normal in the young child, there is gross leg trunk disproportion in the elder.

forces the observations of others that leg ulcers. an accepted feature of the clinical picture in adults, are rare in children.

Finger clubbing has been noted in several of the older children, in none of whom have we found evidence of any of the conditions with which clubbing is usually associated. It has been presumed that clubbing occurred as a manifestation of sickle cell anaemia. Figure 8 shows clubbing in one of our cases.

Haematological Findings

The haematological features of sickle cell anaemia have been well described by many authors. Observations in this section will be confined to certain aspects of the haematology only.

The haemoglobin level in 67 cases on first attendance in hospital is shown in Table II. It will be seen that there is a wide range from

Table II

Haemoglobin Level on First Examination in 67 Cases of Sickle Cell Anaemia

Haemoglobin g. Per Cent. (14.8 g. equals 100 Per Cent.)	Number of Cases
Less than 3 (20 per cent.)	2
3 to 4.4 (30 per cent.)	17
4.5 to 5.9 (40 per cent.)	15
6 to 7.4 (50 per cent.)	17
7.5 to 8.9 (60 per cent.)	12
9.0 to 9.6 (65 per cent.)	4

less than 3 g. per cent. to more than 9 g. per cent. In general, anaemia tends to be more severe among the younger patients. As the first visit is usually precipitated by some exacerbation in the severity of the disease, the findings on first examination do not necessarily reflect the usual state of affairs in these patients. Our clinic follow-up studies show that in the majority the haemoglobin level is maintained between 7 and 8 g. per cent. (45 to 55 per cent.), but some patients run for long periods at lower levels without obvious evidence of incapacity due to anaemia *per se*.

Patients vary in their ability to maintain their haemoglobin level. There are a number of patients who have been under observation for several years who have never required blood transfusions. Many cases, however, become severely anaemic from time to time and require blood transfusion, but there is considerable variability in the rapidity with which severe anaemia develops.

Exacerbation in the severity of anaemia may occur without any increase in the severity of other manifestations of the disease, and conversely "clinical crises" of limb pain, abdominal pain, fever, etc., often occur without increase in the severity of anaemia. Our observations in this latter respect accord with those of Diggs, who in a study of 166 patients with sickle cell anaemia seen in 747 "clinical crises," found that there was no evidence of a more severe anaemia during or following crises compared with the values for erythrocytes and bilirubin previous to crises. He concluded: "The concept of a haemolytic crisis in sickle cell anaemia is a myth which should not be perpetrated in the light of present knowledge" (Diggs, 1956).

In our own cases, while "clinical crises" often occur without exacerbation of anaemia, in some

patients the two coincide. Available data on our patients do not permit an opinion as to whether exacerbation of anaemia is more often due to hyperhaemolysis or temporary bone marrow hypoplasia causing a disturbance of the precarious balance between red cell production and destruction. Recently, four patients have been seen in whom increase in the severity of anaemia was due to folic acid deficiency. The bone marrow in these patients showed megoblasts. Following oral folic acid administration, there was a reticulocyte response and subsequent elevation of the haemoglobin level.

"With continued experience of sickle cell anaemia, the impression has grown that in some cases with very large spleens, "hypersplenism" aggravates the anaemia. This observation has recently been confirmed in one of our cases who was subjected to splenectomy with very satisfying results. The improvement in this case accords with that reported by others who have done splenectomies in selected cases of sickle cell anaemia (Shotten, Crockett and Leavell, 1951; Sprague and Paterson, 1958).

Radiological Findings

We have found radiological examination of the bones a very useful aid to the diagnosis. Radiological changes occur in sickle cell anaemia as a result of—

(1) chronic anaemia;
(2) bone marrow hyperplasia;
(3) infarction in haemopoetic tissues and bones; and
(4) increased susceptibility to infections, especially osteomyelitis.

A very brief account of the common findings follows.

The Chest.—The commonest finding is cardiomegaly. Usually the enlargement is generalised, but sometimes the cardiac silhouette shows greater prominence of one side or the other. Not infrequently the pulmonary conus is prominent, giving the heart shadow a "mitral" configuration. In the younger age groups the pulmonary vessels usually show no abnormality, but with increasing age the main vessels become more prominent, particularly when pulmonary hypertension has developed. In the older children the ribs usually show evidence of marrow hyperplasia.

The Skull.—Changes are usually demonstrable except in the very young. The features most commonly seen are widening of the diploe, thickening of the outer table and increase in the thickness of the frontal and parietal bones,

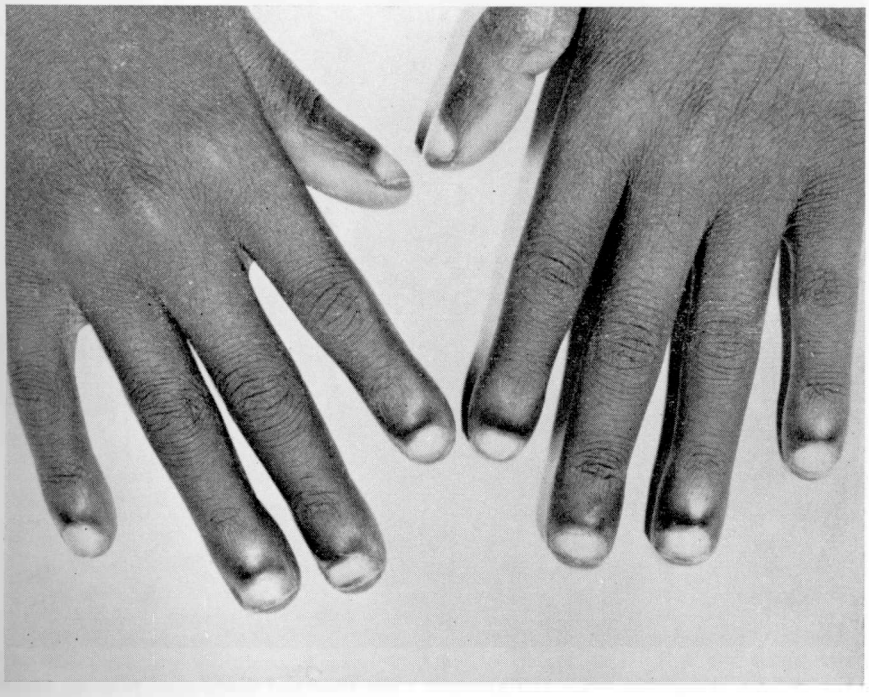

Fig. 8—Clubbing of fingers in sickle cell anaemia.

particularly the orbital roof. Prominence of the diploeic spaces gives the skull a spongy texture especially noticeable in the frontal and parietal regions in the lateral views. The "hair on end" appearance, commonly seen in thalassaemia, is only rarely found. Circumscribed areas of rarefaction probably due to infarcts are sometimes seen.

The Long Bones.—Osteoporosis, a coarse trabecular pattern, widening of the medullary cavity and thinning of the cortices are usual. Other findings which are frequently seen include periosteal reaction and circumscribed areas of rarefaction, sometimes surrounded by sclerotic bone, usually situated in the distal half of the shafts of long bones (Fig. 9). Not infrequently these lesions are multiple and may be bilateral and symmetrical. Osteomylitis is a common complication, presumably due to bacterial invasion of areas devitalised by infarction. Radiological examination often provides evidence of past osteomyelitis.

Among older patients (over 10 years of age) avascular changes in the head of the femur sometimes occur; five instances of this occurrence were recorded in our radiology department during 1958 (Cockshott, 1958).

Hands and Feet.—The general appearances are similar to those described in the long bones. "Cystic" areas are often seen near the distal ends of the shafts of the proximal and middle phalanges, and the tendency to symmetrical arrangement of these is very striking. They appear to be areas of bone absorption, which arise in relation to penetrating vascular channels. Individual small bones of the hand often show sclerosis, distortion or shortening resulting from previous infarction or infection. The swellings of hands and feet mentioned earlier may on occasion be associated with radiological evidence of gross bone destruction.

The Spine.—In older children the vertebral bodies often show increased translucency and prominence of the trabeculae, and sometimes widening and flattening associated with "cupping" in relation to the intervertebral discs. On two occasions we have seen destruction and collapse of individual vertebrae.

A Few Special Considerations

Osteitis in Sickle Cell Anaemia

Sickle cell anaemia often masquerades as osteomyelitis. The combination of fever, local pain and swelling over bone, leucocytosis and

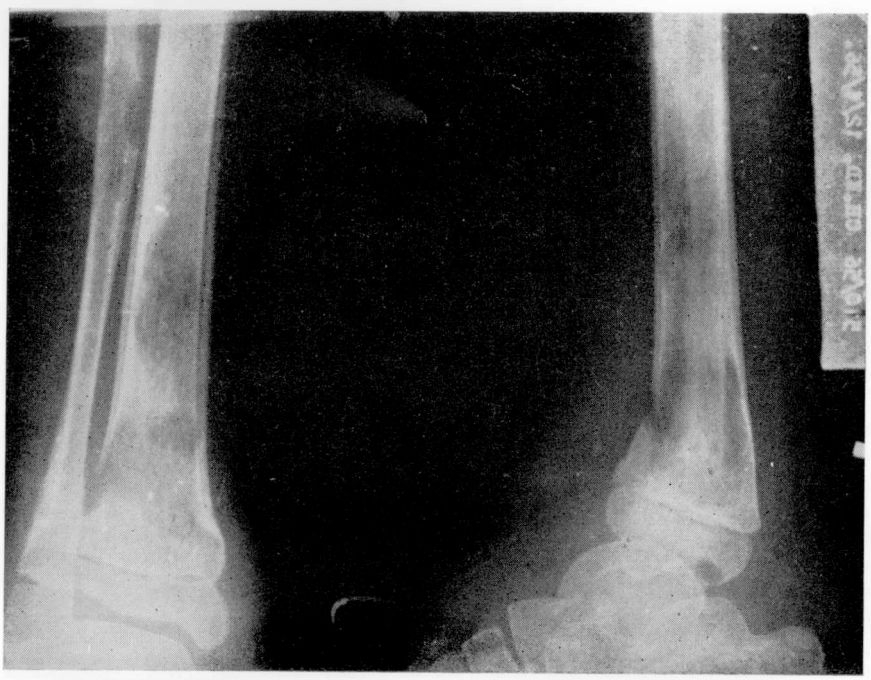

Fig. 9—Bone changes in sickle cell anaemia. The tibia and fibula show multiple areas of bone absorption and periosteal reaction. A pathological fracture is present in the tibia.

radiological changes in bone all strongly suggest bone infection. Usually, however, these episodes subside over a period of days or weeks without suppuration occurring in the affected parts. In a number of patients, however, suppuration does supervene and pathogenic organisms may be isolated from the affected sites. Among our patients who have had frank osteomylitis, several have been due to infection with strains of *Salmonellae*. This finding supports the observation of others that persons with sickle cell anaemia show a peculiar susceptibility to *Salmonella* osteitis which in normal persons is a rare clinical finding (Vandepitte *et al.*, 1953; Vandepitte and Oyo, 1956; Hook *et al.*, 1957).

Liver Function Tests

Table III shows liver function tests and liver sizes recorded in 18 of our cases. While it must be accepted that individual tests have little value as indices of liver function, our results taken as a whole in conjunction with liver size

Table III

SERUM PROTEINS, LIVER FUNCTION TESTS AND LIVER SIZE IN 18 CASES IN THE PRESENT SERIES

Series No.	Age Years	Sex	Serum Proteins			Bilirubin Total	A/Phos. K.A.	T.T. Units	ZnS.T. Units	Liver cms.
			Alb.	Glob.	A/G Ratio					
7	8	F	2.6 2.4	3.1 2.6	0.8 0.9	15.8 D 17.0 D	— —	9.5 14.0	— —	10 10
10	3	M	—	—	—	4.1 D	—	6.5	—	8-10
17	3	F	—	—	—	15.0 D 2.3	9 7.4	12.0 3.0	12.9 6.8	8 0
27		M	3.0	4.3	0.7	1.2 D	20.3	6.0	—	3-8
21	10	F	1.7	6.0	0.28	8.6 D	33.6	6.5	19.0	0
28	10	M	2.9 4.4	3.3 4.3	0.87 1.0	6.5 D 1.2 4.0	13.9 18.0 21.9	4.5 9.6 16.5	— 13.6 13.5	8 8 6
34	9	M	— — — —	— — — —	— — — —	8.8 D 25.0 D 5.0 D 0.45	45.7 33.0 35.2 22.3	8.0 14.2 4.5 5.2	10.6 18.4 — —	2 above umbilicus 2 below umbilicus
38	1¾	M	4.4	3.5	1.2	0.2	30.0	3.5	7.5	2
*39	6	M	2.9	3.2	0.9	4.5 D	37.9	5.0	—	"Huge"
41	1	M	—	—	—	1.2	20.9	4.0	—	0
48	3	F	—	—	—	11.0 D	10.5	3.0	7.0	4-6
60	5	F	1.9	4.7	0.4	5.6 D 5.9 D	28.0 54.0	14.0 11.0	18.6 14.0	3 above umbilicus
61	7	F	1.8 —	4.1 —	0.43 —	3.0 D 2.2	21.1 24.8	9.6 6.9	19.2 14.0	10 10
63	3	M	—	—	—	—	30.5	—	—	0
64	6	M	—	—	—	3.3	12.8	2.5	10.0	6-8
68	4	F	—	—	—	4.3 D	18.9	4.5	11.0	1-4
70	1½	F	—	—	—	0.45	—	7.8	5.6	0
71	9	M	3.0 —	3.7 —	0.81 —	2.56 D 1.5	23.9 26.3	1.6 1.5	4.3 5.8	2 8

Alb. = Albumen. Glob. = Globulin, both expressed in g. per 100 mls. Bilirubin expressed in mg. per 100 ml. D = direct reacting bilirubin. A/phos. = Alkaline phosphatase. K.A. = King Armstrong units. T.T. = Thymol turbidity. ZnS.T. = Zinc sulphate turbidity.

* Needle biopsy showed cirrhosis of the liver.

indicate that in many patients the disease is associated with hepatic dysfunction. This finding is in keeping with that recorded by American authors in adults in the United States, but not usually in children during the first decade (Green *at al.*, 1953). The likely explanation for the earlier onset of hepatic dysfunction in our cases is that chronic protein deficiency (a feature of the average Nigerian diet) renders the organ more susceptible to damage and thus accelerates the pathological processes of the disease.

Malaria and Sickle Cell Anaemia

Much attention has been focussed on the role of malaria in the population dynamics of the sickle cell gene, but the effect of malaria on the clinical course of sickle cell anaemia has received little attention. Malarial parasitaemia is frequently found in our cases, and our findings in respect of spleen size compared with American reports may also be interpreted as evidence of malarial infection. It has been suggested that malaria may act as a precipitating factor in the development of crises in sickle cell anaemia, and a certain amount of indirect evidence cited lends support to this suggestion (Edington, 1953; Colbourne and Edington, 1956).

Apparent response to antimalarial drugs during crises of fever and pain in many of our cases and improvement in the general state of well-being brought about in many by long-term chemoprophylaxis against malaria lend support to the suggestion that malaria adversely affects the course of sickle cell anaemia. The possible role of malaria in determining the less favourable course of sickle cell anaemia in Africa should be borne in mind and influence the management of cases. Experience in Ibadan indicates that regular chemoprophylaxis against malaria should be instituted in all cases likely to be exposed to infection.

Prognosis

Our definite impression is that the prognosis in our cases is better than that recorded in the Belgian Congo and parts of East Africa. The statement that in Africa "the majority of the homozygous (SS) sickle cell anaemia cases die before they are two years old" (J. and C. Lambotte-Legrande, 1958) does not agree with our experience. Our findings in respect of age show that the number of patients presenting for treatment decreases in succeeding age groups. It remains to be shown to what extent increasing mortality or decreasing severity of symptoms with age is responsible for the smaller number of older children seen in hospital. It is of interest to note that during 1958 our central haematology laboratory detected *29* cases of sickle cell anaemia in persons ten years of age, and of these six were over 20 years of age (Watson-Williams, 1958).

Management and Treatment

There is no known specific or curative treatment. Among measures found useful in the management of crises of the disease the following have proved their worth:—

(1) *Blood Transfusions.*—These are invaluable in the management of the acute exacerbations of the disease. Transfusions are generally not indicated if the haemoglobin level exceeds 5 g. per cent., except in patients who are shocked or who have severe pain which fails to respond to other measures. Transfusions are also indicated in cases complicated by serious infections and in those who are to undergo surgical procedures.

Blood transfusion is a hazardous procedure in patients who are in cardiac failure because of anaemia. In such cases an "exchange transfusion" should, if possible, be carried out. In children only a relatively small quantity of blood needs to be exchanged, as the object of the procedure is simply to raise the haemoglobin level without increasing the total blood volume. This is most speedily achieved by using packed cells. The femoral vein is best for this procedure and the technique employed is exactly the same as in exchange transfusions for Rhesus incompatibility.

(2) *Priscoline.*—Smith *et al.* have reported dramatic relief of symptoms following the administration of the vasodilator priscoline in crises of sickle cell anaemia. The use of the drug was based on the assumption that vasospasm may play a part in the pathogenesis of crises of the disease (Smith *et al.*, 1953). Our own experience confirms their observation that priscoline often affords dramatic relief of pain during crisis, beneficial results being obtained in some cases within a matter of minutes.

(3) *Antimalarials.* (See section on malaria.)

(4) *Antibiotics.*—Bacterial infection presents special hazards to persons with sickle cell anaemia. It may cause an anaemic crisis by depressing erythropoiesis (Singer *et al.*, 1950; Chernoff and Josephson, 1951); it frequently complicates ischaemic lesions, as is indicated by the high incidence of osteomyelitis, and it may possibly precipitate clinical crises of the disease

Table IV

Differential Diagnosis of Sickle Cell Anaemia and Sickle Cell-Haemoglobin C Disease in Nigerian Children

Finding	Sickle Cell Anaemia	Sickle Cell-Haemoglobin C Disease (Hendrickse, 1958)
Average age of cases	3.8 years Common in infants	6 years Rarely seen under two years
Limb pain	Frequent; severe	Less frequent and severe, but occasionally marked
Limb swellings— (1) Hands and feet (2) Long bones and joints	Frequent Fairly frequent	Not seen Very occasionally
Habitus	Frequently abnormal	Usually normal
Jaundice	Frequent	Usually absent
Abdominal distention	Often marked	Absent or slight
Liver	Usually enlarged	Usually *not* enlarged
Heart	Often abnormal	Usually normal
Radiological bone changes and osteitis	Common	Rarely seen in young children
Anaemia	Moderate to severe	Mild; may be absent, but may be severe in crisis
Stained peripheral blood films— (1) Sickling (2) Reticulocytosis (3) Target cells	 Usually seen Usually present Usually present	 Usually absent Absent or minimal Always present and numerous
Haemoglobin electrophoresis	Hb. S.	Hb. S. & C.

(Scott *et al.* (1951, 1955) stress the frequent association of respiratory infection and crises of the disease).

Recognition of the several ways in which infection may be deleterious to the patient with sickle cell anaemia has prompted us to use antibiotics freely in the management of exacerbation of the disease, even when overt evidence of infection is lacking.

(5) *Surgery.*—From time to time patients with severe osteomylitis require surgery. A tourniquet should never be employed in limb surgery in sickle cell anaemia (or its genetic variants), as it may precipitate gangrene. Before this was recognised, two cases of gangrene occurred in our hospital from this cause.

Differentiation of sickle cell anaemia from examination is a very useful aid to diagnosis in many cases.

Differential Diagnosis

It is obvious that many of the clinical features of sickle cell anaemia also occur in a number of unrelated conditions prevalent in tropical Africa. Their occurrence in non-sicklers should present no real difficulty, as routine sickling tests will readily eliminate this source of confusion. In children with the sickling trait who present with disease associated with anaemia, splenomegaly, etc., differentiation is less easy, but even without the aid of subtle haematology most cases can be differentiated.

Among the most valuable aids to clinical diagnosis the "rheumatoid" manifestations of sickle cell anaemia (limb pains, joint swellings, swellings of hands and feet, cardiac signs) feature prominently. This is an African paradox. In America differentiation of sickle cell anaemia from rheumatic fever and other rheumatic disorders constitutes a real problem. In tropical Africa rheumatic disorders are rarely seen. "Rheumatism" in an anaemic African child should be regarded as sickle cell anaemia until disproved. In particular, the osteoarticular swellings of the hands and feet in the very young are an invaluable aid to diagnosis; indeed, some authors regard them as pathognomonic (J. and C. Lambotte-Legrande,

1958). Malarial anaemia during infancy in trait carriers can closely simulate sickle cell anaemia, but observation of haematological response to antimalarial drugs will usually resolve the problem. In the former condition, anaemia rapidly disappears and the haemoglobin level usually returns to near normal level within a matter of weeks (Hendrickse and King, 1958). In addition to the foregoing, radiological bone its genetic variant, sickle cell haemoglobin C disease, which occurs with appreciable frequency in Ibadan (Hendrickse, 1958), can usually be made on clinical grounds, but requires electrophoresis of the haemoglobin for final confirmation. Table IV sets out points of difference in the two conditions.

Summary and Conclusions

We have found that sickle cell anaemia in Nigerian children under the age of 10 years is characterised by frequent episodes of fever, limb pains often associated with inflammatory swellings, and various gastro-intestinal complaints, including anorexia and vomiting, abdominal pain and distension, and diarrhoea. Anaemia is constantly found, but varies in severity. Hepatosplenomegaly is present in about 50 per cent. of patients in the first two years of life and increases in frequency thereafter. Inflammatory swellings of the hands and feet are commonly seen in the early years of life. Many patients have cardiomegaly and cardiac murmurs, and the incidence of these increases with age. Evidence of hepatic dysfunction is relatively frequent in the latter half of the first decade. Abnormal radiological appearances in bone are commonly seen. Osteitis is a frequent complication. Some patients show an abnormal habitus. Leg ulcers do not occur and lymphadenopathy is rare.

Comparison of our findings and those of others in Africa with the experience recorded by American authors in sickle cell anaemia shows the following differences:

In Africa the age at onset of severe symptoms is earlier; anaemia tends to be more severe; the incidence of splenomegaly is higher, and spleens tend to be larger; gross hepatomegaly and evidence hepatic dysfunction generally occur at an earlier age; limb swellings, especially those involving the hands and feet, in the early years of life, are common, whereas they are rarely reported by American authors; radiological evidence of bone involvement is more frequent and the ultimate prognosis appears to be worse.

These differences in general reflect the more rigorous conditions under which children live in Africa, but certain features of the disease, as seen by us, may be attributed to specific environmental factors. Spleen sizes are probably related to endemic malaria, and the earlier onset of liver dysfunction may be related to dietary protein deficiency. The characteristic findings in the hands and feet in African infants may well result from the customary manner in which African mothers carry their babies. The child is placed astride the mother's back, its legs encircling her waist. The position is maintained by a wrapper which covers the child and is tied in front of the mother. In this position the child's limbs are pinioned to the mother and subjected to steady gentle pressure which probably slightly impairs the peripheral circulation. Such impairment, while of no consequence in normal children, may be sufficient in sickle cell anaemia to provoke intravascular sickling in the extremities, with resultant capillary blockage and reactionary swelling.

While differences in the clinical picture of sickle cell anaemia in Africa and America may be attributed to environmental factors, the apparent difference in the severity of the disease in different parts of Africa cannot readily be explained in the same way. Differences in the age incidence in the Belgian Congo and Nigeria are of particular interest. Reference to Figure 1 will show that in the Belgian Congo more children present between the ages of three months and one year than at any other period. It has been shown that in infants in hyperendemic malarial areas the mean parasite rate rises from about 2 per cent. at three months to 80 per cent. at one year (Bruce-Chwatt, 1952). In the Belgian Congo, therefore, it appears that the period during which children acquire their first infection with malaria coincides with the age during which sickle cell anaemia is most frequently diagnosed. This suggests that malaria should be considered as a possible factor determining the age at which sickle cell anaemia presents in the Belgian Congo. Another possible explanation of these age relationships is that some of their cases were examples of primary malarial anaemia in persons with the sickle cell trait. The clinical and haematological findings in such cases can closely simulate those encountered in sickle cell anaemia (Hendrickse and King, 1958). None of the cases reported from the Belgian Congo by the Lambotte-Legrandes (1951, 1955) were confirmed by electrophoretic studies of the haemoglobin.

The apparent differences in the clinical manifestations of sickle cell anaemia in different parts of Africa merit closer study. There are no grounds at present for contending that these differences have a genetic basis, though this possibility should be borne in mind.

A careful appraisal of the influence of environmental factors on the course of the disease might point the way to more successful management of cases and thus bring about an improvement in prognosis.

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