ANAESTHESIA IN WEST AFRICAN PATIENTS WITH SICKLE-CELL ANAEMIA, HAEMOGLOBIN SC DISEASE, AND SICKLE-CELL TRAIT

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SUMMARY

Sickling occurs in sickle-cell anaemia, sickle-cell trait and the mixed sickling haemoglobinopathies such as haemoglobin SC disease. The severity of sickle-cell anaemia is apparently greater in West Africa than in the West Indies. Three cases anaesthetized in Ghana are described. Experience of thirty-three cases of heterozygous sickle-cell states indicates that the danger of anaesthesia is greater in haemoglobin SC disease than in sickle-cell trait. Pre-operative treatment of the anaemia is discussed. Sodium bicarbonate, magnesium sulphate, low-molecular weight dextran, heparin, and the phenothiazine derivatives may be useful in prophylaxis and treatment of crisis in the operative period. Hypoxia, acidosis, stasis and cooling should be avoided during anaesthesia.

The sickling phenomenon occurs in three conditions: (1) sickle-cell anaemia; (2) sickle-cell trait; (3) mixed sickling haemoglobinopathies, of which haemoglobin SC disease is the most common. These conditions are, to a considerable extent, distinguishable on clinical grounds, and are easily and definitely distinguishable by filter paper electrophoresis of the patient's haemoglobin.

Brown (1965) has described operations on sixteen cases of sickle-cell anaemia in Jamaica. There were no complications attributable to the nine general or seven regional anaesthetics. However, Golding (1964) is quoted as stating that the results of surgery in West African patients with sickle-cell anaemia are not so satisfactory.

It has previously been shown (Anderson et al., 1960; Fullerton and Watson Williams, 1962) that the maternal mortality in obstetric patients with sickle-cell anaemia is greater in West Africa than in Jamaica. In haemoglobin SC disease, too, Anderson and his colleagues, as a result of their experience in Jamaica, wrote “It is likely that pregnancy does not materially affect the natural history of haemoglobin SC disease” (Anderson et al., 1960), whereas in West Africa it has been stated “Pregnancy appears to be a definite hazard, and catastrophes are liable to occur, particularly in the third trimester” (Edington, 1957).

The mortality rate in childhood is also apparently higher in Africa than in Jamaica. The likelihood of survival to adult life with sickle-cell anaemia in Africa is probably about 14 per cent (Jacob, 1957) in contrast to the findings of Went and MacIver (1958) that 50 per cent of their patients were adults.

Some of the apparent geographical differences in the sickling diseases may be due to selection, and conclusive proof must depend on larger, more comparable series of cases.

This paper describes anaesthesia in the three sickling conditions in West Africa. There were two deaths among three cases of sickle-cell anaemia. Anaesthesia was followed by complications attributable to sickling in two cases with haemoglobin SC disease. No complications occurred in the cases of sickle-cell trait, although consideration of the effect of high altitude on these patients would indicate that the possibility of sickling under anaesthesia probably exists exceptionally.

THE “SICKLING” PHENOMENON

It was discovered by Herrick (1910) that the erythrocytes of certain American Negroes assume a crescentic or “sickle” shape when deprived of oxygen. In some cases the phenomenon was associated with a severe haemolytic anaemia, the clinical features of which were sufficiently distinctive for “sickle-cell anaemia” to be considered a disease entity. In other cases, however, sickling was observed in the blood of apparently healthy people, and this was called sickle-cell trait. Subsequent research has shown that sickling only occurs
in erythrocytes containing the abnormal haemoglobin now known as haemoglobin S, the occurrence of which is determined by the inheritance, from either or both parents, of a dominant gene.

In the homozygous condition haemoglobin S is formed to the complete exclusion of normal haemoglobin (haemoglobin A). Due to the effect on the erythrocyte of so much haemoglobin S, the cells exhibit the sickling phenomenon, and the effect on the patient is to cause sickle-cell anaemia.

Sickle-cell trait is the result of the inheritance of normal haemoglobin from one parent and haemoglobin S from the other (fig. 1). The smaller proportion of haemoglobin S is of less clinical importance although it is far from completely innocuous (McCormick, 1961). The erythrocytes do, however, contain enough haemoglobin S to sickle in the usual laboratory preparation.

If the gene responsible for the formation of haemoglobin S occurs in a heterozygote with the gene associated with another abnormal haemoglobin (of which more than twenty types have been described) a mixed sickling haemoglobinopathy will result. The cells will exhibit the sickling phenomenon in the laboratory, but the clinical manifestations may range from a severe disability to an almost asymptomatic trait, depending on the amount of haemoglobin S present, and on the nature of the other abnormal haemoglobin. The combination of haemoglobins S and C (haemoglobin SC disease, fig. 2) is common in West Africa, and is known to cause a high maternal mortality in pregnancy (Smith and Conley, 1954) and is frequently associated with a characteristic aseptic necrosis of the head of the femur. The combination of haemoglobin S with a gene which suppresses the formation of haemoglobin A (sickle-cell thalassaemia) can cause severe anaemia and may be difficult to distinguish from homozygous sickle-cell anaemia (Went, 1957). Thus a diagnosis of a haemoglobinopathy is incomplete without a statement of the haemoglobins which are present, usually expressed as the genotype (SS, SC, AS, etc.).

For a more detailed account of the haemoglobinopathies the reader is recommended Lehmann’s very intelligible account of this complicated subject (Lehmann, 1960). Papers written before the actual haemoglobin present could be identified by electrophoresis are liable to be misleading and should be critically evaluated. Haemoglobin S was discovered by Pauling and associates (1949) and it

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**Fig. 1**

Inheritance of sickle-cell anaemia and sickle-cell trait.

A = gene responsible for haemoglobin A.  
S = gene responsible for haemoglobin S.

**Fig. 2**

Genetic mechanism of the formation of a mixed sickling haemoglobinopathy, in this case haemoglobin SC disease.

C = gene responsible for formation of haemoglobin C.
was shown by Ingram (1959) to differ from haemoglobin A by the substitution of a valine radical for a glutamic acid radical in one of the two polypeptide chains which make up the globin moiety. The haem fraction is the same in all the haemoglobins.

**DIAGNOSIS OF SICKLING STATES**

This should rarely be missed if the blood of every Negro patient is checked for sickling. The test is not more difficult than a haemoglobin estimation. Usually a drop of blood is added to the reducing agent sodium metabisulphite on a microscope slide, and the preparation is examined microscopically. If sickling is detected then the more complex task of identifying the abnormal haemoglobins present must follow. This is usually done by filter paper electrophoresis as the haemoglobins have different electrophoretic motilities, which are fairly specific in most cases.

It may be mentioned here that abnormal haemoglobins other than S do not produce sickling or severe clinical syndromes. They may be disregarded unless in combination with haemoglobin S, or with suppression of haemoglobin A (partly or entirely) by the thalassaemia gene.

**GEOGRAPHICAL DISTRIBUTION**

Many papers quote regional incidences of sickle-cell trait, as it may be fairly easily assessed by testing the blood of representative samples of the population for sickling. Figures for the incidence of sickle-cell anaemia, which should be confirmed by the more complex electrophoretic investigation, are rare, and due to the high mortality of the disease they are only correct for the age group examined. The highest incidence of the trait is probably found in East Africa (Lehmann, 1954) where it occurs in more than 30 per cent of the African population. An incidence of over 20 per cent is found in West Africa. Haemoglobin C originated in Northern Ghana and is found in 10-5 per cent of the population (Thompson, 1962). The Vedoid people of South Arabia and South India have been found to have an incidence of sickle-cell trait of over 30 per cent. Parts of the world to which West Africans were taken as slaves also have a high incidence of sickle-cell trait. In American Negroes the incidence has been quoted as 8 per cent (Smith and Conley, 1954) and in Jamaica it has been estimated to be 10-4 per cent (Went, 1957). That the disease is not wholly confined to Negroes is shown by the discovery of the trait in at least 17 per cent of a small community in Greece (Lehmann, 1954). Cases have been reported from all parts of the world and reports from British hospitals (Diamond, 1959; Lewin and Goodell, 1962) emphasize the need for clinicians to be aware of the implications of a positive sickle test even in areas where the abnormality is not found in the native population.

**PATHOLOGICAL MECHANISMS IN SICKLE-CELL STATES**

Haemoglobin S differs from all other haemoglobins in its extreme insolubility in the reduced form. When erythrocytes containing haemoglobin S are rendered hypoxic, the reduced haemoglobin forms long insoluble intracellular chains called tactoids, which distort the cell membrane and cause the cell to assume a sickle shape. The degree of hypoxia required to cause sickling depends on the proportion of haemoglobin S present. In sickle-cell anaemia the red cells contain a very large proportion of haemoglobin S (a little foetal haemoglobin persists), and the venous blood always contains some sickle cells, while a small decrease in available oxygen may provoke massive sickling. In sickle-cell trait, on the other hand, the proportion of haemoglobin S is lower, and the critical degree of hypoxia rarely occurs in vivo, and so many carriers of the trait are asymptomatic. The mixed sickling haemoglobinopathies, such as haemoglobin SC disease, vary in the amount of haemoglobin S present and, therefore, the severity of the resultant symptoms.

The pathological results of sickling may be due to: (i) anaemia; (ii) blockage of blood vessels.

*The anaemia.*

In classical sickle-cell anaemia a moderately severe degree of anaemia is constantly present (Smith and Conley, 1954). It is unusual for the haematocrit to exceed 30 per cent. Most patients with haemoglobin SC disease are free from anaemia during asymptomatic intervals although during crises anaemia may be severe. The anaemia is accounted for by the greatly reduced life span of sickled erythrocytes which are mechanically and osmotically fragile (Harris et al., 1956). The excessive rate of destruction is partly compensated by an increased rate of erythropoiesis by the bone marrow, but this balance results in a subnormal haemoglobin level, usually about 8 g/100 ml. A raised serum bilirubin level is found and patients
are often clinically jaundiced. The high reticulocyte count usually present is evidence of accelerated erythropoiesis. Blood smears from patients with haemoglobin SC disease show large numbers of "target cells", more than 50 per cent of the total erythrocytes being in this form. A leucocytosis, predominantly polymorphonuclear, is a usual finding during a crisis and should not be interpreted as due to an infection.

Episodes of severe acute anaemia may be superimposed on the chronic anaemia causing "haematological crises" as distinct from the "clinical crises" described below. Singer, Motulsky and Wile (1950) refer to aplastic and hyperhaemolytic crises. In the former, a sudden cessation of erythropoiesis combined with the short lifespan of the existing erythrocytes causes a precipitous fall in haemoglobin level. The cause of the suspension of erythropoiesis is not known precisely, but has been seen in association with infection, and possibly after anaesthesia. The existence of hyperhaemolytic crisis is doubtful (Anderson et al., 1960). Acute folic acid deficiency may cause the superimposition of a megaloblastic anaemia on pre-existing sickle-cell anaemia with fatal results (Fullerton and Watson Williams, 1962). Finally, any cause of extensive sickling will cause the spleen and liver to sequestrate the deformed erythrocytes leaving a frequently fatal deficiency in the circulating blood. This syndrome is particularly frequent in the post-partum period.

Infarctive phenomena.

The presence of sickled red cells in blood increases its viscosity (Harris et al., 1956) and it tends to cludge in areas of sluggish flow. Ischaemia results, possibly accentuated by vascular spasm, and a vicious circle arises, as the ischaemia causes further sickling. Patients with sickle-cell anaemia, and some cases of sickle-cell trait and haemoglobin SC disease, suffer periodic painful crises, with malaise, pyrexia, and pain in the abdomen and limbs. These are referred to as "clinical crises" and are not associated with haematological disturbances. They may be due to temporary blockage of small blood vessels but Lehmann has emphasized that before permanent occlusion and infarction can occur the sludge must be bound by clotted plasma.

The effects of infarction due to sickling may be present in any part of the body in the homozygous condition. The spleen, usually enlarged in childhood, is commonly progressively destroyed by repeated infarction and fibrosis, a process described as "autosplenectomy". Repeated pulmonary infarcts and emboli lead to pulmonary hypertension. Renal infarcts occur but complete renal hypertension is uncommon. Cardiac failure may occur as the myocardium, weakened by anaemia, fails to withstand the strain on the right ventricle imposed by the pulmonary hypertension. Cardiomegaly and tachycardia with a systolic bruit and accentuated second heart sound in the pulmonary area are common findings in sickle-cell anaemia. The nervous system may be affected in many ways and transient blindness has been described in the post-operative period (Lewin and Goodell, 1962). Other ocular manifestations are described by Goodman, von Sallmann and Holland (1957). Infarction of the ribs, with secondary infection by E. coli, frequently requires surgical treatment under anaesthesia.

Although perhaps the majority of patients with haemoglobin SC disease have occasional clinical or "painful" crises, permanent infarction is much less common and less serious than in sickle-cell anaemia. The head of the femur is, however, particularly prone to infarction leading to a distinctive aseptic necrosis. Vitreous haemorrhage is also found more commonly in haemoglobin SC disease and a case is described later in this paper.

Patients with sickle-cell trait are usually free from these effects of sickling although they may occur during conditions associated with exceptional ischaemia, such as pneumonia, alcoholic intoxication, or the effects of high altitude.

RELEVANCE OF THE HAEMOGLOBINOPATHIES TO ANAESTHESIA

Sickle-cell trait and haemoglobin SC disease.

It is obvious that while patients with sickle-cell anaemia may be exposed to the danger of massive sickling of their erythrocytes if the oxygen tension of their blood is allowed to fall even slightly during anaesthesia, patients whose erythrocytes contain a smaller proportion of haemoglobin S (i.e. heterozygotes) will not be endangered unless a greater reduction in oxygen tension occurs. Hypoxia may apparently be avoided during anaesthesia but it has been shown (Nunn and Payne, 1962; Conway and Payne, 1964) that a considerable degree of hypoxia may occur during and after an uneventful anaesthetic for a minor operation. These authors state
that the average degree of hypoxia discovered postoperatively corresponds to that which occurs in an unpressurized aircraft flying at an altitude of 10,000 feet above sea level, and the lowest oxygen tension they found would be reproduced in a person in such an aircraft at 17,000 feet. In aircraft at these altitudes, however, passengers with sickle-cell trait and haemoglobin SC disease have suffered from splenic infarction (Smith and Conley, 1955) and so the same accident, or other consequences of sickling, would be expected to occur postoperatively. The authors noted that sickling due to altitude occurred more frequently, and at lower altitude, in haemoglobin SC disease than in sickle-cell trait.

In fact, in thirty-three patients with these diseases who were anaesthetized by the author, no postoperative splenic infarcts occurred, so the risk, if it exists in practice, must be small. Two postoperative complications associated with the sickling disease occurred in this group of patients, and both patients have haemoglobin SC disease.

Case 1.
A male Ghanaian, aged 35 years, was found to be suffering from aseptic necrosis of the head of the femur. The sickling test was positive and electrophoresis showed haemoglobins S and C. He was subject to frequent sickling crises, with malaise and bone pains. In the course of the surgical treatment of the hip disease he was anaesthetized four times. The second of these was for a subtrochanteric osteotomy with insertion of a tibial bone graft from the osteotomy site to the ischium. Anaesthesia on this occasion was induced by thiopentone (300 mg), after which suxamethonium bromide (Brevetil M) 120 mg was given. After oral intubation anaesthesia was maintained by nitrous oxide, oxygen and halothane (1 per cent). Postoperatively he had an unusually severe sickling crisis, and became jaundiced. The serum bilirubin was 5 mg per cent, and reticulocyte count 5 per cent. His haemoglobin was, unfortunately, not recorded but he was not severely anaemic.

Case 2.
A male Ghanaian, aged 37 years. He had frequent attacks of joint pains and malaise as a child but none during the past fifteen years. He had been regarded as a case of sickle-cell trait. Two attacks of vitreous haemorrhage occurred about ten years ago but he recovered full vision in the eye. Whilst pursuing postgraduate studies in Liverpool last year another vitreous haemorrhage occurred and a drainage operation was proposed, to relieve his pain. Local anaesthesia was not considered suitable; general anaesthesia was requested.

Pre-operatively he appeared healthy apart from the ophthalmic condition. The haemoglobin level was 95 per cent and electrophoresis revealed sickle-cell haemoglobin C disease.

Anaesthesia was induced with thiopentone 200 mg, after which suxamethonium chloride 75 mg was injected. The lungs were inflated with oxygen before topical analgesia of the larynx and trachea with 4 per cent lignocaine; a cuffed endotracheal tube was then passed. Anaesthesia was maintained with nitrous oxide (5 l./min), oxygen (3 l./min) and halothane (1-5 per cent for 3 minutes, then 0-5 per cent for the remainder of the anaesthetic). During anaesthesia the systolic blood pressure remained at 110 mm Hg. The respiratory rate was 24/min, and minute volume was 5-54 l./min. A tachycardia of 96 beats/min persisted throughout.

Postoperatively oxygen was administered by nasal catheter for 24 hours. On the third day left-sided pleuritic and shoulder-tip pain accompanied a mild pyrexia. There was no cough or sputum. Percussion note was slightly dull at the left lung base and chest radiography showed increased shadowing in that area. On the sixth day a little blood-stained sputum was produced. No pathogenic organisms were isolated. The incident was at first regarded as being due to pneumonia but in retrospect may well have been due to a small pulmonary infarct. It is of interest that there was no preceding bone pain.

The other anaesthetics in this group of thirty-three patients were all given for orthopaedic operations. All the adults were anaesthetized with halothane, using a similar technique. Anaesthesia in children was induced with thiopentone, endotracheal intubation being aided by suxamethonium.

Anaesthesia was maintained with either nitrous oxide and oxygen in the ratio 3:1 using intermittent positive pressure ventilation and a muscle relaxant, or with nitrous oxide and oxygen (3:1 mixture) and halothane, the patient breathing spontaneously.

Other types of surgery may be attended by a greater risk. Ciliberti and his co-workers (1962) describe a patient with sickle-cell trait, who had been treated with nephrotic syndrome, who died of sickle-cell crisis and nephrotic syndrome after laparotomy at which no surgical lesion was discovered. The anaesthesia was uneventful except for a tachycardia of 100-120 beats/min.

No statistical assessment of the risk of anaesthesia is possible from this small number of cases, but it appears to be low in asymptomatic cases of the trait if careful attention is paid to oxygenation during the operation.

Sickle-cell anaemia.

Three patients with this condition were anaesthetized in the Military Hospital, Accra, between February 1963 and March 1964, and two of them died.

Case 1.
A Nigerian woman, aged about 30 years, was delivered by Caesarean section under general anaesthesia. After induction with thiopentone followed by suxamethonium bromide, endotracheal intubation was performed. Anaesthesia was maintained by pulmonary hyperventilation with nitrous oxide (6 l./min) and oxygen (2 l./min) and relaxation was provided by tubocurarine 30 mg. The
relaxant was reversed at the end of the operation by injection of neostigmine 5 mg preceded by atropine sulphate 1-2 mg. The operation was uneventful and the blood loss was not excessive. On leaving the theatre she was awake, and pulse, blood pressure and respiration were normal. She collapsed and died about 2 hours later. At autopsy massive sickling and severe anaemia were the only abnormalities discovered. The pre-operative haemoglobin level was 80 per cent.

**Case 2.**
A child about 10 years old was anaesthetized for removal of a foreign body from its buttock. Anaesthesia was induced by thiopentone and maintained by nitrous oxide and oxygen (3:1 mixture) with halothane (1·5 per cent). After about 1 hour of uneventful anaesthesia the child collapsed and died.

**Case 3.**
A child about 5 years old was suffering from osteomyelitis of a rib and surgical drainage was necessary. A short anaesthetic was given using thiopentone and suxamethonium for induction and endotracheal intubation. Maintenance was by controlled ventilation with nitrous oxide and oxygen (3:1 mixture) via a T-piece and open-ended bag. Postoperatively the haemoglobin level fell to 50 per cent but she recovered without transfusion.

Descriptions of anaesthesia in sickle-cell anaemia by other authors include the series of fifteen cases described by Shapiro and Poe (1955), although the electrophoretic results are not quoted. Of fifteen general anaesthetics administered to these patients, there were five "definite complications". The case of Lewin and Goodell (1962) has already been mentioned. Anaesthesia administered to an 11-year-old Nigerian girl with proven sickle-cell anaemia was followed by transient blindness, paresis of limbs, jaundice, and disturbance of consciousness. Treatment by Lehmann's regime was followed by recovery.

Brown's report of anaesthesia in Jamaicans with sickle-cell anaemia (1965) has been referred to. No complications occurred in nine general anaesthetics. The risk of anaesthesia and surgery in sickle-cell anaemia in West Africa is undoubtedly high and reflects the previously noted severity of the disease in Africans as opposed to the milder course seen in Jamaica. In the author's cases careful use of orthodox techniques was followed by two deaths. Use of the measures to be described may lead to better results.

**MANAGEMENT OF ANAESTHESIA IN SICKLING STATES**

**Pre-operative preparation.**

As was stated earlier, the increased rate of destruction of erythrocytes is partly balanced by hyperactive erythropoiesis, and a haemoglobin level of about 8 g/100 ml is usual in sickle-cell anaemia. Iron therapy is not usually effective, as stores are usually adequate. In some cases folic acid may be deficient, and a dose of 5 mg twice daily may be helpful. Blood transfusion is of only temporary benefit, because elevation of the haemoglobin level depresses the activity of the bone marrow. Furthermore, Henderson (1950) reported an increased risk of adverse reaction to transfusion in sickle-cell anaemia. Paterson and Sprague (1959) have also suggested that transfusion is, in general, contraindicated. Clinicians have, therefore, been reluctant to treat the anaemia by transfusion unless it is very severe.

A different approach is suggested by Herbert and Hammond (1963) who utilize the aplastic phase, induced by transfusion, to replace the haemoglobin S. Packed cells are transfused at a rate of 11 mg/kg body weight every 12 hours until the haemoglobin level reaches 14–15 g per cent. This may require 3–4 days. An aplastic bone marrow results, and continued daily transfusion is necessary to maintain the haemoglobin level because the patient's cells are destroyed. After about 10 days a virtual exchange transfusion has been effected and the proportion of haemoglobin S may be reduced to about 10 per cent. At this level the danger of sickling should be very slight. If the urgency of the operation will not permit such a protracted delay a reduction in the haemoglobin S level to 40–50 per cent may be achieved in 4 or 5 days. Even this delay may be unacceptable and, from the reports quoted above, there may be a considerable risk of reaction to the numerous transfusions required. It is not known how many patients have been treated by this method, or with what results.

Brown (1965) has pointed out that the haemoglobin level varies cyclically and recommends that, if the operation is not urgent, it should be undertaken when the haemoglobin level is at a peak, jaundice is absent, and a marked reticulocytosis indicates active erythropoiesis. In severe cases of the disease these favourable conditions may occur infrequently, but his attention to these points may partly explain the encouraging results quoted in Brown's series.

Greenberg and Kass (1958) have shown that alkalosis renders the erythrocytes in sickle-cell
anaemia less sensitive to hypoxia, and Lehmann (1963) has suggested that the maintenance of a metabolic alkalosis may protect these patients from sickling crises. No descriptions of the use of this regime during anaesthesia are available, although it has been used at other times. It is suggested that enough sodium bicarbonate should be administered to maintain the urine sufficiently alkaline to turn litmus paper blue. Such a regime could be easily instituted pre-operatively and maintained during the operation and indefinitely afterwards.

Lewis and Hathorn (1963) have noted that deficiency of the enzyme glucose-6-phosphate dehydrogenase protects against sickling, presumably by delaying oxidative reduction of haemoglobin S. As this enzyme can be suppressed by phenothiazine derivatives, this group of drugs may also be expected to protect against sickling. An in vitro and in vivo study tends to confirm this idea (Lewis, 1964) but further research is necessary before administration of phenothiazine derivatives can be recommended to protect against sickling during anaesthesia.

The association of acute sepsis with sickling crises has often been noted, and infection at any time should be vigorously treated. In appropriate cases, prophylactic antibiotic cover may be indicated during the operative period.

Attention should be paid to the patient's general health, which may be undermined by malaria and malnutrition. The absence of malaria in the West Indies may be a factor in the better prognosis of sickle-cell disease as described in reports from Jamaica.

Recommendations concerning the anaesthetic technique.

The method adopted should avoid: (1) hypoxia; (2) acidosis; (3) stasis; (4) cooling.

The necessity of avoiding hypoxia during and after anaesthesia in both the homozygous and heterozygous states has already been mentioned. The premedication chosen should not cause respiratory depression.

The desirability of avoiding acidosis in the homozygous condition has also been mentioned, and an infusion of sodium bicarbonate continued during anaesthesia may, by maintaining a metabolic alkalosis, help to protect against sickling. Pulmonary hyperventilation would, of course, result in a respiratory alkalosis, presumably with a similar protective effect, but the vasoconstriction which hypocarbia tends to produce in the skin and splanchnic areas might cause local hypoxia and initiate sickling of the erythrocytes. It has also been suggested that the protection described by Greenberg and Kass may have been conferred by the elevation of the plasma bicarbonate level rather than by a change in blood pH, in which case respiratory alkalosis, which is associated with a secondary fall in plasma bicarbonate, may actually increase the sensitivity of haemoglobin S to hypoxia.

Other possible causes of stasis must also be avoided during anaesthesia. Lehmann has pointed out that an erythrocyte circulating through an hypoxic part will normally pass to the lungs and be re-oxygenated in less than the 15 seconds required for sickling to occur. The cell will sickle only if it is trapped by stasis. Stasis may occur during anaesthesia due to bad positioning of the patient on the operating table, or due to hypotension. It may also be induced deliberately by the application of a tourniquet to facilitate orthopaedic operations, which in some cases may be impossible without a bloodless field. If the limb is first carefully exsanguinated with an Esmarch’s bandage the procedure appears to be safe in cases of sickle-cell trait and haemoglobin SC disease. The author anaesthetized twelve such cases without incident, and surgeons who had considerably greater experience of the technique were confident of its safety. Tourniquets were not, however, applied to any patients with sickle-cell anaemia.

Cooling during anaesthesia should be avoided in sickling states. It has been shown that the temperature of the blood in the superficial veins in the leg may be as low as 30°C (Rubenstein and Lack, 1959). There is a considerable increase in the viscosity of both normal and sickling blood when cooled from 37°C to 30°C, so cooling may lead to stasis and sickling of the red cells (Rubenstein, 1961).

No research on the effects of anaesthetic agents on sickling is known, so any technique in which hypoxia, acidosis and stasis are avoided would appear to be applicable in these states. If hyperventilation is used, and it is, of course, preferable to hypoventilation, the addition of a vasodilator, such as halothane, would appear to be indicated. It is of interest that in the patient who died after Caesarean
section (case 1 above) pulmonary hyperventilation had been carried out with nitrous oxide and oxygen. The alka-laemia achieved did not adequately protect her from sickling.

Postoperative care.

Mention has been made of the work of Nunn and Payne (1962). Their findings would indicate that oxygen should be administered continuously for 24 hours postoperatively in sickling patients to combat the expected hypoxia. It has been objected that oxygen administration depresses erythropoiesis (Reinhard et al., 1944) in sickle-cell anaemia but this effect only occurred after 4 or 5 days therapy. Added protection could be effected by the continued administration of sodium bicarbonate parenterally at first and orally later.

However, it has been shown that alka-linization of the blood does not relieve the crisis once it has occurred (Schwartz and McElfresh, 1954). Magnesium sulphate has been suggested as a means of preventing the formation of a permanent thrombus and possibly mobilizing sludged erythrocytes, as it combines a mild vasodilatation with prolongation of the clotting time (Huntsman, Hurn and Lehmann, 1960; Anstall et al., 1959). The dosage schedule recommended by Apthorp and Lehmann (1964) for the treatment of a crisis or to cover surgery is: 2 ml of 50 per cent magnesium sulphate by intravenous injection every 4 hours until pain is relieved, followed by 10 ml of 70 per cent magnesium glutamate orally every 6 hours for 5 days.

The use of low-molecular-weight dextran has seemed to several authors to offer a means of mobilizing sickled cells trapped in areas of sluggish blood flow, but reports of its effectiveness are conflicting. Watson Williams (1963) found it effective in terminating or reducing the pain in three cases, but Reidenberg and Barry (1964) did not observe any improvement in two cases in which they tried the same treatment. The latter authors also describe the development of sensitivity to low-molecular-weight dextran in a patient who received the drug on two occasions.

A hazard in the postpartum period is the occurrence of multiple small pulmonary emboli. In the series of twenty-one obstetrical patients described by Fullerton and Watson Williams (1962) five died from bone marrow and fat emboli within 3 days of delivery. Four patients complained of bone pains shortly before death and the fifth was very heavily sedated and might otherwise have been expected to complain. After all patients who complained of bone pain were heparinized until the end of the fourth day after delivery, there were no more deaths in seventeen patients. It is, therefore, possible that any patient should be heparinized if there is complaint of bone pain after operation.

Anaemia in the postoperative period may require transfusion. Anderson and colleagues (1960), after expressing reluctance to transfuse patients suffering from sickle-cell anaemia, state that transfusion is necessary if the haemoglobin falls below 6 g/100 ml. In view of the rapidity with which anaemia can occur in this disease, close vigilance is necessary.

In contrast to the experience of Brown in Jamaica, it appears that in West Africa sickle-cell anaemia considerably increases the dangers of anaesthesia. In the author's experience two patients out of three died during or after anaesthesia which would have been adequate and safe had the patients not suffered from this disease. The heterozygous sickling haemoglobinopathies are less dangerous, but their pathology should be familiar to anaesthetists if the risks are to be reduced to a minimum.

REFERENCES


