THE SICKLE CELL TRAIT AND SICKLE CELL ANAEMIA WITH SPECIAL REFERENCE TO AN INVESTIGATION IN THE GOLD COAST.

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Part I.

A GENERAL ACCOUNT OF THE SICKLE CELL TRAIT AND SICKLE CELL ANAEMIA.

INTRODUCTION.

The sickle cell trait is a hereditary constitutional anomaly of the blood probably limited to those of African descent. It is transmitted by either sex as a dominant Mendelian characteristic and characterised by the tendency of the red blood cells, when deprived of oxygen, to assume a peculiar oat, hollyleaf or sickle shape, (plate, I). The majority of the people exhibiting this trait are symptomless but in certain cases a haemolytic anaemia developes and when such an anaemia occurs it is called sickle cell anaemia. It must be emphasised that the sickle cell trait is a supposedly harmless anomaly of the blood, whereas sickle cell anaemia is a serious pathological condition.

The reported incidence of the sickle cell trait in the African native is much higher than in the American negro. It would appear, however, from the literature that sickle cell anaemia is rare in Africa and common in the United States of America. The present author was also of the opinion that sickle cell anaemia was rare in Africa and, in a publication in association with two medical colleagues, was responsible for the statement that the sickle cell trait was of no practical clinical importance in the group of 255 Gold Coast villagers examined, COLBOURNE, EDINGTON & HUGHES (1950). The incidence of the sickle cell trait in the 255 villagers was reported, in the paper mentioned above, to be 22.4%.

It was therefore considered important to investigate this condition and to attempt to determine the significance of the sickling phenomenon as a cause of morbidity and mortality in the Gold Coast African.

The present paper is the result of two years further work on this problem, undertaken while the writer was attached to the Medical Research Institute, Accra, Gold Coast. The investigation falls naturally into four parts:

1.) Surveys of the population in the Accra District of Gold Coast to determine the incidence of the sickle cell trait and of sickle cell anaemia.

2.) An investigation of all patients suspected to be suffering from sickle cell anaemia referred for examination to the writer by medical colleagues.

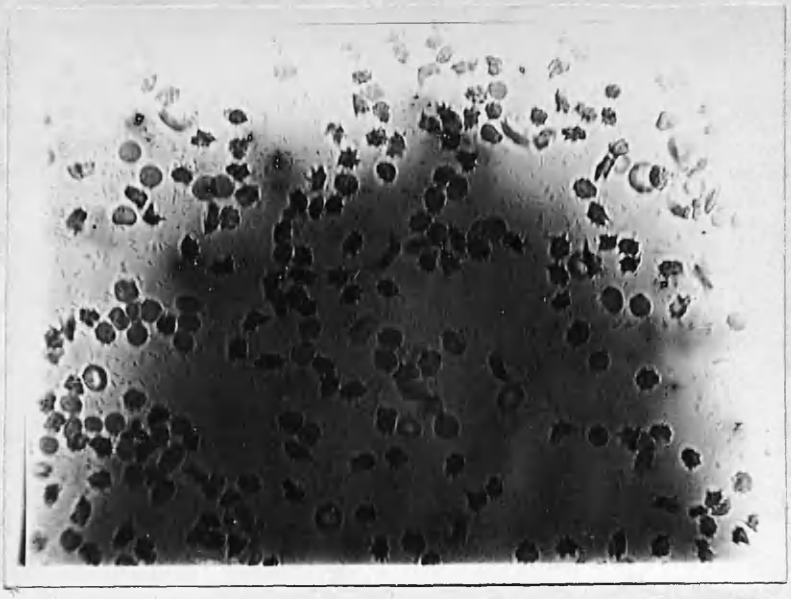
3.) An investigation into the incidence and significance of the target cell in peripheral blood smears of Africans in the Accra District.

4.) A survey of the autopsies performed in the Gold Coast Hospital by the writer to discover if the sickling phenomenon was a cause of mortality.

The original investigation as planned did not include Part 3 above, but the characteristic feature of the first case of sickle cell anaemia diagnosed by the writer was the presence of numerous 'target cells' in the peripheral blood and sternal marrow smear. (PLATE 2.)

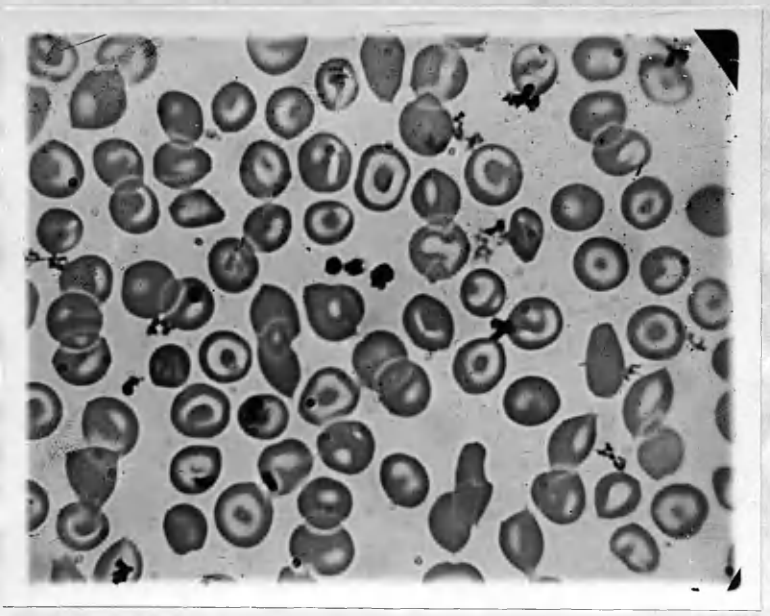
This introduced the additional factor of the significance of the target cell as DAMESHEK (1940) and SCHIEBER (1945)

PLATE 1



ERYTHROCYTES WHICH HAVE BEEN WASHED 10 TIMES IN NORMAL SALINE, SHOWING OAT, HOLLY LEAF AND SICKLED CELLS WITHIN 5 MINUTES WHEN MIXED WITH AN 18 HOUR BACT. COLI CULTURE

PLATE 2



SMEAR OF PERIPHERAL BLOOD OF M.A. SHOWING NUMEROUS TARGET CELLS. (CASE REPORT NUMBER 1, APPENDIX C.) +700

had described a haemolytic anaemia clinically indistinguishable from sickle cell anaemia (apart from the sickling of the red blood cells) in which they considered that the causal agent was the target cell. DAMESHEK named the condition Target Cell Anaemia. This first patient might well have been suffering from 'target cell anaemia' with sickling of the red blood cells a coincidental finding or, on the other hand, this might be a true case of sickle cell anaemia. Accordingly it was considered necessary to investigate the incidence and importance of the target cell in the peripheral blood of Africans in the Accra District of the Gold Coast.

It is stated in COLONIAL RESEARCH (1949) that the condition which has been described as sickle cell anaemia can be recognised in Uganda as being malarial anaemia in persons harbouring the sickle cell trait. Case and autopsy reports have accordingly been given in full in this dissertation as it is felt that the reader must be given every opportunity to criticise the diagnosis of sickle cell anaemia arrived at in a district where malaria is hyper-endemic.

A historical summary and a review of the literature are also included in the first part of this paper.

HISTORICAL SUMMARY.

As the present investigation was performed in Africa the history of the sickle cell trait and of sickle cell anaemia in Africa is given separately below and excluded from the general historical review.

GENERAL HISTORICAL REVIEW.

Elliptical human erythrocytes were described by HAYEM (1899). The brothers SERGENT (1905) described 'corps en demilune' in peripheral blood smears and demonstrated that these corpuscles were not artefacts. BRUMPT (1908) also noted the presence of 'demilune' cells in malaria and considered that they were vacuolated giant corpuscles. LANGERON (1911) claimed that these cells could be produced in rats and guinea pigs by injecting massive doses of lead acetate and considered that the sickled cells were the result of toxic action. This work has never been confirmed.

It was in 1910, however, that HERRICK described a type of anaemia in a negro youth from the West Indies in which the red blood cells were peculiarly elongated and sickle shaped. A similar type of anaemia was reported from Virginia the following year by WASHBURN (1911). A third case was reported by COOK & MEYER (1915) and EMMEL (1917), studying the erythrocytes from this case, was the first to note the changes occurring in the erythrocytes in sealed moist preparations of the peripheral blood. It was also noted that the erythrocytes of the patient's father behaved in

a similar manner. The possiblity of a familial condition was considered. MASON (1922) reported the fourth case and first called the condition Sickle Cell Anaemia.

The real understanding of sickle cell anaemia, however, dates from 1923 when SYDENSTRICKER and his colleagues performed the first autopsy and TALIAFERRO & HUCK described the sickling phenomenon as a dominant Mendelian characteristic. In the same year both HUCK and SYDENSTRICKER demonstrated that the disease was not a rarity and noted that the erythrocytes of apparently normal negroes might sickle. In the following year SYDENSTRICKER (1924, 464, 465) described latent and active forms of sickle cell anaemia. Considerable confusion reigns in the literature of the next decade as many writers did not grasp the fact that the sickling phenomenon could occur in the blood of an otherwise normal negro. In 1926 COOLEY & LEE suggested the term sicklaemia for the latent type of sickle cell anaemia, HAHN (1928) suggested the term 'sickle cell trait'. These are the terms which have been most commonly used in the literature to denoted the harmless form of the sickling aberration. Various other terms have been suggested to distinguish the sickle cell, the sickle cell trait and sickle cell anaemia. GRAHAM & McCARTY (1927) suggested meniscocyte, meniscocytosis and meniscocytaemia and HAHN & GILLESPIE (1927) suggested drepanocyte, drepanocytaemia and drepanocytic anaemia respectively. The same authors noted the importance of anoxaemia in the production of sickled cells and suggested

that the presence of reduced haemoglobin was responsible for the phenomenon. In the same paper the first splenectomy in the treatment of the condition was recorded, although this had been suggested as a possible form of treatment by SYDENSTRICKER in 1924.

The first bone changes on radiological examination were noted by GRULEE & ROSE and reported by COOLEY, WITWER & LEE (1927). CASTANA (1925) reported the first case in a European and COOK in 1930 first drew attention to the cerebral manifestations which might occur in sickle cell anaemia.

It is of interest to note that O'ROKE (1936) noted sickle cell anaemia in 14 out of the 178 deer he examined, and PONDER (1945) recorded the same phenomenon in the elk.

Apart from improved techniques in the detection of the trait and amplification of the clinical and pathological findings little new emerged in the understanding of sickle cell anaemia until NEEL in 1947 suggested that sickle cell anaemia might be a homozygous manifestation of the sickle cell trait. A further advance occurred in 1949 when ITANO & PAULING reported electrophoretic differences in the behaviour of the sickle cell anaemia haemoglobin when compared with normal haemoglobin. These reports will be discussed later.

I suggested this myself in 1945 in letters to Acera A.J.L.

AFRICA

The history of the sickle cell trait and of sickle cell anaemia in Africa lags sadly behind that of its American counterpart. ARCHIBALD (1925) recorded the first case of sickle cell anaemia in Africa and from that date until 1942 there are only six reported cases of sickle cell anaemia available in the literature, and three of these are by one author SMITH (445,446 & 447). The annual medical reports of the various African colonies are not, however, included in this statement as they appear to have escaped the attention of all previous writers. A number of references are available in the annual medical reports of Nigeria and the Gold Coast. The incidence of the trait was first noted to be high in Africa in 1936 GOLD COAST (199) and in the same report it was stated that there was no particular reason to consider the sickle cell trait dangerous.

Since 1942 the volume of literature has increased considerably. The majority of writers stress the high incidence of the trait in Africa and the low incidence of sickle cell anaemia. ROBINSON (1945) was the first to describe the rapid method for detecting the trait utilising bacterial cultures.(PLATE 1). ALTMANN (1947) demonstrated that the normal erythrocytes were not destroyed more rapidly than usual when transfused into a patient suffering from sickle cell anaemia. LEHMANN & RAPER (1949) noted the marked tribal variations in the incidence of the trait and BEET (1949)

studying the genetics of the sickle cell trait in a Bantu tribe, considered that the homozygous theory of the inheritance of sickle cell anaemia was correct. LEHMANN (1951) considered that this was most improbable.

On the whole the reports from Africa are confusing and the part that the sickling phenomenon plays in the appalling morbidity and mortality rates of the African has yet to be assessed.

REVIEW OF THE LITERATURE

As already mentioned much confusion exists in the earlier literature on sickle cell anaemia as many writers did not recognise that sickling of the red blood cells could occur in an otherwise normal individual. A few writers still consider that the sickling phenomenon should always be considered a potential cause of morbidity and BAUER (1940) suggested the term 'sickle cell disease' and considered that persons harbouring the supposedly harmless trait might exhibit symptoms and signs due to blockage of blood vessels by sickled erythrocytes in situations where local anoxaemia had occurred following circulatory stasis. The evidence in favour of this view is unconvincing and is not generally accepted WINTROBE (1947). There is no doubt, however, that sickle cell anaemia has been well named ' A Great Masquerader ' WINSOR & BURCH (1945, 530). It is accepted that the symptomatology, pathological findings and clinical signs described in proven cases of sickle cell anaemia are many and varied. These have been adequately described by WINTROBE (1947) and, as they are referred to later in this paper, are not discussed further in this review. Agreement on the aetiology of sickle cell anaemia, however, has not yet been reached. The literature on this problem is therefore discussed in some detail under various headings in the following paragraphs and in the writer's discussion of the results of the investigations reported in this thesis.

THE INCIDENCE OF THE SICKLE CELL TRAIT

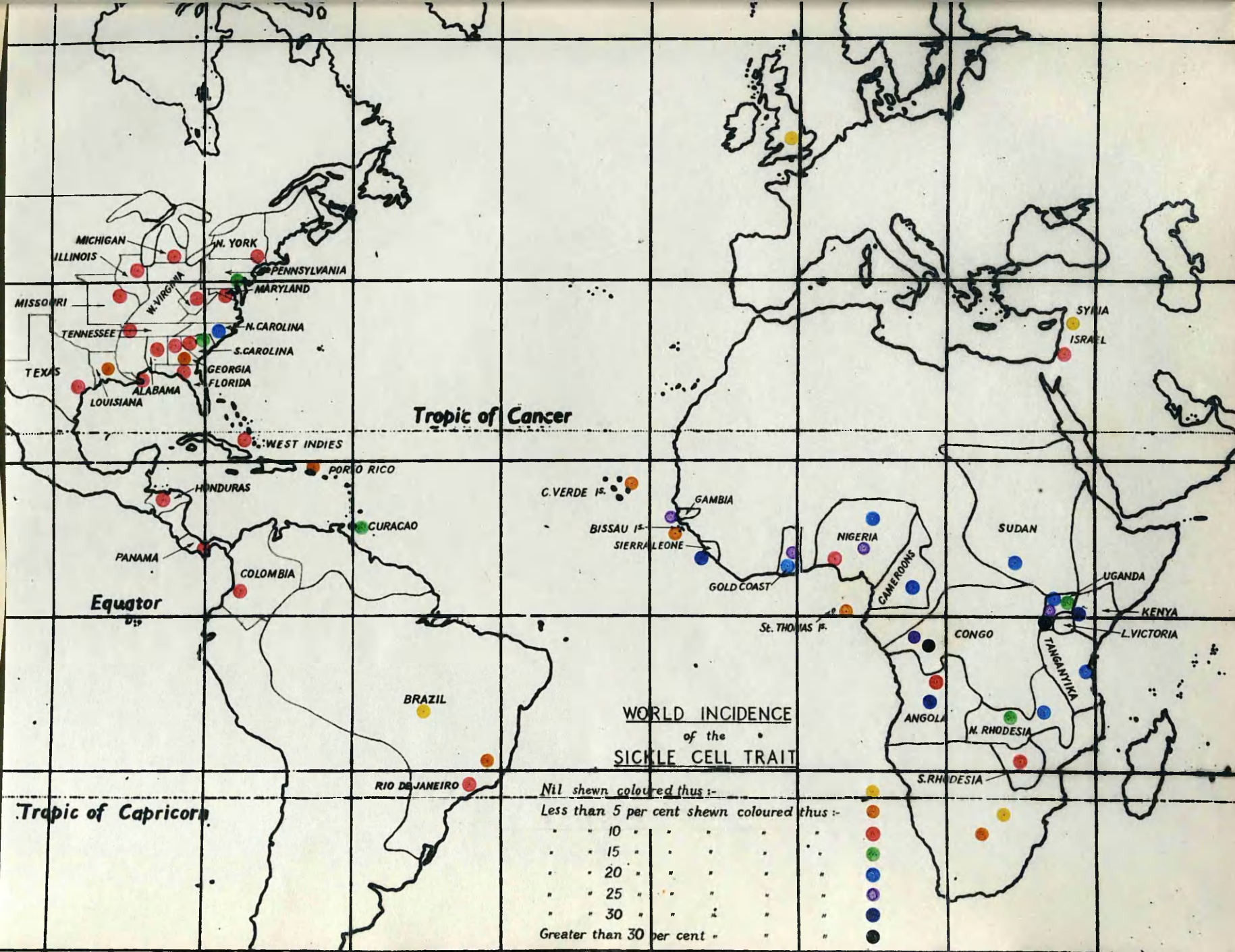
The sickle cell trait is confined exclusively to the Negro race and the presence of the sickling phenomenon in the blood of a white person is evidence of Negro ancestry EDITORIAL, J. AMER. MED. ASS., (1947). The blood of 3,688 non-negroes in various parts of the world has been examined and the sickling phenomenon has never been detected (Appendix A). On the other hand the sporadic occurrence of the sickle cell trait and of sickle cell anaemia has been reported in the white race in 64 instances.* The majority of these reports concern patients of Italian, Greek or Sicilian descent and it is suggested that the possibility of negro ancestry in the distant past cannot be excluded. CHOREMIS (1951), however, reported 15 patients suffering from sickle cell anaemia in a Greek village of 6,000 inhabitants. This fact, in the writer's opinion, throws doubt on the accepted statement that the sickle cell trait in a white person is definite evidence of negro ancestry and the further investigations promised by the above mentioned author should be illuminating. It is also of interest to note that SILVERSTRONI & BIANCO (1946) have reported a congenital type of haemolytic anaemia

(* 12; 50; 74; 79; 84; 89; 90; 96; 100; 105; 165; 183; 208; 207; 217; 305; 306; 334; 307; 355; 379; 402; 434; 435; 438; 501; 508; 510; 518; 536.)

in Italians in which a mixed inheritance of the sickle cell trait and Cooley's trait has been found.

The incidence of the sickle cell trait throughout the world is shown on Map 1. The recent report of the trait occurring in Southern India, LEHMANN & CUTBUSH (1952), is not included. The detailed figures are given in Appendix A. It is at once apparent from the map that the incidence of the trait is much higher in East, West and Central Africa than in the Americas. GRAHAM & McCARTY (1930) suggested in America that sickling might be of ethnological importance and urged workers abroad to investigate this problem, but it was not until 1949 that LEHMANN & RAPER drew attention to the marked tribal differences in the incidence of the trait in Africa and discussed its bearing on ethnology. The incidence of the trait varied in different tribes from 0.2% in the South African Bantu to 86.8% in the Lutomi tribe in Uganda.

HODGES (1950) stated that the incidence of sickling increased with the dilution of the 'pure' negro by small amounts of white blood. In the writer's opinion Map 1 contradicts this statement and would tend to prove that the sickle cell trait has its highest incidence in Central Africa and decreases in incidence in direct proportion to the admixture of other tribal or racial groups. As the aetiology of sickle cell anaemia is not yet fully elucidated, any conclusions drawn from the incidence of the sickling gene in a community must be purely conjectural. It follows that


MICHIGAN
ILLINOIS
N. YORK
PENNSYLVANIA
MARYLAND
W. VIRGINIA
MISSOURI
TENNESSEE
N. CAROLINA
S. CAROLINA
GEORGIA
FLORIDA
TEXAS
ALABAMA
LOUISIANA
Tropic of Cancer
WEST INDIES
PORTO RICO
HONDURAS
CURACAO
PANAMA
COLOMBIA
Equator
BRAZIL
RIO DEJANEIRO
Tropic of Capricorn
C. VERDE Is.
GAMBIA
BISSAU Is.
SIERRA LEONE
GOLD COAST
NIGERIA
CAMEROONS
St. THOMAS Is.
SYRIA
ISRAEL
SUDAN
UGANDA
KENYA
L. VICTORIA
CONGO
TANGANYIKA
ANGOLA
N. RHODESIA
S. RHODESIA
WORLD INCIDENCE
of the
SICKLE CELL TRAIT
Nil shewn coloured thus :-
Less than 5 per cent shewn coloured thus :-
" 10 " " " " "
" 15 " " " " "
" 20 " " " " "
" 25 " " " " "
" 30 " " " " "
Greater than 30 per cent " " "

the ethnological importance of the sickle cell trait cannot be accurately assessed until its importance as a factor in mortality is known.

The incidence of the sickle cell trait has been reported to be ;

A). Higher in the younger age groups. BEET (1947), FINDLAY ET AL (1946) and SWITZER (1950).

B). Similar in all age groups. LEHMANN (1951), McGAVACK & GERMAN (1944), PARENT (1950), RAPER (1949), WATSON (1948) and COULBOURNE ET AL (1950).

C). Lower in the younger age groups. MACKEY (1949).

The incidence of the trait has not been found to be significantly raised in any specific disease.

THE INCIDENCE OF SICKLE CELL ANAEMIA.

The incidence of the sickle cell trait has been easy to assess but it has been found impossible to assess the incidence of sickle cell anaemia either in America or Africa. No statistically significant figures are available in the literature.

The incidence of sickle cell anaemia to the sickle cell trait has been variously reported in America as :

1 : 2 (approx.) WINSOR & BURCH (1945,530);

1 : 2.4 MERA (1943); 1 : 5 OGDEN (1943);

1 : 9 DIGGS ET AL (1933); 1 : 15 HENDERSON & THORNELL (1946);

1 : 40 SYDENSTRICKER (1924, 465) ; and

1 : 71 SWITZER & FOUCHE (1948).

There is obviously great disparity in these figures, but they do prove that sickle cell anaemia is relatively common in America when it is remembered that approximately 900,000 negroes in the United States of America exhibit the trait. BEACHEM ET AL (1950). McGAVACK & GERMAN (1944) considered that sickle cell anaemia was the most common primary blood dyscrasia in negro hospital patients in the Southern United States.

On the other hand, sickle cell anaemia is considered to be rare in Africa in spite of the fact that the incidence of the trait in the African native may be more than double that of the American negro. ROBERTSON ET AL (1947) estimated the incidence of the anaemia to the trait in West Africans

to be 1 : 151. MURRAY LYON (1944) stated that many hundreds of cases in West Africans were tested for the trait and the incidence was 20%. In only a few instances, however, had the men any symptoms or disability. MACKEY (1949) saw only one case of sickle cell anaemia in Dar es Salaam when investigating the incidence although it was estimated that there were 8,000 trait positive Africans in the area. GELFAND (1944) stated in his text book 'The Sick African' that he had never seen a case of sickle cell anaemia in the African native. CULLINAN (1946) discussed medical disorders in East Africa and not only did not mention sickle cell anaemia, but found that the incidence of diseases of the blood was higher in European personnel than in the African native. RAPER (1946,386) stated that the sickling aberration was much less to be regarded as a cause of morbidity amongst Africans than it was amongst negroes in the Unites States of America and elaborated this theme in a further publication RAPER (1950). WILLIAMS (1938), discussing child health in the Gold Coast, did not mention the trait or the anaemia as a probable cause of morbidity in children and stated that acute rheumatism was remarkable for its rarity which leads to the conclusion that the typical haemolytic crises of sickle cell anaemia are indeed rare. The rarity of the anaemia in Africa has been emphasised by other writers. BEET (1947); LEHMANN (1951); TEXEIRO (1944); TRINCAO ET AL (1950); JELLIFFE (1952); EDITORIAL (1952).

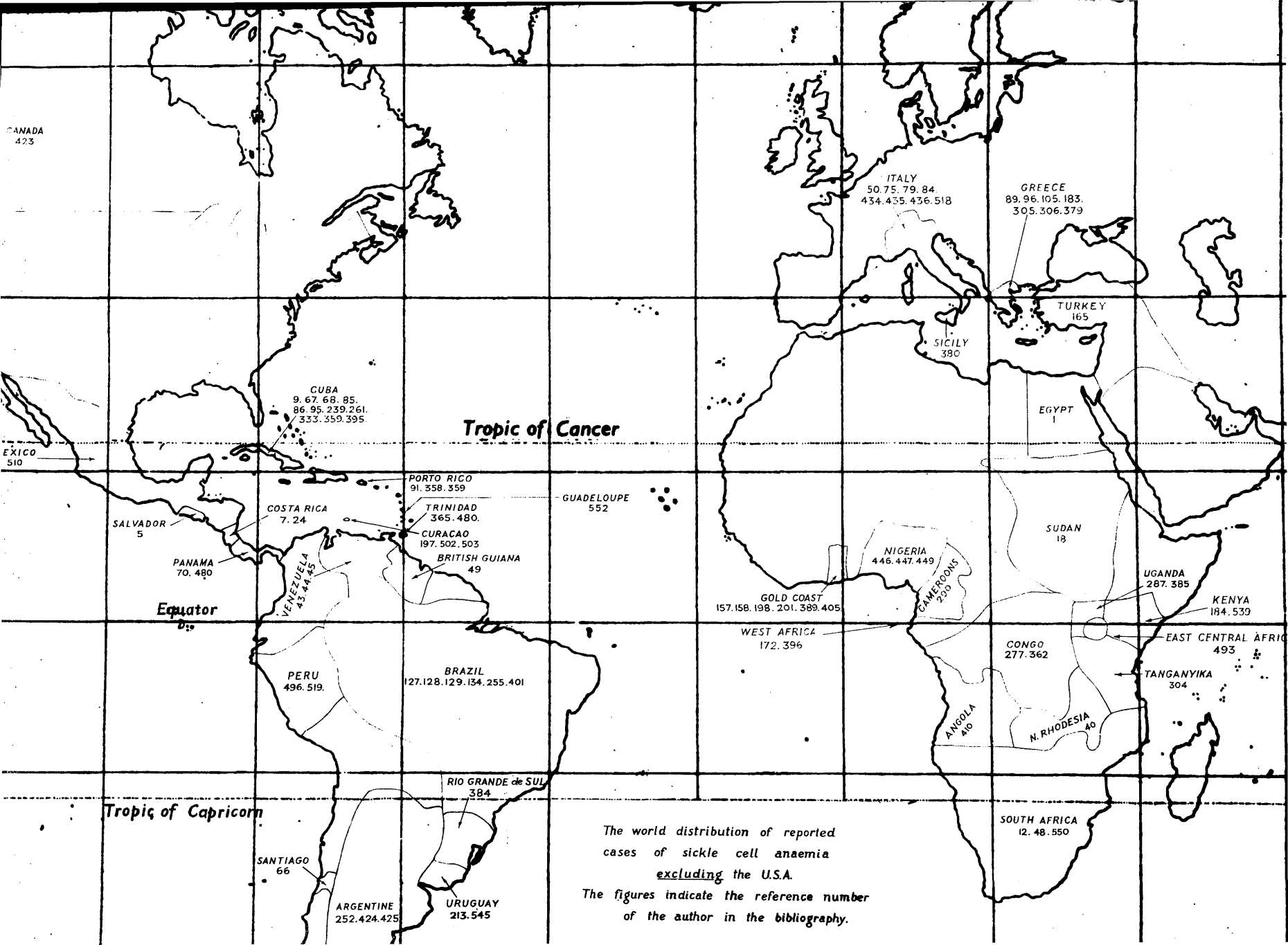
On the other hand, SMITH (1943) estimated the incidence of the anaemia to the trait to be 1 : 5 in Nigeria and since this investigation was commenced two papers have been published tending to discredit previously published work which has emphasised the rarity of sickle cell anaemia in Africa. FOY ET AL (1951) in Kenya, described no cases but stated that there were 4 cases of sickle cell anaemia in the 13 trait positive Africans examined. It was also stated that the anaemia was commonest among infants and newborn babies. This statement, however, cannot be accepted as it has been shown that the neonate is probably protected against sickle cell anaemia WATSON (1948,514). LAMBOTTE (1951) stated that 6% of trait positive Africans in Leopoldville suffer from sickle cell anaemia but, although the paper is reasonable only one case of sickle anaemia was described in detail and the truth of his statements could not be assessed.

It is of interest to note that, of the 161 recorded cases from Africa, details have been given in only 69 and included in these 69 reports are three Indian, two white and one Arab patient. The total cases of sickle cell anaemia reliably reported in the African native is thus 63 which is a surprisingly low figure when it is realised that there are probably ten million trait positive natives in Africa.

The apparent difference in the incidence of sickle cell anaemia in Africa and America was noted by McGAVACK & GERMAN (1944) and they suggested that the admixture of white and

negro blood might be responsible for the anaemia. RAPER (1950) discussed this theory and considered that it was the most likely explanation of the apparent discrepancy in incidence.

The distribution of reported cases of sickle cell anaemia is shown on Map 2 and details are given in Appendix B. The distribution of reported cases in the United States of America has purposely been omitted in view of the many hundreds reported from that country. WINTROBE (1947) has mistakenly stated that cases of sickle cell anaemia have been reported from Algeria. The reference given is SMITH (1933) who reported the cases in question from Nigeria. ABBASSY (1951) has perpetuated this error.



The world distribution of reported cases of sickle cell anaemia excluding the U.S.A.

The figures indicate the reference number of the author in the bibliography.

THE INHERITANCE OF SICKLE CELL ANAEMIA

It is accepted that the sickle cell trait is inherited as a Mendelian dominant characteristic. TALIAFERRO & HUCK (1923) and BEET (1949,41). NEEL & VALENTINE (1947) and NEEL (1949) suggested that there existed one gene which in the heterozygous condition resulted in the sickle cell trait and in the homozygous condition in sickle cell anaemia, the counterpart of Cooley's trait and Cooley's anaemia in the Mediterranean. This was a most attractive theory and was supported by DAMESHEK in an EDITORIAL (160) and by BEET (41) in 1949. There are, however, many reports in the literature of authenticated cases of sickle cell anaemia in which neither or only one of the patient's parents sickled. WATSON (1948,514) discussed this problem and concluded that Neel's theory was not well supported factually. LEHMANN (1951) reviewed the African literature and arrived at the same conclusion. In 1951 NEEL investigated 75 family groups and haematological investigations were performed on 465 individuals. He concluded that the observations were not definitely compatible with the heterozygous-homozygous theory of inheritance and stated that this theory might require to be modified. Two exceptions to the rule that both parents of a child with sickle cell anaemia or one parent of a child with the trait must sickle were discovered. In view of these exceptions the following possible explanations were given :-

(a) certain individuals heterozygous for the sickling gene do not sickle.

(b) the legal father may not be the biological father.

(c) sickle cell anaemia may be due to a single gene with an unknown genetic factor.

(d) an apparently normal parent may contribute a sickle cell gene to one or more of his offspring in consequence of a mutation.

THE HAEMOGLOBIN IN SICKLAEMIA AND SICKLE CELL ANAEMIA.

New facts on the aetiology and inheritance of sickle cell anaemia have been brought to light by recent work on the structure and behaviour of normal and sickle cell haemoglobin. TROUGHT (1932) showed that the normal haemoglobin of the newborn differed from that of the adult and persisted for at least one month after birth and disappeared by 18 weeks. WATSON (1948, 514) examined 226 newborn Negro infants and found that 19 sickled. The sickling of the red blood cells in the infant differed considerably, however, from that of the adult. It was found that the red cells sickled much more slowly and, that, using the most efficient methods of detection, the mean percentage of cells sickling in the 19 infants was 11%. In the adult 100% of the red blood cells sickled. 11 infants were followed up over four months and it was found that the percentage of sickled cells gradually increased to 90%. It was considered that this investigation indicated that the low percentage of sickled cells in the blood of neonates was due to the presence of foetal haemoglobin and

was a protective measure against the low oxygen tension occurring in utero. SCOTT ET AL. (1948) also described a quantitative and qualitative suppression of the sickling phenomenon in newborn negro infants.

It would thus appear that the newborn infant should not suffer from sickle cell anaemia. There are only two reports in the literature of sickle cell anaemia occurring under the age of 4 months.* COHEN ET AL. (1947) described sickle cell anaemia in a Puerto Rican girl aged 1 month. Only 80% of her erythrocytes sickled at the end of 24 hours and the blood of neither of the parents exhibited the trait. Death occurred 6 hours after a laparotomy and, in the writer'S opinion, the autopsy findings were not convincing. FRAZIER & RICE (1950) described a haemolytic anaemia occurring in a 19 day old negro infant. Only 40% of the erythrocytes sickled on the 35th. day.

On the other hand SINGER ET AL. (1951) stated that foetal haemoglobin was found in normal infants up to 2 years of age. They studied 60 individuals with the trait and 36 suffering from sickle cell anaemia. The haemoglobin of the 60 trait carriers behaved normally on alkali denaturation, whereas the haemoglobin of the 36 cases of sickle cell

* HELDRICH, F.J., J.Pediatrics, 39, 90, (1951) has recently reported a third case of sickle cell anaemia in a newborn infant but the author has been unable to consult the paper.

anaemia was resistant. It was suggested that, in contra-distinction to the papers of WATSON & SCOTT mentioned above, in sickle cell anaemia foetal haemoglobin (i.e. resistant to alkali denaturation) might persist into adult life.

PAULING ET AL (1949) reported differences in the electrophoretic behaviour of normal and sickle cell anaemia haemoglobin. The haemoglobin molecule in sickle cell anaemia was found to carry more positive charges than the normal haemoglobin molecule. It was therefore considered that the chemical affinity of this molecule was high and that one end of the molecule was able to form a bond with the opposite end of another. A pseudocrystallisation thus occurred which twisted the red blood cell out of shape. The presence of oxygen prevented this clamping of the molecules. The haemoglobin from carriers of the trait appeared to be a mixture of normal and sickle cell anaemia haemoglobin. Differences in normal and sickle cell anaemia haemoglobin have also been reported by ITANO & PAULING (1949) and HARRIS (1950).

WELLS & ITANO (1951) found that, in 42 trait positive negroes examined, 24-45% of the total haemoglobin was sickle cell anaemia haemoglobin and the remaining 55-76% was normal. In 3 patients suffering from sickle cell anaemia 80-95% of the total haemoglobin was sickle cell anaemia haemoglobin and only 5-20% was normal. This was considered evidence that all shades of clinical variation between the harmless trait and the severe anaemia might

exist. It was also considered that this was evidence rather against the simple homozygous theory of the inheritance of sickle cell anaemia and the possibility of a quantitative type of inheritance as well as a qualitative should be considered.

KAPLAN and his colleagues in 1951 described a third type of haemoglobin occurring in sickle cell anaemia and claimed that this haemoglobin 111 was inherited as a Mendelian dominant and was responsible for a benign form of sickle cell anaemia. This work has not yet been confirmed.

As has been shown in the foregoing paragraphs, the mode of inheritance and the aetiology of sickle cell anaemia are still undecided.

THE MECHANISM OF HAEMOLYSIS IN SICKLE CELL ANAEMIA.

The following abnormalities have been described in sickle cell anaemia.

a.) Sickling of the erythrocytes occurs when the oxygen tension of the blood falls. The critical tension has been stated to be 40-45 mm. Hg. SCRIVER & WAUGH (1930). The majority of the erythrocytes revert to a discoidal form when the blood is reoxygenated but a small percentage may fail to do so.

b.) The haemoglobin is abnormal. (page 18).

c.) The life span of the red blood cell from a patient with sickle cell anaemia when transfused into a normal individual is much shorter than normal. Normal red blood cells when transfused into a patient suffering from sickle cell anaemia survive normally. ALTMANN (1947), CALLENDER & NICKEL (1947) and SINGER ET AL (1948, 443).

d.) The osmotic fragility of the sickle cell is decreased but the mechanical fragility is increased CALLENDER & NICKEL (1949), HARRIS (1950) and SHEN ET AL (1949).

From these observations the explanation of the haemolytic process in sickle cell anaemia would thus appear to be the relatively simple process of anoxia producing sickled erythrocytes which are then dealt with by the reticuloendothelial system and by intravascular fragmentation of the erythrocytes abnormally sensitive to mechanical trauma. In practice, however, this simple explanation has not sufficed and the literature abounds

with conflicting statements.

FINDLAY ET AL (1947) and HENDERSON & THORNELL (1946) found that flying had no adverse effect on trait positive individuals. One of Henderson's patients, suffering from sickle cell anaemia, withstood the lowered oxygen tension effected by ten minutes at 16,000 feet better than normal controls. The exact oxygen tension of the blood was not estimated but DAVIS (1944) found that the mean venous oxygen pressure at 20,000 feet was 19.8 mm. Hg. REINHARD ET AL (1944) and TINSLEY ET AL (1949) noted that oxygen administration of varying duration up to 20 days had an adverse effect on patients suffering from sickle cell anaemia. The haemolysis was not arrested and haemopoiesis was depressed although the degree of intravascular sickling was lowered.

DIGGS (1932) discussed the blood picture in 74 cases and stated that sickled cells in a blood smear were the exception rather than the rule. SINGER & ROBIN (1948) found that there was no correlation between the number of sickled cells in the preparation of the rapidity and degree of sickling present and the presence of either the trait or the anaemia. Other authors have claimed that, as the red blood cell ages, it sickles more readily and does not revert to the normal shape when reoxygenated. LONDON ET AL (1949), by the use of N15 labelled glycine, considered that the red blood cells were destroyed in an indiscriminate manner rather than as a function of their age.

MURPHY & SHAPIRO (1945) studied the pathology of sickle cell disease and considered that the diverse symptoms and signs were explained by mechanical blockage of the smaller blood vessels by sickled erythrocytes with consequent thrombosis, infarction and fibrosis. The haemolytic manifestations of the disease were due to lysis and resolution of these multiple thrombi. Thromboses of blood vessels were the most constant pathological finding in sickle cell disease. PRATT THOMAS & SWITZER (1949), however, considered that thrombi were the exception rather than the rule.

PONDER (1951) considered that stasis, anoxia, the accumulation of metabolites and local tissue lysins might be responsible for the haemolysis. No satisfactory explanation however has been given which will account for the continuous haemolysis and sudden acute episodes found in sickle cell anaemia. As previously stated, lowering the oxygen tension of the blood has had no adverse effect on patients suffering from sickle cell anaemia so there would appear to be some additional factor responsible for the haemolysis. It is interesting to note that JOSEPHS (1938) reported that the injection of normal plasma or of a protein free plasma concentrate reduced the rate of blood destruction in patients suffering from sickle cell anaemia. KAPLAN (1949) confirmed these findings but the effect was transitory and tended to reversal with repeated injections. There may thus be in sickle cell anaemia lack of an undescribed anti-

haemolytic factor in addition to the sickling phenomenon.

Part II.

SURVEYS OF THE POPULATION IN THE ACCRA DISTRICT OF THE GOLD COAST.

Part II of this paper records the results of surveys performed on selected groups of the population in the Accra District of the Gold Coast. Expediency rather than choice determined the groups selected for investigation. It is, unfortunately, most difficult to survey a random sample of the population of the Gold Coast. Illiteracy, polygamy, superstition and family reticence are factors which require endless patience to overcome. Consequently groups had to be chosen which were easily accessible and over which some control could be exercised. The groups investigated are listed below.

a.) 327 inmates of a Boy's Industrial School.

b.) 428 students and nurses in training.

c.) 200 school children.

d.) 123 pregnant patients suffering from anaemia.

e.) 417 mothers and 384 newborn babies.

f.) 125 hospital patients.

An attempt was also made to examine children under the

age of 5 years attending the children's clinic. This was unsuccessful as the number defaulting was high.

In addition to the groups listed above 255 villagers had already been examined (page 1).

The groups are not strictly comparable. The first three (a,b, and c) are composed of 'healthy' Africans and the second three (d, e, and f) of hospital patients. The method of investigation varied with each group and these variations will be described separately as they occur. In all cases however, the rapid bacterial method ROBINSON (1945) was utilised to detect the presence of the sickle cell trait. Haemoglobin was estimated by Sahli's method using two haemoglobinometers which were afterwards kindly calibrated by Dr. J. V. Dacie at the Postgraduate Medical School, Hammersmith, and by Dr. J. N. Marshall Chalmers at St. Georges Hospital. The packed cell volume, when recorded, was estimated by centrifuging oxalated venous blood (Wintrobe's method) in a haematocrit tube at 3,000 revs. per minute for 30 minutes. Similarly red and white cell counts were performed in three sets of commercial pipettes which were checked against each other and against normal individuals (European). They consistently gave similar results and it is not felt that grave inaccuracies have resulted.

It was hoped that the investigation of these groups would reveal not only the incidence of the sickle cell trait in the population but also the incidence of sickle

cell anaemia. The diagnosis of sickle cell anaemia in the Gold Coast African is not a simple task. The 'normal' values of the Gold Coast African in clinical medicine are unknown. The writer, in conjunction with Drs. M.J.Colbourne and M.H.Hughes (COLBOURNE ET AL., 1950), in an attempt to discover the 'normal' clinical findings, thoroughly investigated a village of 255 inhabitants in the Southern Gold Coast. The infirmities from which these villagers suffered were truly appalling and are shown in Table I.

TABLE I.

THE PERCENTAGE INCIDENCE OF DISEASES IN A VILLAGE OF 255 INHABITANTS.

Condition.	%. Incidence.
Ancylostomiasis.	52.
Ascariasis.	76.
Enlargement of the liver.	33.
Enlargement of the spleen.	46.
Guinea worm infestation.	52.
Malarial parasitaemia.	32.
Signs of malnutrition.	26.
Schistosomiasis.	9.
Streptocerciasis.	21.
Yaws.	75.
Herniae.	10.
Sickle cell trait.	22.

The blood counts, haemoglobin and haematocrit values fell much below the normal standards for Britain. Malaria, liver disease, malnutrition, ancylostomiasis and bilharzia infestation are all capable of causing an anaemia and may all be found in one individual. The haematological findings in Africans suffering from anaemia may thus not be clear cut. In one individual there may be present both a

haemolytic factor (malaria) and a macrocytic factor (liver disease and malnutrition) in addition to an iron deficiency (ancylostomiasis and schistosomiasis). The writer thus had difficulty in deciding the criteria necessary for the diagnosis of sickle cell anaemia. It was decided primarily to rely mainly on the history given by the individual and to investigate thoroughly all cases in which a history of recurrent attacks of joint pain, vague ill health or jaundice was given. In addition individuals showing more than 4% of target cells in peripheral blood smears were investigated as DIGGS & BIBB (1939) found these cells without exception in the 47 cases of sickle cell anaemia they investigated. On further investigation sickle cell anaemia was not diagnosed unless the following criteria were fulfilled.

1.) Sickling of the erythrocytes.

2.) Signs of increased haemolysis in the peripheral blood with a persistently raised reticulocyte count.

3.) Lack of response of the haemolytic anaemia to antimalarial therapy.

4.) Absence of any other condition which might be responsible for the haemolytic anaemia.

5.) A low erythrocyte sedimentation rate and lack of response of the joint pains to salicylate therapy.

The method of discovering patients suffering from sickle cell anaemia employed in these surveys is open to criticism but, in the one girl in whom sickle cell anaemia

was diagnosed, the history was dramatic and was not simulated by any of the other individuals examined and questioned. It should be noted that acute rheumatism is extremely rare in the Gold Coast, if indeed it occurs at all.

The result of the investigation on the significance of the target cell in the peripheral blood smear is described in Part IV of this thesis.

a.) 327 INMATES OF A BOY'S INDUSTRIAL SCHOOL.

Three hundred and twenty seven inmates of a Boy's Industrial School were examined. The ages of the boys ranged from 12 to 24 years and 25 Gold Coast tribes were represented. A history was taken and a clinical examination performed on each boy. The haemoglobin content of the blood was estimated and also tested for the sickle cell trait. In addition peripheral blood smears (thick) were examined for the presence of malarial parasites and the number of target cells in thin smears enumerated. A specimen of stool was examined microscopically. The results of the investigation are shown in Table II. The incidence of the target cell is not included in the table and will be discussed later.

TABLE II

THE INCIDENCE OF THE SICKLE CELL TRAIT IN 327 BOYS AND THE RESULTS OF THE INVESTIGATIONS PERFORMED IN THE TRAIT POSITIVE AND TRAIT NEGATIVE GROUPS.

Investigation	Sickling Positive.	Sickling Negative.	Total.
Number examined	48 (14.7%)	279	327
Mean Hb. in G./100 ml. blood.	11.4	11.3	
Splenic enlargement.	12 (25%)	60 (22%)	72 (22%)
Liver enlargement.	2 (4%)	38 (14%)	40 (12%)
Malarial parasites in blood.	14 (29%)	60 (22%)	74 (22%)
Ascariasis.	8 (17%)	54 (19%)	62 (19%)
Ancylostomiasis.	6 (12.5%)	28 (10%)	34 (10%)
History of joint pains (recurrent).	Nil	Nil	Nil

From the above table it will be seen that the findings in the group of boys examined varied very slightly in the sickling positive and negative groups. The haemoglobin values were similar. A history of vague generalised pains is common in the Gold Coast African. Two boys in the sickling positive group who gave this history were thoroughly investigated. Malarial parasites were present in the peripheral blood and their symptoms ceased abruptly with antimalarial treatment. A history of severe recurrent joint pains simulating the haemolytic crises of sickle cell anaemia was not obtained in any instance and sickle cell anaemia was not diagnosed in the group of trait positive boys examined.

b.) THE SICKLE CELL TRAIT IN STUDENTS AND NURSES IN TRAINING

The blood of 428 students and nurses in training whose ages varied from 16-26 years was examined for the presence of the sickle cell trait, the haemoglobin content was estimated and a history was taken. The findings are shown in Table III.

TABLE III

THE INCIDENCE OF THE SICKLE CELL TRAIT AND HAEMOGLOBIN CONTENT OF THE BLOOD IN 343 FEMALE AND 85 MALE STUDENTS AND NURSES IN TRAINING.

	Sickling positive.	Sickling negative.	Total
Females.	78 (22.7%)	265	343
Mean Hb. in G./100 ml. blood.	12.9	12.7	12.8
Males.	12 (14%)	73	85
Mean Hb. in G./100 ml. blood.	13.1	13.4	13.3

It will be seen from the table that the haemoglobin values of those who exhibited the trait did not differ from those who did not. A history of recurrent joint pains was not obtained but in 6 instances a history of recurrent vague ill health was given and, of these 6, the trait was detected in one individual only. This was a girl aged 20 years and the haematological findings were not those of a haemolytic anaemia. The blood Kahn was positive and it was considered that yaws was probably responsible for her complaints.

c.) THE SICKLE CELL TRAIT IN 200 SCHOOLCHILDREN OF THE GA TRIBE.

In conjunction with Doctors [illegible] H. Hughes and J. [illegible] R. Sarkies 200 Ga schoolchildren between 9 and 13 years of age were examined. A history was taken and a full clinical clinical examination performed. The laboratory examinations performed were similar to those already outlined in paragraph (a) page 29. The writer was responsible for the investigations concerning the sickle cell trait and Table IV illustrates the findings.

TABLE IV

THE FINDINGS IN 100 GIRLS AND 100 BOYS SHOWN IN SICKLING POSITIVE AND SICKLING NEGATIVE GROUPS.

	100 Girls		100 Boys	
	Sickling negative.	Sickling positive.	Sickling negative.	Sickling positive.
Total (200)	83	17	81	19
Haemoglobin G./ 100 ml. blood.	12.6	12.0	11.8	12.8
Hepatomegaly	20	3	7	7
Splenomegaly	19	3	21	2
Malarial parasitaemia	25	4	49	12

A history of recurrent joint pains was given by one girl (A.L.) and she was considered to be suffering from sickle cell anaemia. A full report of the investigations performed on this girl is given in Appendix C (Case Report Number 15). Thus in the 200 schoolchildren examined, the incidence of the sickle cell trait was 18% and one girl was found to be

suffering from sickle cell anaemia. It will be seen from the table that neither enlargement of the spleen or liver nor the mean haemoglobin value of the blood in the trait positive schoolchildren were of value in the detection of sickle cell anaemia.

d.) THE SICKLE CELL TRAIT AND ANAEMIA IN PREGNANCY

In an attempt to discover the importance of the sickling phenomenon as an aetiological factor in anaemia in pregnancy, the blood of all patients admitted to the antenatal wards of the Maternity Hospital , suspected to be suffering from anaemia, was examined for the presence of the trait and a full haematological investigation performed.

123 consecutive patients were examined of whom 30 (24%) were primigravida.

The anaemia was classified according to mean corpuscular volume and mean corpuscular haemoglobin concentration. The normal range of M.C.V. was taken to vary from 75 to 98 cu. micra and the terms microcytic, normocytic and macrocytic were based on these figures. Similarly the normal M.C.Hb.Conc. was taken to be from 28 to 34 per cent. defining the terms hypochromic and orthochromic. The findings are shown in Table V. page 34.

TABLE V.

THE INCIDENCE OF THE TYPES OF ANAEMIA OF PREGNANCY AND THE SICKLE CELL TRAIT IN 123 CONSECUTIVE ANAEMIC PATIENTS IN THE MATERNITY HOSPITAL, ACCRA.

Type of anaemia.	No.	Haemoglobin in G./100 ml. of blood.		Erythrocytes in millions per cu. m.m.		P.C.V.%.		No. Sickling.
		Mean.	Range.	Mean.	Range.	Mean.	Range.	
Macrocytic orthochromic.	14	6.31	3.08-10.5	1.86	0.85-3.25	18.96	10-32	1
Macrocytic hypochromic.	18	5.6	2.8 - 9.8	2.302	1.08-3.578	23.8	13-41	2
Normocytic orthochromic.	57	7.74	2.52-14.0	2.82	0.86-5.02	23.7	7-46	2
Normocytic hypochromic.	21	5.36	2.1 - 7.7	2.56	1.05-4.8	22.2	10-37	3
Microcytic orthochromic.	12	5.57	3.22- 9.1	2.318	1.21-3.55	15.7	9-26	1
Microcytic hypochromic.	1	6.3		3.74		27		-
Total.	123							9

No case of sickle cell anaemia was detected in these patients and it is of interest to note that the incidence of the trait was only 7.3 per cent. It is considered, however, that the number examined was too small for this low incidence to be statistically significant.

No comparable figures have been found in the literature on the types of anaemia of pregnancy in West Africans. When these findings are compared with those of GOSDEN & REID (1948) in cases of anaemia in adult Africans in Sierre Leone, the incidence of normocytic orthochromic anaemia conforms fairly closely. The incidence of macrocytic anaemia in the present series was 26% and microcytic 10.6% which is a reversal of the incidence found in Sierre Leone where microcytic anaemia was found to be three times as common as macrocytic. This can be explained by the selected group on which the present findings were obtained.

It would appear from the figures in Table V that the sickle cell trait does not predispose to anaemia in pregnant women. Other factors have, however, to be taken into consideration and the implications of this investigation are discussed later in this thesis following the report of 8 autopsies on pregnant women in whom the sickling phenomenon was thought to be the cause of death.

e.) THE SICKLE CELL TRAIT IN 417 MOTHERS AND 384 NEONATES.

All mothers and babies delivered in the Maternity Hospital, Accra during the last 5 months of 1950 were examined for the presence of the sickle cell trait. In addition, a history was taken from each mother and the haemoglobin content of the blood estimated. An attempt to obtain cord blood from each newly born infant was unsuccessful as specimens were sent spasmodically by the African midwives. It was therefore necessary to examine the peripheral blood of infants on the first day of life. The blood of stillborn infants was consequently not examined in all cases. There were 64 stillbirths, including multiple pregnancies, and in only 10 instances was the cord blood examined. In these 10 babies the blood was negative for the sickle cell trait.

413 mothers were examined and the trait was present in 75 (18.2%). The 413 mothers gave birth to 448 children of whom 384 were born alive and the erythrocytes of 71 (18.4%) sickled.

The results of the investigation are recorded in TABLE VI.

TABLE VI

THE RESULTS OF THE INVESTIGATIONS PERFORMED ON 413 MOTHERS AND 384 NEONATES CORRELATED WITH THE PRESENCE OR ABSENCE OF THE SICKLE CELL TRAIT IN THE MATERNAL BLOOD.

	Sickling negative mothers.	Sickling positive mothers.	Total.
Mothers examined.	338	75	413
Number of primigravida.	157 (47%)	39 (52%)	196 (47%)
Number of multigravida.	181 (53%)	36 (48%)	217 (53%)
Multiple pregnancies	25 (7%)	8 (11%)	33 (8%)
Stillbirths.	54 (16%)	10 (13%)	64 (16%)
Babies born alive.	311	73	384
Mean birth weight of babies.	2,880 G.	3,010 G.	
Mean Hb. in G./100 ml. blood.	11.9	12.2	

The number of primipara in the sickling positive group of mothers was slightly higher but the percentage of stillbirths was less. In this same group the weight of the babies was greater than the weight of those in the sickling negative group. In the group of mothers examined there was no evidence that the presence of the sickling phenomenon influenced adversely the mother or the newborn child.

The 181 non-sickling multigravida had given birth to 525 children, 167 (32%) of whom had died and the 36 sickling positive multigravida had given birth to 129 children, 32 (26%) of whom were dead. The fertility rate of the former group was 2.9 and of the latter 3.3. It would thus appear

that, in multigravida, the sickle cell trait does not have a deleterious effect on fertility. Also the children born of these mothers are not any more likely to die in childhood than are the children of the non-sickling group of multigravida. The history of 32% and 26% of children born in each group not surviving to adult life may seem unnaturally high to practitioners with no tropical experience. It has previously been calculated however, that, in the Gold Coast, 40% of children born do not reach adult life COLBOURNE, EDINGTON & HUGHES (1950).

None of the mothers examined gave a history suggestive of sickle cell anaemia.

THE EFFECT OF THE SICKLE CELL TRAIT IN THE NEWBORN

The sickle cell trait was detected in 71 babies. 41 of these babies were born of sickling positive mothers and 30 of sickling negative mothers. 44 were males and 27 were females and the mean of their respective birth weights was slightly higher than the mean of their non-sickling brothers and sisters. Of 5 sets of twins, both sickled in three and one twin only in two instances.

The percentage of red blood cells sickling in the newborn varied from 0.3 to 48 whereas in the mothers all the erythrocytes sickled. It must be emphasised that the rapid bacterial method was constantly used. An attempt was made to follow up the sickling positive babies but this was found to be impossible in the majority of cases owing to the

disinterested non-cooperation of the African mothers. 6 neonates however, were followed up for periods of 8 to 10 weeks and it was found that the percentage of sickled cells in the peripheral blood increased with age thus confirming the findings of WATSON (1948,514). It would appear that the presence of the sickle cell trait in the blood of the newborn baby does not influence the birth weight and there is no evidence that such an infant is more likely to be stillborn. As few of the peripheral erythrocytes were found to sickle in the newborn, it is unlikely that a newborn baby could suffer from sickle cell anaemia.

f.) THE SICKLE CELL TRAIT IN HOSPITAL PATIENTS.

85 hospital patients, suffering from either a respiratory or hepatic condition, and 40 blood donors were examined for the presence of the trait or the anaemia. 21 (16.8%) exhibited the trait and no history of recurrent joint pains was obtained. Evidence of a chronic haemolytic anaemia was not obtained in any of the 21 trait positive individuals.

SUMMARY OF PART II

The blood of 2,255 Africans has been examined for the presence of the sickle cell trait. Sickling was present in 407 instances (18.1%). The findings are summarised in Table VII.

TABLE VII.

THE INCIDENCE OF THE SICKLE CELL TRAIT IN 2255 AFRICANS SHOWING AGE, SEX AND TYPE OF GROUP EXAMINED.

Age Groupd	Type of Group	Total Examined	Number Sickling	Males		Females	
				Total	Sickling	Total	Sickling.
Newborn	Newborn	384	71	211	44	173	27
8 - 12yrs	Schoolchildren	200	36	100	19	100	17
12-24 yrs	Boys	327	48	327	48		
16-26 yrs	Nurses (b)	428	90	85	12	343	78
Adults	Anaemia (d)	123	9			123	9
Adults	Pregnancy (e)	413	75			413	75
Adults	Patients (f)	125	21	62	11	63	10
All ages	Villagers	255	57	113	22	142	35
	Total.	2255	407(18%)	898	156(17.4%)	1357	251(18.4%)

No significant difference in the incidence of the trait in age or sex groups was noted. The incidence of the trait in the 621 hospital patients examined was 15.8% which was less than the incidence found in the general population.

Although only one case of sickle cell anaemia was diagnosed in the 2,255 Africans examined, this does not give the incidence of sickle cell anaemia in the population. As previously stated it is most difficult to examine a random sample of the population of the Gold Coast and in this investigation the age group 6 months to 8 years was unavoidably neglected. It can be stated that, from the investigations performed, no ill effects were attributed to the presence of the trait in 406 out of the 407 Africans exhibiting it. The implications of the investigations described in Part II of this paper are discussed further on page 71.

Part III.

SICKLE CELL ANAEMIA IN THE ACCRA DISTRICT OF THE GOLD COAST.

INTRODUCTION

Sickle cell anaemia has been diagnosed in 25 instances. In 5 patients however only one examination was possible. These 5 patients are consequently not considered in the review of the cases although the haematological findings have been included in Appendix C in which detailed case reports of the remaining 20 patients have been given.

The following methods of investigation were employed to discover the 20 patients suffering from sickle cell anaemia.

1) One patient was discovered on the routine surveys of the population discussed in Part II of this thesis (page 32).

2) Patients in the Gold Coast Hospital, in whom a sickling test had been requested and found positive, were examined. 60 sickling positive patients were investigated and 4 were considered to be suffering from sickle cell anaemia.

3) Patients in the Gold Coast Hospital showing many target cells in the peripheral blood smear on which routine differential counts were being performed were examined. 50 patients were investigated and 2 were considered to be suffering from sickle cell anaemia.

The remaining 13 cases were discovered in patients suspected to be suffering from a haemolytic anaemia who

were referred to the author for investigation by medical colleagues.

2 of the 20 patients exhibited microaneurysms of the retinal vessels, signs previously unreported in sickle cell anaemia. These findings were published by EDINGTON & SARKIES (1952). The case histories and clinical details of these 2 patients have been included in Appendix C and considered in this review.

METHODS EMPLOYED IN THE INVESTIGATION.

Specialised laboratory investigations are not available at present in the Gold Coast. It was not possible to perform investigations requiring the use of a colorimeter. The faecal urobilinogen output or haemolytic index could not thus be estimated.

The majority of the haematological methods employed have already been described. (page 26). Reticulocytes were counted by the coverslip method using an alcoholic solution of brilliant cresyl blue. 500 cells were counted. Target cells were enumerated on a thin blood smear stained by Leishman's method. 500 cells were counted by moving transversely across the centre of the smear and the percentage of target cells to the nearest whole number calculated. Serum bilirubin was estimated by the use of a Lovibond's comparator. Coombs' test was performed using dried anti-human globulin serum supplied by the Ministry of Health Blood Group Reference Laboratory. The erythrocyte sedimentation rate was performed in the manner described by WINTROBE (1947).

No correction for anaemia was made.

The bromsulphalein excretion test was performed with a dosage of 2 mgm./ kilo. and blood was withdrawn at the end of 30 minutes. An alkalinised portion of the serum was compared with prepared known percentage standards and acidified serum.

REVIEW OF 20 CASES OF SICKLE CELL ANAEMIA.

3 females and 17 males representing 6 Gold Coast tribes were considered to be suffering from sickle cell anaemia. (See Table VIII.)

TABLE VIII.

THE AGE AND SEX GROUPS OF 20 CASES OF SICKLE CELL ANAEMIA.

Sex.	0-5 yrs.	6-10 yrs.	11-20 yrs.	21-30 yrs.	31-40 yrs.	Over 40 yrs.
Males (17).	-	3	8	4	1	1
Females (3).	-	2	-	-	1	-

Examination of the families :-

In only 5 patients was it possible to examine both parents and they all exhibited the sickling phenomenon. In another patient one parent was available for examination and the erythrocytes also sickled. None of the parents were found to be suffering from sickle cell anaemia. 23 siblings were examined and 5 were considered to be suffering from sickle cell anaemia. 3 of the 5 cases were in one family (A.L. Case Report Number 15) and a fourth child in this

family was considered a probable case. The results of the examination of the families agreed with the homozygous inheritance theory discussed in the review of the literature on page 17.

Previous Histories :-
The previous history in all cases apart from S.A. (Case Report Number 5) was strikingly similar. A history of severe recurrent attacks of pain in the larger joints of the limbs was given. The first attack had occurred in 'infancy' in 12 instances and the latest onset of the attacks occurred at the age of 7½ years. The number of attacks per year varied from 'continuous' to nil (J.A.H. Case Report Number 6 who stated that the attacks had ceased at the age of 35 years). In 9 instances it was stated that the attacks had become less severe as the patient became older and in 10 instances the attacks of joint pain were associated with cold weather. Cold weather was considered a possible factor in precipitating the acute episodes of sickle cell anaemia by GRAHAM (1924) and BERK & BULL (1943). WINTROBE (1947) does not mention that sickle cell anaemia may become less severe with age. In the Gold Coast, however, cold weather is associated with the rainy season and with an increase in the mosquito population and a corresponding increase in malarial infestation. KNISELY & BLOCH (1942) described massive intravascular agglutination in vivax and falciparum malaria with local haemoconcentration and tissue anoxaemia resulting from the clumping of the erythrocytes. They reported similar findings in the one case of sickle cell anaemia examined. Malaria may

thus act as the 'trigger' mechanism in precipitating a crisis in sickle cell anaemia. Intravascular sickling could be produced by the local anoxaemia caused by the malarial parasite with resultant increased stasis, increased sickling and a further increase in the local tissue anoxaemia. A vicious circle would thereby be established. The history of a decrease in the number of attacks as the patient becomes older is also compatible with the theory that malaria may be a precipitating factor in the crises - the attacks lessening in frequency as the patient's premunition immunity to malaria developes. It is tentatively suggested that in the Gold Coast the association between cold weather and the acute episodes of sickle cell anaemia are in all probability associated with the greater incidence of malarial infestation found during the rainy season.

Symptomatology :-
7 out of the 20 patients were not complaining at the time of examination. The symptoms complained of in order of frequency were :- joint pains (11), fever (9), nausea (9), headache (5), abdominal pain (4), pains in the limbs (4), pain in the chest and lumbar pain (2), weakness (2), yellow eyes (2), eye complaints (2), dizziness (1), leg ulcer (1) and palpitation (1). In general the symptoms complained of are those usually described in the literature. The eye complaints were however, unusual and microaneurysms of the retinal vessels were found in the 2 patients with eye complaints.

Clinical Signs :-
11 of the patients were asthenic and resembled the type of habitus described by WINSOR & BURCH (1944) with a short trunk and long slender limbs and fingers. 'Tower' skull was noted in 2 patients and mongoloid features in 2. Jaundice was noticeable in 9 and scars of leg ulcers in 7. Active leg ulcers were present in 1 patient only. The elbow joint was swollen in 1 patient and the small joints of the fingers in another.

The heart was considered to be enlarged clinically in 5 patients. Systolic bruits were present at the mitral area in 4 and pulmonic area in 1 patient. The blood pressure was consistently low. The incidence of cardiac complications in this series (25%) is lower than that usually reported and figures as high as 95% have been recorded WINSOR & BURCH (1945,529).

Enlargement of the lymph glands was not a striking feature although cervical glands were palpable in 8 patients.

The liver and spleen were palpable in 11 and 15 patients respectively. The diagnostic importance of enlargement of the liver or spleen in the Gold Coast African is difficult to assess. 'Normally' in children the liver may be palpable in 58% and the spleen in 86%. In adults the figures are lower and are in the region of 21% and 24% respectively. COLBOURNE, EDINGTON & HUGHES (1950). The spleen in sickle cell anaemia is enlarged in the younger age groups and diminishes in size with the progress of the

disease until finally only a fibrosed remnant may be found. The spleen in races living in a hyperendemic malarial area follows a similar course but the histological appearances are different and the small fibrosed spleen of sickle cell anaemia is not seen. In the writer's opinion no reliance can be placed on enlargement of the spleen or liver as diagnostic points in sickle cell anaemia in the Gold Coast African.

As already noted 2 patients revealed aneurysms of the retinal vessels and tortuous and dilated retinal vessels were noted in a further 4.

Blood Findings:-

The types of anaemia found in the 20 cases of sickle cell anaemia are shown below.

Normocytic	orthochromic	7.
" "	hypochromic	4.
Macrocytic	orthochromic	1.
" "	hypochromic	4.
Microcytic	orthochromic	3.
" "	hypochromic	1.

These findings are discussed later. The haemoglobin varied from 4.0 to 14.2 G./100 ml. blood with a mean of 10.1G., the packed cell volume from 14% to 41% with a mean of 31% and the white blood cells from5,400 to 25,300 per cu.mm. with a mean of 11,200.

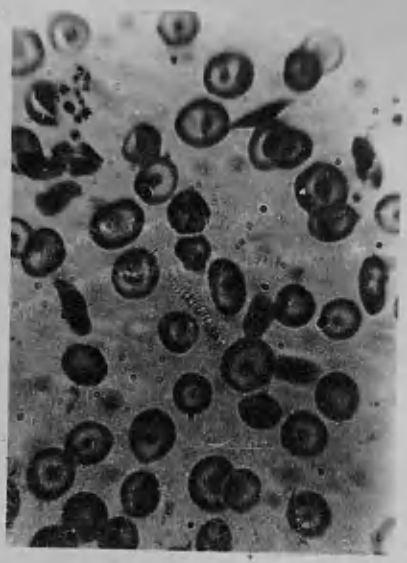
The most striking and constant feature, however, was the presence of numerous target cells in the thin blood smears of each patient. The number varied from 32 - 87%. (See plates 3, 4, 5). Sickled or oat shaped cells were seen in 10 instances and nucleated red cells in 14. The

NUMBERS REFER TO CASE REPORTS

APPENDIX C

PLATE 3

5



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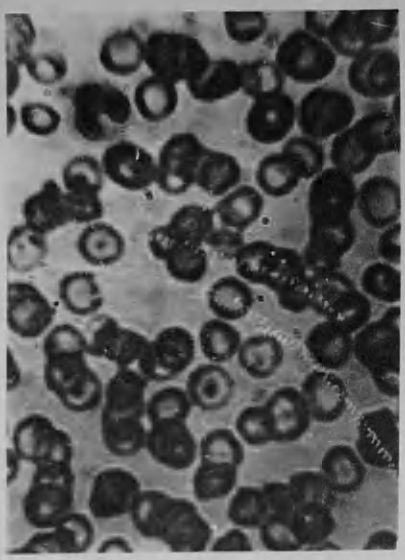

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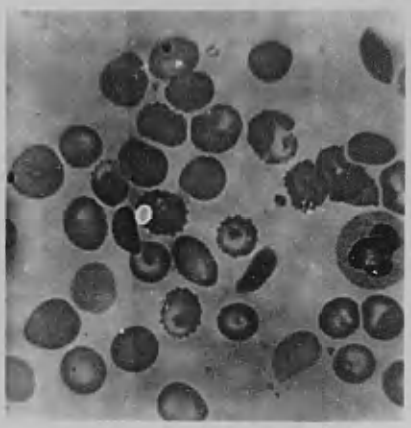

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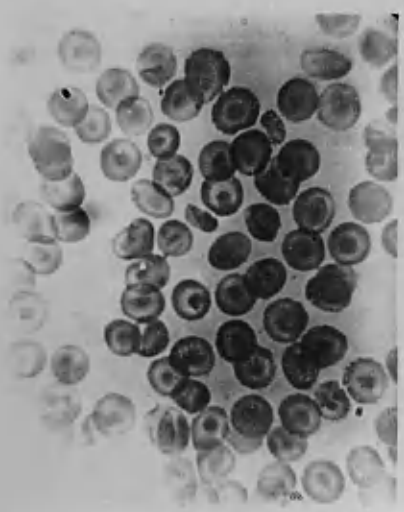

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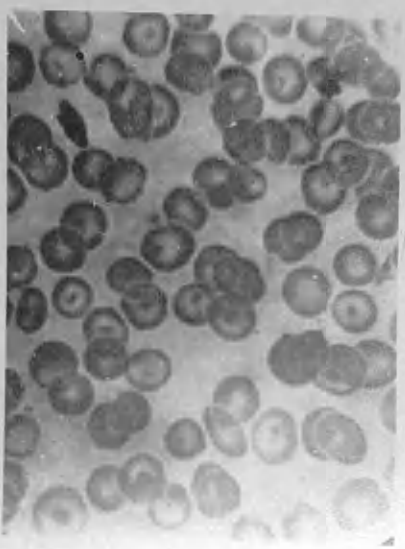

PLATE 4

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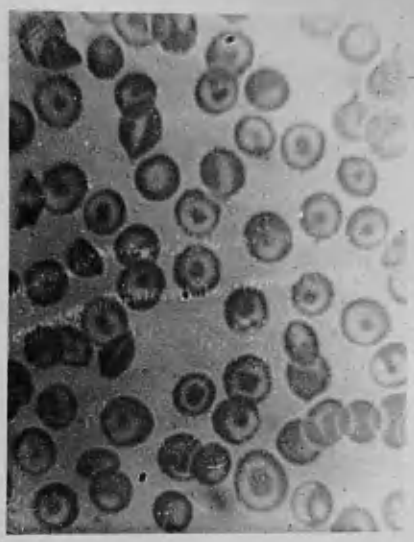

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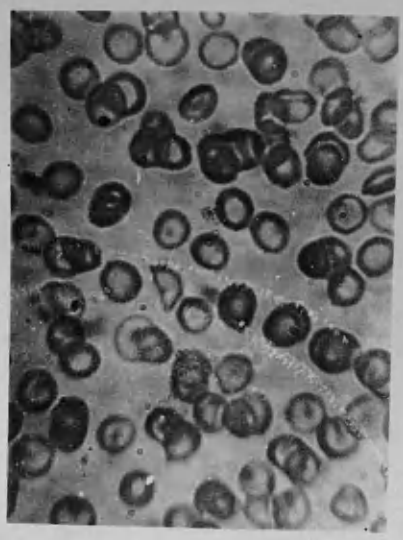

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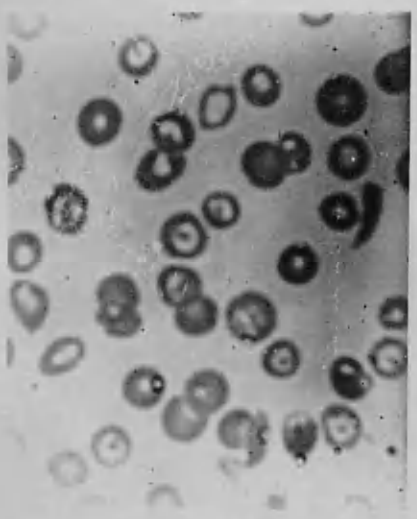

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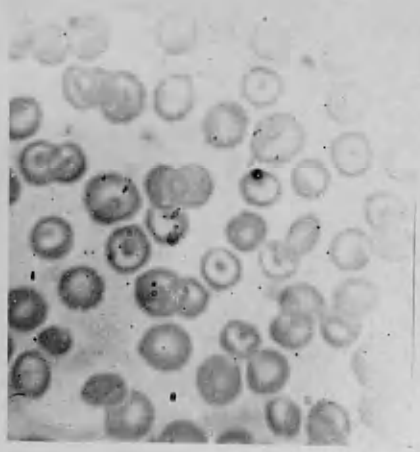

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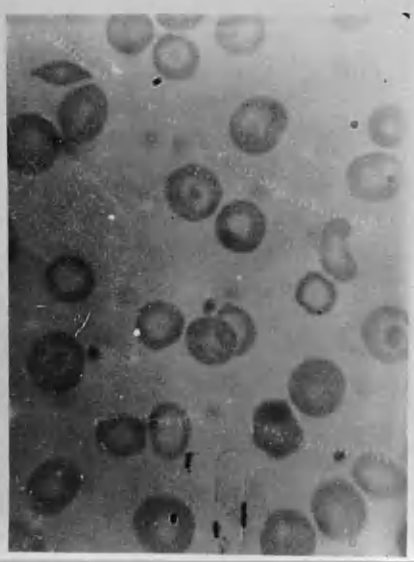

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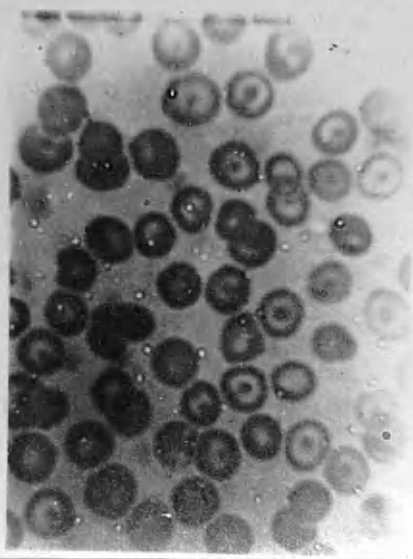

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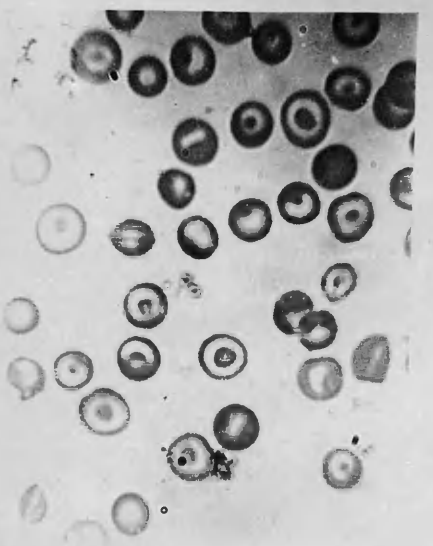

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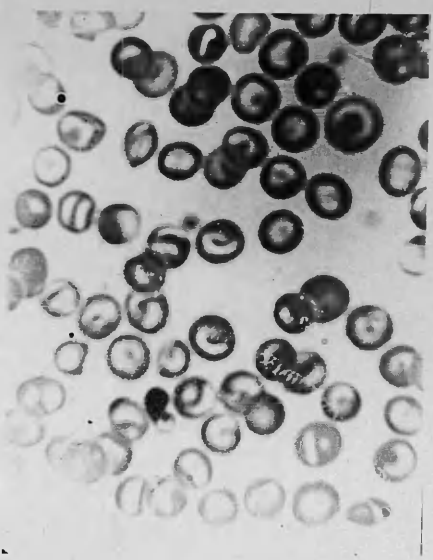

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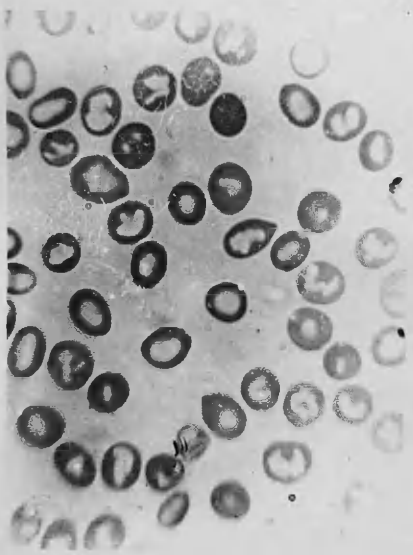

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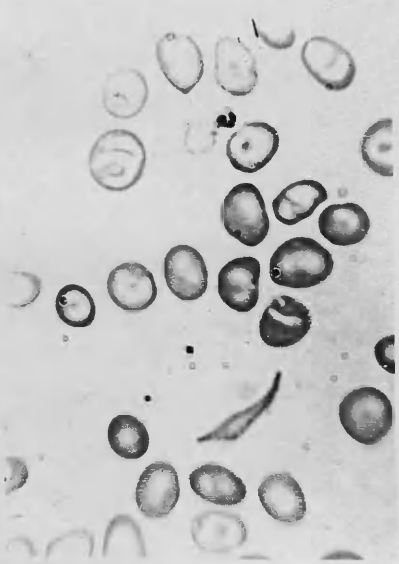

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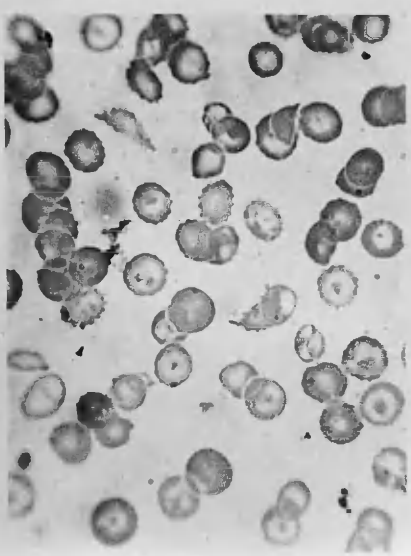

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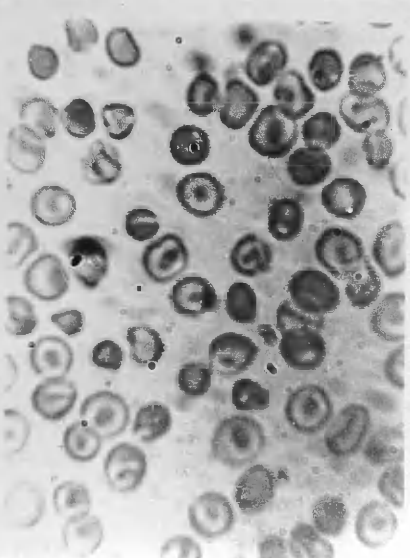


thin smear of A.B. (Case Report Number 14) contained more nucleated red cells than white. Anisocytosis and poikilocytosis were features of the severe cases only. The reticulocytes varied from 3.4 to 25% and the serum bilirubin from 0.8 to 14 mgm. per 100 ml. blood. The Coombs' test was negative in the 9 instances in which it was performed. Howell Jolly bodies were seen in 3 instances and Cabot's rings in one. The erythrocytes were in all instances more resistent to hypotonic saline than normal controls. The E.S.R. varied from 3 to 40 mm. in the hour.

The haematological findings in these cases agree closely with the reported findings of DIGGS & BIBB (1939) who reviewed 44 cases. The procedure with the least number of variables in routine haematology is the packed cell volume. Unfortunately in sickle cell anaemia the reverse is true. The rapidity and degree of sickling vary from patient to patient and the replacement, in varying proportions, of the flexible biconcave disc by a rigid oat or sickled shaped cell cannot but influence the packed cell volume (author's observation). This change also influences the sedimentation rate of the erythrocytes which is slow in sickle cell anaemia. ALTMANN (1945), BUNTING (1939) and DIGGS & BIBB (1939). The variation in the types of haemolytic anaemia diagnosed can be explained by this variability of the packed cell volume from which the absolute values, used in the classification of the anaemia, are calculated.

THE EXAMINATION OF THE BONE MARROW.

TableIX illustrates the findings in 9 patients in whom sternal marrow puncture was performed. The marrow in all cases was of thin consistency and marrow fragments could not be satisfactorily separated from blood. The recorded results are therefore those of the 'haemomyelogram'. The nomenclature adopted was that of ISRAELS (1948). At least 500 cells were counted and the results are shown in percentages. The cells enumerated under the heading 'Macronormoblast' resembled superficially the megaloblast but the nuclear chromatin was clumped in blocks and could not be mistaken for the fine network arrangement of the true megaloblast. In certain instances the differentiation between the cell termed the macronormoblast and the megaloblast was difficult but in no instance could any of the nucleated red cells be definitely termed megaloblastic.

Sickled erythrocytes were rarely seen in smears and target cells were much more common although in no case did they approach the numbers seen in the peripheral blood smears (Plates 6 and 7). Nucleated red cells were never seen to be sickled in form in direct smears although it is known that they are capable of sickling. DIGGS & BIBB (1939), HERRICK (1910), SYDENSTRICKER (1924,465) and WATSON (1948,515).

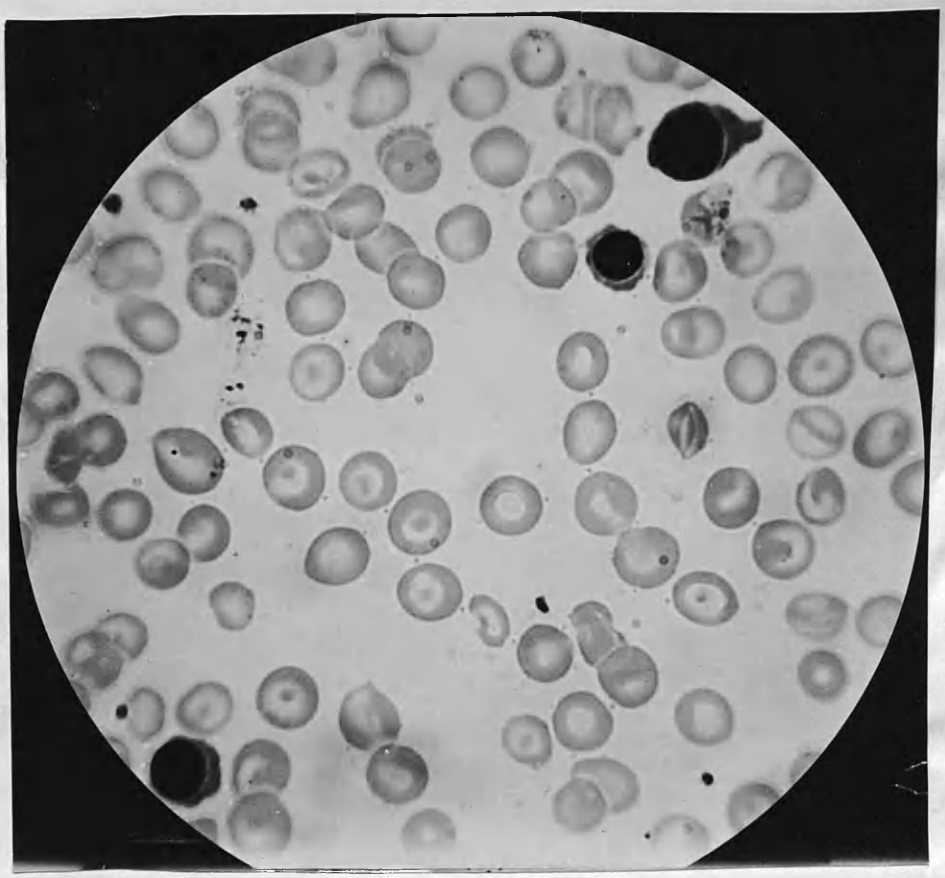
Malarial parasites were not detected in any of the marrow smears. In all cases a normoblastic hyperplasia was present ; the myeloid-erythroid ratio varied from 1.6 : 1 to 1 : 5.5

TABLE IX.

THE RESULTS OF MARROW BIOPSY DIFFERENTIAL COUNTS IN PERCENTAGE.

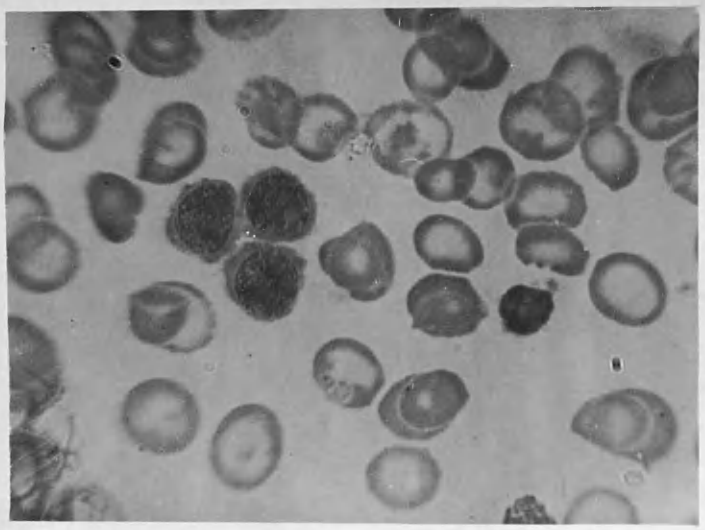
	Case Report No. 1	Case Report No.2.	Case Report No.4.	Case Report No.5.	Case Report No. 7.	Case Report No.10	Case Report No.11	Case Report No.14	Case Report No.19
Haemoglobin inG/100 ml.	9.1	6.1	7.5	7.5	9.0	7.7	4.0	6.6	14.2
P.C.V.	26%	21%	22.5%	26%	25%	26%	14%	22%	40%
W.B.C. per cu.m.m.	9,000	6,600	14,200	23,000	14,000	5,400	10,000	25,200	6,200
Haemocytoblast.	-	0.2	0.4	0.1	0.5	0.2	2.2	0.6	-
Proerythroblast	2.6	3.8	1.6	4.0	2.0	0.6	10.2	5.2	3.6
Normoblast									
Early.	3.2	6.6	2.0	3.0	4.0	1.2	3.6	8.6	4.0
Intermediate.	1.8	11.6	5.6	8.0	14.0	14.0	8.2	12.0	7.0
Late.	48.6	28.8	50.0	30.0	20.0	18.0	36.4	31.2	28.2
Mitotic.	0.8	1.8	3.2	2.0	1.0	-	6.4	3.0	1.2
Macronormoblast									
Early.	-	-	-	-	-	-	-	-	-
Intermediate.	-	-	0.2	-	-	-	1.6	-	-
Late.	1.6	1.0	7.0	2.0	-	1.2	3.4	4.4	0.2
Myeloblast	-	-	-	1.5	0.5	0.4	2.0	-	2.0
Promyelocyte	1.0	0.8	0.4	2.5	6.0	3.0	5.0	-	6.2
Neutrophil									
Myelocyte.	0.2	1.0	1.0	3.0	3.0	8.0	5.6	0.4	8.2
Metamyelocyte.	2.0	3.4	1.4	8.0	20.0	16.0	7.4	3.0	12.4
Polys.	25.0	34.2	18.0	22.0	21.0	26.0	2.8	22.4	20.0
Eosinophils (total)	3.0	0.6	-	1.5	1.0	2.0	1.4	2.0	2.0
Basophils (total).	-	1.0	-	0.5	-	0.2	-	0.2	0.2
Lymphocytes.	9.0	5.0	6.0	11.0	5.0	8.4	3.4	6.0	4.8
Monocytes.	0.2	0.2	0.2	0.5	0.5	0.8	0.4	0.8	-
Plasma cells.	1.0	-	3.0	0.4	1.5	-	-	0.2	-
Megakaryocytes.	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Myeloid-erythroid ratio.	1:1.2	1:1.3	1:3.3	1:1.2	1.3:1	1.6:1	1:2.8	1:2.3	1.1:1

PLATE 6



STERNAL MARROW SMEAR OF M.A. SHOWING TARGET CELLS, A PROERYTHROBLAST AND NORMOBLASTS. CASE REPORT NUMBER 1.

PLATE 7



STERNAL MARROW SMEAR OF D.B. SHOWING SCANTY TARGET CELLS AND EARLY NORMOBLASTS. CASE REPORT NUMBER 2.

Radiology :-
Radiological changes which were considered to be due to sickle cell anaemia were found in 9 of the 17 patients who were Xrayed.

The radiological changes in sickle cell anaemia have been discussed by a number of authors *.
Two mechanisms are thought to be involved in their production.

a.) Hyperplasia of the bone marrow producing non-specific lesions which have been described in other haemolytic anaemias, the most important being Cooley's.

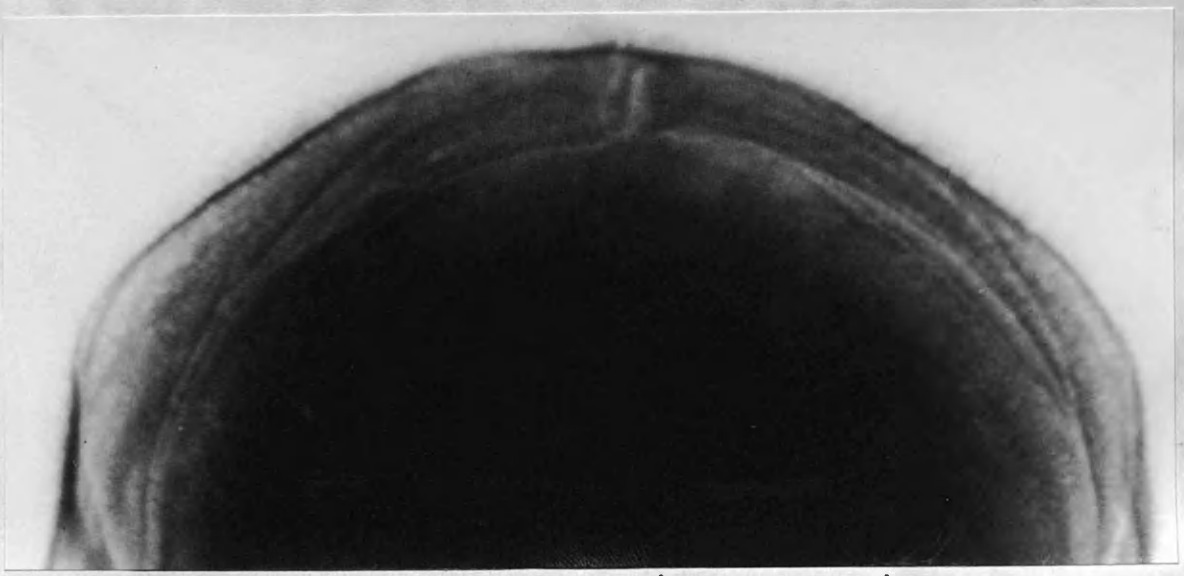
b.) Lesions produced in bone by the blockage of blood vessels by sickled erythrocytes with consequent infarction.

Lesions due to hyperplasia of the bone marrow were seen in 9 patients and infarctive lesions were present in 3. (Plates 8,9,10 and 11).

Absence of a well defined outer table of the skull with perpendicular trabecular striations radiating outwards from the inner table, giving the 'hair on end' appearance, was the most common lesion and was seen in 8 patients.
A generalised mottling of the ribs with trabeculation in the direction of the long axis and enlargement of the heart were seen in 2 instances. Changes in the femora were noted in 4 patients and in the tibia and fibula in one.

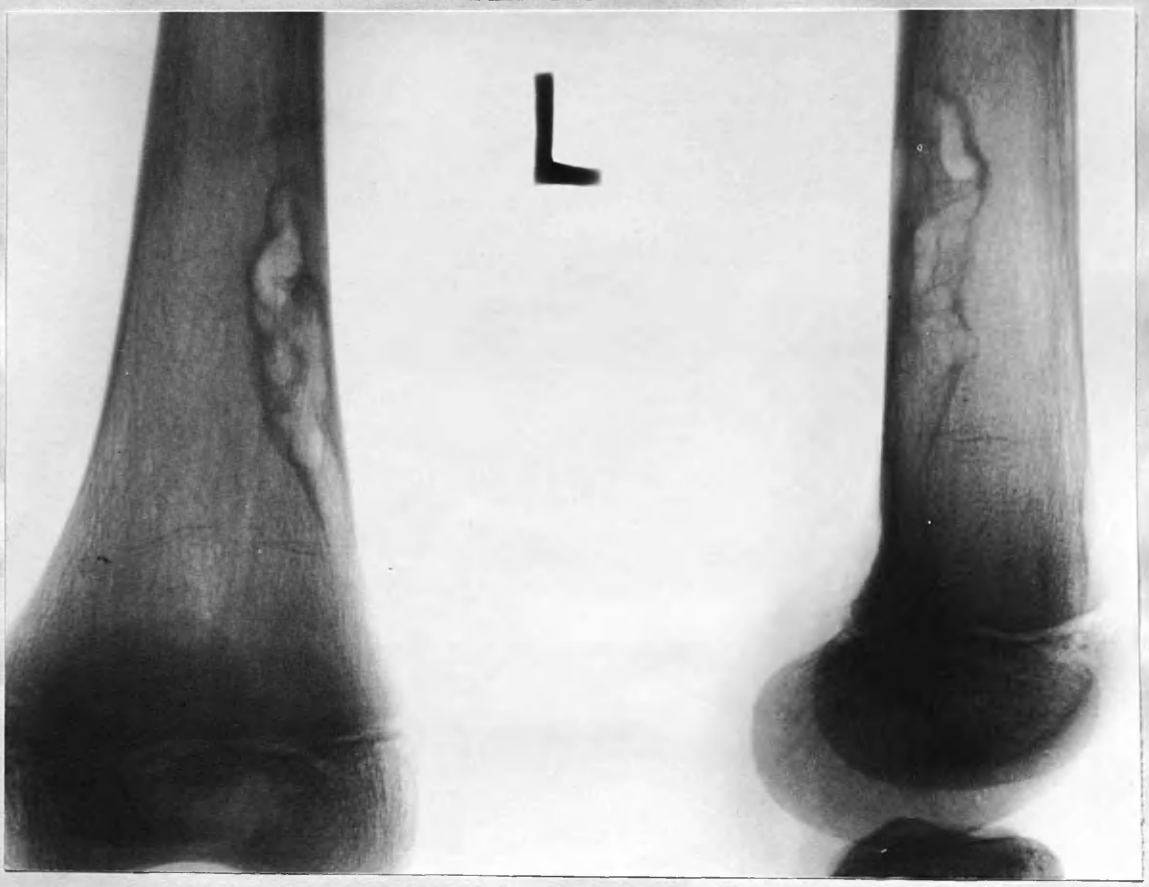
* 69, 82, 142, 144, 210, 211, 229, 238, 274, 284, 295, 296, 303, 308, 340, 400, 505.

PLATE 8



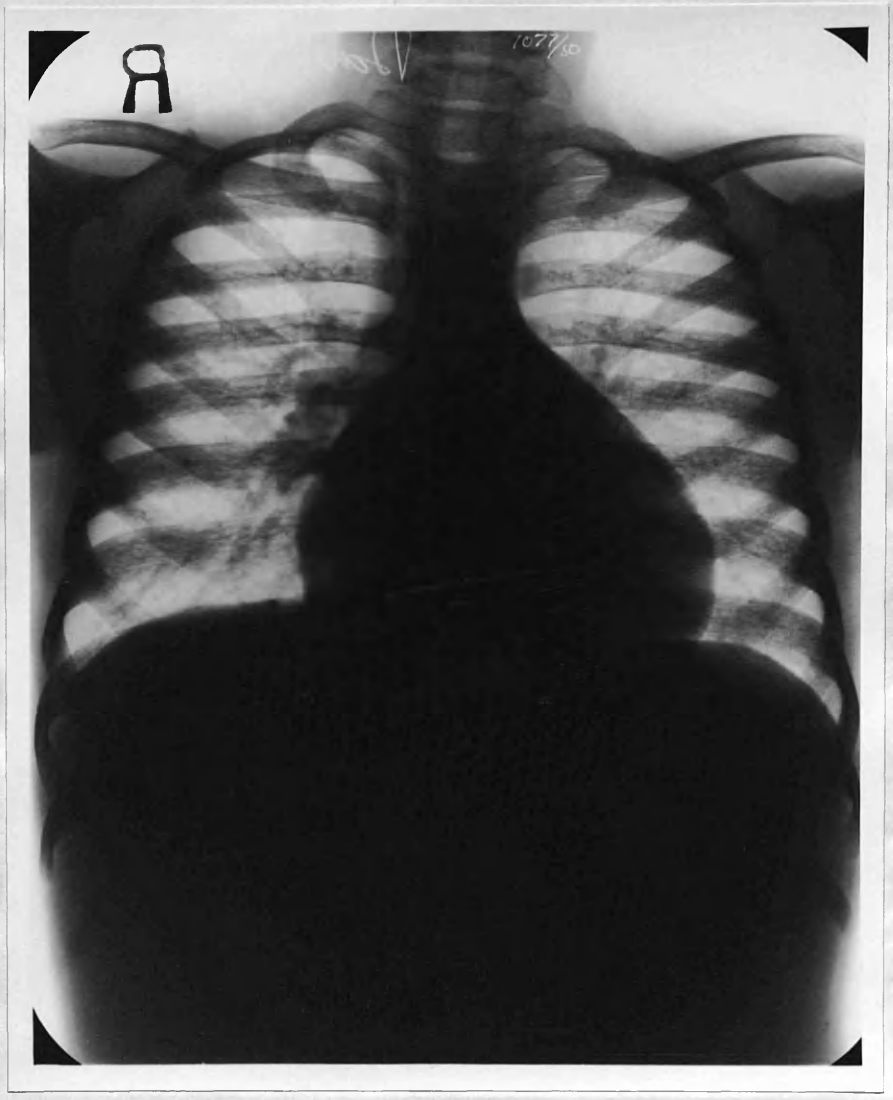
RADIOGRAPH OF SKULL OF D.B. SHOWING 'HAIR ON END' APPEARANCE. CASE REPORT NUMBER 2.

PLATE 9



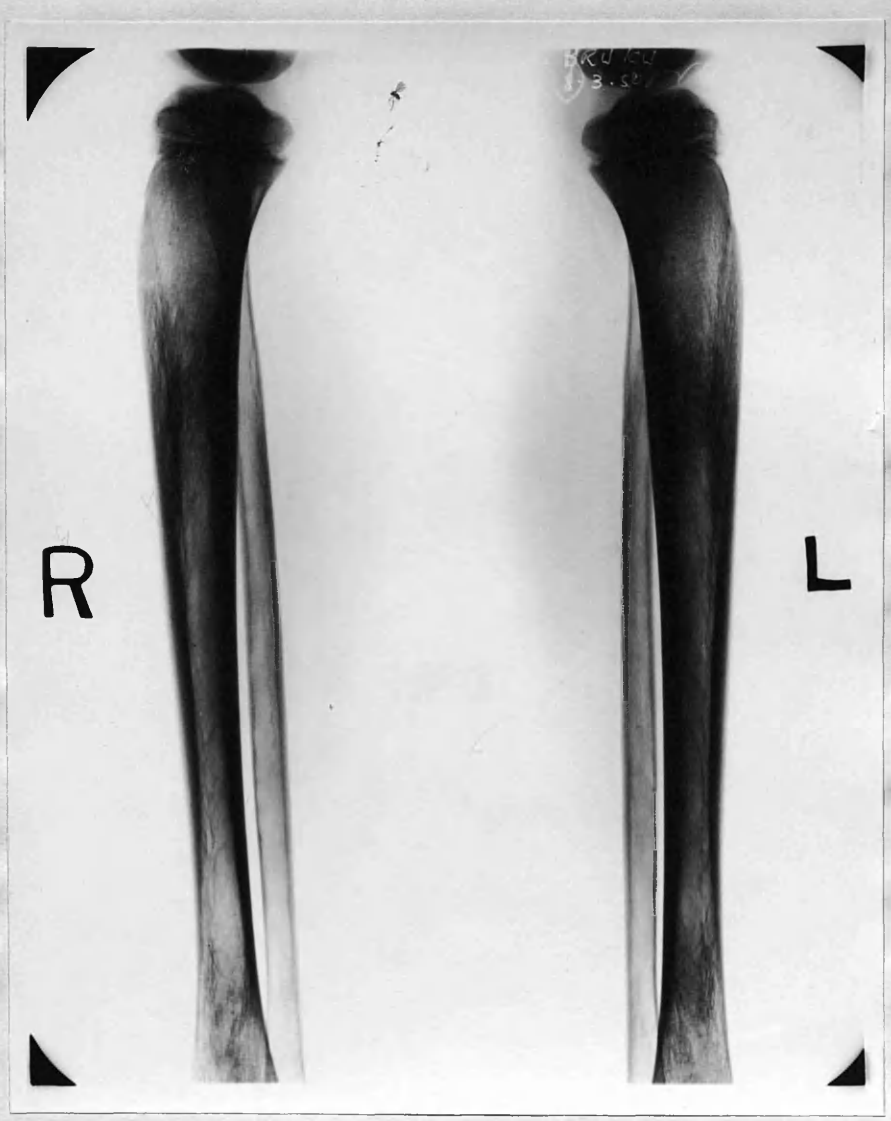
ANTERO-POSTERIOR AND LATERAL VIEWS OF THE LEFT FEMUR OF D.B. ILLUSTRATING AN INFARCTIVE LESION. ACCENTUATED GROWTH LINES CAN ALSO BE DISTINGUISHED. CASE REPORT NUMBER 2.

PLATE 10



RADIOGRAPH OF CHEST OF D.B. SHOWING ENLARGEMENT OF THE HEART. OSTEOPOROSIS AND INCREASED TRABECULATION OF THE RIBS CAN ALSO BE DISTINGUISHED. CASE REPORT NUMBER 2.

PLATE 11



RADIOGRAPHS OF THE BONES OF BOTH LOWER LEGS OF D.B. SHOWING OSTEOPOROSIS AND INCREASED TRABECULATION. CASE REPORT NUMBER 2.

Treatment :-
Antimalarial treatment, consisting of mepacrine hydrochloride 0.1 G. t.d.s. for 5 days followed by proguanil 0.1 G. t.d.s. for 5 days, was given to 17 patients without relief and crises occurred in 2 patients who were on suppressive proguanil therapy. Salicylates and aspirin did not relieve the joint pains nor arrest the condition. Liver and iron therapy had apparently no effect on the anaemia.

Splenectomy was advised by the author in 2 patients for the mechanical relief that was felt would follow the removal of the grossly enlarged spleen. (D.B. and A.B.). The surgeon, however, considered that, inview of the poor results of splenectomy in sickle cell anaemia recorded in the literature and the absence of readily available blood for transfusion, the risks involved were not justified. It has since been discovered that D.B. Case Report Number 2 died some months after discharge from hospital. The cause of death could not be ascertained as no medical officer was in attendance and the parents had,no doubt, resorted to 'native medicine' in view of our failure to cure the condition.

It was considered that the various treatment described above had no effect on the course of the disease in any patient.

Many drugs have been prescribed in sickle cell anaemia but few,if any,have proved of value. DIGGS (1934) reviewed the literature and personally treated 7 cases of sickle cell

anaemia. Iron, copper, liver, and hog's stomach were therapeutically valueless. MURPHY & SHAPIRO (1945) confirmed these findings and added anticoagulants, blood transfusion and salicylates to the list. Oxygen therapy has also been reported to have little effect on the crises of sickle cell anaemia HUGHES ET AL (1940) and TORRANCE & SCHNABEL (1952). LEIVY & SCHNABEL (1932) and TORRANCE & SCHNABEL (1952) considered that the administration of alkali and potassium sulphocyanate relieved the crises and GREK & FINDLAY (1951) considered that oxygen inhalation combined with nicotinic acid given intravenously was of help if administered early in the acute crisis.

Differential Diagnosis :-

20 patients have been investigated and a clinical 'triad' Of a history of recurrent joint pains, many target cells in the peripheral blood smear and sickling of the erythrocytes has invariably been associated with signs of increased haemolysis in the peripheral blood. In the writer's opinion three imporatant conditions have to be considered in the differesntial diagnosis. These are acute rheumatic fever, a chronic haemolytic anaemia due to malaria and so-called 'Mediterranean Anaemia'.

The absence of a history of sore throat, palpable nodules, joint swellings or evidence of valvular disease of the heart with, in many instances a normal sedimentation rate, eliminates the possibility of this condition being a rheumatic manifestation. In addition there was no response

to salicylate therapy.

Malarial parasites were detected in the blood of only 4 patients and there was no haematological or symptomatic response to antimalarial therapy in any of the 20 patients. In addition in 5 instances the spleen was not palpable and the history of recurrent joint pains given by these 20 patients was striking and was not simulated by any of the many hundreds of Africans examined and questioned - all of whom were developing or had developed their premunition immunity to malaria. From these facts it is felt that malaria can.be excluded from the list of possible diagnoses.

It is difficult to exclude Cooley's anaemia as, apart from the sickling of the erythrocytes, sickle cell anaemia and Cooley's anaemia may present an identical blood picture in fixed films. Many patients showing target cells in the peripheral blood smears were investigated, however, and in no instance was the syndrome described in these 20 cases found in the absence of the sickling phenomenon.

Finally it is considered that the case reports recorded in Appendix C conform to the recognised descriptions in the literature of sickle cell anaemia.

Part IV

THE SIGNIFICANCE OF THE TARGET CELL IN PERIPHERAL BLOOD SMEARS.

The target corpuscle was first described in sickle cell anaemia by HADEN & EVANS (1937) as the 'Mexican hat' cell and is a constant finding in the peripheral blood films of patients suffering from sickle cell anaemia DIGGS & BIBB (1939). A number of authors have attributed a haemolytic anaemia to the presence of this cell in the blood DAMESHEK (1940), WINTROBE ET AL (1940) and SCHEIBER (1945). The target cell is also the characteristic cell of Mediterranean anaemia. DAMESHEK (1940) considered that these cells might be the result of a hereditary defect of red cell production. The present author was struck by the many target cells seen in the peripheral blood film of the first patient who was considered to be suffering from sickle cell anaemia (Plate 2). Was this patient suffering from target cell anaemia with the sickling of the red blood cells a coincidental finding ? On the other hand, SINGER & ROBIN (1948) considered that there might be an additional structural alteration of the anaemia cell in sickle cell anaemia in addition to the sickling process. Might this additional factor be the target cell and might the reported rarity of sickle cell anaemia in Africa be due to the rarity of the target cell in Africa ?

The following paragraphs give an account of the investigations performed in an attempt to answer these

questions.

A preliminary examination was performed on 165 'healthy' boys aged 8-18 years to determine the incidence of the target cell in peripheral blood smears. The method employed to detect and count the target cells has already been described on page 43. 61 of the 165 boys showed target cells in the smears and the percentage of target cells varied from 0.02 to 81. If, however, the significant level of target cells in the peripheral blood smear was taken to be 4% as suggested by DAMESHEK (1940), a very much lower incidence was obtained. Table X shows the number of individuals showing more than 4% of target cells in peripheral blood smears in 527 normal Africans, 157 Africans exhibiting the sickle cell trait and 25 Africans suffering from sickle cell anaemia.

TABLE X.

THE NUMBER OF INDIVIDUALS SHOWING MORE THAN 4% OF TARGET CELLS IN PERIPHERAL BLOOD SMEARS IN 704 EXAMINATIONS.

GROUP	NON-SICKLING		SICKLAEMIC		S.C. ANAEMIA	
	Number examined	Target Cells	Number examined	Target cells	Number examined	Target cells
Boys	360	61	67	14	14	14
Girls	83	8	45	3	4	4
Adults	84	4	45	-	7	7
Total	527	73 15.8%	157	17 10.9%	25	25 100%

In addition 50 hospital patients whose blood slides showed many target cells were examined (page 42). They were found to be suffering from many different diseases and 3 were suffering from sickle cell anaemia. Only 2 of the 11 parents of children who were suffering from sickle cell anaemia showed target cells in the peripheral blood film.

From Table X it would appear that the incidence of the target cell in those with sicklaemia does not differ from the incidence in those with normal erythrocytes. The incidence of the target cell is higher in the younger age groups. There is no evidence that the target cell is inherited from the parents in sickle cell anaemia and no patient has been found to be suffering from a haemolytic anaemia in whom the peripheral blood film showed many target cells in the absence of the sickling phenpmenon.

The target cell was found to be a striking feature in the peripheral blood films of all patients suffering from sickle cell anaemia.

DISCUSSION

The number of children in the general population exhibiting target cells in peripheral blood films is surprisingly high. Target cells have been described in many conditions in the literature *. It would appear that these cells are found normally in a certain number of Gold Coast Africans. The writer is inclined to agree with LUBITZ (1945)

* 28, 51, 119, 120, 174, 206, 301 and 498.

who stated that this cell was non-specific.

It's presence in the Gold Coast African could be explained by the high parasitic infestation found in the general population with special emphasis on the malarial parasite. This would explain the higher incidence of the target cell in the younger age groups and would agree with the conclusions of BOHROD (1941) who considered that the target cell was a newly formed cell produced by the bone marrow in response to blood loss. There is no doubt, however, that the examination of a peripheral blood film in the Gold Coast African for the presence of target cells is a useful negative diagnostic procedure in differentiating the sickle cell trait from sickle cell anaemia. The presence of the target cell is by no means diagnostic of sickle cell anaemia but their absence renders the possibility of a diagnosis of sickle cell anaemia most improbable. In each instance that the writer has examined an African complaining of recurrent attacks of joint pain and has found numerous target cells in the blood smear, signs of increased haemolysis have always been present in the peripheral blood and the erythrocytes have sickled.

Part V.

A SURVEY OF 203 AUTOPSIES PERFORMED IN THE GOLD COAST HOSPITAL.

INTRODUCTION.

203 autopsies, excluding subjects in which decomposition was advanced, were performed by the author. In each instance the heart's blood was tested for the presence of the sickle cell trait. The trait was present in 44 instances. In 13 of these 44 subjects the sickling of the red blood cells was thought to be an important factor in the cause of death and these autopsy reports are given in full in Appendix D. In the remaining 31 subjects sickling of the red blood cells was found in the heart's blood and in histological sections but no pathological lesion could be ascribed to this abnormality. The causes of death in these 31 autopsies are listed below.

TABLE XI.

CAUSE OF DEATH IN 31 SUBJECTS EXHIBITING THE SICKLE CELL TRAIT.

Deaths due to trauma	7
Acute Yellow Atrophy (liver)	3
Cirrhosis of the liver	1
Pneumococcal septicaemia	3
Peritonitis	4
Meningitis (pneumococcal)	2
" " (meningococcal)	1
Empyema thoracis	2
Tuberculosis	2
Malaria	1
Reticulosis	1
Onyalai	1
Chloroform poisoning	1
Congenital abnormality	1
Chronic nephritis	1

It should be noted that a number of these autopsies were selective and that these figures cannot therefore be used to assess the incidence of the trait or of sickle cell anaemia in the population. The series of 13 autopsies in which the sickling aberration was thought to be an important factor in the cause of death consisted of 10 females and 3 males and the ages varied from 4 to 48 years with a mean of 22.8 years. Once again no conclusions can be drawn from the preponderance of females in this series as in the early stages of this investigation the author performed autopsies on 2 young African primigravida who died suddenly in the last months of pregnancy. Death in both instances was considered to be due to an acute sickle cell crisis. The findings in both cases were strikingly similar and the autopsy reports were subsequently published. EDINGTON (1951). These autopsy reports have been included in Appendix D. Attention was thus directed to the possibility of sudden death in pregnant women being due to a sickle cell crisis and an attempt was made to obtain permission for a post mortem examination on all similar cases. 6 similar autopsies were performed and this selection is responsible for the greater number of female autopsies reported.

In the review of the autopsies, autopsy number 1 is discussed first as it exhibited the classical pathological findings described in the literature in sickle cell anaemia. Autopsies 2 to 9 inclusive are then reviewed separately as they occurred in pregnant women and presented, in the author's

opinion, a definite pathological syndrome. Lastly autopsies 10 to 13 are briefly discussed.

Methods employed in the investigation :-
The first autopsy was the only one in which the author was able to perform antemortem investigations and the haematological methods employed have already been described on pages 26 and 43.

All autopsy sections were collected in neutral 10% formol saline. Zenker's was not used as a fixative as it causes the majority of the erythrocytes to resume the discoidal shape GRAHAM (1924) and HAHN & GILLESPIE (1927). Sections were stained routinely with haemalum and eosin and Perl's stain was used to detect the presence of iron containing pigment. Calcium was detected by von Kossa's method.

With the materials available it was not possible to perform more complicated staining procedures. 2 sections of the spleen were, however , stained for reticulin by Dr. C. V. Harrison at the Postgraduate School of Medicine, Hammersmith.

AUTOPSY REPORT NUMBER 1.

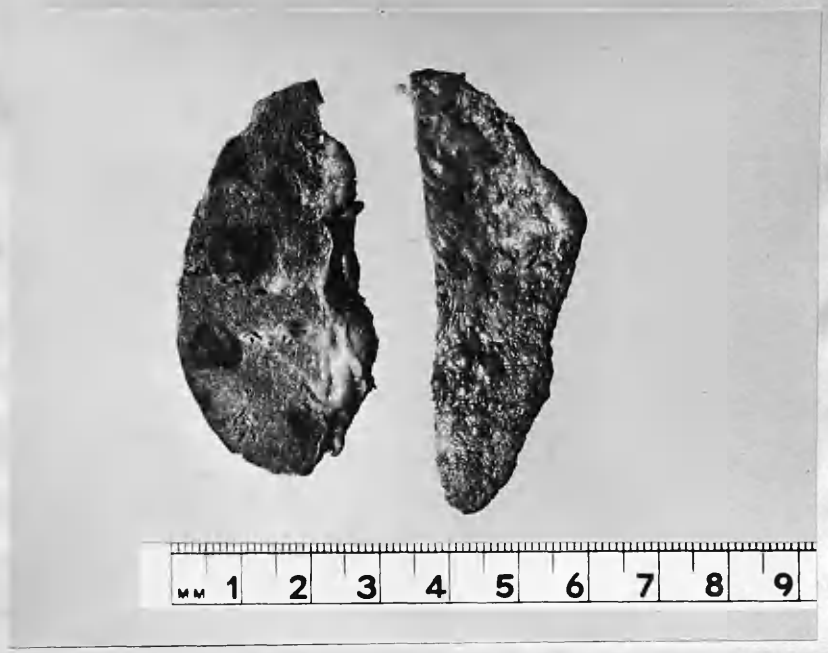
The findings in this patient were similar to those described in the majority of cases of sickle cell anaemia upon whom autopsies have been performed and recorded in the literature. The patient gave a history of recurrent attacks of joint pains and jaundice. A leg ulcer was present and there was evidence of increased haemolysis in the peripheral

blood with sickling of the erythrocytes. The destructive lesion of the hip joint demonstrated radiologically has also been described in sickle cell anaemia by HUCK (1933), MACHT & ROMAN (1948) and by CARROLL & EVANS (1949). The striking autopsy findings were the intense erythrophagocytosis by the Kupffer cells in the liver and the small fibrosed spleen containing much iron and calcium-containing pigment. (Weight 19 G.). These lesions are shown in Plates 12 to 17 inclusive.

Fibrotic nodules containing iron pigment have been described in the spleen in many conditions and were first described by STENGEL (1904). McNEE (1929) reviewed the literature on this subject (excluding sickle cell anaemia) and examined over 100 spleens containing these nodules. In every instance the spleen was larger than normal. The writer has not found the small siderofibrotic spleen described in the literature in any other condition apart from sickle cell anaemia although LEARMONTH (1951) mentioned atrophy of the spleen, of unknown aetiology, in a man of 53 years. BAUER (1940) and STASNEY (1943) considered that the small siderofibrotic spleen was pathognomonic of sickle cell anaemia.

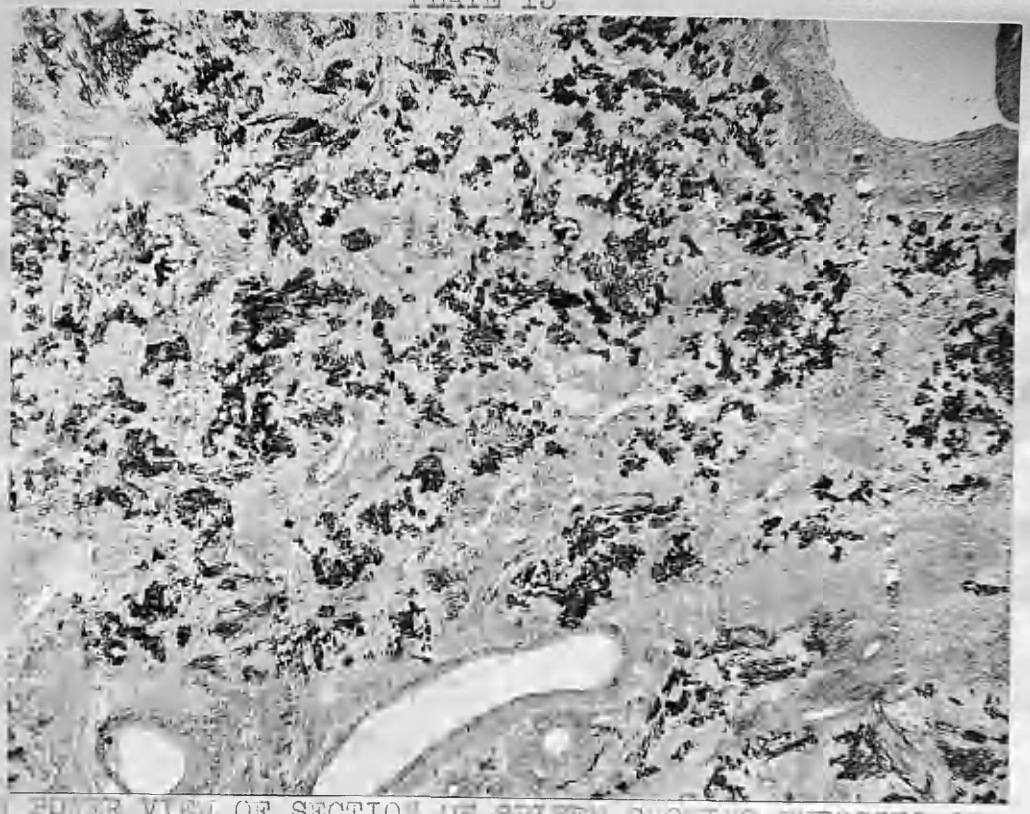
The pathology of the spleen in sickle cell anaemia has been excellently described by DIGGS (1935) and macroscopically and histologically this specimen conforms exactly to his description of the siderofibrotic spleen. It is considered that these changes in the spleen are due

PLATE 12



THE SMALL FIBROSED SPLEEN IN AUTOPSY NUMBER 1. WEIGHT 19 Grams.

PLATE 13

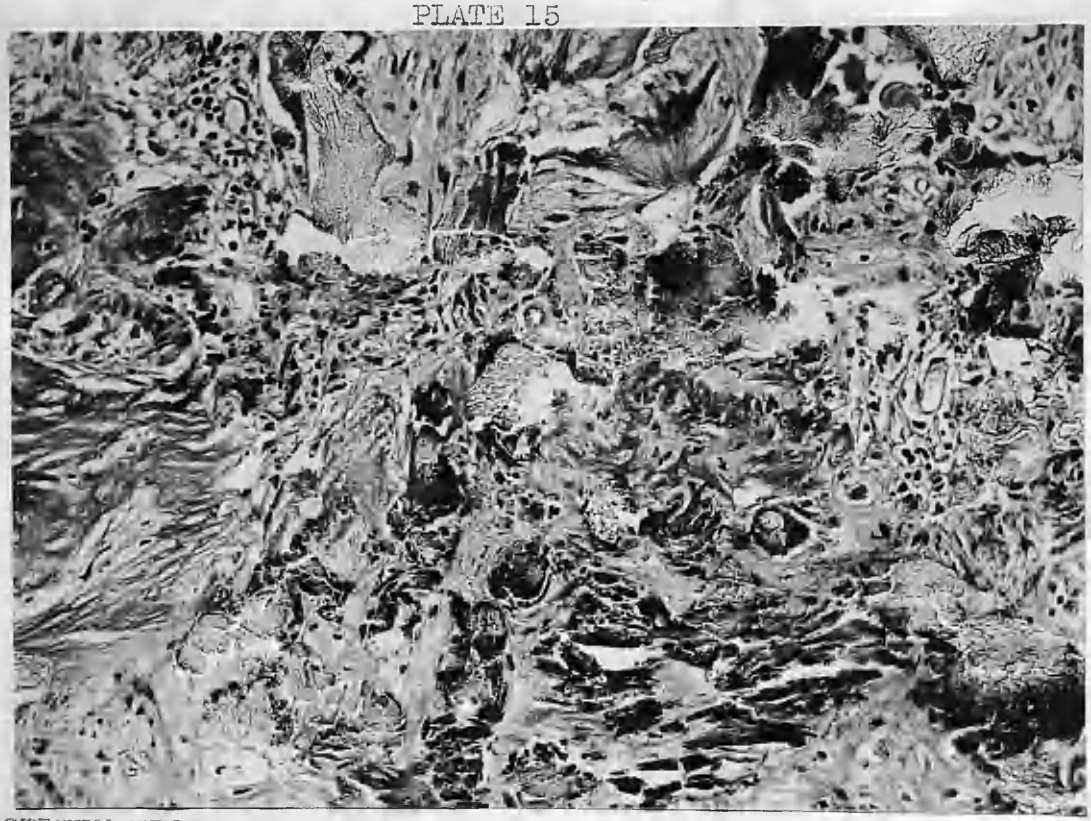


LOW POWER VIEW OF SECTION OF SPLEEN SHOWING DEPOSITS OF PIGMENT, FIBROSIS AND INTIMAL PROLIFERATION OF THE BLOOD VESSELS. AUTOPSY NUMBER 1. (PERL'S STAIN) ×33

PLATE 14

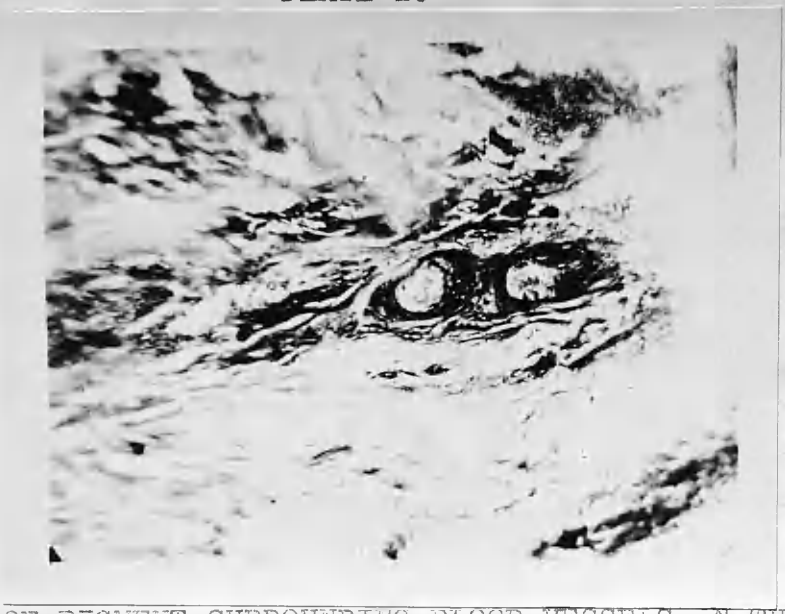
THE ROD SHAPED ERYTHROCYTES SEEN IN THE FIBROTIC SPLENIC TISSUE. AUTOPSY NUMBER 1. (H & E.)

PLATE 15



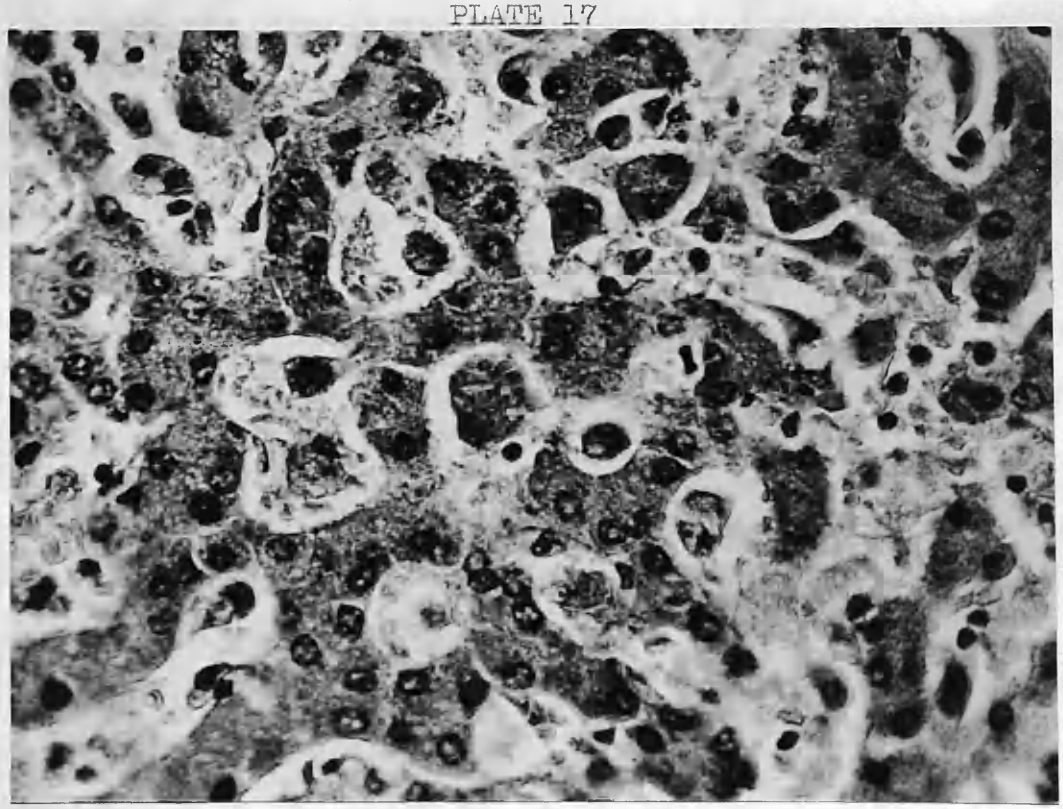
SPLEEN FROM AUTOPSY NUMBER 1 SHOWING GIANT CELLS ENGULFING THE YELLOW STAINING PIGMENT. THERE IS COMPLETE DESTRUCTION OF THE NORMAL SPLENIC ARCHITECTURE. (H.& E.) × 190

PLATE 16



DEPOSITS OF PIGMENT SURROUNDING BLOOD VESSELS IN THE SPLEEN. AUTOPSY NUMBER 1. (PERL'S STAIN)

PLATE 17



THE LIVER FROM AUTOPSY NUMBER 1 SHOWING THE INTENSE ERYTHROPHAGOCYTOSIS BY THE KUPFFER CELLS. (H.& E.) ×520

to the organisation and fibrosis of repeated haemorrhages and infarctions with the concomitant deposition of iron and calcium salts. Eventually the spleen may be represented by a fibrotic remnant only. In the same article a spleen was described weighing 0.87 G. in a 23 year old negress and DIGGS & CHING (1934), in a 51 year old male, could not find any splenic tissue at autopsy.

It is considered that the antemortem and postmortem findings recorded in Autopsy Report Number 1 are characteristic of sickle cell anaemia and that no other diagnosis is possible.

AUTOPSY REPORTS NUMBER 2 TO 9 INCLUSIVE.

These 8 autopsies were performed on African females who died suddenly during or immediately after the termination of pregnancy. The earliest death occurred in the 28th. week of pregnancy and the latest 2 days after delivery. 5 of the females were young primipara and the remaining 3 were multipara who had previously given birth to 10 children, 5 of whom are alive and well. In the present pregnancies one pair of twins and one baby were born alive. The remaining children did not survive. 2 of the 7 babies examined exhibited sickling of the red blood cells at autopsy at the end of 28 weeks of intrauterine life.

History and Clinical Examination :-

In all cases the records of the histories and clinical examinations were scanty. The relatives were questioned but only in 2 instances was a history of previous repeated

attacks of ill health given. The typical history of recurrent attacks of joint pains described earlier in this paper was not obtained and pain in the joints was only recorded on the case sheets of 2 patients. In 2 other patients a rapid fall in the haemoglobin from 6.8 G. to 4.1 G./100 ml. blood and 6.7 G. to 4.7 G./100 ml. blood in 2 days was recorded. In all patients the onset was sudden and dramatic and the condition of none of the patients had previously given rise to anxiety. The patient suddenly collapsed complaining of difficulty in breathing, vague pains in the chest and profound weakness. Restlessness was present and delirium and coma followed. Death occurred within a short time. One patient complained of ' a bell ringing in her ears'. On clinical examination the patients appeared to be in a state of shock.

Autopsy Findings :-
The macroscopic appearances at autopsy were similar in all cases. The subjects were all well nourished and slightly jaundiced. There was gross pallor of all organs with the exception of the liver in 3 cases and the spleen in all cases. The spleen was enlarged and deep blue in colour. It was firm in consistency, did not bleed on section and appeared to be packed with red blood cells. The weight of the spleen varied from 190 to 1,422 G. with a mean of 787 G.. The liver was pale in colour in 4 instances, normal in 1 and congested in 3. It was enlarged in all cases and varied from 1,927 to 2,950 G. with a mean of 2,254 G.

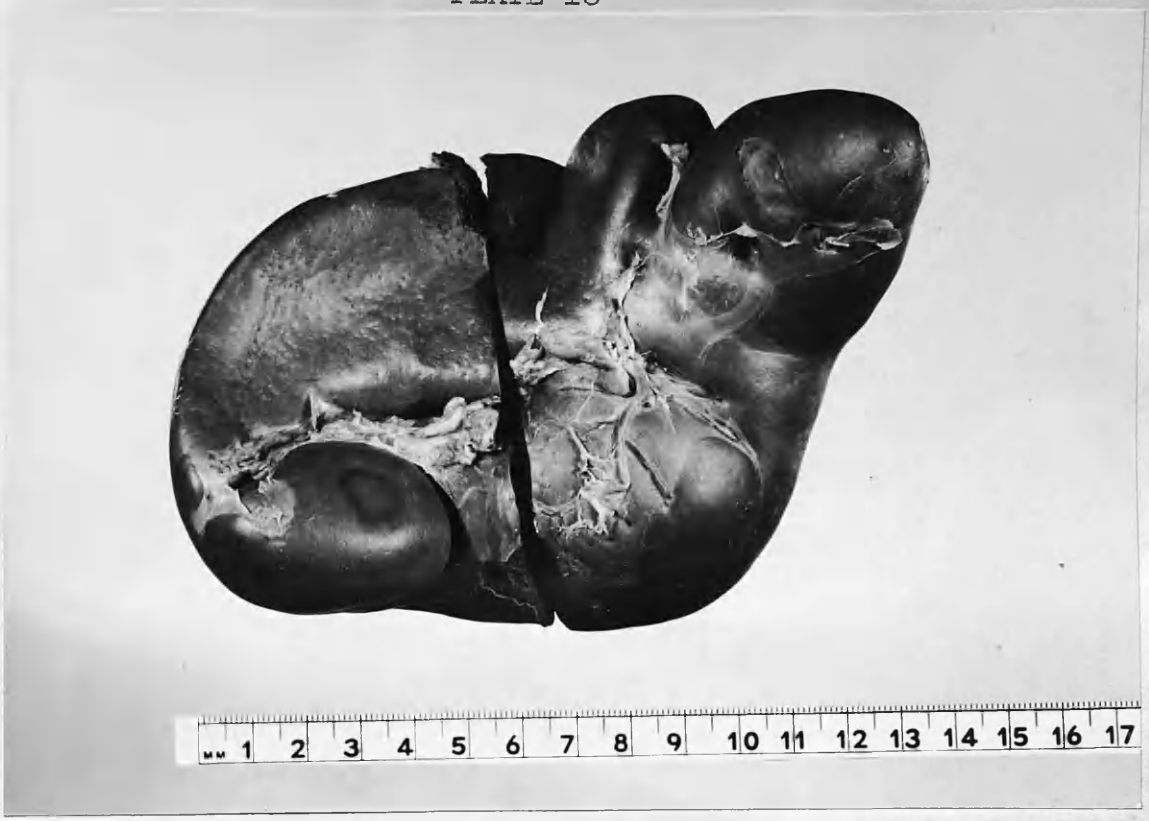
The lungs were frothy, bulky and pale. The heart

was enlarged in 2 patients but no valvular disease was detected. The kidneys were pale and oedematous. The bone marrow was hyperplastic in the 4 instances that it was examined. Malarial parasites were detected before death in 2 primipara and the 3 multiparous patients exhibited Ps. pyocyanea in the urine, a right pyonephrosis and delay in labour respectively.

Histologically the organ most greatly affected appeared to be the spleen but intense erythrophagocytosis was noted in the Kupffer cells of the liver in 5 of the 8 autopsies. The lungs were oedematous and in 2 patients masses of conglutinated sickled erythrocytes blocking the smaller blood vessels were noted.

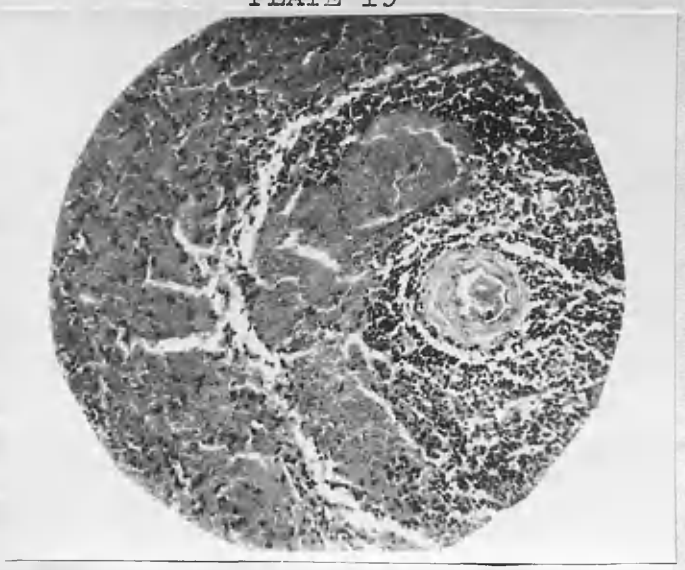
The spleen presented a characteristic histological picture. The pulp and sinuses were packed with sickled erythrocytes. The malpighian corpuscles were small and widely separated and were surrounded, in many instances, by haemorrhages. The tissue was so tightly packed with erythrocytes that it was impossible to say if erythrophagocytosis was present apart from the 1 spleen in which it was observed. There was much pigment giving a variable reaction for iron in the endothelial cells and pulp phagocytes. The trabeculae were thickened and haemorrhages were present. The blood vessels showed intimal proliferation with narrowing of the lumen. The sheets of pigment described in the small fibrosed spleen were not seen. Plates 18 to 25 illustrate certain

PLATE 18



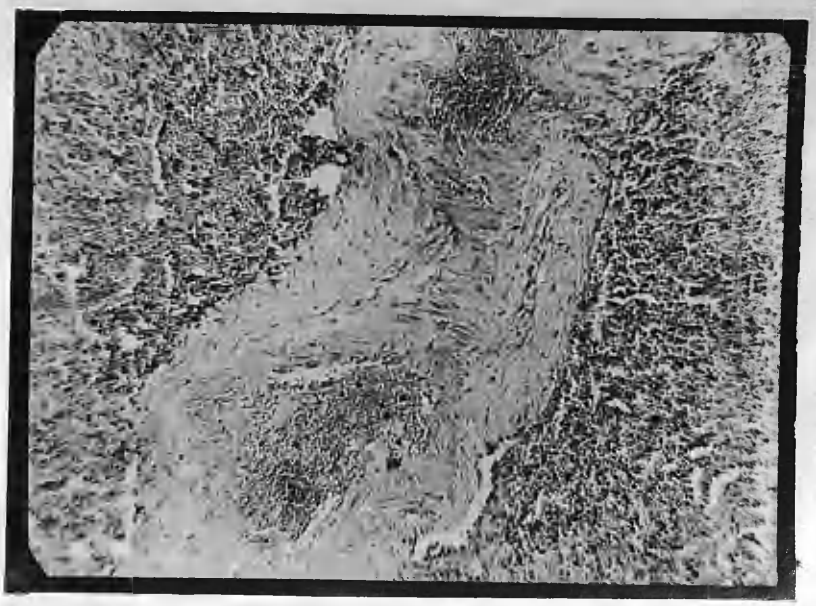
THE ENLARGED CONGESTED SPLEEN FROM AUTOPSY NUMBER 8. WEIGHT 475 GRAMS. COMPARE WITH PLATE 12.

PLATE 19



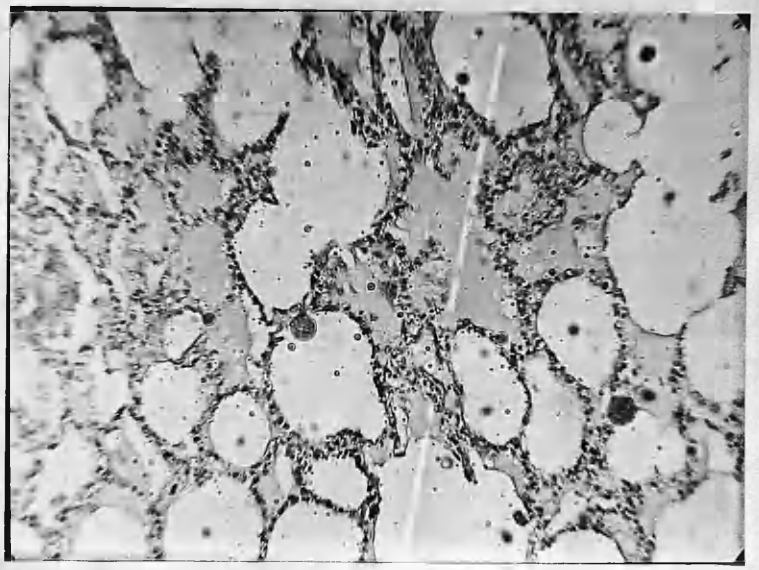
HISTOLOGICAL APPEARANCE OF SPLEEN SHOWN ABOVE. HAEMORRHAGE INTO AND SURROUNDING THE MALPIGHIAN CORPUSCLE. DENSE CONGESTION OF THE PULP WITH SICKLED ERYTHROCYTES. (H.& E.)

PLATE 20



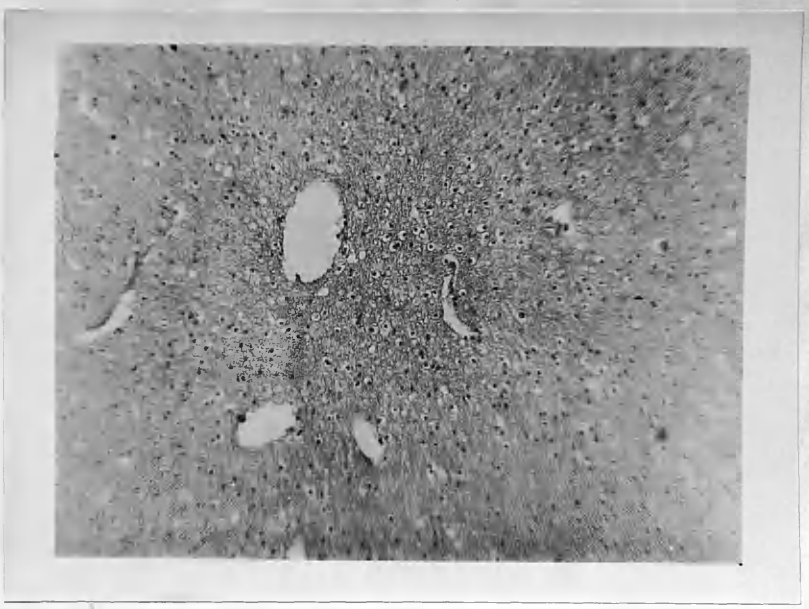
HAEMORRHAGES INTO THE TRABECULAE OF THE SPLEEN. AUTOPSY NUMBER 8. (H.& E.)

PLATE 21



GROSS OEDEMA OF THE LUNG. AUTOPSY NUMBER 2. (H.& E.)

PLATE 22

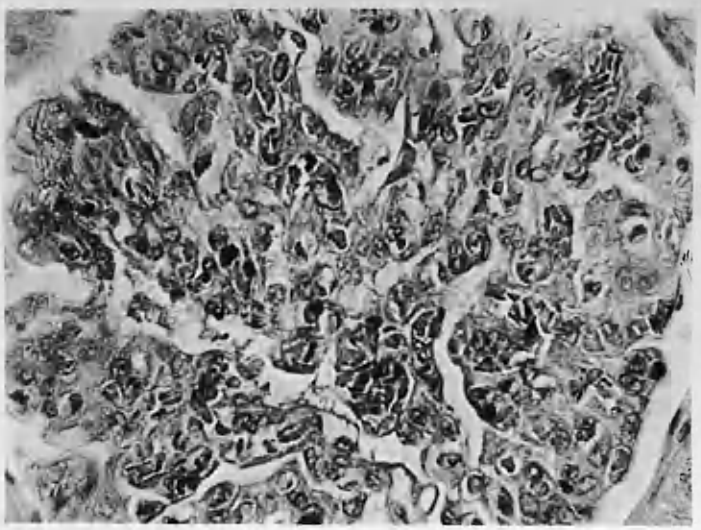


EMPTY CAPILLARIES IN THE BRAIN. AUTOPSY NUMBER 2. (H.& E.)

PLATE 23

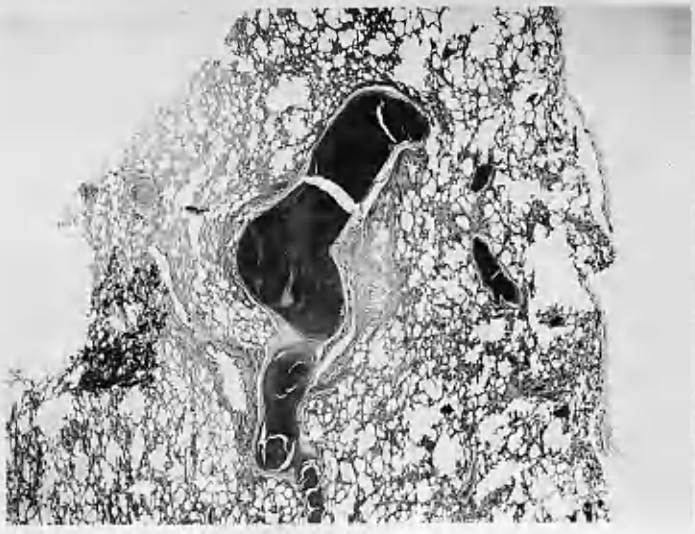
EXTRAVASATION OF SICKLED ERYTHROCYTES INTO THE ALVEOLI OF THE LUNG. AUTOPSY NUMBER 4. (H.& E.)

PLATE 24



CONGESTION OF THE GLOMERULI WITH SICKLED ERYTHROCYTES. AUTOPSY NUMBER 4. (H.& E.)

PLATE 25



LUNG SHOWING BLOOD VESSELS BLOCKED WITH SICKLED, CONGLUTINATED ERYTHROCYTES. AUTOPSY NUMBER 7. (H.& E.)

of these features.

Sickle cell anaemia complicating pregnancy has been described by many authors *. BEACHAM ET AL (1950) reviewed the literature and concluded that the maternal mortality in patients suffering from sickle cell anaemia was 25% and maternal morbidity during gestation was 100%. 35% of patients did not present symptoms until after the 6th. month of pregnancy. One patient, a 19 year old primipara, suddenly became acutely ill for the first time at term but she recovered following delivery. FOUCHE & SWITZER (1949) reported 6 cases of sickle cell anaemia and reviewed the literature. 2 necropsies were reported and the weight of the spleens were 2 and 95 G.. They stated that 55% of the reported cases of sickle cell anaemia associated with pregnancy were in primipara with no previous history suggestive of the disease. In the literature the author has only found 5 reported autopsies which resembled the 8 discussed above. LASH (1934) reported the sudden death of a 21 year old primipara following Caesarian section performed under local anaesthesia. The weight of the liver was 2,420 G. and of the spleen 960 G.. The histology of the spleen resembled those described above and the cause of death was thought to be shock and sickle cell anaemia.

* 15, 55, 76, 113, 149, 157, 176, 182, 201, 235, 244, 265, 272, 281, 296, 312, 342, 354, 361, 389, 395, 394, 396, 427, 453, 456, 469, 502, 503, 547 and 542.

HOYES (1946) performed an autopsy on a 32 year old multipara who had never previously been ill until the 7th. month of her present pregnancy. Death occurred suddenly following respiratory embarrassment. The liver weighed 2,030 G. and the spleen 740 G. at autopsy. Death was considered to be due to sickle cell anaemia, the predominating factor being generalised ischaemia due to conglutination of the sickle cells in the capillaries. REID (1936) described 3 cases of unexpected death in young African women dying shortly before or after delivery. The livers were congested and the spleens were enlarged but few details were given. Sickling of the red blood cells, however, was considered to be a factor in the cause of death.

It is considered that the cause of death in the 8 autopsies described was an acute sickle cell crisis. This condition may occur suddenly in pregnant African women shortly before or after labour. The history is brief and dramatic and may occur in women who superficially appear healthy and who give no previous history suggestive of sickle cell anaemia. At autopsy the gross pallor of the mother's mucosae and organs (excluding the liver) contrasts with the dark slaty blue appearance of the enlarged firm spleen and also with the organs and dark red blood of the fully haemoglobinized child. The macroscopic appearances suggest that the patient died from haemorrhage and that the sickled red cells had been withdrawn from the general circulation and packed tightly into the spleen.

A haemolytic element must also be presumed as icterus was present and erythrophagocytosis was marked in the liver in 5 of the autopsies. In addition conglutinated masses of erythrocytes were noted in sections from 2 autopsies. A possible explanation of the mechanism of this condition may be the relative anoxaemia produced in the maternal blood by the increased need of the child added to the haemoconcentration which has been reported to occur in the last months of pregnancy MULL & BILL (1945). An acute sickling crisis would thereby be initiated with subsequent sequestering of the rigid sickled erythrocytes in the spleen. An additional precipitating factor may be the presence of infection. Malarial parasites were present in 2 of the primipara and it is interesting to note that the three multipara, who had previously delivered children without mishap, suffered in 2 instances from an additional infection and in the third patient the labour had been long and exhausting.

AUTOPSY REPORTS 10-13 INCLUSIVE.

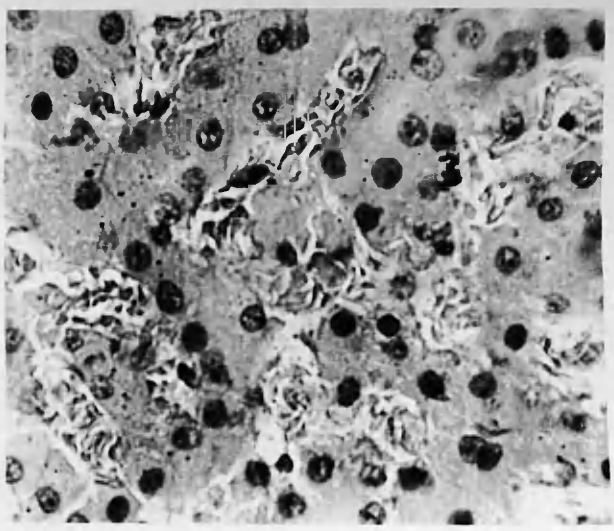
These autopsies record 3 cases of sudden death in 2 males aged 48 and 5 years and 1 female aged 4 years and a death caused by evipan in a male aged 19 years. The patients dying suddenly resembled the acute sickle cell crisis already described but the histological findings were not exactly similar. The predominating feature, apart from the enlarged spleen, was the intense congestion of all organs with sickled erythrocytes. The spleen in each instance

was enlarged and resembled those described in the previous paragraph (page 65). Erythrophagocytosis by the Kupffer cells and congestion of the liver sinusoids was marked in 3 autopsies. The male, aged 19 years, died suddenly when less than 1 G. of Evipan had been given. At autopsy the spleen was enlarged (280 G.) and packed with sickled erythrocytes. The other organs showed congestion. (See Plates 26, 27 and 28).

Discussion :-
BAUER (1940) stated that sickle cell anaemia was not infrequently entirely overlooked by the clinician and was discovered only by the pathologist at necropsy, the diagnosis being established by the observation of a small markedly atrophic spleen consisting of a mass of partially calcified fibrotic tissue. Although this type of spleen is most commonly reported at autopsy in sickle cell anaemia, the enlarged congested spleen is not uncommonly found *. TOMLINSON (1945) described the spleen as enlarged and rubbery in 8 out of the 11 cases discussed and described 4 autopsies in children, one of whom died suddenly in convulsions, which resembled the 3 cases of sudden death described above. The weight of the largest spleen was 1,425 G. in a girl of 19 years. SHOTTON ET AL (1951) removed a spleen weighing 1,850 G. from a girl of 8 years. Josephs in 1938 described an autopsy on a 3 year old child in which the findings

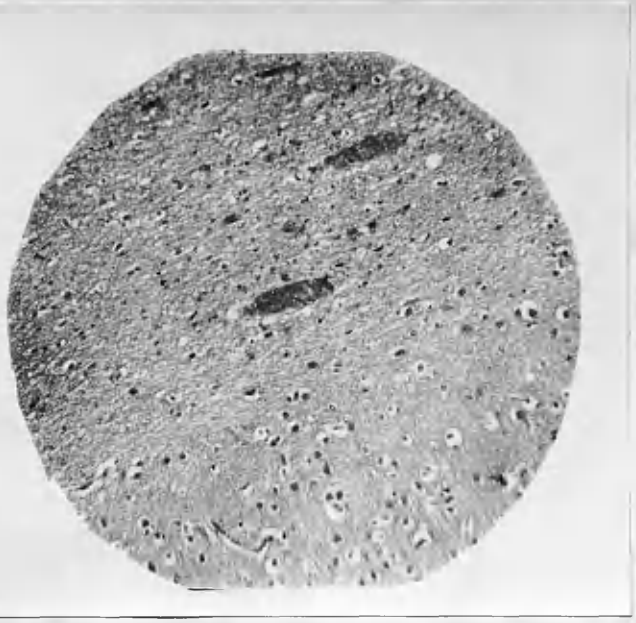
* 32, 143, 172, 219, 255, 258, 278, 314, 406, 432, 465, 478, 495, 508.

PLATE 26



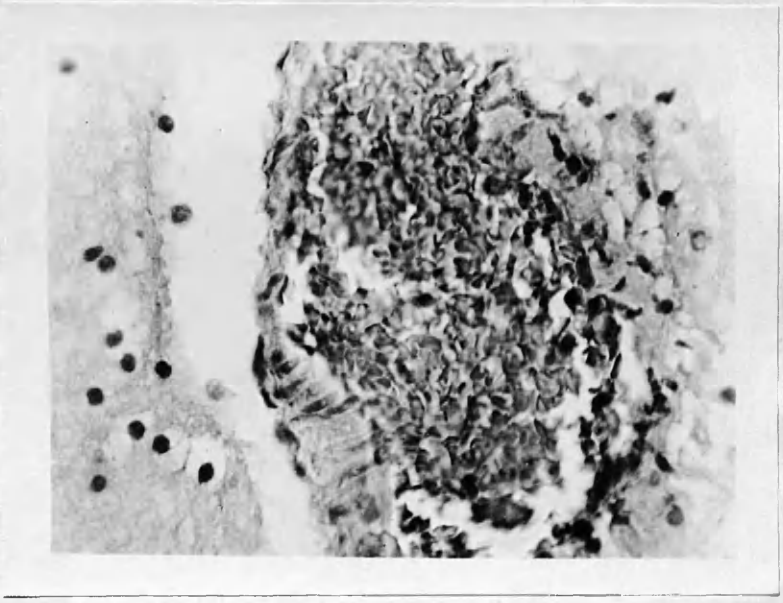
THE LIVER SHOWING CONGESTION OF THE SINUSOIDS AND ERYTHROPHAGOCYTOSIS BY THE KUPFFER CELLS. AUTOPSY NUMBER 10. (H.& E.)

PLATE 27



THE BRAIN SHOWING CONGESTION. AUTOPSY NUMBER 12. (H.& E.)

PLATE 28



THE BRAIN SHOWING A FOCAL HAEMORRHAGE. THE ERYTHROCYTES ARE SICKLED. AUTOPSY NUMBER 11. (H.& E.)

suggested that the child had bled to death into the spleen. It is also recognised that the administration of an anaesthetic to a patient suffering from sickle cell anaemia is dangerous and a number of deaths have been reported in the literature following surgical procedures WINSOR & BURCH (1945).

The mechanism of death in the 4 autopsies reviewed would once again appear to be an acute sickle cell crisis with circulatory stasis in the blood vessels and spleen. The precise mechanism whereby the erythrocytes are packed into the spleen is not known. RICH (1928) described a congenital malformation of the sinuses of the spleen in sickle cell anaemia but TOMLINSON (1945) perfused the arterial and venous channels of the spleen and could not confirm that a congenital abnormality was present. It was considered that mechanical impaction of the sickled erythrocytes in the smaller blood vessels with consequent blockage and passive dilatation would account for the pathological changes. It is possible that an active hypersplenetic process is also a factor in this condition. A haemolytic element must also be present in view of the erythrophagocytosis seen in the liver although the absence of jaundice would suggest that this might be an agonal phenomenon. The precipitating factor in Autopsy Number 11 was considered to be the anoxaemia produced by the anaesthetic and, in Autopsy Number 12, bronchopneumonia. No precipitating factors were found in the remaining 2 autopsies.

Part VI.

DISCUSSION, SUMMARY AND CONCLUSIONS.

DISCUSSION.

The majority of the problems and facts discovered in the investigations recorded in Parts II to V of this paper have been discussed as they have arisen. The probable incidence of sickle cell anaemia in the Gold Coast, however, has not been considered. If the homozygous theory of the inheritance of sickle cell anaemia is correct, the incidence of the anaemia in the Accra District can be calculated as follows if the incidence of the trait in the general population is taken to be 19%.

Suppose the sickling gene, S, to have the frequency 'p' and, s, the frequency 'q' in the general population where 'p' + 'q' = 1. Then, if the sickling gene is distributed at random in the population, the genotype ,SS, has the frequency 'p^2', Ss has the frequency '2pq' and ss 'q^2'. If the incidence of the sickle cell trait is in the region of 19% or 0.19 then ,ss, = 81% or 0.81 = 'q^2' and hence 'q' = 0.9 and 'p' = 0.1. Similarly SS = 'p^2' = 0.01. This implies that 1% of Africans in the Accra District should suffer from sickle cell anaemia.

The writer examined 8,255 Africans and only diagnosed sickle cell anaemia in one instance, giving an incidence of approximately 0.0005%. This figure is, however, completely fallacious as multiparous women, mothers at term and newborn infants were included in the survey. It is most

probable that the incidence of sickle cell anaemia in mothers at term and in multiparous women is extremely low as, excluding the mortality from the anaemia in the younger age groups, the writer has described 4 autopsies, performed on primigravida dying suddenly before term, in which the cause of death was thought to be an acute sickle cell crisis. It is also unlikely that the newborn child would suffer from sickle cell anaemia. (page 39). Pregnant women suffering from anaemia were also examined and , as there were only 30 primigravida in this group of 123, it is improbable that a case of sickle cell anaemia would be detected. In addition, in the survey mentioned above, the age groups most likely to exhibit the active disease (infancy and early childhood) were, unavoidably, not examined. It is perhaps significant that, in the group of 200 young schoolchildren examined whose ages ranged from 9 to 13 years, one girl was found to be suffering from sickle cell anaemia - an incidence of 0.05%. The surveys recorded in Part II, therefore, neither prove nor disprove the theory that sickle cell anaemia may be due to the homozygous inheritance of the sickle cell trait gene.

Case reports of 20 patients and haematological details of a further 5 who were diagnosed as sickle cell anaemia have been included in Appendix C. Both parents of 5 of the reported cases were examined and in each instance the trait was present in the peripheral blood. Examination of the families agreed with the homozygous-heterozygous theory.

On the other hand it has been reported in Part V of this paper that the blood of twins and one baby of 28 weeks maturity and 2 babies of 36 weeks maturity did not exhibit the sickling phenomenon although the mothers had died in an acute sickle cell crisis. This is apparently evidence against the homozygous theory of the inheritance of sickle cell anaemia as, if the mother is of the genotype SS, the child must inherit the sickling gene. The following explanations, however, could be offered.

1) The method employed to detect the trait in the baby was not efficient.

2) The acute sickle cell crisis in pregnant women is an emergency occurring in a carrier of the sickle cell trait and is not a manifestation of sickle cell anaemia.

3) The acute sickle cell crisis in pregnancy is not an entity and the deaths ascribed to this condition are due to some other undiscovered cause.

In the author's opinion the third possibility can be dismissed as the acute sickle crisis in pregnancy has been described in 8 autopsies in Appendix D and similar reports have been discovered in the literature. (page 66).

The rapid bacterial method was employed to detect the trait ROBINSON (1945) and in every instance a known positive control was included in the series. The trait was detected by this method in 71 newborn babies and was found to be simple and efficient. It is possible, however, that a very low percentage of the babies' erythrocytes sickled

and were missed by the author on microscopic examination. It has already been noted that the percentage of red blood cells sickling in the newborn may be as low as 0.3 (page 38). It is also a possibility that there may be a quantitative as well as a qualitative type of inheritance of sickle cell anaemia (page 21) haemoglobin and it is possible that a baby could thus be born of a homozygous mother and not exhibit the sickle cell trait at birth.

In 6 of the 8 autopsies performed on pregnant women dying of an acute sickle cell crisis, no previous history suggestive of sickle cell anaemia was obtained (page 63). This statement, however, cannot be taken factually as the history was taken from relatives, usually through an interpreter, and none of these women had been examined prior to the onset of pregnancy. In a personal communication, Professor L.W. Diggs, commenting on the 2 autopsy reports of the acute sickle cell crisis in pregnancy published by the author EDINGTON (1951), stated that similar cases have been fairly frequently observed in the armed services. The following is an extract from his communication. ' It is our opinion that these cases have the sickle cell trait without the characteristic sickle cell anaemia. Any factors which may produce hypoxia may cause the haemoglobin to crystallise which in turn leads to increased viscosity of the blood, stasis and circulatory failure with a shock like state and often times death.' FOUCHE & SWITZER (1949) stated that 55% of the

reported cases of sickle cell anaemia associated with pregnancy were in primipara with no previous history. There is thus some evidence that an acute episode may occur in an adult who gives no previous history suggestive of the anaemia. There are, however, no records in the literature of haematological examinations having been performed prior to the onset of these crises. In the author's opinion the evidence at present is insufficient to prove that the acute sickle cell crisis can occur in a carrier of the trait as the patients reported in the literature and in Autopsies 2-9 inclusive in this thesis might well have been suffering from a mild form of anaemia prior to, and the acute episode precipitated by, pregnancy. It would be wrong to deduce that the harmless trait might suddenly become lethal in pregnant women as this would imply that, in certain parts of Africa, 30% of women are liable to die in pregnancy.

The author is unable to explain satisfactorily why the 5 babies of mothers who died in an acute sickle cell crisis did not exhibit the sickling phenomenon in their blood. It is possible that there may be a quantitative suppression of the trait in these babies or, alternatively, the mothers may have been carriers of the trait only, and the acute crisis caused by some unknown additional factor in addition to pregnancy.

Sickle cell anaemia has been diagnosed with certainty in 20 patients and incomplete details of a further 5 possible cases have been given in Appendix C. The sickling phenomenon was also considered to be the cause of death in the 13 autopsies recorded in Appendix D. It is concluded that the sickling phenomenon is a cause of morbidity and mortality in the Gold Coast African and that sickle cell anaemia is not rare.

The frequent statements in the literature that sickle cell anaemia is rare in Africa are most probably wrong and are due to a number of factors which are listed below.

1) Large scale surveys of the younger age groups have never been performed. Many conclusions have been drawn from the examination of adults although it is most probable that many of the children suffering from sickle cell anaemia never reach adult life. Two autopsies on children aged 4 years have been reported in this thesis.

2) Laboratory facilities are primitive in most parts of Africa and the relatively specialised and time consuming procedures required to diagnose a haemolytic anaemia are not available to the majority of medical officers. A medical officer may be responsible for the health of 50,000 to 300,000 Africans and, when the multiple infections and infestations which affect the African are remembered (TABLE I), it is not surprising that a congenital haemolytic anaemia is not diagnosed.

3) The many and varied symptoms and signs which can be found in sickle cell anaemia are realised by very few clinicians in Africa. Few textbooks of tropical medicine discuss the anaemia at any length and it is neglected in most courses in tropical medicine. The writer did not receive any information in this subject while attending the course at the School of Tropical Medicine, London. The medical officer may thus be apt to overlook the condition and, when many cases of sickle cell anaemia are not diagnosed in America until autopsy BAUER & FISHER (1943) in spite of modern laboratory facilities being available, there is every excuse for a hard pressed medical officer missing the condition in Africa.

A number of interesting facts have arisen in the course of this investigation. All grades of severity of the anaemia were seen but even when the haemoglobin was as high as 14.2 G./100 ml. blood signs of increased haemolysis were constantly present in the peripheral blood. The relationship of the acute crises with the malarial season and the decrease of the severity of these attacks as the patient became older may be of significance in the aetiology of sickle cell anaemia in the Gold Coast.

In the autopsies it was unusual to obtain a history of previous ill health but unfortunately there are no records of previous haematological examinations having been performed. It is thus impossible to say if these deaths

occurred suddenly in persons who had no previous manifestations of the anaemia or if signs of increased haemolysis had been present in the peripheral blood for some time before death. Whether the person carrying the supposedly harmless trait can suddenly manifest symptoms of the disease must remain an open question. As mentioned above, however, all patients suffering from sickle cell anaemia examined by the author have at all times shown evidence of increased haemolysis and no evidence has been found which would lead to the belief that the harmless trait may suddenly become lethal.

The pathological findings in each autopsy were not constant and one or other of the following features might predominate.

1) Signs of haemolysis as shown by jaundice and erythrophagocytosis by the cells of the reticulo-endothelial system might be present.

2) The spleen might be fibrosed and small or enlarged and congested.

3) The viscera may be congested or exhibit extreme pallor depending upon whether the emphasis is on the spleen which is enlarged and packed with blood or upon the capillaries which may be blocked with masses of agglutinated erythrocytes.

4) Thromboses and infarctions may occur in the organs following capillary blockage as shown by the spleen in

Autopsy Number 1.

Thus the controversy in the literature about the pathological findings in sickle cell anaemia is more apparent than real as the pathologist's opinion will depend upon whichever of the above possible findings have predominated in the autopsies which he has performed.

SUMMARY AND CONCLUSIONS.

a) The literature on the sickle cell trait and sickle anaemia has been reviewed.

b) 2,255 Gold Coast Africans have been examined for the presence of the trait and the anaemia. Sickling of the erythrocytes was present in 407 instances - an incidence of 18.1 per cent.. No ill effects were attributed to the presence of the trait in 406 Africans. The remaining African girl was suffering from sickle cell anaemia. The incidence of sickle cell anaemia could not be calculated from this survey.

c) It was confirmed that the percentage of red blood cells sickling in the newborn was low and gradually increased with age.

d) The case reports of 20 patients suffering from sickle cell anaemia have been discussed. It has been found that, in the Gold Coast, a history of recurrent attacks of pain in the joints and the presence of many target cells in the peripheral blood smear has invariably been associated with sickling of the erythrocytes and signs

of increased haemolysis in the peripheral blood. The importance of malaria as a 'trigger' mechanism in initiating the crises of the anaemia has been considered.

e) The significance of the target cell in peripheral blood smears of Africans has been investigated. This cell, in numbers greater than 4%, has been found in 10 per cent. of 'normal' Africans. It has been present in large numbers in all cases of sickle cell anaemia. The examination of a peripheral blood film in the Gold Coast African for the presence of target cells is a useful negative diagnostic procedure. It's absence renders the diagnosis of sickle cell anaemia most unlikely. No case of Cooley's anaemia was detected. The incidence of the target cell was higher in the younger age groups. It is considered that the target cell is a non-specific cell.

f) The pathological findings in 13 patients dying from sickle cell anaemia or in an acute sickle cell crisis have been described.

g) The sickling phenomenon was found to be the cause of morbidity or mortality in 38 Africans. It is concluded that sickle cell anaemia is not rare in the Gold Coast and is probably not rare in Africa. It has not been possible to assess the incidence of sickle cell anaemia in the Accra District of the Gold Coast but the writer considers that the calculated incidence of 1% may well be correct which would agree with the homozygous theory

of the inheritance of sickle cell anaemia.

h.) A bibliography is appended.

It is concluded that, although the author has shown that sickle cell anaemia is not rare in the Gold Coast, further work on this problem is required. Wide scale surveys should be carried out on the younger age groups. An attempt should be made to examine a selected number of trait positive African girls before puberty and careful records made of their subsequent medical history with special reference to their behaviour in pregnancy. Unfortunately in the present state of our medical knowledge in the Gold Coast a comparable number of non-sickling controls would also have to be examined. This investigation would be outwith the scope of one medical officer and a team of full time workers would be required. Until the aetiology of sickle cell anaemia is understood, little can be done to prevent the disease occurring in many unsuspecting Africans.

APPENDIX A.

THE WORLD INCIDENCE OF THE SICKLE CELL TRAIT.

THE INCIDENCE OF THE SICKLE CELL TRAIT.

Author.	Date.	Locality.	Number examined.	% with trait.
		AFRICA, EAST.		
Foy et al.	1951	Kenya.	-	25.0
English.	1945	N. Rhodesia.	717	17.5
Beet.	1946	N. Rhodesia.	815	12.9
Beet. (39)	1949	N. Rhodesia.	616	13.2
Beet. (41)	1949	N. Rhodesia.	1,755	12.5
Gelfand.	1946	S. Rhodesia.	500	8.0
Mackey.	1949	Tanganyika.	1,036	19.4
Lehmann.	1949	Uganda.	71	18.3
Lehmann & Raper.	1949	Uganda.	4,564	17.8
Lehmann & Milne.	1949	Uganda.	294	24.2
Lehmann.	1951	Uganda.	53	86.8
Raper (385)	1949	Uganda.	1,286	10.7
		AFRICA, SOUTH.		
Murray.	1943	Johannesburg,	50	Nil.
Altmann (11)	1945	Bantu tribe.	403	0.25
Griffiths.	1950	Bantu tribe.	600	0.33
		AFRICA, SUDAN.		
Abbott.	1950	Zande tribe.	100	18.0
		AFRICA, WEST.		
Sarmento	1944	Angola.	418	8.4
Texeira.	1944	Angola.	186	28.0

Author.	Date.	Locality.	Number examined.	% with trait.
Trincao et al.	1950	Bissau Is.	500	3.0
Evans.	1944	Cameroons.	138	15.2
Nogueira et al.	1950	Cape Verde Is.	2,500	3.0
Parent.	1950	Congo, Belge.	1,004	30.4
Lambotte.	1951	Congo, Belge.	716	23.5
Evans.	1944	Gambia.	136	23.5
Gold Coast (199).	1936	Accra.	380	16.0
Evans.	1944	Gold Coast.	132	16.6
Gold Coast (201)	1945	Accra.	2,015	17.3
Findlay et al.	1946	Gold Coast.	888	16.0
Colbourne et al.	1950	Gold Coast.	255	22.4
Evans.	1944	Nigeria.	224	22.3
Smith.	1943	Nigeria.	500	6.0
Adamson.	1951	Nigeria.	100	16.0
Jelliffe & Humphreys.	1952	Nigeria	1,881	23.7
Trincao.	1944	St. Thomas Is.	100	1.0
Gosden & Reid.	1948	Sierre Leone.	1,035	27.0
Findlay et al.	1946	West Africa	5,500	12.4
		BRAZIL.		
DeMendonca.	1942	Mixed races. Negroes.	1,043 168	3.5 9.4
DaSilva.	1944	Rio de Janeiro.	1,368	9.5

Author.	Date.	Locality.	Number examined.	% with trait.
DaSilva.	1948	Indians.	1,379	Nil.
		Mixed.	166	1.8
		BRITISH WEST INDIES.		
Tomlinson, 480	1945	Natives.	998	9.6
		COLOMBIA.		
Mera.	1943	Puerto Tejado.	489	9.4
		CURACAO.		
Van der Sar.	1949	Natives.	2,499	11.7
		HONDURAS.		
McGavack & German.	1944	Tela.	300	8.0
		INDIA.		
Lehmann & Cutbush.	1952	Nilgris.	774	5.4
		ISRAEL.		
Dreyfuss & Benyesch.	1951	Yemenite Jews.	105	6.6
		PANAMA.		
Tomlinson.	1945	Canal Zone.	1,777	7.8
Calero.	1946	Santo Tomas.	896	6.0
		PUERTO RICO.		
Pons & Oms.	1934	San Juan.	388	2.3
		THE UNITED STATES OF AMERICA.		
Sydenstricker et al.	1923	Georgia.	300	4.3
Cooley & Lee.	1926	Michigan.	400	7.5
Miyamoto & Korb.	1927	Missouri.	300	6.3
Josephs.	1928	Baltimore.	250	6.4

THE UNITED STATES OF AMERICA. (Cont.)

Author.	Date.	Locality.	Number examined.	% with trait.
Smith.	1928	New Orleans.	100	5.0
Wollstein & Kreidel.	1928	New York.	150	8.6
Levy.	1929	New York.	213	5.8
Dolgopol & Stitt.	1929	New York.	77	5.2
Graham & McCarty.	1930	Alabama	1,500	8.1
Brandau.	1930	Texas.	150	6.7
Sydenstricker (465,464,466).	1932	Georgia.	1,800	5.5
Diggs.	1932	Tennessee.	827	8.2
Diggs et al.	1933	Florida.	674	9.6
Diggs et al.	1933	Tennessee.	2,539	8.3
Hargrove & Mathews.	1933	General	137	3.6
Beck & Hertz.	1935	Pa.	100	13.0
Wallace & Killingsworth	1935	Texas.	1,205	5.4
Hansen-Pruss.	1936	N. Carolina.	100	15.0
Cardozo.	1937	Illinois.	1,263	9.4
Johnson & Townsend.	1937	S. Carolina.	719	7.9
Tomlinson.	1941	W. Virginia.	275	6.5
Ogden.	1943	New Orleans.	692	6.5
Winsor & Burch, 530.	1945	Louisiana.	612	4.4

THE UNITED STATES OF AMERICA (Cont.)

Author.	Date.	Locality.	Number examined.	% with trait.
Henderson & Thornell.	1946	General.	312	7.3
Scott et al.	1948	Maryland.	471	5.3
Switzer & Fouche.	1948	S. Carolina	1,000	14.0
Watson, 514.	1948	New York.	452	8.2
Hodges.	1950	Philadelphia.	1,500	11.5
Switzer.	1950	S. Carolina.	3,066	13.4
Neel.	1951	Michigan.	1,000	9.1

THE INCIDENCE OF THE SICKLE CELL TRAIT IN THE WHITE RACE.

Miyamoto & Korb.	1927	U. S. A.	100	Nil.
Sydenstricker. 464 to 467.	1929	U. S. A.	1,000	Nil.
Diggs & Bibb.	1933	U. S. A.	309	Nil.
Wallace & Killingsworth.	1935	Mexicans.	239	Nil.
Killingsworth & Wallace	1936	U. S. A.	322	Nil.
Mera.	1943	Colombia.	88	Nil.
Ogden.	1943	U. S. A.	910	Nil.
Findlay et al.	1946	Syrians. British.	188 568	Nil. Nil.
Boturao, E.& E.	1947	Brazilians.	64	Nil.

APPENDIX B.

THE WORLD DISTRIBUTION OF REPORTED CASES OF SICKLE CASES ANAEMIA.

THE WORLD DISTRIBUTION OF REPORTED CASES OF SICKLE CELL ANAEMIA.

The reported cases of sickle cell anaemia in Africa are shown in detail. In the remaining countries of the world the author's reference is given only. The distribution of reported cases of sickle cell anaemia in the United States of America has purposely been omitted in view of the many hundreds of cases reported from that country.

AFRICA.

Author.	Locality.	No. of cases.	Remarks.
Trowell, (1945)	Africa, East.	35.	
Altmann, (1945)	Africa, South.	1	European.
Berk & Bull, (1943)	Africa, South.	1	Indian.
Grek & Findlay, (1951)	Africa, South.	1	Liberian.
Evans, (1945).	Africa, West.	4	
Robertson & Findlay, (1947)	Africa, West	61	None described.
Sarmento, (1945)	Angola.	1	
Abbassy, (1951)	Egypt.	1	
Edington, (1951)	Gold Coast.	2	
Edington & Sarkies, (1952).	Gold Coast.	2	
Gold Coast, 198	Gold Coast.	1	
Gold Coast, 201	Gold Coast.	6	No details.
Reid, (1936)	Gold Coast.	3	No details.
Russell & Taylor, (1932)	Gold Coast.	1	

Author.	Locality.	No. of cases.	Remarks.
Leroy & Linhard, (1943)	Cameroons.	2	
Foy et al. 184 (1951).	Kenya.	4	Not described.
Wright, (1949)	Kenya	2	Indians.
Lambotte (1951)	Leopoldville.	?11	1 described.
Parent, (1950).	Leopoldville.	2	
Smith, 446,447 & 448.	Nigeria.	10	
Beet, 40. (1949)	Rhodesia	1	
Archibald(1925)	Sudan	1	Arab boy.
Mackey, (1949)	Tanganyika.	1	Not described.
Lehmann & Milne, (1949)	Uganda	2	Not described.
Raper, (1950)	Uganda	5	

ARGENTINE.
JAHARA, (1949) ; SEGURA ET AL. (1942) & (1944).

BRAZIL.
DASILVA, (1945), (1946) & (1948). ; DECASTRO (1934) ; JAMRA ET AL. (1944) ; ROSENFELD, (1944).

BRITISH GUIANA.
BETTENCOURT-GOMES (1947).

CANADA.
SCRIVER & WAUGH (1930) ; MCKENDRY, (1944).

COSTA RICA.
AGUILAR & BLANCO, (1945) ; BAHIA ET AL., (1947).

CUBA.
ALONSO-PATINA ET AL., (1938) ; CASTELLANO, (1929) ; CABRERA CALDERIN ET AL., (1942) & (1937) ; CHEDIAK ET AL., (1959) ; COMBY, (1928) ; HERNANDEZ & MARTINEZ (1939) ; JORGANES, (1945) ; MORAGUES, (1941) ; ORTIZ, (1932) ; RIOLEON & HERNANDEZ, (1942).

CURACAO.
GODFRIED, (1949) ; VAN DER SAR, (1942) & (1949).

GREECE.
CHOREMIS ET AL., (1951) ; COMNINOS ET AL., (1950) ; COOLEY & LEE, (1927) ; FOY ET AL, (1951), 183 ; MAGGIORE, (1935) ; MAKRYCOSTAS, (1940) ; PONTONI, (1936) & (1939).

GUADELOUPE.
LANGUILLON, (1951).

ITALY.
BIANCO, (1948) ; CAPRIGLIONE, (1945) ; CARNEVALE, (1943) ; CASTANA, (1925) ; SILVERSTRONI, (1946) & (1948) ; SILVERSTRONI & BIANCO, (1946). ; WEINER (1937).

MEXICO.
WALLACE & KILLINGSWORTH, (1935).

PANAMA.
CALERO, (1946) ; TOMLINSON, (1945).

PERU.
URTEAGA, (1943) ; WEISS ET AL., (1935).

PUERTO RICO.
COHEN ET AL., (1947) ; ORTIZ, (1932) & (1940).

RIO GRANDE DE SUL.
RANGEL, (1946).

SALVADOR.
ACCIOLY, (1947).

SANTIAGO.
BUENO TORRES, (1944).

SICILY.
POWELL ET AL., (1950).

TRINIDAD.
PAWAN, (1937) ; TOMLINSON , (1945).

TURKEY.
EGELI, (1946).

URUGUAY.
GUERRA ET AL., (1942) ; ZERBINO ET AL., (1942).

VENEZUELA.
BENAIM PINTO ET AL., (1946), (1946) & (1947).

APPENDIX C.

CASE REPORTS OF TWENTY PATIENTS SUFFERING FROM SICKLE CELL ANAEMIA.

CASE REPORT NUMBER 1.
An African boy aged 15 years.

Present History. An African boy, M.A., of the Akim tribe was admitted to the Gold Coast Hospital, Accra on 20-12-49 complaining of pain in the joints, limbs and chest, nausea and weakness of 10 days duration. The pain complained of was deep seated in the large joints and muscles of the limbs and was 'gnawing' in character. It was now much less severe than it had been at the onset. Headache and fever had also been present before admission.

Family History. The father was alive but had suffered from attacks of 'rheumatism' all his life. The mother, 3 sisters and 1 brother were alive and well. The brother aged 24 years was the only member of the family available for examination (see below).

Previous History. The patient gave a history of frequent attacks of weakness, dyspnoea, swelling of the legs and severe pains in the joint and limbs at intervals of 2 months. These attacks had commenced in 'infancy'. His average yearly attendance at school was about 6 months. The patient had been in hospital twice at the age of 6 years suffering from yaws ulceration and had received 'many' injections. No history of jaundice was obtained.

Physical Examination. Reasonably comfortable asthenic youth. Temperature 99.2' F. Pulse and respiration rates 100 and 22 per minute respectively. The mucous membranes were pale. No jaundice or oedema. The features were not mongoloid.

There were extensive papery scars on the extensor aspects of both forearms, anterior aspects of both lower legs and right knee. The anterior cervical glands were slightly enlarged and rubbery. The lungs were clear. The heart was not enlarged and there was a systolic apical murmur. The blood pressure was 95/60. The liver and spleen were palpable 3 cm. and 2 cm. below the costal margins respectively. No joint changes or neurological abnormalities were noted. Ophthalmoscopic examination revealed dilated and tortuous retinal vessels.

Laboratory Investigations.

Urine :- albumin present for 2 days only. No bile. Schlesinger's test for urobilinogen strongly positive each day in hospital. Stool :- no ova, amoebae or cysts seen. Kahn test :- negative. No malarial parasites seen in blood smears.

Blood :- Hb. 9.1 G./100 ml. ; R.B.Cs. 3,510,000 per cu. mm. ; P.C.V. 26% ; M.C.V. 74.1 cu. micra ; M.C.Hb. 25.9 micro micrograms ; M.C.Hb.Conc. 35% ; W.B.Cs. 9,000 per cu. mm. Blood film :- mild anisocytosis, occasional poikilocyte and sickle cell ; many target cells (60%), Plate 1. ; occasional polychromatic cell ; no stippling. The reticulocyte count was 6.4%. Differential count :- metamyelocytes 2%, neutrophil polys. 45%, eosinophils 11%, small lymphocytes 16%, large lymphocytes 23%, monocytes 5%. 1 normoblast seen per 200 white blood cells. Sickling of the red blood cells 100% by the rapid method. Fragility

test showed haemolysis to commence in 0.3% and was complete in 0.15% saline. (Control 0.4 and 0.25%). E.S.R. 10 mm. in 1 hour. The serum bilirubin was 1.8 mgm.%.

Sternal puncture was performed on the 9th. hospital day and revealed a normoblastic hyperplasia of the bone marrow (TABLE IX). Target cells were present but no sickled cells were noted (Plate 6).

Radiography of the skull revealed no abnormality.

Bromsulphalein liver function test :- no retention of dye at the end of 30 minutes.

Course. The rheumatic like pains slowly improved and disappeared on the 6th. hospital day. The temperature fluctuated between 98.6 and 100' F. for 5 days and then returned to normal. Antimalarial therapy, sedatives and iron were prescribed. The patient remained in hospital until 17-1-50 when he was discharged at his own request. TABLE XII illustrates the haematological findings. The blood smears and differential counts were essentially similar to the findings reported above.

It will be seen from TABLE XII on page 4 that, during the 25 days that the patient was under observation, signs of increased haemolysis were constantly present in the peripheral blood. Antimalarial therapy had no effect on this haemolysis.

The patient's brother aged 24 years was examined. No abnormality was detected in the blood apart from sickling of the erythrocytes. A history of recurrent illness

simulating the crises of sickle cell anaemia was not given.

TABLE XII.

SERIAL BLOOD COUNTS PERFORMED ON M.A.

Date	.23-12-49	.30-12-49	.10- 1-50	.17- 1-50 .
Hb. in G./ 100 ml.	9.1	9.9	10.9	10.6
RBCs. in millions	3.51	3.6	3.96	4.0
WBCs. per cu.mm	9,000	7,400	8,600	8,200
P.C.V. %	26	28	32	31
M.C.V. in cu.micra.	74	78	81	78
M.C.Hb.Conc.	35	35	34	34
Retics.	6.4	5.3	6.1	7.0
Bilirubin mgm./100 ml.	1.8	1.4	1.5	1.5

Comment. The findings are suggestive of a chronic haemolytic anaemia with decreased fragility and sickling of the erythrocytes. A history of recurrent attacks of joint pains was given. Antimalarial therapy did not affect the haemolysis. The characteristic cell in the peripheral blood smear was the target cell.

CASE REPORT NUMBER 2.
An African boy aged 12 years.

Present History. An African boy, D.B., of the Krobo tribe was admitted to the Gold Coast Hospital, Accra on 6-5-50 complaining of nausea, fever and pain in the left side of the abdomen and large joints of the limbs of 5 days duration.

Family History. The father, mother and 2 brothers were alive and well. 1 sister aged 10 years was stated to suffer from 'rheumatism'. The sister was the only member of the family available and, on examination, was found to be suffering from sickle cell anaemia - Case Report Number 3.

Previous History. Ahistory of recurrent and frequent attacks of fever with abdominal and joint pains was given. The attacks commenced in 'infancy' and occur about 8 times in the year. The eyes have at times been yellow. There was no history of yaws.

Physical Examination. A rather thin,fairly comfortable boy, small for his years. Temperature 100' F. Pulse and respiration rates 124 and 28 per minute. The mucous membranes were poorly coloured. Slight icterus of the sclerae. There was no oedema and the features were not mongoloid. No ulcers or scars. The anterior cervical glands were enlarged and rubbery. The lungs were clear. The heart was enlarged but there were no bruits. The blood pressure was 100/55. The liver was not palpable. The spleen extended into the left iliac fossa and was

firm and tender. No joint changes or neurological abnormalities were noted. The fundi were normal.

Laboratory Investigations. Urine :- trace of albumin, no bile, Schlesinger's test for urobilin strongly positive. Stool :- scanty hookworm ova present. No pathogenic organisms were isolated on culture. Kahn test :- negative, No malarial parasites seen in smears.

Blood :- Hb. 6.1 G./100 ml. ; R.B.Cs. 1,900,000 per cu. mm. ; P.C.V. 21% ; M.C.V. 110.5 cu.micra ; M.C.Hb.Conc. 29% ; W.B.Cs. 6,600 per cu. mm.. Blood film :- anisocytosis, poikilocytosis, occasional sickle cell, many target cells (61%) and polychromatic macrocytes present - Plate 5. The reticulocyte count was 20.2%. Differential count :- metamyelocytes 1%, neutrophil polys. 56%, eosinophils 1%, basophils 1%, lymphocytes 37%, monocytes 4%. 10 nucleated red cells seen per 100 whites. Sickling of the red blood cells 100% by the rapid method. Fragility :- commenced 0.55 and was complete 0.1% saline. (Control 0.5 and 0.25%). E.S.R. 18 mm. in 1 hour. The serum bilirubin was 1.6 mgm. %. The Coombs' test was negative. Plasma protein 8.5 G.%. - albumin 4.4 G. and globulin 4.1 G. Blood culture, Widal and Weil Felix tests were negative. Sternal puncture was performed on the third hospital day and revealed a normoblastic hyperplasia - see TABLE IX and Plate 7.

Radiological Examination. Plates 8,9,10 and 11.
Skull :- perpendicular trabecular striations radiating

outwards from the inner table and absence of a well defined outer table. 'Hair on end' appearance.

Chest :- the transverse diameter of the heart is increased. The ribs show a generalised mottling with increased trabeculation in the direction of the long axis.

Femora :- there are translucent areas surrounded by sclerosis at the lower end of the left femur. There is a mild increase in the vertical lines of the cortex and horizontal growth lines can be distinguished.

Tibiae and fibulae :- there are increased trabecular markings and some endosteal proliferation. An area in the upper third of the left tibia appears to be a healing infarctive lesion.

Course. The original attack settled after three days in hospital when the temperature became normal. Two further exacerbations of fever and joint pains were complained of while the patient was under observation. These attacks lasted for 7 days. They commenced with severe pain in the joints and abdomen and a sudden rise of temperature to 103' F. The temperature settled by lysis and was normal in 7 days. Blood counts were performed during these attacks on 13-4-50 and 27-5-50 and are shown in TABLE XIII . The fall in haemoglobin and the increase in circulating reticulocytes and nucleated red cells are consistent with the increased haemolysis expected in a haemolytic crisis. The spleen did not appear to vary in size but the pain and tenderness increased with the onset of the crises.

Liver, iron, salicylates, sedative and antimalarial drugs were prescribed without relief during the attacks. Morphia was necessary to relieve the joint pains. Splenectomy was considered but was thought by the surgeon to be unjustified. Tetrachlorethylene was prescribed for the hookworm infestation. The patient was discharged from hospital on 30-5-50. There was no improvement in his condition. TABLE XIII illustrates the haematological findings during the 11 weeks D.B. was under observation.

TABLE XIII.

SERIAL BLOOD COUNTS PERFORMED ON D.B.

Date	6-3-50	22-3-50	13-4-50	1-5-50	27-5-50
Hb. in G./100 ml.	6.1	6.8	4.6	7.6	6.2
RBCs. in millions.	1.9	2.46	1.34	2.45	1.85
WBCs. per cu. mm.	6,600	5,000	10,200	6,400	10,600
P.C.V. %.	21	22	16.5	24	20
M.C.V. in cu. micra.	110.5	91	123	100	108
M.C.Hb.Conc.	29	30	29	30	30
Retics. %.	20.2	11.8	27.2	14.4	26
Bilirubin mgm./100 ml.	1.6	1.3	1.8	1.5	2.5
Nucleated reds/100 white cells.	10	3	29	4	11

In all cases the thin blood films showed target cells, poikilocytosis, anisocytosis, sickle cells, basophilic stippling and polychromatic macrocytes.

Comment. See Case Report Number 3.

CASE REPORT NUMBER 3.
An African girl aged 10 years.

Present History :- G.B., a sister of D.B., was not complaining at the time of the examination.

Family History. As for D.B. Case Report Number 2.

Previous History. The patient gave a history of periodic attacks of fever and joint pains occurring about 4-6 times a year. The only abnormal finding on physical examination was an enlarged spleen which was palpable 8 cms. below the costal margin.

Laboratory Investigations.
Urine :- no albumin or bile present. Schlesinger's test for urobilin strongly positive. Stool :- no ova, amoebae or cysts seen.

Kahn test :- weakly positive. No malarial parasites in a blood smear.

Blood :- Hb. 9.5 G./100 ml. ; R.B.Cs. 2,820,000 per cu. mm. ; P.C.V. 27% ; M.C.V. 96.4 cu. micra ; M.C.Hb.Conc. 35% ; W.B.Cs. 11,600 per cu.mm.

Blood film :- anisocytosis , poikilocytosis, target cells (47%) and polychromatic macrocytes. The reticulocyte count was 14.4%. Differential count :- metamyelocytes 2%, neutrophil polys. 51%, eosinophils 2%, lymphocytes 45%. 2 normoblasts seen per 100 white blood cells. Sickling of the red blood cells 100% by the rapid method.

Fragility :- haemolysis commenced 0.3 and was complete 0.05% saline. E.S.R. 25 mm. in 1 hour. The serum bilirubin was 1.6 mgm.%.

Radiological Examination.

Skull :- the frontal and parietal bones show the 'hair on end' appearance.

Femora and knee joints :- No abnormality detected.

Course. An antimalarial course extanding over 10 days was given and a course of N.A.B. instituted. The blood findings were unchanged at the end of the 10 days. The girl unfortunately did not return for further investigation or completion of the course of arsenical therapy.

Comment on Case Reports Number 2 and 3.

D.B. and his sister G.B gave gave a history. suggestive of haemolytic crises and signs of increased haemolysis were constantly present in the peripheral blood.. The erythrocytes of both sickled. Salicylates and antimalarial therapy had no effect on the haemolysis.

CASE REPORT NUMBER 4.
An African boy aged 16 years.

Present History. An African boy, P.H., of the Ga tribe was admitted to the Gold Coast Hospital, Accra on 14-2-50 complaining of generalised pains in the limbs and joints, pain in the upper abdomen and a yellow discolouration of the eyes of 6 days duration. Headache and nausea were also present.

Family History. The mother, father, 5 sisters and 2 brothers were alive and well. The second child and the third child born in the family had died at the same time in a yellow fever outbreak in 1937. The family were examined and the haematological findings are shown in TABLE XV.

Previous History. The patient gave a history of attacks of 'rheumatism' from the age of 4 years. These attacks were thought to be associated with the rainy season and cold weather. Pains in the larger joints and limbs associated with headache and fever were present in these attacks which lasted for 2-3 weeks and they occur 4-6 times in the year. The eyes were first noted to be yellow at the age of 12 years. In a typical attack pains in the joints and limbs occur first and then the patient feels cold and in a few days the eyes become yellow. The patient was a schoolboy and sickness records records were available. Since admission to school in 1948 the boy has lost 95 schooldays in 5 attacks of illness during terms. The diagnoses have been 1) Fever N.Y.D twice. 2) 'Rheumatism'. 3) Tonsillitis

and 4) Malaria. The haemoglobin has ranged from 40 - 60% Sahli during this time.

Physical Examination. Comfortable asthenic African youth. Temperature 101' F. Pulse and respiration rates 90 and 24 per minute respectively. Jaundice of the sclerae. The features were mongoloid and the skin coffee coloured. The hair was soft and slightly reddish in colour. The mucous membranes were poorly coloured and the tongue was smooth and pale. The anterior cervical glands were slightly enlarged and rubbery. The lungs were clear. The heart was not enlarged and there were no bruits. The blood pressure was 90/55. The liver was palpable 9 cms. below the right costal margin in the mid-clavicular line. It was slightly tender and the edge was smooth and soft. The tip of the spleen was just palpable. No joint changes or neurological abnormalities were noted. Ophthalmoscopic examination revealed dilated and tortuous retinal vessels.

Laboratory Investigations.
Urine :- albumin nil. Bile pigments and urobilin present.

Stool :- no ova, cysts or amoebae seen. Trace of bile present.

Kahn test :- negative. No malarial parasites in blood smears.

Blood :- Hb. 7.5 G./ 100 ml. ; R.B.Cs. 2,200,000 per cu. mm. ; P.C.V 22.5% ; M.C.V. 101.3 cu.micra. ; M.C.Hb.Conc. 33% ; W.B.Cs. 14,200 per cu.mm..

Blood film :- anisocytosis, poikilocytosis, occasional

sickle cell, many target cells (48%), occasional Howell Jolly bodies and polychromatic macrocytes present - Plate 5. The reticulocyte count was 7%.

Differential count :- metamyelocytes 0.2%, neutrophil polys. 63%, basket cells 4%, lymphocytes 29%, monocytes 3.8%. 3 normoblasts seen per 100 white blood cells. Sickling of the red blood cells 100% by the rapid method.

Fragility :- haemolysis commenced 0.3% and was complete 0.1%. (Control 0.4-0.25%). E.S.R. 40 mm. in 1 hour.

The serum bilirubin was 14.0 mgm.%. Coombs' test negative. Culture of the blood and stool revealed no pathogenic organisms. Bromsulphalein liver function test showed 35% retention of the dye at the end of 30 minutes.

Sternal puncture was performed on the 5th. hospital day and revealed an intense normoblastic hyperplasia of the marrow - TABLE IX. Scanty target cells were present.

Radiography of the gall bladder, skull and long bones revealed no abnormality.

Course.

Antimalarial, iron and liver therapy were prescribed. The patient's jaundice gradually diminished in intensity but never completely disappeared. Bile pigments slowly disappeared from the urine and reappeared in the stool. Urobilinogen did not noticeably diminish in the urine and was still present on discharge from hospital on 8-3-50. The temperature was irregular and fluctuated between 99 and 102' F. from admission until 1-3-50. Blood cultures and

serological tests were all negative.

The haematological details are shown on the following table (TABLE XIV).

TABLE XIV.

SERIAL BLOOD COUNTS PERFORMED P.H.

Date	15-2-50	25-2-50	14-3-50	15-8-50
Hb. in G./100 ml. blood.	7.5	8.0	8.4	7.9
RBCs. in millions	2.2	2.64	2.65	2.95
WBCs. per cu. mm.	14,200	13,000	11,500	17,400
P.C.V. %.	22.5	22.0	23.0	23.0
M.C.Hb. Conc.	33	36	36	34
M.C.V. in cu. micra.	101	83	87	79
Retics.%.	7	14.2	8.4	9.8
Bilirubin in mgm./100 ml.	14.0	12.5	4.6	5.0
Nucleated reds / 100 wh.	3	7	2	5
Bile in urine	++++	+++	Trace	Nil
Urobilin in urine.	++	++	++	++

From the above table it will be seen that signs of haemolysis in the peripheral blood were still present 5 months after discharge from hospital. The physical signs were as reported above. The jaundice, however, was much less noticeable and the liver was smaller, being palpable 7 cms. below the costal margin. Bromsulphalein retention was less than 5% at this time. Normoblasts, anisocytosis, poikilocytosis, sickle cells, many target cells and occasional Howell Jolly bodies were still present in the

blood smear.

Investigation of the family. The haematological findings are shown in TABLE XV. The features of the mother tended to be mongoloid and it is of interest to note that the blood film in this case showed poikilocytosis and target cells although no history of haemolytic crises was given and there was no evidence of increased haemolysis.
The patient P.H. and Barbara aged 13 years had definitely mongoloid features. The liver was only palpable in P.H. but the spleen was palpable in P.H., Mariana aged 9 years, Joel aged 6 years and Virginia aged 13 months.

Virginia was the only other member of the family who showed signs of increased haemolysis in the peripheral blood and she was considered to be suffering from sickle cell anaemia.

Comment. The history given by P.H. was suggestive of recurrent haemolytic crises. Signs of increased haemolysis were present in the peripheral blood over a 6 month period. The hepatic insufficiency, which was the predominating feature when the patient was first seen, gradually improved without improvement in the anaemia or in the signs of increased haemolysis. The aetiology of hepatic insufficiency in sickle cell anaemia is obscure but has already been described in 5 patients by HENDERSON (1950).

Antimalarial, iron and liver therapy did not affect the course of the haemolysis or improve the anaemia.

The mother and father both exhibited the trait and

TABLE XV HAEMATOLOGICAL FINDINGS IN FAMILY P.H.

	Age	Hb.G/100 ml.	R.B.Cs. in millions.	W.B.Cs. per cu.mm.	P.C.V.%.	MC.V. in cu. micra.	M.C.Hb.C.%.	Sickling.	Fragility % saline.	Bilirubin mgm.%.	Reticulocytes %.
Father.	45	14.2	5.48	5,800	44	80.3	32.2	+ve.	0.4 -0.2	0.1	-
Mother.	43	13.3	4.7	9,000	42	89.4	31.6	+ve.	0.4 -0.1	0.2	-
Peter.	16	Reported case.									
Barbara.	13	12.5	4.56	5,800	37	81.1	34.0	+ve.	0.45-0.2	0.1	0.8
John.	11	12.9	4.83	6,400	40	82.8	30.0	+ve.	0.45-0.25	0.2	0.6
Mariana.	9	13.4	5.2	7,800	39.5	76	34	+ve.	0.4 -0.2	0.2	1.2
Joel.	7	13.2	4.9	8,000	40	81.6	33	-ve.		0.1	D.1
Regina.	6	12.6	4.79	10,800	37	77.2	34	+ve.	0.35-0.05	D.2	0.4
Margaret.	5	10.8	4.3	6,400	34	79.0	30.2	-ve.	nd.	0.8	1.2
Virginia*.	13/12	9.5	3.8	12,600	32	84	30.2	+ve.	nd.	1.4	8.4

* Blood film showed Anisocytosis, Poikilocytosis many target cells and 5 nucleated red cells per 100 white cells.

the examination of their 8 children was considered to agree with the homozygous-heterozygous theory of the inheritance of the sickle cell trait and sickle cell anaemia - TABLE XV.

CASE REPORT NUMBER 5.
An African boy aged 8 years.

Present History. An African boy, S.A., of the Ga tribe was admitted to the Gold Coast Hospital, Accra on the 8-5-50 complaining of fever, pain in the abdomen and large joints of the limbs, dizziness, headache and nausea. These symptoms had been present almost continuously for 6 months.

Family History. The father, mother, 1 brother aged 6 years and 2 sisters aged 4 years and 15 months were alive and well. The maternal grandfather was stated to have suffered from 'rheumatism' all his life. The siblings unfortunately were not available for examination. The results of the parents' blood examinations are recorded below. (TABLE XVII).

Previous History. Apart from chicken pox and an occasional attack of fever, the patient had been well until 6 months ago. No history of joint pains or jaundice previous to this time was obtained.

Physical Examination. Comfortable fairly well nourished boy. Temperature 101.8' F. Pulse and respiration rates 120 and 26 per minute. The mucous membranes were pale. There was slight icterus of the sclerae. Old scars were present on both ankles. The lungs were clear. The heart was not enlarged and there were no bruits. The blood pressure was 90/50. The liver edge was soft and smooth and was palpable 6 cms. below the right costal margin in the mid clavicular line. The spleen was not felt.

No joint changes or other abnormalities were noted. The fundi were normal.

Laboratory Investifations.
Urine :- Trace of albumin for 2 days only. Schlesinger's test for urobilin constantly strongly positive throughout stay in hospital. No bile pigments.
Kahn test :- negative. Malarial parasites (P. malariae) were present in a blood smear on admission but were repeatedly negative following antimalarial therapy.
Blood :- Hb. 7.5 G./100 ml. ; R.B.Cs. 2,310,000 per cu. mm. ; P.C.V. 26%. ; M.C.V. 112.5 cu.micra ; M.C.Hb. 33 micro-micrograms ; M.C.Hb.Conc. 29% ; W.B.Cs. 23,000 per cu.mm..
Blood film :- anisocytosis, poikilocytosis, sickle cells, occasional polychromatic macrocyte, Howell Jolly bodies and many target cells.Plate 3.
The reticulocyte count was 6.2%. Differential count :- metamyelocytes 3%, neutrophil polys. 47%, eosinophils 2%, lymphocytes 38% and monocytes 10%. 5 nucleated red cells (4 normoblasts and 1 macronormoblast) per 100 white cells.
Sickling of the red blood cells 100% by the rapid method.
Fragility :- haemolysis commenced 0.4% and was not complete in 0.05% saline. E.S.R. 12 mm. in 1 hour. The serum bilirubin was 1 mgm.%. The Coombs' test was negative.
Culture and microscopy of the stool and urine revealed no pathogenic organisms. The Widal, Weil Felix and melitensis agglutination reactions were within normal limits on the 10th. and 20th. hospital days.

Sternal puncture was performed on the 8th. hospital day and revealed a normoblastic hyperplasia (TABLE IX). Bromsulphalein was not retained at the end of 30 minutes. Radiography of the skull and long bones revealed no abnormality.

Course. The severity of the joint pains slowly lessened but were present throughout the patient's stay in hospital until his discharge on 11-6-50 (40 days). A low grade pyrexia was also continuously present until 4-6-50. On discharge from hospital there was little improvement in the patient's condition in spite of treatment with salicylates, oral iron, parenteral liver and antimalarial drugs. The haematological findings are shown in TABLE XVI.

TABLE XVI

SERIAL BLOOD COUNTS PERFORMED ON S.A.

Date	4-5-50	18-5-50	9-6-50	12-6-50
Hb. in G./100 ml. blood.	7.5	8.1	9.4	8.7
RBCs. in millions.	2.31	2.51	2.67	2.7
WBCs. per cu. mm.	23,000	14,000	10,200	11,000
P.C.V. %.	26	27	28	27
M.C.V. in cu. micra.	113	108	105	100
M.C.Hb.Conc.	29	30	34	32
Retics. %.	6.2	8.2	5.4	6.1
Bilirubin in mgm./100 ml.	1	1	0.8	0.8
Nucleated reds	10	4	6	4

Thin blood films in all cases showed many target and sickle cells

Investigation of the Family.

As previously stated the parents were the only members of the family available for examination. The following table illustrates the blood findings.

TABLE XVII.

HAEMATOLOGICAL FINDINGS OF THE PARENTS OF S.A.

Parent	Father	Mother
Hb. in G./100 ml. blood.	13.2	12.3
RBCs. in millions	4.29	4.3
WBCs. per cu. mm.	7,000	6,800
P.C.V. per cent.	40	41
M.C.V. in cu. micra	93	95
M.C.Hb.Conc. per cent.	33	30
Reticulocytes per cent.	0.2	0.4
Bilirubin mgm./100 ml.	0.2	0.2
Sickling	+ve.	+ve.

The differential counts of both parents were within normal limits. The thin blood films of each parent showed scanty target cells but no other abnormality.

Comment. The findings are those of a chronic haemolytic anaemia with decreased fragility and sickling of the erythrocytes. A history of continuous attacks of joint pain was given. Therapy did not influence the condition. Both parents exhibited the sickle cell trait but were otherwise healthy.

CASE REPORT NUMBER 6.
An African male nurse aged 44 years.

Present History. An African male, J.A.H., of the Fanti tribe was admitted to the Gold Coast Hospital on 25-2-50 suffering from a typical attack of dengue fever. A routine blood film, however, showed many target cells and the patient was investigated. The course of the dengue fever is not discussed and only findings relevant to the present investigation are given.

Family History. The father, mother and 4 brothers were alive and well. 1 sister died of plague in 1924. The patient has 3 wives, by whom he has had 6 children. 3 children of the third wife are alive and well. 1 child by the second wife died of tetanus neonatorum. The 2 children of the first wife died in infancy of 'anaemia' and typhoid fever respectively. The third wife was the only member of the family available and her blood count was within normal limits and the erythrocytes did not sickle.

Previous History. The patient gave a history of recurrent attacks of severe 'rheumatism' since infancy. These attacks consisted of severe pain in the larger joints of the limbs and muscles accompanied by headache and fever. The attacks became less severe as he became older and finally ceased at the age of 35 years. The attacks were very severe when he was young and occurred 6-8 times in the year. The intervals between the attacks became longer with advancing years until they ceased at the age of 35.

The patient had also suffered from occasional attacks of 'fever' which he considered to be malaria and which he distinguished from the attacks of 'rheumatism'. There was no history of yaws, jaundice or anaemia.

Physical Examination. Well nourished healthy male. A typical dengue rash was present. The liver was firm and smooth and was palpable 4 cms. below the right costal margin in the mid clavicular line. No other abnormal findings were noted.

Laboratory Investigations.

Urine :- Schlesinger's test for urobilin strongly positive.

Stool :- no ova, amoebae or cysts seen.

Kahn test :- negative. No malarial parasites seen in blood smears.

Blood :- Hb. 12.7 G./100 ml. blood ; R.B.Cs. 4.950,000 per cu.mm. ; P.C.V. 38% ; M.C.V. 77 cu. micra ; M.C.Hb. 25.7 micromicrograms ; M.C.Hb.Conc. 33% ; W.B.Cs. 4,800 per cu.mm. Blood film :- poikilocytosis and many target cells (84%) - Plate 3. The reticulocyte count was 4.2%. Differential count :- neutrophil polys. 92% and lymphocytes 8%. Sickling of the red blood cells 100% by the rapid method. Fragility :- haemolysis commenced 0.35% and was complete 0.1% saline. E.S.R. was 3 mm. in 1 hour. The serum bilirubin was 0.8 mgm.%. There was no retention of bromsulphalein at the end of 30 minutes.

Radiography of the skull, long bones and joints revealed no abnormality apart from mild arthritic changes in the left knee joint.

Course. The symptoms referable to the attack of dengue fever cleared in 7 days. A further blood examination on the 10th. hospital day was similar to the first apart from the white blood count and differential count which were 8,600 and neutrophil polys. 76%, lymphocytes 20% and monocytes 4% respectively. Antimalarial therapy was prescribed on the 2nd. hospital day.

Comment.

This patient was a nurse and gave an accurate history of what he termed 'rheumatism'. There was decreased fragility of the erythrocytes to hypotonic saline and evidence of a mild haemolytic process in the peripheral blood which did not improve with antimalarial therapy. The blood exhibited the sickle cell trait and there were many target cells in the thin films. The patient could distinguish the attack of 'rheumatism' from the attack of malaria.

CASE REPORT NUMBER 7.
An African boy aged 12 years.

Present History. An African boy, T.A., of the Ga tribe was admitted to the Gold Coast Hospital on 29-3-50 complaining of pain and swelling of the left elbow joint of 5 days duration. The condition occurred suddenly with the onset of severe pain in the region of the joint and in a few hours the affected part became swollen. There was no history of injury. Vague generalised pains, most marked in the region of the cervical spine, mild headache, nausea and general malaise were also complained of.

Family History. The previous history of the father was not known. The mother and 6 siblings were alive and well. There was no history of 'rheumatism' in the family. The mother was the only member of the family available for examination. Her blood count was within normal limits but the erythrocytes sickled 100%.

Previous History. The patient gave a history of recurrent attacks of joint pain and fever since infancy. No joint had been swollen previously. The patient suffered from 'many' of these attacks in the year. The joints most often affected were both knee joints and the cervical and lumbar regions of the spine. There was no previous history of jaundice or yaws.

Physical Examination. An asthenic African boy with mongoloid features. Temperature 101' F.. Pulse and respiration rates 122 and 28 per minute. The mucous membranes were pale. There was no jaundice or oedema.

There were small keloids on the chin and right ear. There was a fusiform swelling of the left elbow joint which was tender on palpation. Movement of the joint was limited and painful. The surface temperature of the skin overlying the joint was not raised. The anterior cervical glands were slightly enlarged and shotty. The lungs were clear. The heart was slightly enlarged but there were no bruits. The blood pressure was 100/70. The liver and spleen were palpable 5 cms. and 2 cms. below the costal margins respectively. Neither were tender. No neurological abnormalities were noted. The fundi were normal. Scars were present on both lower legs.

Laboratory Investigations.

Urine :- trace of albumin present for 3 days. Urobilin was constantly present. Stool :- microscopy and culture revealed no abnormality.

Kahn test :- negative. No malarial parasites seen in blood smears.

Blood :- Hb. 9.0 G./100 ml. blood ; R.B.Cs. 3,050,000 per cu. mm. ; P.C.V. 25% ; M.C.V. 83 cu. micra. ; M.C.Hb. 29.5 micromicrograms ; M.C.Hb.Conc. 36% ; W.B.Cs. 14,000 per cu. mm.. Blood film :- anisocytosis, poikilocytosis, many target cells (52%), occasional sickle cell and polychromatic macrocyte - Plate 4. The reticulocyte count was 4.6%. Differential count :- metamyelocytes 3%, neutrophil polys. 41%, eosinophils 6%, basophils 1%, lymphocytes 45%, monocytes 4%. 3 normoblasts per 100 white blood cells. Sickling of the red blood cells 100%

by the rapid method. Fragility :- haemolysis commenced 0.45% and was complete in 0.05% saline. E.S.R. 32 mm. in 1 hour. The serum bilirubin was 1.0 mgm.%. There was no retention of bromsulphalein at the end of 30 minutes. Blood culture was sterile. Sternal puncture revealed a normoblastic hyperplasia of the marrow - TABLE IX.

Radiography of the affected joint revealed no abnormality.

Course. The temperature gradually settled and became normal on 10-4-50 (12th. hospital day). The swelling of the left elbow joint slowly diminished and tenderness was maximal over the lower end of the humerus but could never be definitely localised. Movement of the joint gradually became less painful and on discharge 29-4-50 no abnormality could be detected. Blood smears for malarial parasites were repeatedly negative. On discharge the liver had not diminished in size but the spleen could not be felt. Rest and local applications were applied to the affected joint. Mist. aspirin, iron and antimalarial therapy were prescribed. The haematological findings on 29-4-50 were unchanged, that is one month after the original examination.

Comment. The patient gave a history of recurrent attacks of joint pain. A normocytic haemolytic anaemia with sickling of the erythrocytes was present following antimalarial therapy. Many target cells were present in the peripheral blood film.

CASE REPORT NUMBER 8.
An African male aged 22 years.

Previous History. An African male, H.T., of the Ashanti tribe was admitted to the Gold Coast Hospital on 16-5-50 complaining of swelling of the right side of the face, pain in the right knee joint and backache of 4 days duration. Headache, fever and nausea were also complained of.

Family History. The father and 2 brothers were alive and well. The mother and 1 sister were alive but were said to suffer from 'rheumatism'. The members of the family were not available for examination.

Previous History. The patient gave a history of frequent attacks of pain in the larger joints associated with fever and nausea since infancy. He associated these attacks with cold weather and the rainy season. The eyes have often been yellow. There was no history of yaws.

Physical Examination. Fairly comfortable asthenic male African. Temperature 101' F.. Pulse and respiration rates 98 and 24 per minute. There was a diffuse swelling of the tissues of the right cheek and right alveolar margin. The swelling was uniform, firm, slightly tender and did not pit on pressure. The mucous membranes were well coloured. The sclera were slightly jaundiced. There was no oedema. The lungs were clear. The heart was not enlarged but there was a systolic murmur at the apex. The blood pressure was 105/60. The spleen was palpable 5 cms. below the costal margin. There was uniform

swelling of the right knee joint. The fundi were normal.

Laboratory Investigations.

Urine :- light cloud of albumin. Pus, epithelial and red blood cells present. Ova of S. haematobium present. Schlesingers test for urobilin strongly positive.

Stool :- microscopy and culture revealed no abnormality.

Kahn test :- negative. No malarial parasites seen in blood smears.

Blood (not examined until 8th. day in hospital) :- Hb. 11.1 G./100 ml. blood ; R.B.CS. 3,500,000 percu.mm. ; P.C.V. 30% ; M. C. V. 86 cu. micra ; M.C.Hb. 32 micro-micrograms ; M.C.Hb.Conc. 37% ; W.B.Cs. 9,400.

Blood film :- anisocytosis, poikilocytosis, sickle cells and many target cells (55%) - Plate 3. The reticulocyte count was 4.2%. Differential count :- neutrophil polys. 53%, eosinophils 9%, lymphocytes 35% and monocytes 3%. Sickling of the red blood cells 100% by the rapid method. Fragility :- haemolysis commenced 0.3% and was complete 0.1% saline. E.S.R. 5 mm. in 1 hour. The serum bilirubin was 1 mgm%. Blood culture was sterile.

Course. The patient's symptoms rapidly subsided with penicillin therapy (1,000,000 units). Antimalarial therapy was also given. He was discharged on 30-5-50 for out patient treatment of the schistosomiasis. A blood count on discharge revealed that signs of increased haemolysis were still present in the peripheral blood.

Comment. This report is inconclusive as the haematological examination was not performed until the patient had been in hospital for 8 days and the second investigation was performed on the day of discharge only 6 days after the first. The presence of schistosomiasis was also a complicating factor and the patient did not return for further investigation or treatment. However the syndrome of a history of recurrent joint pains, sickling of the erythrocytes, a mild haemolytic anaemia and many target cells in the blood smear was again present.

CASE REPORT NUMBER 9.
An African male aged 39 years.

Present History. An African male, L.A.P., of the Ga tribe was admitted to the Gold Coast Hospital on 16-6-50 complaining of pain in the right thigh, hip and knee joint of 4 days duration. The pain was deepseated and aching in character. The patient also complained of weakness, palpitation, fever and swelling of the small joints of the fingers. The swellings of the fingers were slightly painful and movement was rendered difficult. The urine was dark in colour.

Family History. The mother died aged 55 of diabetes and the father aged 27 years of an unknown cause. The patient's wife and 5 children were alive and well. The family were examined and the result is recorded below.

Previous History. The patient gave a history of recurrent attacks of 'rheumatism' since infancy occurring 4-6 times in the year. He associates the onset of the attacks with cold or wet weather and they are aggravated by cold baths. The attacks last 2-3 weeks and commence with pain in the larger joints, palpitation and fever. The joints involved have never been swollen previously. The attacks were much more severe when the patient was younger. The eyes have never been yellow but the patient noticed that his urine 'changes colour' in these attacks.

Physical Examination. Well nourished African male. Temperature 99.6' F.. Pulse and respiration rates 92 and 22 per minute. The mucous membranes were well coloured.

There was no jaundice or oedema. There was a slight diffuse swelling of the fingers which was not tender and did not pit on pressure. Movement of the right hip and knee joint was not limited but was painful. There was indefinite diffuse tenderness on palpation of the right femur. The lungs heart and abdomen revealed no abnormality. The fundi were normal.

Laboratory Investigations.

Urine :- light cloud of albumin present for a few days only ; urobilin constantly present ; no pus ; culture was sterile.

Stool :- microscopy and culture revealed no abnormality.

Kahn test :- negative. No malarial parasites seen in blood smears.

Blood :- Hb. 13.2 G./100 ml. blood ; R.B.Cs. 4,870,000 per cu.mm. ; P.C.V. 41% ; M.C.V. 85 cu.micra ; M.C.Hb. 27 micromicrograms ; M.C.Hb.Conc. 32% ; W.B.Cs 12,000 per cu.mm. Blood film :- anisocytosis, poikilocytosis and many target cells (80%). The reticulocyte count was 3.5% Differential count :- neutrophil polys. 36%, eosinophils 3%, lymphocytes 55%, monocytes 5%. Sickling of the red blood cells 100% by the rapid method. Fragility :- haemolysis commenced 0.3 and was complete 0.01% saline. E.S.R. 4 mm. in 1 hour. The serum bilirubin was 0.8 mgm.%.

Radiological Findings (2302/50)

Skull :- the 'hair on end' appearance is present although it is not well marked.

Femora :- trabeculation is present with some cortical thickening.

Course. The patient's symptoms improved gradually and he was discharged well on 29-6-50 and at that time there was no change in the haematological findings. Antimalarial therapy and salicylates were prescribed in hospital. The patient did not return as requested for further haematological investigations.

TABLE XVIII.

HAEMATOLOGICAL FINDINGS IN THE FAMILY OF L.A.P.

	Mrs. P.	Kate	John	Ellen	Joseph	Hansen
Age	35	11	10	7	5	2½
Hb. G./100 ml. blood.	11.9	11.9	10.6	9.2	10.6	10.3
RBCs. in millions	3.8	4.2	4.2	3.6	4.0	3.7
P.C.V.%.	36	39	37	34	36	-
M.C.V. in cu. micra	95	93	89	95	90	-
M.C.Hb. Conc	33	30	29	27	30	-
Retics.%.	1.5	0.4	1.5	0.8	1.8	2.2
Bilirubin mgm.%.	0.2	0.2	0.4	0.2	0.5	0.6
WBCs. per cu.mm.	8,200	7,200	5,400	6,200	7,400	5,200
Sickling	-ve	+ve	+ve	+ve	+ve	+ve

The blood film of Hansen showed scanty target cells (1.4%) and ring forms of P. falciparum. None of the family were considered to be suffering from sickle cell anaemia.

Comment. The patient gave a history of recurrent joint pains decreasing in severity with advancing years.

There was evidence of increased haemolysis in the peripheral blood, the erythrocytes sickled and there were many target cells in the thin blood smear - Plate 5. In addition there were bony changes suggestive of a haemolytic anaemia. The patient's wife did not sickle but all the children did which is compatible with the homozygous- heterozygous theory of the inheritance of sickle cell anaemia.

CASE REPORT NUMBER 10.
An African female aged 52 years.

Present History. An African female, A.O., of the Ga tribe was admitted to the Gold Coast Hospital on 3-6-50 complaining of fever, nausea and severe pains in the arms, legs, chest and back of 3 days duration. The pain was gnawing in character and was most severe in the larger joints of the limbs.

Family History. Both parents were dead. The present husband's whereabouts was not known. The patient has had 2 children both of whom are dead. The first died at the age of 15 years of 'fever with yellow eyes' and the second at the age of 8 years of 'fever'.

Previous History. The patient has suffered from recurrent attacks of pain in the joints, limbs and back since childhood. Weakness and nausea accompany the pain and these attacks last from 4 to 7 days and occurred about 6 times in the year when the patient was younger. The attacks are much less severe now than they were in her younger days and from the age of 26-30 years the patient was free of these attacks. Cold and wet weather seem to aggravate the condition. The menses were irregular and scanty. No trouble was experienced in her 2 pregnancies.

Physical Examination. Asthenic African female. Temperature 99.2' F.. The pulse and respiration rates were 86 and 22 per minute. The mucous membranes were poorly coloured and the tongue was pale and smooth. No

jaundice or oedema. The lungs and heart were clinically within normal limits. The blood pressure was 100/65. The liver was just palpable and the spleen was palpable 5 cms. below the costal margin. There were no joint abnormalities. Scars were present on both lower legs. The fundi were normal.

Laboratory Investigations.

Urine :- trace of albumin, few pus and epithelial cells present, culture was sterile, excess urobilin present.

Stool :- no abnormality was detected on microscopy or culture.

Kahn test :- negative. No malarial parasites seen in blood smears.

Blood :- Hb. 7.7 G./100 ml. blood ; R.B.Cs. 3,080,000 per cu.mm. ; P.C.V. 26% ; M.C.V. 84.4 cu. micra ; M.C.Hb. 25 micromicrograms ; M.C.Hb.Conc. 30% ; W.B.Cs. 5,400 per cu.mm.. Blood film :- anisocytosis, poikilocytosis, target cells (28%), sickle cells, basophilic stippling and polychromatic macrocytes present - Plate 5. The reticulocyte count was 6.4%. Differential count :- metamyelocytes 2%, neutrophil polys. 54%, eosinophils 6%, basophils 3%, lymphocytes 33% and monocytes 2%. 2 normoblasts seen per 100 white blood cells. Sickling of the red blood cells 100% by the rapid method. Fragility :- haemolysis commenced 0.3% and was complete 0.1% saline. (control 0.45 and 0.2%). E.S.R. 30 mm. in 1 hour. The serum bilirubin was 1.0 mgm.%.. The Coombs'

test was negative. There was no retention of bromsulphalein at the end of 30 minutes.

Sternal puncture was performed and revealed a normoblastic hyperplasia - TABLE IX.

Course. The temperature gradually returned to normal and the patient was discharged on 15-6-50. Antimalarial, salicylate and iron therapy had been prescribed. The patient was re-examined on 26-6-50 when she had no complaints. The haemoglobin was 8.8 G./100 ml. but there was still evidence of increased haemolysis in the peripheral blood and excess urobilin in the urine.

Comment. This patient gave a history of recurrent attaks of joint pain decreasing in severity with age. There was evidence of increased haemolysis in the peripheral blood, the erythrocytes sickled and there were many target cells in the peripheral blood smear.

CASE REPORT NUMBER 11.
An African boy aged 5 years 10 months.

Present History. An African boy, E.K.D., of the Fanti tribe was referred for investigation by the medical officer stationed at Winneba in view of the history of pain in the joints and the many target cells seen in the thin blood film. The patient was admitted to the Colonial Hospital, Winneba on 13-6-50 complaining of pain in the larger joints of the limbs, fever and yellow eyes of 7 days duration. Antimalarial treatment had been prescribed before the following examination was made on 22-6-50.

Family History. The mother was alive and well. The father was alive but gave a history of long standing rheumatic like pains. The patient had 2 brothers and 2 sisters alive and well with no history suggestive of rheumatism. The mother and father were the only 2 members of the family available and the results of their blood examinations are recorded below.

Previous History. The patient was well until the age of 4½ years when he had an attack of pain in the joints and fever. These have recurred at intervals of about 6 weeks and have necessitated admission to hospital on one previous occasion when the eyes were yellow. No history of jaws was given.

Physical Examination. Asthenic African boy.
Temperature 100.4' F.. Pulse and respiration rates 90

and 34 per minute. The mucous membranes were poorly coloured. The tongue was smooth and pale. The sclerae were icteric. There was no oedema. The anterior and posterior cervical glands were enlarged and rubbery. There was no sign of leg ulceration. The lungs were clear. The heart was not enlarged and there were no bruits. The liver and spleen were palpable 2 cms. and 5 cms. below the costal margins respectively. No joint or neurological abnormalities were noted. The fundi were normal.

Laboratory Investigations.

Urine :- albumin and bile pigments absent. Schlesinger's test for urobilin strongly positive. Stool :- no ova, amoebae or cysts seen.

Kahn test :- negative. No malarial parasites seen in blood smears.

Blood :- Hb. 4 G./100 ml. blood ; R.B.Cs. 1,280,000 per cu.mm. ; P.C.V. 14% ; M.C.V. 117 cu. micra ; M.C.Hb. 31 micromicrograms ; M.C.Hb.Conc. 28.5% ; W.B.Cs 10,000 per cu.mm.. Blood film :- anisocytosis, poikilocytosis, many polychromatic red cells, basophilic stippling, Howell Jolly bodies, Cabot's rings, sickle cells and target cells (28%) - Plate 4. The reticulocyte count was 25%. Differential count :- metamyelocytes 3%, neutrophil polys. 58%, basophils 2%, lymphocytes 36% and monocytes 1%. There were 26 nucleated red cells per 100 white cells and 24 were normoblastic , including mitotic figures, and 2 were macronormoblasts. Sickling of the red blood cells

100% by the rapid method. Fragility :- haemolysis commenced 0.35% and was complete in 0.05% saline. E.S.R 22 mm. in 1 hour. The serum bilirubin was 3 mgm.%. The Coombs' test was negative. There was no retention of bromsulphalein at the end of 30 minutes.

The sternal marrow revealed a normoblastic hyperplasia TABLE IX.

Radiological Findings.

Skull :- marked 'hair on end' appearance.

Long bones of the limbs :- no abnormality was detected.

Examination of the Parents. The mother gave no history suggestive of haemolytic crises. The father gave a history of recurrent attacks of pain in the larger joints, mainly the knee and elbow, since infancy. These attacks were sévere when he was young, were aggravated by cold or wet weather and finally ceased at the age of 25 years. His father had also suffered from 'rheumatism' and died at the age of 75 years of 'old age'. The haematological findings are shown in TABLE XIX. It will be seen from the table that there is no evidence of increased haemolysis in the mother's blood. Both differential counts were within normal limits. The urine of the father contained much urobilin and the thin smear contained many target cells (10%). The reticulocyte count was also slightly raised.

TABLE XIX.

HAEMATOLOGICAL FINDINGS IN THE PARENTS OF E. K. D.

	Father.	Mother
Age in years	45	39
Hb. in G./ 100 ml. blood	13.2	13.5
RBCs. in mills. per cu. mm.	5.42	4.96
P.C.V.%.	49	46
M.C.V. in cu. micra.	91	94
M.C.Hb.Conc.	27	30
W.B.Cs. per cu. mm.	6,4000	6,800
Retics. %.	3.5	1.0
Bilirubin in mgm.%.	0.6	0.2
Sickling	+ve	+ve

Comment. It was only possible to perform one investigation on E.K.D. However there were signs of marked haemolysis in the peripheral blood despite previous antimalarial therapy. The erythrocytes sickled and there were many target and sickled cells in the blood smear. Both parents exhibited the sickling phenomenon. A personal communication from the Medical Officer, Winneba (M.J.Colbourne) stated that the child did not improve on iron and liver therapy and was eventually discharged from hospital with a haemoglobin value of 5.4 G./100 ml. and a reticulocyte count of 9,6 %.

CASE REPORT NUMBER 12.
An African male aged 22 years.

Present History. An African male, T., of the Ga tribe was referred for examination by the Medical Officer, Winneba in view of a history of recurrent attacks of generalised bodily pains since infancy and the presence of many target cells in a thin blood smear. (.The author had previously communicated his opinion on this syndrome to Dr.M.J.Colbourne, the Medical Officer in question.) The patient when seen was not complaining but stated that he had recovered from a typical attack one week ago.

Family History. The father died at the age of 46 years of an unknown cause. The mother, 4 sisters and 2 brothers were alive and well. A third brother was said to suffer from attacks of 'rheumatism'. No members of the family were available for examination.

Previous History. The patient gave a history of recurrent attacks of pain in the joints and long bones of the limbs since infancy. The attacks commenced with pain in the limbs and joints, a feeling of cold was then experienced and the pain gradually disappeared in 7-14 days. The attacks were much worse in infancy and were exaggerated by cold or wet weather or bathing in cold water. They occurred 4-5 times in the year. The eyes have never been yellow during an attack but the urine is dark in colour. No history of yaws was given.

Physical Examination. Well nourished African male. The temperature, pulse and respiration rates were normal. The mucous membranes were well coloured and there was no oedema or jaundice. The lungs were clear. The heart was not enlarged and there were no bruits. The liver was not palpable. The spleen was palpable 3 cms. below the left costal margin. No joint changes or neurological abnormalities were noted. The fundi were normal.

Laboratory Investigations.
Urine :- Schlesinger's test for urobilin was strongly positive. Stool :- no ova, cysts or amoebae see. Kahn test :- negative. Scanty ring forms of P.falciparum were seen in a blood smear.
Blood :- Hb. 11.2 G./100 ml. blood ; R.B.Cs. 4,510,000 per cu.mm. ; P.C.V. 35% ; M.C.V. 78 cu. micra ; M.C.Hb. 25 micromicrograms ; M.C.Hb.Conc. 32% ; W.B.Cs. 10,600 per cu. mm.. Blood film :- slight anisocytosis and poikilocytosis and target cells (35%) present - Plate 4. The reticulocyte count was 4.4%. Differential count :- metamyelocytes 1%, neutrophil polys. 34%, eosinophils 11%, lymphocytes 44% and monocytes 8%. 1 normoblast seen per 200 white blood cells. Sickling of the red blood cells 100% by the rapid method. Fragility :- haemolysis commenced 0.3% and was complete in 0.1% saline. E.S.R. 8 mm. in 1 hour. The serum bilirubin was 1 mgm.%.

Radiological Report.

Skull :- there are changes in the parietal bones of the skull suggestive of a haemolytic anaemia.

Femora :- there is some increased trabeculation present.

Course. A course of antimalarial therapy was prescribed. There was no change in the haemolytic process in the peripheral blood at the termination of this course.

Comment. The patient gave a history of recurrent pain in the limbs and joints since infancy. The blood showed signs of a mild haemolytic process uninfluenced by antimalarial therapy. The thin smears showed many target cells and the erythrocytes sickled. There was radiological evidence of bone changes suggesting a haemolytic anaemia. One brother was said to suffer from a similar complaint.

CASE REPORT NUMBER 13.
An African male aged 24 years.

Present History. An African male nurse,B., of the Akim tribe was referred for examination in view of a history of recurrent attacks of joint pain since infancy. The thin blood smear revealed many target cells. The patient at the time of examination was not complaining.

Family History. The father was alive and well. The mother died when the patient was very young. 9 siblings were alive and well. 1 brother suffers from a similar complaint. An aunt on the paternal side also suffers from 'rheumatism'. None of the family were available for examination.

Previous History. The patient gave a history of recurrent attacks of joint pain since infancy. These attacks are associated with cold or wet weather, severe excercise or bathing in cold water. They were much more severe when the patient was younger. The pains are felt 'deep in the bones' of the limbs and in the joints, especially the knee and elbow. The eyes have never been yellow. No history of yaws was given.

Physical Examination. Well nourished African male. The relevant findings were an enlarged liver, palpable 1 cm. below the costal margin,and an enlarged spleen which was palpable 4 cms. below the costal margin. The fundi were normal.

Laboratory Investigations.
Urine :- Schlesinger's test for urobilin strongly positive. Kahn test :- negative. No malarial parasites seen in blood

smears. Stool :- no ova, cysts or amoebae seen. Blood :- Hb. 11.2 G./100 ml. blood ; R.B.Cs. 4,590,000 per cu.mm. ; P.C.V. 38% ; M.C.V. 88 cu. micra ; M.C.Hb. 25.5 micromicrograms ; M.C.Hb.Conc. 29.5% ; W.B.Cs. 9,000 per cu.mm.. Blood film :- slight anisocytosis and poikilocytosis, occasional polychromatic red blood cell and many target cells (61%) - Plate 4. The reticulocyte count was 3.4%. Differential count :- metamyelocytes 4%, neutrophil polys. 55%, eosinophils 15%, basophils 1%, lymphocytes 26% and monocytes 1%. 1 normoblast per 100 white blood cells. Sickling of the red blood cells 100% by the rapid method. E.S.R. 10 mm. in 1 hour. The serum bilirubin was 1 mgm.%. There was no retention of bromsulphalein at the end of 30 minutes.

Radiological examination of the skull and long bones revealed no abnormality.

Course. The haematological findings were unchanged 14 days later following a course of antimalarial therapy.

Comment. The patient gave a history of recurrent pain in the joints and limbs, the erythrocytes sickled and there was evidence of a mild haemolytic process in the peripheral blood. Thin blood films showed anisocytosis, poikilocytosis and many target cells.

CASE REPORT NUMBER 14.
An African boy aged 7 years.

Present History. An African boy, A.B., of the Ga tribe was admitted to the Gold Coast Hospital on 31-7-50 complaining of ulcers on both legs of 14 days duration and pain in the limbs and joints of 10 days duration. Pain was also felt in the left hypochondrium and fever, malaise and nausea were also present.

Family History. The grandparents on the maternal side only were available for examination. The father of the patient could not be traced and the mother had died at the age of 24 years of 'fever'. His only sister had died at the age of 11 months of 'weakness'. The grandparents were examined and no abnormality was detected apart from sickling of the red cells in the case of the grandfather. There was no history of 'rheumatism' in the family.

Previous History. (from grandparents)
The patient had been strong and healthy until the age of 18 months when it was noticed that his abdomen was protuberant. Since then the patient has always been sick and feverish and has complained frequently of severe pains in the abdomen, joints and limbs. The attacks of pain are present almost continuously but vary in severity. There has been considerable loss of weight.

Physical Examination. Thin, undersized African boy.

The patient was rather distressed. Temperature 99.8' F.. The pulse and respiration rates were 84 and 22 per minute. The mucous membranes were poorly coloured and the tongue was smooth and pale. The features were not mongoloid but the skull was a peculiar shape. It appeared to be compressed laterally giving the 'tower skull' appearance. The anterior and posterior and inguinal glands were slightly enlarged and rubbery. The sclerae were greenish. There was no oedema. There were ulcers on the internal malleoli of both ankles, 2.5 and 1.5 cms. in diameter. The ulcers were punched out involving the whole thickness of the skin and were septic. The percussion note was impaired at the base of the right lung and air entry was diminished. The apex beat of the heart was palpable 2 cms. outside the nipple line in the 5th. interspace. There were no bruits. The blood pressure was 95/55. The liver edge was palpable 5 cms. below the right costal margin in the mid-clavicular line. It was smooth and soft. The spleen was firm, tender and was palpable 10 cms. below the left costal margin. The fundi were normal.

Laboratory Investigations.

Urine :- No albumin or bile. Schlesinger's test for urobilin strongly positive. Stool :- no abnormality detected on microscopy or culture.

Kahn test :- negative. No malarial parasites seen in blood smears.

Blood :- Hb. 6.6 G./100 ml. blood ; R.B.Cs. 5,180,000 per

cu.mm. ; P.C.V. 22%. ; M.C.V. 70 cu.micra ; M.C.Hb. 21.2 micromicrograms ; M.C.Hb.Conc. 30% ; 25,200 (corrected for nucleated reds - 11,000) W.B.Cs. per cu.mm..

Blood film :- anisocytosis, poikilocytosis, polychromatic cells, basophilic stippling, sickle cells and target cells (21%) - Plate 3. The reticulocyte count was 16.2%.

Differential count :- metamyelocytes 2%, neutrophil polys. 37%, eosinophils 4%, lymphocytes 54% and monocytes 3%. 110 nucleated red blood cells per 100 white cells and 4% of the nucleated red cells were macronormoblasts. Many mitotic figures were present. Sickling of the red blood cells 100% by the rapid method. E.S.R 19 mm. in 1 hour.

Fragility :- haemolysis commenced 0.3% and was complete 0.05% saline. (control 0.4% - 0.25%). The serum bilirubin was 2 mgm.%. Coombs' test was negative. There was no retention of bromsulphalein at the end of 30 minutes. Blood culture was sterile.

Sternal puncture was performed on the 6th. hospital day and revealed an intense normoblastic hyperplasia - TABLE IX.

Radiological Examination.

Chest :- osteoporosis and increased trabeculation of the ribs. Increase in the transverse diameter of the heart.

Skull :- no abnormality detected.

Femora :- the ends of the shafts show transverse lines of arrested growth which are usually associated with deficient nutrition or frequent disease in childhood. A small area of rarefaction consistent with an infarctive

lesion is present in the upper third of the right femur.

Course. The temperature settled on 3-8-50 and the symptoms improved. There was a further exacerbation of symptoms on 10-8-50 and the temperature rose to 100.1' F. These gradually subsided and on 18-8-50 the temperature was normal and the joint pains had disappeared. Antimalarial treatment was prescribed on admission to hospital and, in addition, salicylates were given. The second exacerbation occurred while the patient was on suppressive proguanil 0.05 G. daily. The patient was discharged from hospital on 22-8-50 with little improvement in his condition. The haematological findings are shown in TABLE XX.

TABLE XX.

SERIAL BLOOD COUNTS PERFORMED ON A.B.

Date	1-8-50	11-8-50	21-8-50
Hb. in G./100 ml.	6.6	5.3	6.6
RBCs. in millions	3.18	2.5	3.2
P.C.V. %.	22	22	24
M.C.V. in cu. micra	70	88	75
M.C.Hb. Conc.%.	30	24	28
Reticulocytes %.	16.2	20	18
Nucleated reds / 100 whites	110	65	71

Comment. A patient with increased haemolysis, sickled cells and target cells in the peripheral blood uninfluenced by antimalarial therapy. A history of recurrent joint pain was given and bone changes were seen on Xray examination.

CASE REPORT NUMBER 15.
An African girl aged 8 years.

Present History. This patient, A.L., an African girl of the Ga tribe was discovered during a medical survey of 200 schoolchildren. At the time of the examination she was not complaining.

Family History. The mother and father are alive and well. There are 5 brothers, 1 of whom was said to suffer from attacks of abdominal and joint pains. The examination of the family is recorded below- TABLE XXL.

Previous History. The patient was well until the age of 5 years when she complained of severe pain in the joints and fever. The eyes at this time were slightly yellow and the attack lasted for 3 weeks. Since that time the patient has always been sickly and thin. She has suffered occasionally from pain in the larger joints and fever. The eyes are always slightly yellow and the urine high coloured. She is a bright child and, in spite of frequent absences, is 3rd. in the class of 45 children. During the wet season she has been given 0.05 G. of proguanil daily.

Physical Examination. An asthenic African girl. Height 51.5 inches and weight 47 lbs. The skull appeared to be compressed laterally and the features were mongoloid. The temperature was 99' F.. The pulse and respiration rates were 90 and 20. There was mild cheilosis of the lips and 2 teeth were carious. The mucous membranes were

poorly coloured and the tongue was smooth and pale. The sclerae were greenish. The hair was straight, dull and soft. There was depigmentation of the skin, most marked on the face. The skin overlying the knee and elbow joints was hypertrophied and mosaic on the shins. Folliculitis of the chest and thighs was present. The anterior and posterior cervical glands were slightly enlarged and rubbery. There were scars of healed ulcers on the lower limbs. The lungs were clear. The heart was not enlarged and there were no bruits. There was a small umbilical herniae. The liver was palpable, smooth and soft 5 cms. below the right costal margin. The spleen was not palpable. No joint or neurological abnormalities were noted. The fundi were normal.

Laboratory Investigations.

Urine :- Schlesinger's test for urobilin was strongly positive. Stool :- scanty ova of A. lumbricoides present. Kahn test :- negative. Scanty ring forms of P. falciparum present in a blood smear.

Blood :- Hb. 8.4 G./100 ml. blood ; R.B.Cs. 3,400,000 per cu.mm. ; P.C.V. 30%. ; M.C.V. 88 cu. micra ; M.C.Hb. 25 micromicrograms ; M.C.Hb.Conc. 28% ; W.B.Cs 20,000 per cu.mm.. Blood film :- anisocytosis, poikilocytosis, polychromatic red cells, basophilic stippling, Howell Jolly bodies, sickle cells and many target cells (44%) - Plate 4. The reticulocyte count was 9.5%. Differential count :- metamyelocytes 0.6%, neutrophil polys. 50.6%,

eosinophils 12%, lymphocytes 53.4% and monocytes 3.4%. 13 normoblasts seen per 100 white blood cells. Sickling of the red blood cells 100% by the rapid method. E.S.R. 22 mm. in 1 hour. Fragility :- haemolysis commenced 0.45% and was complete 0.1% saline. The serum bilirubin was 1.3 mgm.%. The Coombs' test was negative. There was no retention of bromsulphalein at the end of 30 minutes.

Radiological Findings. 2948/50

Skull :- there is thinning of the outer bony table. There are perpendicular striations running from the inner table giving the 'hair on end' appearance.

Course. The patient was treated with mepacrine 0.1 G. t.d.s. for 5 days and proguanil 0.05 G. t.d.s. for 5 days. The haematological findings were unchanged at the end of this treatment. Suppressive proguanil therapy was prescribed and a further examination performed 8 weeks later. Evidence of increased haemolysis was still present in the peripheral blood and the haemoglobin was 9.1 G./ 100 ml. blood.

Examination of the family. The results of the haematological investigations performed on the family are shown in TABLE XXI. The mother and father had no complaints and their blood counts were within normal limits. 4 of the 6 children exhibited the sickle cell trait and all 4 of these children showed evidence of increased haemolysis in the peripheral blood and sickled and target cells in thin

TABLE XXI. THE FAMILY OF A.L.

	Sickling.	History of joint pains.	Palpable spleen.	Palpable liver.	Haemoglobin in G./100 ml.	R.B.Cs. in mill. per cu.mm.	W.B.Cs. per cu.mm.	P.C.V. %	M.C.V. cu. micra.	M.C. Hb. Conc.	Reticulocytes %.	Bilirubin mgm.%.	Nucleated R.B.Cs. per 100 whites.	Malarial Parasites	Radiography.
Mr. L.	+	-	-	-	13.9	5.6	5,600	41	73.21	34.0	0.5	0.4	-	-	-
Mrs. L.	+	-	-	-	12.5	5.1	6,000	39	76.47	32.0	0.25	0.2	-	-	-
Fred.	-	-	-	-	11.9	4.5	4,800	38	84.4	30.0	0.8	0.4	-	-	-
A.L.≠	+	+	-	+	8.4	3.4	20,000	30	88.23	28.0	9.5	1.3	13	+	+
John. ≠	+	+	-	+	5.9	2.5	24,000	24	96.0	24.6	5.5	1.0	3	-	+
Horace.	-	-	-	-	11.2	4.6	7,400	37	80.4	30.0	1.4	0.6	-	±	-
Kenneth.≠	+	+	+	+	6.3	2.3	12,000	22	95.6	28.6	8.3	1.2	7	+	-
Boye. ≠	+	-	-	-	5.9	nd.	nd.	nd.	nd.	nd.	nd.	nd	2	-	-

≠ Blood films showed Anisocytosis, Poikilocytosis, sickle cells and many target cells.

smears. John aged 7 years , in addition to A.L., gave a history of recurrent joint pains. The xray of his skull also showed the 'hair on end' appearance. In only one child, the patient A.L., was it possible to prescribe antimalarial therapy and perform further investigations. Thus, although the remaining 3 children exhibiting the sickling phenomenon were suffering from a haemolytic anaemia indistinguishable from sickle cell anaemia, malaria could not be excluded as a possible causal factor. The diagnosis of sickle cell anaemia in these 3 children must be tentative and cannot be taken as proved.

Comment. The patient gave a history of recurrent attacks of joint pain. There were signs of increased haemolysis in the peripheral blood, the erythrocytes sickled and sickle and target cells were present in thin films. Bony changes were also present. The condition did not respond to antimalarial therapy. The father and mother both exhibited the sickling phenomenon. 3 other children in the family were suffering from a haemolytic anaemia possibly sickle cell anaemia.

CASE REPORT NUMBER 16.
An African male aged 16 years.

Present History. An African male student, A.K.A., of the Ga tribe was admitted to the Gold Coast Hospital on 5-8-50 complaining of dull aching pain in the arms, hands, legs and chest of 7 days duration. The pain had been present constantly and was most marked in the larger joints of the limbs. The patient also complained of anorexia, nausea and feeling cold.

Family History. The mother and 1 sister were alive and well. The father was alive but had suffered from attacks of 'rheumatism' all his life. None of the family were available for examination.

Previous History. The patient gave a history of recurrent attacks of 'rheumatism' since infancy, occurring almost every month, varying in severity and incapacitating him for approximately 3 months in every 12. The duration of the attack varies from 7-14 days. The eyes have at times been yellow during these attacks no history of abdominal pain or leg ulcers was obtained. The attacks are associated especially with cold weather.

Physical Examination. Well nourished, small African youth. Temperature 99.2' F.. The pulse and respiration rates were 90 and 22 per minute. The mucous membranes were well coloured. The tongue was smooth and rather pale. There was no oedema, jaundice or scars present. The anterior cervical glands were slightly enlarged and rubbery.

The lungs were clear. The heart was not enlarged and there were no bruits. The liver could not be felt. The spleen was palpable 2 cms. below the left costal margin and was firm. Movement of the limbs was unrestricted and no joint or neurological abnormalities were noted. The fundi were normal.

Laboratory Investigations.

Urine :- trace of albumin. Schlesinger's test for urobilin strongly positive throughout stay in hospital. Stool:- scanty ova of A. lumbricoides present.

Kahn test :- negative. No malarial parasites seen in blood smears.

Blood :- Hb. 12.5 G./100 ml. blood ; R.B.Cs. 5,630,000 per cu. mm. ; P.C.V. 38% ; M.C.V. 67.5 cu. micra ; M.C.Hb 22.2 micromicrograms ; M.C.Hb.Conc. 33% ; W.B.Cs. 6,800 per cu.mm.. Blood film :- mild anisocytosis and poikilocytosis, no sickle cells, many target cells (63%)- Plate 3. The reticulocyte count was 5.2%.

Differential count :- neutrophil polys. 37%, eosinophils 10%, lymphocytes 52% and monocytes 1%. Sickling of the red blood cells 100% by the rapid method. Fragility :- haemolysis commenced 0.3% and was complete 0.15% saline. (Control 0.45% and 0.25%). E.S.R. 4 mm. in 1 hour. The serum bilirubin was 1.6 mgm.%. The Coombs' test was negative. There was no retention of bromsulphalein at the end of 30 minutes.

A course of antimalarial treatment was given. The patient's symptoms gradually subsided but blood counts performed on the 11-8-50 and 16-8-50 revealed findings essentially similar to those recorded above. The haemoglobin was 13 G./100 ml. on discharge on the 16-8-50 but signs of increased haemolysis were still present and many target cells were present in the thin smear.

Comment. The patient gave a history of recurrent attacks of joint pain, signs of increased haemolysis were present in the peripheral blood and a thin blood film showed anisocytosis, poikilocytosis and many target cells. The erythrocytes sickled. Antimalarial therapy had no effect on the condition.

CASE REPORT NUMBER 17.
An African male aged 18 years.

Present History. An African male, L.K.K., of the Ewe tribe was referred for examination on 23-3-50 in view of a history of recurrent joint pains of many years duration. The patient was not complaining at the time of examination.

Family History. The mother, father, 2 brothers and 4 sisters were alive and well. 1 brother aged 15 years was said to suffer from recurrent attacks of pain in the joints. None of the family were available for examination.

Previous History. The patient gave a history of recurrent attacks of pain in the joints and limbs since the age of 4 years. The attacks occurred about twice a month when the patient was younger but are now much less frequent and occur about 4 times in the year. The attacks last about 7 days and are associated with the cold weather. The pain is dull and aching in character and cannot be accurately located but occurs most frequently in the larger joints of the limbs. Headache, anorexia and fever accompany the pain which is usually the first indication of an attack.

The patient was in hospital in April 1949 when the diagnosis was Fever N.Y.D.. The haemoglobin at that time, according to the records, was 70% Sahli. The patient was said to have suffered from yaws at the age of 4 years and was treated with many tablets of stovarsol. Since then the patient has had many courses of N.A.B. and many courses

of quinine and mepacrine without relief of symptoms.

The last attack occurred in January, 1950. There is no history of jaundice.

Physical Examination. Well nourished African male. The mucous membranes were well coloured. No jaundice or oedema. The lungs were clear. The heart was slightly enlarged clinically and there was a systolic murmur at the apex. The liver edge was smooth and soft and was palpable 3 cms. below the right costal margin. The spleen was firm and was palpable 3 cms. below the left costal margin. No joint or neurological abnormalities were noted. The retinal vessels were dilated and tortuous.

Laboratory Investigations.
Urine :- Schlesinger's test for urobilin strongly positive.
Stool :- no ova, cysts or amoebae seen.
Kahn test :- negative. No malarial parasites seen in blood smears.
Blood :- Hb. 13.9 G./100 ml. blood ; R.B.Cs. 4,880,000 per cu.mm. ; P.C.V. 39% ; M.C.V. 81 cu. micra. ; M.C.Hb. 28.5 micromicrograms ; M.C.Hb.Conc. 36% ; W.B.Cs. 7,600 per cu. mm.. Blood film :- anisocytosis, poikilocytosis and many target cells (55%) - Plate 3. The reticulocyte count was 3.8%. Differential count :- metamyelocytes 1%, neutrophil polys. 47%, eosinophils 3%, lymphocytes 48%, monocytes 1%. Sickling of the red blood cells 100% by the rapid method. Fragility :- haemolysis commenced

0.45% and was complete 0.1% saline (Control 0.45% and 0.25%). E.S.R. 7 mm. in 1 hour. The serum bilirubin was 0.8 mgm.%. There was no retention of bromsulphalein at the end of 30 minutes.

Radiological Examination.

No abnormality detected in the skull or femora.

Course; Antimalarial therapy was prescribed for 10 days and the blood re-examined. The haemoglobin was 15.4 G./100 ml. blood and the reticulocyte count was 6.5%.

Comment. The patient gave a history of recurrent attacks of joint pain decreasing in severity with advancing years. There were signs of slightly increased haemolysis in the peripheral blood, the erythrocytes sickled and a thin blood film revealed anisocytosis, poikilocytosis and many target cells. Antimalarial therapy did not appear to influence the condition.

CASE REPORT NUMBER 18.
An African male aged 18 years.

Present History. An African male, S.A.N., of the Akim tribe was referred for investigation on 21-3-50 in view of a history of recurrent attacks of pain in the limbs and joints. The patient was not complaining at the time of the examination.

Family History. The father, 1 brother and 1 sister are alive and well. The mother is alive but is said to suffer from recurrent joint pain. 2 brothers have died of unknown causes. None of the family were available for examination.

Previous History. The patient gave a history of recurrent attacks of pain in the arms and legs from the age of 6 years. The attacks were more frequent when the patient was younger and now occur about 3 times in the year. The attack lasts from 7-14 days and the patient has been hospitalised on 3 occasions. No definite diagnosis was reached on these admissions. The eyes have at times been yellow and the urine dark in colour. The patient is said to have suffered from yaws in infancy and was treated by injections. A further course of injections was given at the age of 18 years. The patient has had many courses of quinine and mepacrine.

Physical Examination. A small, asthenic African male. The temperature, pulse and respiration rates were normal. The mucous membranes were well coloured. The sclerae were

greenish. The epitrochlear and inguinal glands were just palpable. The lungs were clear. The heart was slightly enlarged clinically and there were systolic murmurs at the mitral and pulmonic areas. The spleen was just palpable. No joint or neurological abnormalities were noted. Scars were present on both lower legs. The retinal vessels were dilated and tortuous.

Laboratory Investigations.
Urine :- Schlesinger's test for urobilin strongly positive.

Stool :- no ova, cysts or amoebae seen.

Kahn test :- negative. No malarial parasites seen in blood smears.

Blood :- Hb. 13.2 G./100 ml. blood ; R.B.Cs. 4,630,000 per cu.mm. ; P.C.V. 40% ; M.C.V. 87 cu. micra ; M.C.Hb. 28.5 micromicrograms ; M.C.Hb.Conc. 33% ; W.B.Cs 9,400 per cu. mm.. Blood film :- anisocytosis, poikilocytosis and many target cells (87%) - Plate 5. The reticulocyte count was 6.6%. Differential count :- metamyelocytes 1%, neutrophil polys. 40%, eosinophils 7%, lymphocytes 44% and monocytes 8%. 2 normoblasts per 100 white cells. Sickling of the red blood cells 100% by the rapid method. Fragility :- haemolysis commenced 0.3% and was complete in 0.05% saline. E.S.R. 12 mm. in 1 hour. The serum bilirubin was 1.2 mgm.%.

Radiological Examination.
No abnormality was detected in the skull or femora.

Course. Antimalarial therapy was prescribed and the blood

was re-examined on 3-4-50. The findings were essentially similar to those reported above. The reticulocyte count was still raised and the serum bilirubin was 1.2 mgm.%.

Comment. This patient gave a similar history to L.K.K. Case Report Number 17 (page 59) and the haematological findings also were similar.

CASE REPORT NUMBER 19.
An African boy aged 16 years.

Present History. An African youth, J.Q., of the Ga tribe reported to the out-patient department of the Gold Coast Hospital on 10-3-50 complaining of pain and redness of both eyes of 3 weeks' duration.

Family History. The father, mother, 1 sister and 2 brothers were alive and well. A second sister aged 8 years was said to suffer from attacks of 'rheumatism'. The haematological findings of the father, mother and the second sister (the only members of the family available) are shown in TABLE XXII.

Previous History. The patient gave a history of recurrent attacks of deep-seated pain in or near the large joints of the limbs occurring 3 to 4 times in the year. These attacks had persisted since infancy when they were more severe.

Physical Examination. Fairly well developed African youth. The conjunctiva were moderately injected and slit lamp microscopy revealed superficial punctate corneal staining with fluorescein in both eyes. In the left fundus were 2 small aneurysms, well out to the periphery and directly below the macula. They were near, but not associated with, a branch of the inferior temporal vein. Near one aneurysm was a small retinal haemorrhage. The visual acuity was 6/5 in either eye. (Dr. J.W.R. Sarkies). No other abnormality was detected on physical examination.

Laboratory Investigations.
Urine :- Schlesinger's test for urobilin strongly positive, no sugar, albumin or bile pigments present. Stool :- no abnormality detected.

Kahn test :- negative. No malarial parasites were seen in blood smears.

Blood :- Hb. 14.2 G./100 ml. blood ; R.B.Cs. 4,180;000 ; P.C.V. 40% ; M.C.V. 96 cu. micra ; M.C.Hb.Conc. 35.5 % ; W.B.Cs 6,200 per cu.mm.. Blood film :- anisocytosis, poikilocytosis, occasional sickled cells, basophilic stippling, polychromatic macrocytes and many target cells (60%) - Plate 5. The reticulocyte count was 6.1%. Differential count :- metamyelocytes 1%, neutrophil polys. 47%, eosinophils 3%, lymphocytes 48% and monocytes 1%. 1 nucleated red cell per 100 white cells. Sickling of the red blood cells 100% by the rapid method. Fragility :- haemolysis commenced at 0.3 and was complete 0.1% saline. (Control 0.4 to 0.25%). E.S.R. 8 mm. in 1 hour. The serum bilirubin was 1.1 mgm.%.. The Coombs' test was negative.

A sternal puncture revealed a normoblastic hyperplasia

TABLE IX.

Radiological Examination.
The bones of the vault of the skull show changes associated with anaemia.

Course. The blood picture was unaltered following 14 days of antimalarial therapy ; the keratitis cleared

after 3 weeks of symptomatic treatment. 10 weeks later the patient reported fever and joint pains ; the haemoglobin at this stage was 13.3 G./100 ml., the serum bilirubin 1.2 mgm.%. and the reticulocyte count was 10.1%. Scanty malarial parasites were present in a blood smear. The blood picture was unchanged following a further 2 weeks of antimalarial therapy. Apart from the original film malarial parasites were not found although daily smears were examined.

Investigation of the Family. The haematological findings are shown on TABLE XXII.

TABLE XXII.

HAEMATOLOGICAL FINDINGS IN THE FAMILY OF J.Q.

	Mother	Father	Sister
Age	45	50	8
Hb. in G./100 ml.	13.5	13.7	13.3
RBCs. in millions per cu.mm.	4.77	4.37	4.15
P.C.V. per cent.	40	40	37
M.C.V. cu.micra.	84	91	89
M.C.Hb.Conc.	34	34	36
Reticulocytes.	0.2	0.8	3.8
Bilirubin mg.%.	0.6	0.4	1.3
WBCs. per cu.mm.	7,400	7,800	8,400
Sickling	+ve.	+ve.	+ve.

The sister aged 8 years gave a history of recurring attacks of pain in the abdomen and joints and, as will be seen

from the table, there was evidence of increased haemolysis in the peripheral blood. Her spleen was palpable 8 cms. below the costal margin. The thin blood film showed anisocytosis, poikilocytosis, an occasional sickle cell and many target cells (45%). 1 normoblast was seen per 100 white blood cells. Antimalarial therapy was prescribed but the patient did not return for further investigation. This sister can only be regarded as a probable case of sickle cell anaemia as malaria has not been excluded as a possible causal factor. The 3 other siblings in the family who were not available for examination did not, however, give a history of recurrent joint pain although they were also acquiring their premunition immunity to malaria.

Comment. The case report of this patient has previously been published EDINGTON & SARKIES (1952). The investigation of the family was not, however, included and has been added in this report. This patient, J.Q., once again gave a history of recurring attacks of joint pain, signs of increased haemolysis were present in the peripheral blood, the erythrocytes sickled and thin smears showed anisocytosis, poikilocytosis and many target cells. Antimalarial therapy did not appear to influence the haemolysis. The examination of the family agreed with the homozygous theory of the inheritance of sickle cell anaemia. A sister, aged 8 years, was also possibly suffering from sickle cell anaemia.

CASE REPORT NUMBER 20
An African male aged 22 years.

Present History. An African male, A.K.K., of the Ga tribe reported to the out-patient department of the Gold Coast Hospital complaining of gradual loss of vision in the left eye during the previous 3 weeks.

Family History. The mother and 6 siblings were alive and well. The father had died while undergoing a herniotomy in 1943 and 1 brother had died of an 'unknown cause'. There was no family history of rheumatism.

Previous History. The patient gave a history of recurring attacks of pain in the large joints, back and muscles occurring about 6 times in the year. The attacks had been decreasing in frequency and severity since infancy.

Physical Examination. Asthenic African male. The sclerae were greenish. Vision in the right eye was 6/5 and in the left was reduced to light perception only. The light reaction of the left pupil was sluggish. There was a dense vitreous haemorrhage on the left side and slit lamp microscopy showed the anterior vitreous to be full of red cells. On the right dide there was a small morula-shaped aneurysm arising from the inferior temporal vein at the periphery of the fundus at 8 o'clock from the disc ; there was also a smaller aneurysm of the superior temporal vein at 11 o'clock from the disc. (Dr. J.W.R. Sarkies).

The patient had a dorsal scoliosis (said to date from a fall in childhood). The spleen was palpable 6 cms. below

the left costal margin.

Laboratory Investigations.
Urine :- Schlesinger's test for urobilin strongly positive. No sugar, albumin or bile pigments present.

Stool :- no abnormality detected.

Kahn test :- negative. No malarial parasites seen in blood films.

Blood :- Hb. 13.5 G./100 ml blood ; R.B.Cs. 5,100,000 per cu.mm. ; P.C.V. 37% ; M.C.V. 73 cu.micra ; M.C.Hb. Conc. 36.5%. ; W.B.Cs. 9,200. Blood film :- anisocytosis, poikilocytosis and many target cells (74%) - Plate 4. The reticulocyte count was 6.6%. Differential count :- neutrophil polys. 52%, eosinophils 11%, lymphocytes 33% and monocytes 4%. 1 normoblast seen per 100 white cells. Sickling of the red blood cells 100% by the rapid method. The serum bilirubin was 1.3 mgm.%.

Radiological Examination.
Skull :- lateral radiographs show changes of Cooley's erythroblastic or sickle cell anaemia from the region of the coronal suture for about 2½ inches backward along the vault of the parietal bones.

Course. Antimalarial therapy was prescribed for 14 days and the blood was again investigated. Evidence of mild haemolysis as reported above was still present.

Investigation of the Family. Only one sister was available for examination. She gave no history of joint pains, the blood picture was within normal limits and the red blood cells exhibited the sickling trait.

Comment. This is the second case report published by Edington & Sarkies (1952). The patient gave a history of recurrent joint pains, signs of haemolysis were present in the peripheral blood, the erythrocytes sickled and thin smears showed aniaocytosis, poikilocytosis and many target cells. Antimalarial therapy had no effect on the haemolysis.

The case report of this and the previous patient were published in view of the occurrence of microaneurysms in the retinal vessels. These had not previously been reported as occurring in sickle cell anaemia. In the article mentioned above the literature on aneurysms of the retinal vessels was briefly discussed. It was considered that stasis and subsequent thrombosis following blockage of the blood vessel by sickled erythrocytes was the probable cause of the microaneurysms found in sickle cell anaemia.

APPENDIX D.

THIRTEEN AUTOPSY REPORTS.

AUTOPSY REPORT NUMBER 1

An African female aged 38 years.

Present History :- A.A., an African female of the Ga tribe was admitted to the Gold Coast Hospital, Accra on 24-4-50 complaining of generalised muscular and joint pains, fever, headache, vertigo and vomiting of two days duration. Mild diarrhoea was also present. A small ulcer on the left ankle had been treated at the out patient department for four weeks. On the day before admission the patient noticed that her eyes were yellow and that the urine was dark in colour.

Family history :- The patient was married and had one child aged 5 years who was alive and well. The husband's whereabouts were unknown and the patient's parents were both dead. The cause of their death was unknown.

Previous History :- The patient gave a history of frequent attacks of generalised pains in the limbs and joints, accompanied by fever, headache and nausea of ten years duration. The eyes had often been yellow. The right hip joint had been especially affected and for many years was always painful. It had not been so painful during the last year and the patient stated that she could not move the right upper leg.

Physical Examination :- Thin ill looking African female. Mentally slow. Temperature 99'F. Pulse 106. Respirations 30. The mucous membranes were pale. There was a shallow, healing ulcer 2.5 cm. in diameter on the outer aspect of the left ankle. The lungs were clear. The heart was not enlarged and there were no bruits. There was tenderness and guarding in the

epigastrium and right hypochondrium. The liver was just palpable. The spleen could not be felt. The reflexes were sluggish and the abdominals could not be elicited. The right hip joint was ankylosed.

Laboratory Investigations :-
Urine :- heavy cloud of albumin ; bile pigments and urobilin present ; scanty pus, red blood and epithelial cells seen microscopically ; culture revealed the presence of Bact. coli.

Stool :- greyish in colour ; trace of bile present ; unfertilised ova of A. lumbricoides present ; culture revealed no pathogenic organisms.

The Kahn test was negative.

No malarial parasites were detected in repeated blood smears.

Blood findings :- haemoglobin 7.3 G./100 ml. ; r.b.cs. 2,200,000 per cu.mm. ; PCV 29% ; MCV 131.8 cu.micra ; MCHb 33 ; MCHbConc. 25% ; WBCs 27,000 per cu.mm. ; differential count :- myelocytes 1%, metamyelocytes 2%, neutrophil polys. 85%, eosinophils 1%, lymphocytes 10% and monocytes 1%.

Blood smear :- anisocytosis, poikilocytosis, polychromatic macrocytes, basophilic stippling and target cells. There were 18 normoblasts per 100 white cells.

The reticulocyte count was 7.6%. The erythrocytes sickled 100% by the rapid method.

The serum bilirubin was 16 mgm.%.

X ray report 1554/50 :- No gall stones detected.
1509/50 :- Right hip joint. There is deformity and flattening of the head of the femur with loss of joint space. Bony ankylosis and a great increase in the density

of the adjacent femoral and acetabular bone is present.
The condition may have resulted from an old infective arthritis.
(a similar condition has been described in sickle cell anaemia
- see page 62).

Course :- The patient's condition slowly deteriorated. Intense pruritis was complained of on 2-5-50. On the day before death, 7-5-50, there were sordes on the lips and the patient was delirious. The haemoglobin had fallen to 4 G./100 ml. blood. (i.e. a drop of almost 50% of the original value in 13 days) She sank into coma and died 8-5-50.

Treatment :- Vitamin K, penicillin and antimalarial therapy had been prescribed.

AUTOPSY 103/50 (6 hours after death)
The body was that of a thin jaundiced African female. The heart and lungs were normal. The liver was enlarged and bile stained. The bile ducts were patent and there were no gall stones. The spleen was densely adherent to the surrounding organs and was small and fibrosed. (Weight 19 G. - see plate 12). It was dull greyish brown in colour and the surface was nodular. It was gritty on section, the capsule was greatly thickened and dense bands of fibrous tissue stood out from the reddish slate grey colour of the cut surface. Grey and red nodules from 2 to 6 mm. in diameter were scattered throughout. The kidneys were enlarged and oedematous. The marrow of the femur was red and hyperplastic.

Histological Findings :-
Liver :- The lobular pattern was well preserved. There was no necrosis or evidence of biliary obstruction. The most striking feature was the intense erythrophagocytosis exhibited

by the Kupffer cells. They were distended with masses of sickled erythrocytes filling the cell. (see PLATE 17). The larger blood vessels contained serum only. Granules of pigment giving a variable reaction for iron (but mostly non iron containing) were present in the Kupffer and parenchymal cells.

Kidney :- The glomeruli and parenchyma were congested with sickled erythrocytes. A number of the glomeruli were hyalinised. and the capsular membrane of others was thickened. A few glomerular adhesions were present. The proximal tubules were dilated and there were densely staining casts in the collecting tubules. Granules of iron containing pigment were present in the tubular epithelium. The intertubular capillaries were packed with red blood cells which appeared to be agglutinated and sickled.

Spleen :- The normal splenic architecture was completely destroyed. There were dense masses of yellowish dark brown pigment enmeshed in fibrous tissue. (see PLATE 13). In some instances the pigment appeared to be in bundles resembling bamboo and in others it was surrounding the blood vessels giving a laminated appearance. (see PLATE 16). Giant cells were engulfing the pigment. (PLATE 15). The pigment gave the reaction for calcium and iron. Malpighian corpuscles were absent. The overall picture was that of progressive fibrosis with calcium and iron deposition, Masses of sickled erythrocytes were enmeshed in the interstices of the fibrous tissue.

AUTOPSY REPORT NUMBER 2
An African primigravida aged 21 years.

Previous History (from relatives) ; Suddenly collapsed 2 days before death complaining of weakness and difficulty in breathing : became delirious and died on the way to hospital. The patient had never been a strong woman and was subject to attacks of fever but no history of jaundice was given.

AUTOPSY 123/49 (15 hours after death)
A well nourished African female. Slight oedema of the ankles and jaundice of the sclera. The subcutaneous fat was not icteric. The meninges and brain were normal apart from their extreme pallor with which the blood vessels, containing pale watery blood, were in striking contrast. No malarial parasites were found in a smear from the brain. The mouth and throat were normal and the trachea contained frothy mucus. The lungs were pale bulky and oedematous. Much froth exuded on section. There was 60 ml. of clear straw-coloured fluid in the pericardium. The heart was pale, collapsed and not enlarged. There was gross pallor of the abdominal organs. The spleen, in contrast to this pallor, was a dark slaty blue colour and was grossly enlarged. (1,422 G.) It was adherent to the surrounding organs but could easily be freed. It was firm in consistency, the pulp was dark red in colour and did not bleed on section. The liver was enlarged and pale in appearance. (2,268 G.). The kidneys and suprarenal glands showed no gross abnormality. Uniovular twins were removed from an extremely pale uterus of 28 weeks enlargement. Their blood did not exhibit the sickle cell trait.

Histological findings :-
Brain :- the capillaries were empty and no sickled red blood cells were seen (PLATE 22).

Liver :- considerable autolysis, non iron containing pigment present, no congestion or necrosis and no sickled red blood cells seen.

Kidneys :- tubular degeneration, no congestion and very few red blood cells present.

Lungs :- gross oedema with scanty red blood cells present and a few sickled forms (PLATE 21).

The Spleen :- packed with sickle cells forming lakes of blood around the malpighian corpuscles which were scanty and widely separated. Much iron free pigment present.

The heart's blood showed 100 per cent. sickled red blood cells on direct examination.

Culture from the spleen and intestine revealed no pathogenic organisms.

AUTOPSY REPORT NUMBER 3
An African primigravida aged 20 years.

Extract from Clinical Notes :- No history of previous illnesses. Suddenly became unwell on 8-10-49 complaining of breathlessness, swelling of the face and legs and a 'bell ringing' in her ears. She was admitted to hospital on 9-10-49 collapsed and delirious. No jaundice. The temperature was 102' F. on admission. Scanty malarial parasites were present in a blood smear. The patient died shortly after admission. No history suggestive of previous haemolytic crises could be obtained.

AUTOPSY 169/49 (9 hours after death)
A well nourished African female. Oedema of the ankles and (?) slight jaundice of the conjunctivae. The macroscopic appearances of the organs were exactly similar to AUTOPSY NUMBER 2 apart from the thyroid gland which was diffusely enlarged. Again the slaty blue colour of the spleen was in striking contrast to the pallor of the other organs (weight 802 G.). Weight of the liver 1927 G. The heart's blood showed 100 per cent. sickling of the red blood cells on direct examination.
A male child of 28 weeks maturity was removed from a pale uterus. The child showed no abnormality apart from sickling of the red blood cells (10% by the rapid method) and the weight of the spleen was 3.2 G.
Cultures of the intestinal contents and splenic pulp of the mother revealed no pathogenic organisms.

Histological Findings :-
The brain, kidney and lungs were similar to Autopsy number 2. The thyroid gland showed a diffuse colloid enlargement with an occasional sickle cell present.

Liver :- diffuse hyaline degeneration with some round celled infiltration. Scanty red blood cells present. No evidence of haemorrhage or necrosis.

Heart :- the muscle was oedematous

Spleen :- packed with sickled erythrocytes. Lakes of blood obliterating the normal structure of the gland. Much iron free pigment was present.

The sternal marrow preparation was , unfortunately, unsatisfactory.

AUTOPSY NUMBER 4
An African primigravida aged 19 years.

Previous History (from relatives) :- The patient had been well throughout her pregnancy apart from occasional complaints of feeling tired and of vague pains in the limbs. Twins were delivered normally at 11 a.m. on 3-12-49. The labour was not unduly long, there were no apparent complications nor undue blood loss. The girl suddenly collapsed and 'became weak' after delivery. She was rushed to the hospital but died on the way at 1 p.m.

Autopsy 206/49 (2 hours after death) :-
Well nourished African female. Neither oedema nor jaundice present. The brain and meninges were pale and no malarial parasites were present in a smear. The oesophagus and trachea were normal. The lungs were pale, bulky and oedematous. The heart was pale,flabby and collapsed. It was not enlarged. The liver was enlarged and pale. (2,002 G.) The spleen weighed 190 G. and presented the typical slaty blue appearance of those previously described. The stomach and intestines were pale. There was some perirenal oedema but the kidneys otherwise appeared normal. The uterus was contracted and there was no evidence of haemorrhage or excessive trauma in the reproductive organs. The erythrocytes of the heart's blood sickled 100 per cent.. Culture from the spleen was sterile.

Histological findings :-
Liver :- The lobular pattern was well preserved. There was no necrosis. The blood vessels and sinusoids were congested with sickled erythrocytes. There was erythrophagocytosis by the Kupffer cells. A small amount of non iron containing

p

pigment was present.

Lungs :- There was congestion and extravasation of sickled erythrocytes in the alveoli. (PLATE 23). The smaller blood vessels were blocked by conglutinated masses of sickled erythrocytes.

The heart muscle was oedematous.

Spleen :- There was intense congestion of the pulp and sinuses and there were haemorrhages surrounding the malpighian corpuscles. The pulp and endothelial phagocytes had engulfed many red cells. Much non-iron and a little iron containing pigment was present.

Kidney :- A few of the glomeruli were hyalinised and the remainder were congested and packed with conglutinated masses of sickled red cells. (PLATE 24). No casts or pigment were seen.

AUTOPSY NUMBER 5

An African primigravida aged 17 years.

Previous History (clinical notes) :- Four days history of generalised pains, nausea and weakness.. Admitted to the Maternity Hospital, Accra on 14-12-49. The patient was a primigravida almost at term. She was weak and jaundiced on admission and malarial parasites were present in a blood smear. Bile pigments and urobilin were present in the urine. The haemoglobin was 6.8 G./100 ml. of blood. An injection of mepacrine was given intramuscularly on admission at 9 a.m. and qunine gr. 9 given intramuscularly just before a normal delivery at 2.30 p.m. the same day. The male child was alive and well. (2,168 G.) It's blood did not exhibit the sickle cell trait. The patient's temperature varied between 100' and 103'F. for the next 2 days. The lochia was not offensive and a blood culture was sterile. On the 16-12-49 the patient suddenly collapsed and became delirious. She died at 5.15 p.m. The haemoglobin was 4.1 G./100 ml. on the day of death.

Autopsy 215/49 (15 hours after death)

Well nourished African female. No oedema was present. There was jaundice of the sclerae and subcutaneous tissues. The meninges and brain were normal apart from their extreme pallor. No malarial parasites were present in a smear. The mouth and throat were normal. The trachea contained frothy mucus. The lungs were pale, heavy, frothy and oedematous. There was 55 ml. of bile stained fluid in the pericardium. The heart was slightly enlarged (330 G.), collapsed and the muscle was pale. The stomach and intestines were very pale.

The spleen was slaty blue in colour, enlarged and the cut surface was dark red and did not bleed on section. It was firm in consistency and a smear of the pulp was negative for malarial parasites although malarial pigment was present. The weight of the spleen was 765 G. The liver was enlarged and congested (2,142 G.). The pancreas was pale and firm. The shaft of the femur contained red marrow but there was considerable autolysis and the cellular components could not be satisfactorily identified. The kidneys and suprarenal glands showed no abnormality.. The heart's blood showed many sickled red blood cells on direct examination.

Histological findings :-
There was considerable autolysis of all organs.

Brain :- The capillaries were empty and no sickled erythrocytes were seen.

Liver :- No congestion nor necrosis. Iron and non-iron containing pigment present.

Kidney :- No congestion and no sickled erythrocytes seen.

Lung :- There was marked congestion and oedema with small haemorrhages present. The majority of the erythrocytes were discoidal but scanty sickled forms were present.

Spleen :- The splenic pulp was congested and packed with sickled cells. There were haemorrhages surrounding the malpighian corpuscles which were widely separated by the masses of sickled erythrocytes. Much iron and non-iron containing pigment was present.

AUTOPSY NUMBER 6

An African primigravida aged 18 years.

Extract from clinical notes :- The patient (28 weeks pregnant) was admitted to the Maternity Hospital, Accra on 24-3-50 complaining of pain in the joints of 24 hours duration. The general condition on admission was fairly good.

Laboratory investigations :- Urine :- albumin nil, no bile pigments but urobilin present. The Kahn test was negative. No malarial parasites were detected in blood smears. Hamoglobin 45% Sahli.; RBCs. 2,250,000 per cu.mm.. Sickling of the red blood cells 100 per cent. in 24 hours.

Antimalarial treatment was prescribed. Iron and marmite were given orally and hepolon intramuscularly.

Course :- The patient's condition gave no cause for anxiety until 1-4-50 when she suddenly became distressed and dyspnoeic. Oxygen was thought to improve the dyspnoea. The patient collapsed and died suddenly.

Autopsy 69/50 (6 hours after death)

Well nourished African female. There was no oedema but slight icterus of the sclerae was present. The meninges and brain showed extreme pallor. The blood vessels contained thin watery blood. No malarial parasites were found in a smear. The lungs were pale, bulky and oedematous. There was much froth in the trachea and bronchi. The heart was pale flabby and eo collapsed (261 G.). There was gross pallor of the abdominal organs. The spleen was a dark slaty blue colour and was greatly enlarged (1234 G.). It was firm in consistency and the pulp was dark red in colour and did not bleed on section. The liver

was pale (2,190 G.). The kidneys were pale and oedematous (275 G.). A male infant of about 28 weeks maturity was removed from a pale uterus. The child showed no abnormality, the blood was dark red in colour and did not exhibit the sickle cell trait. The weight of the liver was 27 G. and of the spleen 4 G. No abnormality was noted histologically in these organs. The heart blood of the mother showed 80 per cent. sickled forms on direct examination and 100 per cent by the rapid method.

Histological findings :-
Brain :- the majority of the blood vessels were empty. Others contained serum and white cells only.

The lungs showed congestion and oedema.

The heart muscle was oedematous and fatty degeneration was present.

Liver :- intense erythrophagocytosis by the Kupffer cells. The sinusoids were congested and nucleated red cells and polymorphs could be distinguished. The blood vessels contained serum and white cells only. Fine granules of non-iron containing pigment in the liver cells and a few iron containing granules in the Kupffer cells.

Spleen :- packed with sickled erythrocytes. Haemorrhages forming lakes of blood around the malpighian corpuscles. Iron and non-iron containing containing pigment in the pulp phagocytes and endothelial cells.

There was marked congestion of the kidneys.

AUTOPSY NUMBER 7
An African multipara aged 30 years.

Extract from clinical notes :-
The patient had only been unwell for the last 7 days although she had never been a strong woman. She had had 3 children of whom 2 were alive and the third was dead of an unknown cause. The patient complained of pain in the larger joints of the limbs, weakness, vertigo and palpitation on 19-5-49. These complaints became more severe and she was admitted to the Maternity Hospital, Accra on 22-5-49. On admission the patient's condition did not give rise to anxiety. She was considered to be 36 weeks pregnant. The temperature was 100'F. A blood smear for malarial parasites was negative and Ps. pyocyaneus was isolated from the urine. Suddenly on 4-6-49 the patient complained of difficulty in breathing and collapsed. On examination she appeared shocked. The patient died within 2 hours. Unfortunately no haematological investigations were recorded.

Autopsy 86/49 (4 hours after death.)
Well nourished African female. Slight icterus of the sclerae and mild oedema of the ankles. The brain and meninges were pale. No malarial parasites were seen in a smear from the brain. The lungs were bulky and oedematous. The heart was enlarged. (365 G.). The liver was enlarged and congested. The spleen was enlarged (604 G.) and resembled those previously described. The kidneys were congested. The erythrocytes of the maternal blood sickled 100 per cent. on direct examination. A macerated full term infant was removed from a pale uterus.

Histological findings :-

Lungs :- there was much congestion and the blood vessels were packed with conglutinated masses of sickled erythrocytes (PLATE 25).

Liver :- the blood vessels and sinusoids were packed with sickled erythrocytes. There was no necrosis. There was marked erythrophagocytosis by the Kupffer cells. No pigment was detected.

Kidney :- congestion of the glomeruli and blood vessels with sickled erythrocytes. Iron containing pigment in the epithelium of the tubules.

Spleen :- the pulp was congested and there were lakes of blood surrounding the malpighian corpuscles and haemorrhages into the trabeculae (PLATE 20). There was some fibrosis and thrombosed vessels were present. Iron and non-iron containing pigments were present in the endothelial and pulp phagocytes.

AUTOPSY NUMBER 8.
An African multipara aged 26 years.

Extract from the clinical notes :-
Previous History :- the patient had had 3 previous children. One child had died of an unknown cause and the other 2 are alive and well. The labours had been normal. The patient had suffered from osteomyelitis some years ago.

Present History :- the patient was admitted to the Maternity Hospital, Accra at 11 a.m. on 29-3-50 complaining of pain in the chest, cough and swelling of the ankles of one week's duration.

The general condition on admission was fairly good and the significant findings were as follows. There was oedema of the ankles and slight icterus of the sclerae. A radiograph of the chest was within normal limits. There was a systolic apical murmur. The liver and spleen were just palpable. The uterus was enlarged (full term). The foetal heart sounds were normal and there was no disproportion.

Laboratory investigations :- the urine showed a heavy cloud of albumin and urobilin was present but no bile pigments were detected. There were many pus cells present. No malarial parasites were detected in blood smears. The haemoglobin was 6.7 G./100 ml. blood. The stool was liquid and mucus was present but culture revealed no pathogenic organisms.

The patient suddenly became dyspnoeic, restless and delirious on 31-3-50 when the haemoglobin was 4.7 G./100 ml. Her condition quickly deteriorated and she died at 6.15 a.m. on 2-4-50. The blood urea after death was 60 mgm.%.

Autopsy 70/50 (3 hours after death).
Reasonably well nourished African female. There was slight icterus of the sclerae and oedema of the ankles. There was an old healed sinus on the outer side of the left thigh. The brain and meninges were excessively pale. The blood was pale and watery and no malarial parasites were detected in a smear. The lungs were pale and oedematous and much froth exuded on section. There were a few pleural adhesions in the left chest cavity. The heart was collapsed, pale and flabby (289 G.). The liver was enlarged but of normal colour (2,300 G.) The spleen was dark slaty blue in colour and there were a few adhesions to the surrounding structures (475 G.- PLATE 18). The cut surface was dark red, firm and did not bleed on section. The stomach and intestines were pale. The left kidney was rather pale (160 G.) and there was a pyonephrosis of the right (215 G.). There was sclerosis and cortical thickening of the middle third of the left femur. The marrow cavity contained reddish yellow marrow which could easily be scooped out. There was an increase in cellularity and many nucleated red cells were present. The erythrocytes of the maternal blood sickled 100 per cent. A full term male infant was removed from a pale uterus. No abnormality was detected in the infant. The blood was dark red in colour and did not exhibit the sickle cell trait.

Histological findings :-
Brain :- the capillaries were empty and the larger blood vessels contained serum only. No sickled erythrocytes were seen.

Heart :- there was oedema of the muscle and hyaline degeneration

of the fibres.

Lungs :- there was marked oedema.

Liver :- there was congestion of the blood vessels and sinusoids by sickled erythrocytes. Erythrophagocytosis by the Kupffer was present. There were small granules of iron containing pigment in the liver cells.

Kidney :- the right kidney showed the histological features of pyelonephritis and the left was normal apart from congestion by sickled erythrocytes.

Spleen :- the spleen was packed with sickled erythrocytes. There were haemorrhages into the trabeculae and surrounding the malpighian corpuscles (PLATE 19). The pulp histiocytes had engulfed many sickled cells. Iron and non-iron containing pigments were present.

Autopsy Number 9
An African multipara aged 30 years.

Extract from the clinical notes :-
Previous history :- the patient had had 4 previous children. 3 were stillborn and 1 was alive and well. The labours had all been long and difficult.

Present history :- the patient was admitted to the Maternity Hospital, Accra at 10 a.m. on 27-3-50 with a history of having been 4 days in labour. The membranes had ruptured 3 days previously. The general condition on admission was fairly good. Slight uterine contractions were noted and the cervical os was not fully dilated. The temperature was 102'F. The pulse rate was 140 and the respiration rate 24 per minute. There was an offensive vaginal discharge (native medicine had been inserted into the vagina). There was a trace of albumin in the urine and the haemoglobin (Tallquist) was 50%. The patient died suddenly in a state of shock at 10.45 p½m. on the day of admission.

Autopsy 65/50 (12 hours after death).
Well nourished African female. There was jaundice of the sclerae. No oedema was present. The meninges and brain showed extreme pallor. The lungs were pale, bulky and oedematous. The heart was hypertrophied. The liver was enlarged and congested (2,950 G.). The spleen resembled those previously reported and weighed 800 G. It's dark blue colour contrasted sharply with the pallor of the stomach and intestines. The kidneys were pale and oedematous. The erythrocytes of the heart's blood sickled 100 per cent. on direct examination. A normal full term infant was removed from a pale uterus.

The erythrocytes of the infant's blood sickled 1 per cent. by the rapid method. (ROBINSON, 1945).

Histological findings :-

Liver :- the sinusoids were congested with sickled erythrocytes. Intense erythrophagocytosis by the Kupffer cells was present. The larger blood vessels contained serum and white blood cells only. There was alymphocytic infiltration of the portal tracts. A considerable amount of iron containing pigment was present in the liver cells and was most marked in the periportal areas.*

Spleen :- there was intense congestion of the pulp and sinuses. The endothelial cells of the sinuses and phagocytes of the pulp had engulfed many sickled erythrocytes. In addition they contained iron and non-iron containing pigments.

Kidney :- the large blood vessels contained serum only. Albuminous casts were present in the proximal convoluted tubules.

* The significance of this deposit of iron pigment in the liver cells of Africans is unknown. The writer has found this type of pigment in about 10% of unselected liver sections examined.

AUTOPSY NUMBER 10
An African male aged 40 years.

K.Y., an African male, was admitted to the Gold Coast Hospital in the afternoon of 3-11-51. He was complaining of severe substernal pain and breathlessness of sudden onset. There was no history of vomiting or sweating. No relevant previous history was noted.

Examination (Dr. A. J. Hawe, Senior Specialist).
Temperature 98°F. The pulse rate was 136 and the respiration rate 36 per minute. The patient appeared shocked and the extremities were cold. Examination of the cardiovascular and respiratory systems revealed no abnormality apart from a few crepitations at the lung bases. The blood pressure rather surprisingly was 160/105. The spleen and liver were palpable. The fundi were normal.
The urine contained a slight cloud of albumin and there was no excess of urobilin. A blood smear was negative for malarial parasites. No diagnosis was reached and the patient died on 6-12-51.

Autopsy Report 251/51
The body was that of a rather emaciated African male. There was no jaundice oedema or clubbing of the fingers.
The trachea contained frothy mucus. The left lung was adherent to the chest wall. The adhesions were fine and did not appear to be of long standing. The apical lobe of the left lung was dark red and firm and lobar pneumonia was tentatively diagnosed. The right lung was congested and oedematous.
The heart showed no abnormality. The coronaries were patent and there was no sign of infarction. The throat and pharynx were normal. The stomach and upper part of the small intestine were

dilated. The mesenteric vessels were normal. The liver was congested,1,770 G..The gall bladder was normal and there was no obstruction to the bile ducts. The pancreas was firm. The kidneys were dark and congested (245 G.). A few small yellowish nodules were were scattered throughout both kidneys, mostly subcapsular in position. There was a small area of ulceration in the trigone of the bladder. The testes were small. The prostate was not enlarged and the seminal vesicles were normal. The spleen was enlarged (710 G.), dark red and congested. The lymphatic glands were not enlarged.
The brain was not examined.

Histological findings :-
Lungs :- the apex of the left lung did not show pneumonic consolidation. The smaller blood vessels were packed with conglutinated masses of sickled erythrocytes. Many of the alveoli were collapsed and in others there was a fibrinous exudate with macrophages containing pigment.
Liver :- the sinusoids were grossly congested with sickled erythrocytes. Erythrophagocytosis by the Kupffer cells was present (PLATE 26). The usual portal lymphocytic infiltration so common in the African was marked. No pigment was present.
Spleen :- the splenic pulp and sinuses were grossly congested and there were haemorrhages into and surrounding the malpighian corpuscles. The erythrocytes were sickled. The phagocytes contained pigment which did not give the staining reaction for iron. There was some erythrophagocytosis present.
Kidney :- the nodules mentioned above were papillary adenomata with granular calcification present. The glomeruli were

congested and a number were hyalinised. There was a mild fibrosis of the interstitial tissue and some lymphocytic cellular infiltration. There were a few casts in the tubules. The vessels showed intimal proliferation.

Heart :- the muscle fibres were small and separated. The blood vessels were normal. The mitral valve was thickened by a fibrous tissue reaction but there was no evidence of infection.

The pancreas showed no gross abnormality. There was a mild non specific infection of the bladder. The testes were atrophied.

The sternal marrow smear could not be interpreted as post mortem changes had occurred.

AUTOPSY NUMBER 11
An African male aged 19 years.

A healthy male African out patient died under Evipan anaesthesia which was being given to enable a urethral stricture to be dilated. Less than 1 G. of Evipan had been given when the patient stopped breathing. Attempts at resuscitation failed.

Autopsy 17/50 (4 hours after death).
Well built African male. The brain was congested. The lungs were oedematous and congested and there was blood stained froth in the trachea. The heart was not enlarged (210 G) but the right ventricle was dilated. The liver was dark and congested (1,280 G.). The spleen was enlarged (280 G.), dark blue in colour and the cut surface was dark red and did not bleed on section. No abnormality was detected in the stomach or intestines. There were a few enlarged lymph glands in the mesentery. The kidneys were dark and congested. The bladder wall was thickened. A chronic fibrous urethral stricture was present. The erythrocytes of the heart's blood sickled 100 per cent.

Histological findings :-
Lungs :- there was intense congestion. The vessels were packed with sickled erythrocytes. The alveoli were oedematous and there was a mild extravasation of red cells.

Brain :- the capillaries of the brain were congested and small focal haemorrhages were present (PLATE 28).

Spleen :- the spleen was packed with sickled erythrocytes and there were haemorrhages surrounding the malpighian corpuscles.

The bladder wall showed chronic fibrosis and congestion.

AUTOPSY NUMBER 12
An African female child aged 4 years.

Extract from the clinical notes :- The child suddenly became distressed, semiconscious and dyspnoeic. She was admitted to the Gold Coast Hospital, Accra on 26-6-49 at 5.20 a.m. and quinine hydrochloride grain iii was given intramuscularly. The temperature was 102'F. The pulse and respiration rates were 102 and 24 respectively. The result of the blood smear was not recorded. The pulse rate rose to 144 and the temperature fell to normal and then rose to 102'F. just before death which occurred at 7.25 p.m. on the day of admission.

Autopsy 112/49 (17 hours after death)
The body was that of a well nourished African girl. The meninges and brain were intensely congested but showed no other abnormality. No malarial parasites were found in a smear. There was much froth in the air passages. The lungs were congested and oedematous. The heart appeared normal. The liver was enlarged and yellowish brown in colour. The spleen was enlarged (82 G.). It resembled those previously described. The kidneys, stomach and intestine revealed no abnormality apart from congestion. A culture from the splenic pulp revealed no pathogenic organisms. The erythrocytes in the heart's blood sickled 100 per cent.

Histological findings :-
Brain :- the capillaries were dilated and packed with sickled red blood cells. No malarial parasites or haemorrhages were noted. (PLATE 27).

Lung :- The alveoli showed much oedema. The smaller blood

vessels were packed with sickled erythrocytes. In a few areas there was an infiltration of polymorphonuclear cells in the alveoli.

Spleen :- The spleen was packed with sickled red blood cells. There were haemorrhages surrounding the malpighian corpuscles. Erythrophagocytosis was noted in the pulp and endothelial phagocytes. Iron and non-iron containing pigments were present.

Liver :- there was marked fatty infiltration. The sinusoids were congested with sickled erythrocytes. The Kupffer cells were packed with ingested erythrocytes. There was much pigment in the portal tracts and parenchymal cells which gave a variable reaction for iron.

AUTOPSY NUMBER 13
An African boy aged 5 years.

Extract from the clinical notes :- the boy was admitted to the Gold Coast Hospital, Accra on 5-1-50 at 10.30 a.m. with a history of convulsions of some hours duration. On examination the patient was having a major epileptic fit. The temperature was 98'F. The pulse and respiration rates were 82 and 22 per minute. Clinical examination revealed no abnormality. No malarial parasites were present in a blood smear. Quinine grains X were given intramuscularly. A second fit occurred at 3.30 p.m. and 2 ml. of paraldehyde was given intramuscularly. This was repeated at 10.30 p.m. when a third fit occurred. The temperature, pulse and respiration rates rose steadily during the day and just before death at 6.30 a.m. on 6-1-50 were 104'F., 160 per minute and 40 per minute respectively.

Autopsy 6/50 (1½ hours after death).
Moderately well nourished African boy. Neither jaundice nor oedema were present. The brain was markedly congested. No malarial parasites were found in a smear. The lungs were bulky and oedematous. No abnormality was detected in the heart or pericardium (113 G.). The liver appeared normal (496 G.). The spleen was enlarged and was dark slaty blue in colour (101 G. The stomach and intestines were pale. The kidneys appeared normal (85 G.). 20 per cent. of the erythrocytes of the heart's blood sickled on direct examination and 100 per cent. when the rapid bacterial method was used.

Histological findings :-
Brain :- there was marked congestion of the blood vessels which were packed with sickled erythrocytes. There was no evidence of malaria and no haemorrhages were seen.

Liver :- the Kupffer cells were packed with ingested sickled erythrocytes. The sinusoids and blood vessels were congested with sickled erythrocytes. Considerable fatty infiltration was present. Pigment giving a variable reaction for iron was present in the portal tracts and parenchymal cells.

Spleen :- the sinuses and pulp were packed with sickled erythrocytes. There were haemorrhages around the malpighian corpuscles. The endothelial cells of the sinuses and pulp phagocytes contained ingested red blood cells. Much pigment giving a varying reaction for iron was present also in these cells.

APPENDIX E.

BIBLIOGRAPHY.

BIBLIOGRAPHY

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