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Sickle cell disease and anaesthesia

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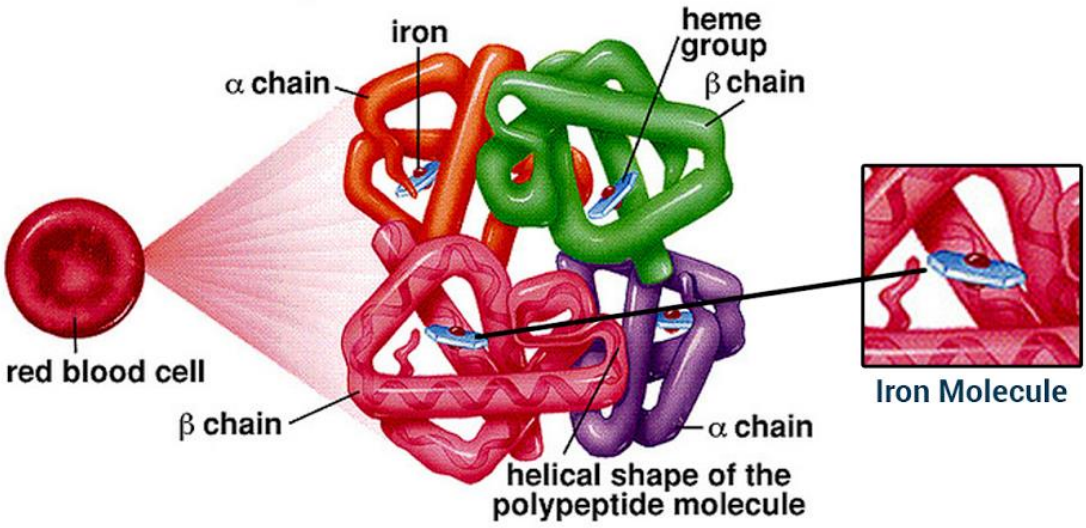
Introduction

Sickle-cell disease (SCD) is a group of blood disorders typically inherited from a person's parents. The most common type is known as sickle-cell anaemia. It results in an abnormality in the oxygen-carrying protein haemoglobin (hemoglobin S) found in red blood cells.

About 80% of sickle-cell disease cases are believed to occur in sub-Saharan Africa. It also occurs relatively frequently in parts of India, the Arabian peninsula, and among people of African origin living in other parts of the world. In the UK it is estimated up to 10% of men of African descent have sickle cell disease.

Haemoglobin (Hb) is contained in red blood cells (270 million in each cell) and is capable of combining with oxygen in the lungs, transporting it to the tissues and releasing it there. Normally it is composed of 4 polypeptide chains combined with 4 haem radicals.

When the haemoglobin is combined with oxygen it is said to be **oxygenated**. When it is not combined with oxygen it is **deoxygenated** (sometimes also called "reduced").



Sickle cell disease is a genetically inherited abnormality of haemoglobin in which valine (an amino acid) replaces glutamine at the sixth position on the beta chains of the haemoglobin molecule. This haemoglobin is termed Haemoglobin S (usually written HbS).

Unfortunately when HbS becomes deoxygenated it comes out of solution forming long crystals called "tactoids" which distort the red cell.

Two types of sickle cell illness are described depending on the genetic make-up.

Sickle cell trait

Everyone has 2 genes responsible for haemoglobin synthesis. When a person has one normal (HbA) gene and one sickle (HbS) gene they make a mixture of HbA and HbS. They are called heterozygous patients (meaning that they have both genes present) and are said to have **Sickle cell trait**.

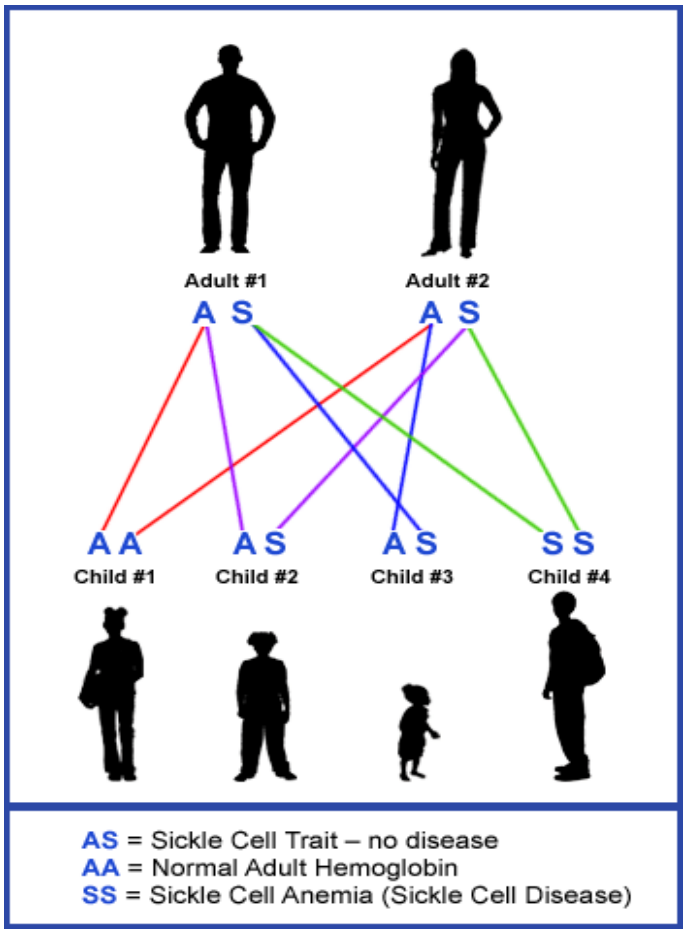
The mixed haemoglobin is described as HbAS; their blood contains around 20-45% HbS, the rest being HbA. Because their HbS is mixed with normal HbA, they are much less susceptible to the problems of sickle cell disorders described below.

Sickle cell disease or Sickle cell anaemia

Patients who have 2 sickle genes can only produce sickle haemoglobin which is called HbSS. They are said to be homozygous, meaning that both of their genes are abnormal.

Their haemoglobin is 85-95% HbS, the remainder being made of HbF, a small amount of which is still produced in these patients. Fetal hemoglobin (HbF) is normally completely replaced by adult hemoglobin by approximately 6 months postnatally.

They are described as suffering from **Sickle cell disease** or **Sickle cell anaemia**.



Pathophysiology

Deoxygenated HbS is 50 times less soluble in blood than deoxygenated HbA.

When HbS becomes deoxygenated it comes out of solution forming long crystals called “tactoids” which distort the red cell and cause it to become crescent shaped.

Initially this is reversible with oxygenation but repeated sickling in the low oxygen tension of the microcirculation causes membrane damage. The cell wall becomes brittle and permanently deformed or “sickled”.

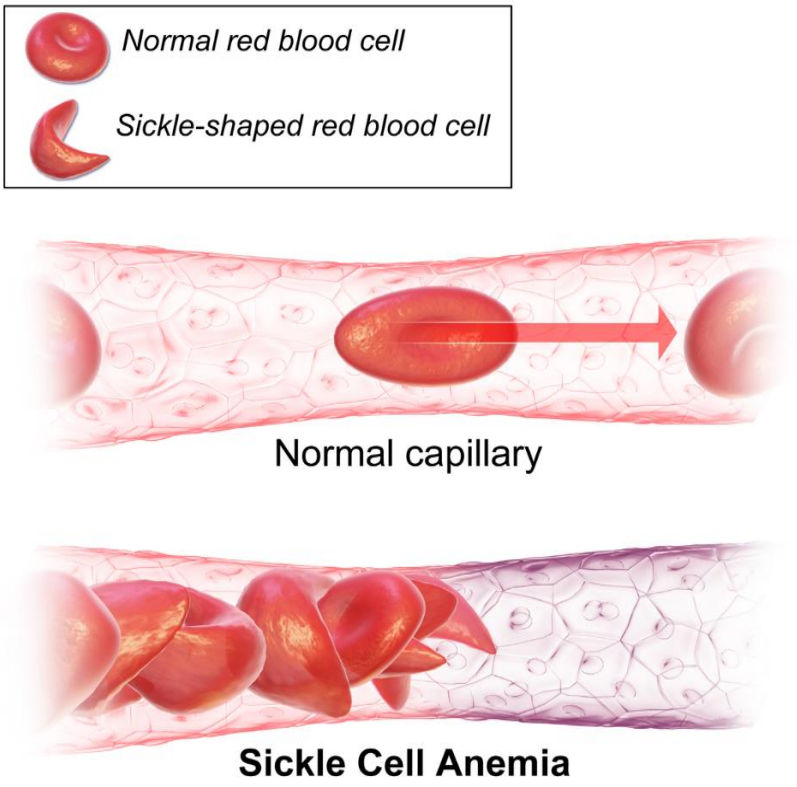
These cells are then susceptible to premature destruction resulting in a lifespan of only 10-20 days as opposed to a normal 120 days. This causes a chronic haemolytic anaemia with a haemoglobin of around 5-8g/dl.

The structural change and associated increase in blood viscosity promotes venous stasis. A vicious cycle is initiated with local blood vessel obstruction leading to tissue hypoxia producing further deoxygenation which promotes further sickling.

This leads to cell death and tissue infarction at the site of obstruction. This is termed **a sickle cell crisis.**

These vaso-occlusive episodes commence from about 6 months of age after the reduction in fetal haemoglobin (HbF) which initially acts as a protective mechanism.

Some sufferers are fortunate to maintain a higher than normal HbF production throughout their lives which improves their condition.



Many episodes of sickling occur spontaneously although certain factors may increase the risk. Apart from hypoxia, acidosis (irrespective of the prevailing oxygen tension) is important and is the principle reason for most sickling occurring in the venous circulation.

Infections (bacterial or viral) are potent inducers. Hypothermia and dehydration are also important causing venous stasis and hypoxia via vasoconstriction.

Clinical Features

Patients with sickle trait are usually fit and healthy. However patients with sickle cell disease will usually demonstrate multiple organ damage through repeated veno-occlusive episodes superimposed on a history of poor development and failure to thrive.

Haematological. An acute fall in Hb is usually secondary to infection induced haemolysis or an acute sequestration syndrome in the spleen (infants and children) or liver (children and adults). Blood transfusion is often essential. Bone marrow failure (aplastic crisis) also occurs with a high mortality. Damage to the spleen with increased susceptibility to infections occurs with age.

Respiratory. Dyspnoea, cough, haemoptysis and pleuritic chest pain are classical features of the "acute chest syndrome". Repeated episodes can lead to compromised lung function, pulmonary hypertension and respiratory failure.

Genitourinary. The relative hypoxia and hyperosmolarity of the renal medulla creates an environment for sickling in the vasa recta. The long Loops of Henle are destroyed causing renal failure as the kidney loses its ability to concentrate urine. Haematuria is also a complicating feature. Priapism (prolonged painful penile erection due to venous occlusion) is common, often requiring surgical decompression.

Liver. Jaundice and gallstone formation are a consequence of chronic haemolysis. Liver failure may supervene as a result of multiple infarcts or haemosiderosis from frequent blood transfusions.

Skeletal. Sickling and microvascular occlusion within bones and epiphyseal plates often leads to shortening of the limbs and gross deformity of joints. Osteomyelitis may occur.

Skin. Leg ulcers following skin infarcts are common and often complicated by trauma and poor hygiene.

Neurological. "Acute brain syndrome" is rare but serious. It is characterised by confusion with variable neurological defects. Whilst most resolve spontaneously permanent damage can occur. There is an increased incidence of subarachnoid haemorrhage, blindness and deafness.

Many patients with sickle cell anaemia have frequent hospital admissions for exacerbations of the disease. This can alter their mental health to an extent that considerable psychological, as well as physical, support is essential to their well-being.

Preoperative assessment

1. A careful medical history and examination should be performed in susceptible patients as not all patients have obvious symptoms or signs of the disease.
2. If improvements can be made to the function of the cardiovascular or respiratory systems then the operation should be deferred if possible until this has been achieved.
3. In patients with haemoglobinopathy the need for an operation should be considered very carefully, as sickle cell crises can mimic acute surgical events eg an acute abdomen.

Investigations

The following tests are useful to complement the history and examination.

1. **Full blood count**. If the haemoglobin level is normal then sickle cell disease can effectively be excluded. The presence of anaemia however does not always imply sickle cell disease. Further investigations should include blood microscopy to check for sickle cells, Howell Jolly bodies and sideroblasts, all features of the disease.
2. **Sickling** ("Sickledex") **test**. Mixing blood with the reducing agent, sodium metabisulphite, will induce sickling in susceptible cells. The test is simple and quick and the results can be viewed under a microscope after 20 minutes. Haemoglobin electrophoresis will differentiate between homozygous and heterozygous conditions. In the absence of electrophoresis, a positive sickling test associated with a normal haemoglobin is likely to indicate a patient with sickle cell trait.
3. **Urea and electrolyte estimations** will help to assess renal function.
4. **Liver function tests**. A raised alkaline phosphatase (Alk Phos) reflects obstructive liver disease and elevated aspartate transferase (AST) indicates intrinsic damage. Unconjugated bilirubin may be raised in the blood as a result of the haemolytic anaemia.
5. **ECG** to look for evidence of cardiac damage.
6. **Chest X-ray** to assess lung fields and cardiac size.

Unfortunately many hospitals do not have access to such investigations and in this situation patients thought to be at risk should be treated as if they were susceptible.

General anaesthesia for elective Surgery

The aim is to prevent a sickle cell crisis whilst providing anaesthesia. Attempts should be made to improve the patient's condition preoperatively and to avoid hypoxia, acidosis, hypotension, dehydration and hypothermia perioperatively.

Anaesthesia Planning

1. Optimise haemoglobin. Blood transfusion should be considered preoperatively with a haemoglobin of less than 7g/dl particularly when major surgery or considerable blood loss is anticipated. Transfuse slowly to avoid an increase in blood viscosity. Aim to achieve HbA levels of more than 70% to limit sickling crises. Exchange transfusions have been used in emergencies but are not often practical. In the long term it is better to limit blood transfusions to avoid the problems of chronic iron deposition and formation of irregular antibodies.
2. Preoperative physiotherapy and breathing exercises decrease the incidence of postoperative atelectasis and lung collapse.
3. Premedication. If premedication is planned anxiolytics are preferable to opiates which may depress the respiration.
4. Avoid dehydration by instituting an intravenous infusion if the patient cannot take adequate fluids orally.
5. Preoxygenate for 2-3 minutes. Hypotension on induction should be avoided by careful titration of induction agents.
6. If there is any doubt about the airway a rapid sequence induction with intubation should be performed. Except for the shortest procedures ventilation should be controlled to ensure oxygenation and normocarbia (normal CO_2 level). A 30-50% inspired oxygen level is advisable.
7. Close monitoring of anaesthesia should prevent hypoxia, cardiovascular depression or acidosis developing. Clinical observation can be usefully supplemented by pulse oximetry, blood pressure measurement, ECG and end tidal CO_2 monitoring when available.
8. Replace fluid loss promptly. A central venous pressure line may help monitor fluid replacement. Monitor urinary output.
9. Temperature loss should be measured and minimised. Creating a warm ambient temperature is important. Cover all exposed parts of the body. Used warmed fluids. Inspired gases can be partly warmed using a condenser humidifier such as a "Humidivent".
10. Venous stasis should be minimised. This may be a particular problem in the prone (face down) position when compression of the inferior vena cava may occur. Pay attention to the placement of supports.
    The use of tourniquets is controversial. Previously contraindicated, an increasing number of reports have shown no evidence of sickling with the use of tourniquets when there is an absolute need for a bloodless field. It is of no importance in sickle cell trait, contrary to popular opinion.

Regional anaesthesia and Sickle cell anaemia

Certain regional techniques may have advantages over general anaesthesia and should be considered whenever possible. Benefits include:

1. Peripheral vasodilation secondary to sympathetic block. This improves blood flow to the extremities thereby limiting the possible devastating consequences of vasoconstriction.
2. Analgesia is improved in the early postoperative phase and may help to prevent the increased oxygen demand imposed by pain and shivering.
3. Skeletal abnormalities arising from the consequences of sickle cell disease may make intubation difficult. This potential problem is avoided with local anaesthesia.

There are disadvantages, however. Regional blocks may cause hypotension and hypoperfusion. Prevent these with adequate fluid loading and a careful technique. Use small doses of vasoconstrictors only if absolutely necessary. Do not mix adrenaline with the local anaesthetic as it may exacerbate a crisis.

Emergency anaesthesia

The same guidelines should be followed as detailed above. Although less time for preoperative assessment will be available, prepare the patient as thoroughly as possible in the time available.

Postoperative Period

The immediate postoperative period is a critical time for patients with sickle cell disease. Hypoventilation resulting from general anaesthesia can easily result in a sickling crisis. The risk can be reduced by:

1. Careful monitoring of vital signs and conscious level. Ensure a clear airway, and where possible, postoperative oxygen therapy.
2. Neuromuscular function must be fully returned to normal before extubation is contemplated. Unless a nerve stimulator is available test this by checking if the patient can perform a sustained head lift (5 seconds) or a strong hand grip on command. Ventilation should be continued until these are apparent.
3. Extubation should be preceded by 2 - 3 minutes of breathing 100% oxygen and supplementary oxygen should be continued postoperatively. This will help to overcome the effects of any residual depressant effects of general anaesthesia, any shunt present in the lungs and will compensate for the increased oxygen demand resulting from pain or shivering.
   Regular chest physiotherapy should be available with the aim of preventing a chest infection.
4. Adequate analgesia is essential but must be balanced against the problems of hypoventilation with the use of opiates. Titrate the dose carefully. Regional and local blocks are useful. Non-steroidal anti-inflammatory drugs can be used unless renal function is impaired.
5. Maintenance of intravenous fluids is essential until the patient is able to eat and drink.

Summary

Sickle cell disease is an important cause of morbidity and mortality worldwide. When a patient presents for surgery an understanding of the implications of the illness will, when combined with careful preoperative preparation and anaesthesia lead to a successful outcome in most circumstances.

Note

Over the years there have been various treatments attempted in the management of Sickle cell disease. These have all failed to make an impact. Some are listed below.

1. Alkalisation using magnesium glutamate or sodium bicarbonate in an attempt to increase oxygen affinity to haemoglobin in the red blood cell.
2. Antiplatelet and anticoagulants to reduce infarction.
3. Hyperbaric oxygen, high concentration oxygen therapy.

Original article from http://www.wfsahq.org