# CHAPTER 7
# HAEMOGLOBINOPATHIES

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## Introduction

Children with haemoglobin disorders are more likely than the general population to need to undergo surgery during their lifetimes to treat the common surgical manifestations of their condition. However, they are also more likely to experience complications as a result of that surgery, with complication rates as high as 32% in patients with sickle haemoglobinopathies. Careful peri- and postoperative management is required to minimise the risk of complications. Furthermore, the prevalence of haemoglobinopathies, with an estimated 269 million carriers worldwide, means that the possibility of an undiagnosed haemoglobin disorder should be considered prior to undertaking a surgical procedure in any child.

## Demographics

The haemoglobinopathies are the most common genetic disorders worldwide. One in 20 people are carriers of a defective haemoglobin gene, and 300,000 babies are born each year with a major haemoglobin disorder. Africa is disproportionately affected, shouldering two-thirds of the disease burden, with sickle cell disease particularly prevalent.

The distribution of sickle cell disease across the continent is influenced by the resistance to severe malaria conferred by carrying a single copy of the sickle cell gene. Even though malaria resistance does not extend to those affected by homozygous sickle cell disease itself, the survival advantage for carriers means that the sickle cell trait is selected for in areas where malaria is endemic. As a result, sickle cell disease is more prevalent in sub-Saharan Africa, particularly those countries bordering the equator. Sickle cell disease is an especially significant problem in Nigeria, where 24% of the population are carriers and the condition affects 2 in every 100 live births. This means that in Nigeria alone, 150,000 children are born with sickle cell anaemia each year.

## Aetiology/Pathophysiology

Haemoglobinopathies are disorders that affect the globin part of the haemoglobin molecule. Genetic defects can lead to either decreased globin *synthesis*, producing the thalassaemia syndromes, or abnormal globin *structure*, resulting in disorders that include sickle cell disease (SCD).

The haemoglobin molecule comprises four globin chains (two alpha and two beta chains), which are genetically coded: different types combine to make different subtypes of haemoglobin. Of note, two distinct globin chains (each with its individual haem molecule) combine to form a haemoglobin.

Sickle cell disease is caused by an abnormal beta chain due to an amino acid substitution, valine for glutamic acid at β6. Other structural qualitative haemoglobinopathies include haemoglobin C (glutamic acid to lysine at β6) and haemoglobin E (lysine for glutamic acid at β 26). Sickle cell disease comprises a group of clinical disorders, which includes homozygous sickle cell anaemia (HbSS), sickle cell haemoglobin C disease (HbSC), sickle cell thalassaemia disease (HbS/β thal) and other compound heterozygous conditions. The carrier state, sickle cell trait HbAS, is not usually associated with increased morbidity or mortality.

As a result of the abnormal globin protein, both the haemoglobin molecules and the erythrocytes that contain them are unstable and can break down under predisposing conditions (hypoxia, acidosis, hypertonicity), releasing free haemoglobin radicals that lead to oxidative stress on the vascular endothelium. This sets up a chronic inflammatory process in the vasculature of patients with SCD, and this is thought to be the starting point for many of the pathological processes observed. The abnormal globin chain also causes the red cells to become less deformable and to stick more readily to the vascular endothelium. The downstream result is vaso-occlusion, leading to pain, ischaemia, and infarction, which can occur anywhere in the body, including the bones, abdominal viscera, and penile vasculature. Accelerated haemoglobin breakdown also leads to chronic haemolysis and a persistent state of anaemia.

Chronic haemolysis is also a central feature of the thalassaemias, and the major clinical manifestations of these conditions relate to variably severe anaemia. Other complications occur due to iron overload with end organ damage due to iron deposition.

The laboratory tests required to make a diagnosis of a haemoglobinopathy are described in Table 7.1. An important part of the diagnostic process is having a high index of suspicion in at-risk populations. The possibility of an undiagnosed haemoglobinopathy should be actively considered in any child who could potentially require surgery.

*Table 7.1: Laboratory Investigations for the haemoglobinopathies.*

| Investigation | Typical finding |
|---|---|
| Full blood count | Normocytic anaemia (SCD)<br>Microcytic anaemia* (thalassemia/HbSC) |
| Blood film | May show sickled erythrocytes, target cells, and nucleated red cells in sickle cell disease. Basophillic stippling is a nonspecific finding in some thalassaemias. |
| Haemoglobin electrophoresis | Demonstrates a single band of HbS in sickle cell anaemia or HbS with another mutant haemoglobin in compound heterozygotes. A raised level of HbA2 is consistent with β-thalassaemia. |
| Red cell staining | Reveals aggregates of β globin protein in α-thalassaemia |
| Sickle solubility and instability tests | A number of rapid screening tests are available for the detection of sickle haemoglobin. Although helpful in some settings, their use is not appropriate for definitive diagnosis because they miss other variants |
| DNA analysis | Often not required, but may be helpful in ascertaining diagnosis of thalassaemias. |

* Iron studies should be sent to exclude iron deficiency.

## Surgical Manifestations of Sickle Cell Disease

### Acute Abdominal Pain

Acute abdominal pain in children with sickle cell disease presents a significant diagnostic challenge. Painful vaso-occlusive crises can mimic surgical pathologies and are difficult to differentiate on clinical

grounds. Diagnosis is further confounded by the range of abdominal disease seen in this population. Important differentials to consider are shown in Table 7.2.

## Acute Splenic Sequestration Crisis

Acute splenic sequestration is a life-threatening complication of sickle cell disease. It mainly occurs in children with homozygous sickle cell disease (HbSS) who have not undergone autosplenectomy and older patients with HbSC disease or HbSβ thalassaemia. It affects between 7% and 30% of children with sickle cell anaemia and is less common in other forms of SCD. It is the second most common cause of death in children with sickle cell anaemia under the age of 10. Acute hepatic sequestration is much rarer, but has also been described in this population (Figure 7.1).

In acute splenic sequestration, splenic outflow obstruction leads to massive sequestration of red cells and platelets in the spleen, often causing a significant decrease in circulating blood volume. Patients present with abdominal pain and distention and signs of haemodynamic compromise. The diagnosis is based on evidence of acute splenic enlargement accompanied by a rapid decrease in the haematocrit, usually to half the patient's "baseline value", as well as brisk reticulocytosis with increased nucleated red cells and moderate to severe thrombocytopaenia.

Acute splenic sequestration is a medical emergency, and treatment in the form of blood transfusion should be instigated rapidly to restore circulating volume and replenish red cell mass. Adequate analgesia is also important.

Patients who recover from a first episode of acute splenic sequestration have a 50% chance of having further episodes. Two possible management strategies can prevent this: children can be enrolled in a transfusion programme or undergo a splenectomy. There is no high-quality evidence to support one of these approaches over the other, and both are associated with potential complications.

The particular concern following total splenectomy is infection, so partial splenectomy has been proposed as an alternative to retain some immune function. A recent case series by Vick et al. showed that sickle cell patients who underwent a partial splenectomy were not subject to increased rates of infection. Nevertheless, a theoretical risk of seques-

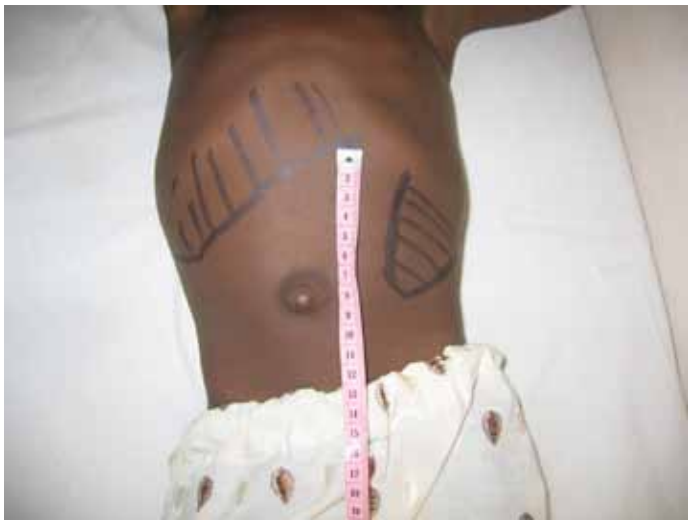

*Figure 7.1: Acute liver enlargement should raise suspicions of a hepatic sequestration crisis.*

*Table 7.2: Differential diagnosis of acute abdominal pain in sickle cell disease.*

| Cause | Frequency | Characteristic features | Investigations |
|---|---|---|---|
| **Vaso-occlusive painful crises** | Very common | May mimic acute surgical disease with guarding and distention; often attributed to micro-infarcts of mesentery and abdominal viscera | A specific cause is rarely identified |
| **Gallstone disease** | | | |
| ***Biliary colic*** | Relatively common | Epigastric pain that comes on gradually over several hours and subsides over a similar period | Pigment stones may be visible on a plain abdominal radiograph |
| ***Acute cholecystitis*** | Relatively common | Persistent right upper quadrant pain with or without guarding; possible fever | Ultrasound shows pericholecystic fluid and thickening of the gallbladder |
| ***Cholangitis*** | Uncommon | Right upper quadrant pain with or without guarding; fever and rigors; jaundice | Ultrasound shows dilatation of the common bile duct |
| **Acute splenic sequestration** | Common, occurring in up to 30% of patients | Left upper quadrant pain; acute splenic enlargement; hypovolaemic shock | Falling haemoglobin, often with a 2 g/dl drop below baseline; thrombocyopaenia; erythrocytosis |
| **Liver Disease** | | | |
| ***Acute sickle hepatic crisis*** | Common, affecting approximately 10% of patients | Right upper quadrant pain; low-grade fever; nausea; increasing jaundice; tender hepatomegaly | Mild to moderate elevation of liver transaminases, bilirubin level generally less than 15 mg/dl (257 µmol/l) |
| ***Hepatic sequestration*** | Uncommon | Right upper quadrant pain, acute liver enlargement, hypovolaemic shock | Falling haemoglobin; thrombocytopaenia; erythrocytosis |
| ***Sickle cell intrahepatic cholestasis*** | Rare | Right upper quadrant or epigastric pain; acute liver enlargement; fever; nausea and vomiting | Significant hyperbilirubinaemia |
| ***Viral hepatitis*** | Increased risk due to multiple transfusions | Malaise; jaundice; low grade fever; tender hepatomegaly | Elevated liver transaminases; positive viral serology |
| **Pancreatitis** | Increased risk due to pigment gallstones | Epigastric pain radiating through to the back; fever; nausea and vomiting | Raised amylase |
| **Appendicitis** | Less than in general population | Right iliac fossa pain with or without guarding; nausea and vomiting; fever | |
| **Ischaemic colitis** | Rare | Sudden onset of abdominal pain and distention; can pass bloody stool | Raised lactate |
| **Urinary tract infection** | Common | Dysuria, frequency, fever | Positive urine dip and culture |

tration in the splenic remnant still exists, so this approach needs further evaluation. In the meantime, splenectomy should generally be reserved for selected patients with recurrent splenic sequestration crises or those who develop red cell alloantibodies following transfusion therapy.

## Gallstone Disease

Pigment gallstones are a frequent complication of sickle cell disease because continuous haemolysis leads to increased bilirubin excretion and subsequent stone formation. Although many children are asymptomatic, they can experience the full range of gallstone disease from biliary colic to cholangitis.

Management of the acute complications of gallstones is the same as in the general population, and elective cholecystectomy is recommended in patients with symptomatic cholelithiasis. The management of asymptomatic gallstones is less clear, but many would advocate cholecystectomy to avoid subsequent difficulty in distinguishing acute cholecystitis from vaso-occlusive painful episodes.

## Orthopaedic Manifestations

Bone-related symptoms are the most common reason for children with sickle cell disease to present to hospital. The osteoarticular manifestations of sickle cell disease can be classified as acute or chronic, as shown in Table 7.3.

*Table 7.3: Osteoarticular manifestations of sickle cell disease.*

| |
|---|
| **Acute** |
| Vaso-occlusive crises (including dactylitis and diaphyseal infarction) |
| Osteomyelitis |
| Septic arthritis |
| Pathological fractures |
| **Chronic** |
| Avascular osteonecrosis |
| Chronic arthritis |
| Osteoporosis |
| Osteomyelitis |

### Acute

In a child presenting with acute bone pain, the most important distinction to make is between bone infarction and bone infection. Although the vaso-occlusive crises that lead to bone infarction are up to 50 times more common than osteomyelitis, there is potential for extensive damage to the bone and surrounding structures as well as overwhelming sepsis if an infection remains untreated.

It is difficult to distinguish between the two conditions on clinical criteria alone because the archetypal features of osteomyelitis—namely, pain, swelling, and fever—are also common in vaso-occlusive crises. A history of a painful episode that has lasted longer than 1 to 2 weeks or pain in a distribution that does not conform to previous painful crises should raise suspicions of an alternative underlying cause. Infection is not the only differential; stress fractures should also be considered.

Both vaso-occlusive crises and osteomyelitis are most common in the long bones of the arms and legs, but can involve any part of the skeleton. Dactylitis, with swelling of the hands or feet, occurs in young children between the ages of 6 months and 4 years, and can be one of the earliest signs of sickle cell disease. Careful examination should be made for evidence of a draining sinus or bony deformity, which would suggest chronic or subacute bone infection. Adjacent joints should be assessed for evidence of an effusion, and the range and ease of movement noted.

Preliminary laboratory investigations are often unhelpful in distinguishing infection from infarction because both conditions can cause a leucocytosis with raised inflammatory markers. Blood cultures taken before the commencement of antibiotics can be invaluable, as can culture of a bone or joint aspirate if there is evidence of fluid accumulation.

Imaging investigations are also confounded by the similarity between the radiographic appearances of bony infarction and infection. Plain radiographs can be normal in the early stages of both conditions, and the periositis and osteopaenia seen in acute osteomyelitis can also occur in vaso-occlusion. The imaging modality of choice for suspected osteomyelitis is magnetic resonance imaging (MRI), where it is available, but even this is not 100% specific for differentiating infection from infarction. Ultrasonography, which is showing promise in the diagnosis of osteomyelitis in children in particular, should be used to guide any aspiration procedures.

The management of vaso-occlusive crises is largely supportive, focusing predominantly on pain management. By contrast, the first line management of osteomyelitis requires urgent parenteral antibiotics, ideally directed at whatever organism has been isolated. When antibiotics are being started empirically, it is important to bear in mind that patients with SCD are more predisposed than the general population to contracting *Salmonella* osteomyelitis. Other organisms that cause bone infection in this population include *Staphylococcus aureus*, *Haemophilus influenzae*, and *Escherichia coli*. Third-generation cephalosporins are often used in this setting, and treatment should continue for at least 6 weeks.

Surgical drainage is generally believed to be required only in those cases of osteomyelitis that are not responding to antibiotics or where there is evidence of abscess formation. However, the exact timing and method of surgical intervention remains controversial.

### Chronic

Avascular osteonecrosis is the most common chronic complication of sickle cell bone disease and is believed to affect up to 41% of these patients. It occurs when repeated bone infarction leads to destruction and breakdown of an area of bone, and it most often occurs at the femoral head. Other areas affected include the head of the humerus, the knee, and the small joints of the hands and feet.

Sufferers describe pain and limited movement at the affected joint; examination may reveal localised tenderness, with restriction of both active and passive joint movements. Initial investigations should include a plain radiograph, which may be diagnostic in more advanced cases, showing flattening or collapse of the articular surfaces and subchondral radiolucency. Less advanced cases may show evidence of sclerosis. MRI is the second-line investigation of choice.

When considering treatments for avascular necrosis in patients with SCD, it is important to note the differences between this population and nonsickle patients with the same condition. Not only is the pathophysiology of osteonecrosis in SCD thought to differ from that of osteonecrosis from other causes, but the quality of the surrounding bone is often much poorer in this group of patients. Combined with their increased anaesthetic risk, this makes SCD patients less attractive surgical candidates.

A lack of quality data currently precludes any definitive recommendations for the surgical management of avascular necrosis in patients with SCD. The available data confirm a high rate of surgical complications and procedure failures. Much interest has been shown in hip core decompression as a measure to prevent progression of early femoral head disease; however, the only randomised controlled trial that has been carried out failed to provide a clear mandate for this procedure. In fact, the only intervention that has been shown to be effective in preventing progression is bed rest. Clearly, a more feasible long-term solution needs to be found.

### Genitourinary Manifestations

The most common genitourinary manifestations of sickle cell disease are haematuria, urinary tract infection, and priapism. The haematuria is often painless and is thought to result from microinfarctions of the renal papillae. Management is predominantly conservative.

Urinary tract infection (UTI) is more common in patients with SCD compared to the general population. The reason for this is remains unclear, but children found to have a UTI should undergo the same careful urological evaluation as nonsickle children.

Priapism is a well-recognised complication of SCD and can be challenging to manage. The condition involves prolonged and painful penile erection, which can lead to irreversible fibrosis and impotence if it persists. About 90% of cases lasting longer than 24 hours have been associated with subsequent erectile dysfunction. Priapism occurs most commonly in children aged 5–13 years (and in adults aged 21–29 years) and affects 28% of the male paediatric sickle population. The majority of children presenting with priapism have sickle cell disease.

The most important history to obtain in a patient presenting with priapism pertains to the duration of the current episode and to previous episodes and their treatment. Alternative causes of priapism, including trauma, drugs, and malignancy, should be excluded.

Examination generally demonstrates rigid corpora cavernosa with a soft glans penis and corpus spongiosum. Involvement of the glans can suggest corporeal infarction.

Investigations should seek to establish or exclude the diagnosis of a haemoglobinopathy in all cases of priapism if this is not already known. Many centres recommend blood gas analysis of blood aspirated from the corpus cavernosum to exclude nonischaemic causes of priapism. Compared to the ischaemic, low-flow priapism most typical in SCD, nonischaemic priapism is a high-flow state with causes that include cavernous artery fistulas. It is normally relatively pain-free and will often resolve without treatment. In ischaemic priapism, aspirated cavernosal blood is expected to appear dark in colour with an oxygen saturation of less than 4 kPa (30 mm Hg) and a pH < 7.25. Where the resources are available, this analysis can be supplemented by colour duplex ultrasonography.

The evidence base for the management of priapism is poor; as a result, considerable variation exists in current management practices. The following discussion is derived largely from the American Urological Association guidelines, which are based on a review of the limited evidence and consensus opinion.

Initial management for all sickle patients presenting with priapism should involve analgesia and hydration. In the past, additional measures, including ice packs, heat packs, and spinal anaesthesia with hypotension, have been advocated, but these measures are now thought to be counterproductive. The role for blood transfusion in this setting, although commonly used, is unproven, and in some cases, transfusion has been associated with serious adverse effects.

Priapism that persists for greater than 4 hours requires urgent focal treatment that should be carried out in conjunction with the systemic treatments described above. The initial intervention can be either a therapeutic aspiration of corporeal blood or an intracavernous injection of a sympathomimetic agent. Both procedures can be carried out under local anaesthetic, following a dorsal nerve block or a penile shaft block.

A therapeutic aspiration is often carried out first, using an 18- or 19-gauge butterfly needle inserted into either corpora cavernosa. Blood can then be aspirated, accompanied by irrigation with saline if so desired. If this procedure fails to achieve detumescence, it should be followed by the intracavernous administration of phenylephrine, an α-1 adrenergic agonist. Depending on the age of the child, a small quantity of the drug diluted in normal saline can be injected with careful monitoring for any side effects including hypertension or arrhythmias. This can be repeated every 3–5 minutes, as required, for approximately 1 hour before an assessment of the treatment's efficacy is made.

Surgery should be considered only if these measures are unsuccessful. The aim of the surgery is to allow the blood from the engorged corpora cavernosa to return to the systemic circulation, most commonly via the corpus spongiosum. A cavernoglanular shunt is the easiest to perform and has the fewest complications. It can be performed with a large biopsy needle (Winter shunt) or a scalpel (Ebbehøj shunt) inserted percutaneously through the glans. It can also be performed by excising a piece of the tunica albuginea at the tip of the corpus cavernosum (Al-Ghorab procedure). If such measures fail to achieve detumescence, a more proximal procedure to create a cavernospongiosal shunt (Quackel's procedure) or to anastomose the saphenous vein to one of the corpora cavernosa (Grayhack procedure) may be warranted.

Recurrent priapism is a common problem, and much effort has been focused on developing a preventive therapy. Gonadotropin-releasing hormone analogues and, more recently, 5α-reductase inhibitors appear to be effective in controlling recurrent priapism, but they have significant side effects and are not currently licensed for use in children. Phosphodiesterase inhibitors are also under evaluation.

### Skin

Leg ulcers are less common in children than in adults and affect approximately 3% of patients between the ages of 10 and 19 years with sickle cell anaemia. The ulcers occur spontaneously or as a result of local trauma with subsequent infection and skin necrosis, but no specific organisms have been incriminated. The majority of ulcers are located on the lower leg (Figure 7.2); they can also involve the dorsum of the foot and, more rarely, the sole. Ulcers typically persist for prolonged periods of time and take up to 16 times longer to heal than venous ulcers.

Surgical intervention can be required to debride infected necrotic ulcers or for skin grafting in intractable cases. Various techniques have been deployed, including myocutaneous flaps and split thickness skin grafts but, as with other surgery in this population, such procedures are plagued by a poor success rate.

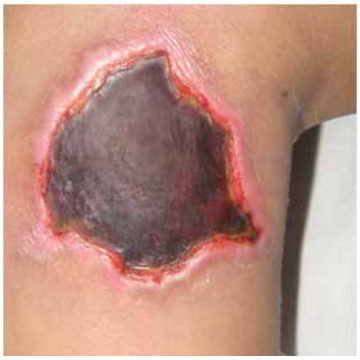

*Figure 7.2: Leg ulcer in a patient with sickle cell disease.*

## Surgical Manifestations of the Thalassaemias

Compared to sickle cell disease, there are relatively few surgical manifestations of the thalassaemias. As in SCD, chronic haemolysis can lead to gallstone formation and symptomatic gallstone disease may require cholecystectomy. Splenectomy is sometimes carried out to treat painful splenomegaly or hypersplenic pancytopaenia; it can also be in used to decrease a patient's transfusion requirement.

## Postoperative Complications

Patients with sickle cell disease clearly experience a higher rate of postoperative complications than the general population. Observed complications include the acute chest syndrome, painful vaso-occlusive crises, neurological events, acute kidney injury, and postoperative infections. The high postoperative complication rate has traditionally been attributed to unfavourable intraoperative conditions precipitating erythrocyte sickling and leading to vascular occlusion and subsequent

end organ damage. Preventive measures have therefore focused on measures designed to prevent sickling.

Newer models of sickle cell disease have suggested, however, that chronic vascular inflammation and endothelial dysfunction may instead underlie many of the pathological processes. The logic behind measures aimed primarily at preventing sickling has been called into question. An example of such a measure is the common practice of exchange transfusion prior to undertaking surgery. The idea is to dilute the sickle haemoglobin with normal red cells, thereby decreasing the risk of intraoperative sickling. Nevertheless, there is no evidence to suggest the superiority of this approach over a simple "top-up" transfusion; indeed, the case for universal preoperative transfusion remains to be definitively proven (see Table 7.4).

It has been suggested that laparoscopic surgery could diminish the risk of sickle-related complications for patients undergoing abdominal surgery, but this has not been demonstrated to date. Patients undergoing laparoscopic surgery have been shown to have shorter hospital stays, however, so, where feasible, a laparoscopic approach should be considered.

Current advice for the perioperative management of children with sickle cell disease is as follows:

- All teams involved in the patient's surgery should be aware of the diagnosis of sickle cell disease and the need for special attention.
- Preoperative assessment should consider the following indicators of increased operative risk in patients with sickle cell disease:
  - frequent recent hospitalisations;
  - sickle cell lung disease;
  - history of early onset dactylitis (a predictor of severe disease);
  - coexisting chest or urinary tract infection; and
  - previous stroke.
- Simple transfusion to achieve a haemoglobin concentration of approximately 10 g/dl should be performed before all but the lowest risk procedures.
- Careful attention should be paid to avoiding hypoxia, although this should not preclude the use of opiate analgesia for pain management or anxiolytic medication, if required.
- Dehydration and hypothermia should be avoided.
- Early mobilisation, effective postoperative pain control, and chest physiotherapy with incentive spirometry may decrease the risk of chest complications.

## Prevention

Many of the conditions discussed in this chapter are unavoidable manifestations of a group of complex multisystem diseases. A number of measures could improve the outcomes for these children, however, including those listed here.

- Early diagnosis of a haemoglobinopathy is essential for appropriate management; the onus lies with the medical team to suspect it in at-risk groups and with certain typical presentations.
- Education of patients and their parents about their condition can help to avoid dangerously late presentations. Parents of infants with sickle cell disease should be taught how to palpate their infants' spleens and when to suspect a splenic crisis; warning signs of other serious complications should also be discussed.
- Penicillin prophylaxis reduces the incidence of infection in children with sickle cell anaemia and heterozygotes with HbS-$\beta^0$ thalassaemia. This preventive treatment should be started between 2 and 4 months of age and continued at least until the age of 5.
- All children with sickle cell disease and splenectomised children with thalassaemia should receive immunisation against pneumococcus, *H. influenzae*, meningococcus, influenza, and *Salmonella typhi* (in endemic areas) as well as routine vaccines. Hepatitis B vaccination should be considered in all children with a haemoglobinopathy.
- Careful foot care and well-fitting shoes can help to prevent the development of leg ulcers.

## Evidence-Based Research

Table 7.4 presents a study comparing preoperative transfusion regimes for patients with SCD.

*Table 7.4. Evidence-based research.*

| | |
|---|---|
| **Title** | Preoperative blood transfusions for sickle cell disease |
| **Authors** | Hirst C, Williamson L |
| **Institution** | AstraZeneca, Alderley Park, UK. |
| **Reference** | *Cochrane Database of Systematic Reviews* 2001, Issue 3. |
| **Problem** | There is a high rate of perioperative complications in patients with sickle cell disease. |
| **Intervention** | Preoperative blood transfusion. |
| **Comparison/ control (quality of evidence)** | This study is a meta-analysis of two randomised controlled trials comparing an aggressive preoperative transfusion regimen, designed to decrease the sickle haemoglobin level to less than 30%; a conservative regime, designed to increase the haemoglobin level to 10 g/dl; and a group receiving no preoperative transfusion. |
| **Outcome/ effect** | The study found that the conservative transfusion regime was as effective as the aggressive regimen in preventing surgical complications, and was associated with fewer transfusion-related adverse events. There was insufficient evidence to demonstrate a clear advantage to preoperative blood transfusion compared with a nontransfused group. |
| **Historical significance/ comments** | The potential risks associated with blood transfusions vary significantly according to the setting. In areas of the world where resources are limited, and clean, infection-free blood products cannot be guaranteed, a risk-benefit analysis is likely to favour less frequent usage of preoperative transfusions. |

## Key Summary Points

1. Haemoglobinopathies (sickle cell disease/thalassaemias) are associated with increased morbidity and mortality.
2. Due to the surgical manifestations of haemoglobinopathies, surgical intervention is a common occurrence and is associated with a higher risk of complications for these patients than for the general population.
3. Basic knowledge of the pathophysiology of sickle cell disease and the principles behind its clinical management is essential for the paediatric surgeon to achieve successful outcomes in sickle cell patients under their care.
4. A multidisciplinary team approach is needed.
5. Careful perioperative management is required to minimise the risk of surgical complications, including the consideration of blood transfusion prior to surgical procedures, paying careful attention to oxygenation and hydration in the intra- and postoperative period, providing adequate pain control, and encouraging early mobilisation.

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