<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP’s role</td>
<td>3</td>
</tr>
<tr>
<td>Prevalence of haemoglobinopathies</td>
<td>4</td>
</tr>
<tr>
<td>Investigations</td>
<td>4</td>
</tr>
<tr>
<td>Investigations of carriers for haemoglobinopathies in general</td>
<td>4</td>
</tr>
<tr>
<td>FBE and ferritin</td>
<td>5</td>
</tr>
<tr>
<td>Haemoglobinopathy testing</td>
<td>5</td>
</tr>
<tr>
<td>Interpretation of results</td>
<td>6</td>
</tr>
<tr>
<td>DNA testing</td>
<td>7</td>
</tr>
<tr>
<td>Prenatal diagnosis</td>
<td>8</td>
</tr>
<tr>
<td>Referral</td>
<td>8</td>
</tr>
<tr>
<td>β-Thalassaemia</td>
<td>8</td>
</tr>
<tr>
<td>Clinical features</td>
<td>8</td>
</tr>
<tr>
<td>Genetics</td>
<td>9</td>
</tr>
<tr>
<td>Prevalence</td>
<td>9</td>
</tr>
<tr>
<td>Investigations</td>
<td>9</td>
</tr>
<tr>
<td>For affected individuals</td>
<td>9</td>
</tr>
<tr>
<td>For potential or identified carriers</td>
<td>10</td>
</tr>
<tr>
<td>Management</td>
<td>10</td>
</tr>
<tr>
<td>α-Thalassaemia</td>
<td>10</td>
</tr>
<tr>
<td>Clinical features</td>
<td>10</td>
</tr>
<tr>
<td>Genetics</td>
<td>11</td>
</tr>
<tr>
<td>Prevalence</td>
<td>11</td>
</tr>
<tr>
<td>Investigations</td>
<td>11</td>
</tr>
<tr>
<td>For affected individuals</td>
<td>11</td>
</tr>
<tr>
<td>For potential or identified carriers</td>
<td>12</td>
</tr>
<tr>
<td>Management</td>
<td>12</td>
</tr>
<tr>
<td>Sickle cell disease (HbS disease)</td>
<td>12</td>
</tr>
<tr>
<td>Clinical features</td>
<td>12</td>
</tr>
<tr>
<td>Genetics</td>
<td>12</td>
</tr>
<tr>
<td>Prevalence</td>
<td>13</td>
</tr>
<tr>
<td>Investigations</td>
<td>13</td>
</tr>
<tr>
<td>Management</td>
<td>13</td>
</tr>
<tr>
<td>Other haemoglobinopathies caused by structural change</td>
<td>14</td>
</tr>
<tr>
<td>Further information</td>
<td>15</td>
</tr>
<tr>
<td>Bibliography</td>
<td>15</td>
</tr>
<tr>
<td>Patient and family fact sheet:</td>
<td></td>
</tr>
<tr>
<td>Haemoglobinopathies (including thalassaemias)</td>
<td></td>
</tr>
</tbody>
</table>
GP’s role

- Haemoglobinopathy carrier testing is recommended and should be discussed as part of pre-conceptional/antenatal care in the following individuals:
  > With a family history of anaemia/thalassaemia/abnormal haemoglobin variant
  > With any of the following ethnic backgrounds: Southern European, Middle Eastern, African, Chinese, South East Asian, Indian subcontinent, Pacific Islander, New Zealand Maori, South American and some northern Western Australian and Northern Territory Australian Indigenous communities
  > Partners of known or identified haemoglobinopathy carriers
  > When MCV <80fL or MCH <27pg

- Test partners of pregnant at-risk women at the same time as the pregnant woman where possible.

- Investigate with the following:
  > FBE
  > Iron studies (ferritin)
  > Haemoglobin electrophoresis

- Indications for DNA testing:
  > Possible carrier for α-thalassaemia (low-borderline MCV or MCH, normal ferritin and normal haemoglobin electrophoresis).
  > Proven carrier for β-thalassaemia and partner is also a carrier for thalassaemia or other haemoglobinopathy.
  > Confirmation of carrier status for a haemoglobin variant.

- Where a DNA test is positive, refer to specialist service (haematology clinic, Genetics Services, thalassaemia clinic).

- If both partners of a couple are carriers, refer to Genetics Services and/or haematology clinic for genetic counselling and testing. **This is particularly urgent for pregnant couples** (see Contacts, support and testing).

- Cascade genetic testing is recommended and should be discussed (see Contacts, support and testing).

- Refer the family to a relevant support group (see Contacts, support and testing).
Haemoglobinopathies

Prevalence of haemoglobinopathies

- Figure 1 illustrates the global distribution of haemoglobin conditions in terms of number of affected infants per 1,000 births.
- The World Health Organization (WHO) estimates that globally at least 5% of adults are carriers for a haemoglobin condition: approximately 2.9% for thalassaemia and 2.3% for sickle cell disease.
- Most countries have an uneven distribution of carriers because their populations include different ethnic groups (with different carrier rates, types of haemoglobinopathy and mutations) that have become co-located as a result of migration.

Investigations

Investigations of carriers for haemoglobinopathies in general

- Genetics Services and haematologists can provide advice regarding appropriate testing.
- It is considered good practice to investigate all women of childbearing age with FBE and ferritin, and Hb electrophoresis for women from an at-risk group (see Figure 2).
- Investigation for haemoglobinopathy carrier state is usually a multi-step process, with results of FBE, ferritin studies and clinical picture influencing decisions regarding haemoglobinopathy testing and DNA analysis.
- All indications for investigation should be given, including pregnancy, gestation, ethnicity and family history, to assist the laboratory in interpreting test results.

It is not always possible to assume ethnicity from country of birth or surname. More information can be obtained by asking patients where their parents, grandparents or great-grandparents were born.

Figure 1. Global distribution of haemoglobin disorders, in terms of births of affected infants per 1000 births (WHO)
**FBE and ferritin**

- FBE and ferritin identify individuals who require further investigation; however, not all carriers for a haemoglobinopathy will be identified. For example, carriers for α-thalassaemia with a one-gene deletion will usually have **borderline to normal** red cell indices, while carriers for sickle cell disease will usually have normal red cell indices.
- Ferritin is ordered to identify iron deficiency. Iron deficiency may mask thalassaemia carrier status. If the woman is not pregnant, FBE should be repeated when iron stores are replete. If the woman is pregnant, her partner should be investigated before iron stores are corrected. If the partner is shown to be a carrier for a haemoglobinopathy, DNA studies on both partners may be appropriate.

**Possible results**

- The majority of carriers for α-thalassaemia and individuals with two or three copies of the α-globin gene deleted will have:
  - MCV <80fL
  - MCH <27pg
  - Slightly low or normal Hb
- The majority of carriers for sickle cell disease will have normal MCV and MCH, but these could be reduced in the presence of another underlying haemoglobinopathy (eg β-thalassaemia carrier status) and/or iron deficiency.

**Haemoglobinopathy testing**

- Haemoglobinopathy testing determines the types, quantity and proportions of haemoglobin in the blood (see ‘Genetics’ below). Techniques for this may include haemoglobin electrophoresis and High Pressure Liquid Chromatography (HPLC) analysis. Blood films and HbH (see ‘Genetics’, under ‘α-thalassaemia’) preparations identify HbH inclusions found in HbH disease and in carriers for two-gene deletion α-thalassaemia (−/−α α or −α/−α).
- Ideally, haemoglobinopathy testing should be performed six months after iron replacement and when iron stores are replete. However, testing should not be delayed if the woman is pregnant. If the woman is pregnant and has low red cell indices, her partner should be investigated.
- Consult a haematologist or thalassaemia service for advice.
- In general, haemoglobinopathy testing should be performed after FBE and ferritin investigations.

<table>
<thead>
<tr>
<th>Haemoglobinopathy testing should be performed concurrently with FBE/ferritin for:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Pregnant woman with low red cell indices</td>
</tr>
<tr>
<td>- Pregnant woman from a high-risk ethnic background</td>
</tr>
<tr>
<td>&gt; Partners of the pregnant woman should be tested at the same time as the pregnant woman</td>
</tr>
<tr>
<td>- Partners of individuals who are carriers for thalassaemia or a haemoglobin variant</td>
</tr>
<tr>
<td>- A family history of haemoglobinopathy or haemoglobinopathy carrier state</td>
</tr>
<tr>
<td>- Individuals from ethnic groups with a high prevalence of haemoglobinopathy</td>
</tr>
<tr>
<td>- Consanguinity</td>
</tr>
</tbody>
</table>
Interpretation of results

- A haematologist or thalassaemia service should be consulted for assistance in interpreting haemoglobinopathy testing results, as interpretation is influenced by the clinical picture.
- β-thalassaemia carrier state is characterised by the presence of increased HbA₂ (see ‘Genetics’), but this can be masked in some circumstances, such as low iron stores.
- α-thalassaemia carrier states are characterised by low red cell indices, with normal HbA₂ and/or haemoglobin electrophoresis results. Individuals with a three-gene deletion and two-gene deletions may be identified by presence of HbH bodies on HbH preparation; however, a normal HbH preparation does not exclude α-thalassaemia carrier state, especially one-gene deletion forms where the MCV & MCH are also usually in the normal range.
- Definitive identification of α-thalassaemia with one- and two-gene deletions requires DNA testing.

Figure 2. Suggested protocol for targeted carrier testing of high risk populations for patients in ANY ONE of the categories below:

- **Family history**
  - Family history of anaemia, thalassaemia or other abnormal haemoglobin variant
- **Ethnic origin**
  - Southern Europe, Middle East, Africa, China, South East Asia, the Indian subcontinent, Pacific Islands, New Zealand (Maori), South America and some northern Western Australian and Northern Territory Indigenous communities
- **Abnormal FBE**
  - MCV < or = 80fL and/or MCH < or = 27pg

**Order the following:**
- FBE
- Haemoglobin electrophoresis
- Iron studies (if indicated)
- Blood for DNA studies

**Any abnormality or diagnosis or suggestion of carrier state in couple**

- **Potential risk for couple:**
  - Both carriers, or status unclear
  - Referral for counselling and risk assessment
  - Urgent if woman is pregnant
  - Couple counselling:
    - Both partners are carriers: discussion about risk to pregnancy from haemoglobinopathy and available options

- **No risk for couple:**
  - One partner is a carrier and the other has been tested and is not a carrier
  - One partner only is a carrier
    - Health professional, eg GP, midwife to disclose carrier status
    - Consider referring to genetic counselling service to discuss issues raised with carrier status

---

1 Petrou V, Bowden D, 2005. Suggested protocol for targeted testing of high risk populations, Medical Therapy Unit, Monash Medical Centre, Victoria, Australia (adapted).
Table 1. Interpretation of haemoglobinopathy carrier testing results

<table>
<thead>
<tr>
<th>MCH (pg)</th>
<th>Ferritin</th>
<th>Haemoglobin electrophoresis</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; or = 27</td>
<td>Normal</td>
<td>Normal</td>
<td>Thalassaemia unlikely but one-gene deletion α-thalassaemia not excluded</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Hbs present</td>
<td>Carrier for sickle cell disease</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Normal</td>
<td>Reduced iron stores or iron deficiency, thalassaemia unlikely but one-gene deletion α-thalassaemia not excluded</td>
</tr>
<tr>
<td>&lt;27</td>
<td>Normal</td>
<td>HbA\textsubscript{2} increased HbH present</td>
<td>Carrier for β-thalassaemia</td>
</tr>
<tr>
<td></td>
<td>HbA\textsubscript{2} normal HbH present</td>
<td>Carrier for α-thalassaemia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HbS present</td>
<td></td>
<td>Carrier for sickle cell disease Possible co-existent thalassaemia carrier state</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Possible carrier for α-thalassaemia DNA testing indicated</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>Normal</td>
<td>Iron deficiency Thalassaemia may coexist If woman is pregnant, seek advice about DNA testing; test partner for full haemoglobinopathy screen</td>
</tr>
</tbody>
</table>

**DNA testing**

*Indications for DNA testing*

- Possible carrier for α-thalassaemia (low-borderline MCV or MCH, normal ferritin and normal haemoglobin electrophoresis).
- Proven carrier for β-thalassaemia and partner is also a carrier for thalassaemia or other haemoglobinopathy.
- Confirmation of carrier status for a haemoglobin variant.
- Patients requiring DNA testing should be referred to specialist services.

DNA testing of couples who are both carriers is necessary for prenatal diagnosis to be available. Testing can be time-consuming and, if possible, couples should be tested and referred prior to pregnancy.
Prenatal diagnosis

- Prenatal diagnosis is available to couples where:
  - There is a risk of having a child affected by a haemoglobinopathy
    and
  - The causative globin mutations carried by the parents are known
- Due to the time-consuming nature of DNA testing to identify causative gene mutations, it is important that, wherever possible, DNA studies are carried out pre-pregnancy.
- Prenatal diagnosis is performed on a sample collected by chorionic villus sampling (see Testing and pregnancy). This is usually performed in the first trimester but, under certain circumstances, may be performed in the second trimester.

Referral

- If both members of a couple are found to be carriers for a haemoglobinopathy, they should be immediately referred to specialist services for information regarding their risk of having a child with a severe form of thalassaemia, and to discuss the need for DNA studies. Some combinations of thalassaemia and haemoglobin variants can result in a clinically affected child.
- Pregnant couples at risk of having a child with a major thalassaemia syndrome or sickle cell disease should be urgently referred to a specialist service for counselling and possible prenatal diagnosis.

Condition-specific information

β-Thalassaemia

Clinical features

- The common clinical features of β-thalassaemia major manifest after birth, usually within six to 12 months and include:
  - Pallor
  - Lethargy
  - Poor appetite
  - Developmental delay
  - Failure to thrive
  - Irritability, difficulty settling
  - Splenomegaly, growth failure with bone changes, fractures and leg ulcers also develop during childhood
  - Haemolytic anaemia
- Carriers for β-thalassaemia are usually asymptomatic but may have mild hypochromic anaemia.
Genetics

- Haemoglobin A (HbA) contains two α-globin chains and two β-globin chains (α₂β₂).
- HbA₂ is a normal variant of haemoglobin and is composed of two α-globin and two δ-globin chains (α₂δ₂). It usually represents 2 to 3.5% of normal total adult haemoglobin.
- HbF refers to fetal haemoglobin, a normal variant in fetal development that persists in small amounts postnatally. It is composed of two α-globin and two γ-globin chains (α₂γ₂) and usually represents less than 1% of normal total adult haemoglobin.
- β-thalassaemia is caused by reduced or absent production of the β-globin chain of the haemoglobin molecule.
- The β-globin gene (HBB) encodes the β-globin chain. Each individual has two copies of this gene, one from each parent.
- β-thalassaemia major is caused by mutations in both copies of the β-globin gene, resulting in virtually no functional β-globin chains being produced. This is a severe medical condition requiring frequent blood transfusions and iron chelation therapy.
- β-thalassaemia minor (also called β-thalassaemia trait) is the carrier state and is caused by a mutation in one copy of the β-globin gene. While this is not a serious medical condition, it manifests as reduced red cell indices and elevated concentrations of HbA₂, and can be mistaken for iron deficiency.
- β-thalassaemia major follows a pattern of autosomal recessive inheritance. Carriers have a 50% chance of passing the mutated β-globin gene to their children. Couples who are both carriers have a 25% chance of having an affected child. This risk applies for every pregnancy of that partnership.
- Co-inheritance of β-thalassaemia minor and a haemoglobin variant (for example, Hb Lepore, HbC or HbE) may result in a form of β-thalassaemia major (see 'Other haemoglobinopathies caused by structural change'). This is known as compound heterozygosity, as the two types of gene mutations are different.
- Couples where one partner is a carrier for β-thalassaemia and the other is a carrier for α-thalassaemia are not at risk of having children with thalassaemia major.

Prevalence

- There are particular sub-groups of the population who are at increased risk of being a carrier for α-thalassaemia:
  > 1 in 5 people of high-risk ethnic background (from the Middle East, Southern Europe, Indian subcontinent, Central and South East Asia and Africa) may carry a β-thalassaemia mutation
  > An individual with an MCH <27pg and/or MCV <80fL is at increased risk of having a thalassaemia minor carrier state. Some labs consider MCH ≤ 27pg and MCV ≤ 81fL
  > Individuals with a family history of β-thalassaemia major and/or β-thalassaemia minor
- Also see 'Prevalence of haemoglobinopathies' above.

Investigations

- See 'Investigations of carriers for haemoglobinopathies in general' above.
- Genetics Services or haematologists can provide advice regarding appropriate testing.

For affected individuals

- FBE usually shows significant anaemia, microcytosis, hypochromia and abnormal red cell morphology, including target cells. Nucleated red blood cells are usually present.
- Haemoglobin electrophoresis testing to determine HbF and HbA₂ levels is usually diagnostic of β-thalassaemia. Affected children over the age of six months usually have markedly elevated levels of HbF and elevated HbA₂.
- Compound heterozygous states result in a variety of abnormal results on haemoglobinopathy testing. Contact a haematologist for advice.
For potential or identified carriers

- It is considered good practice to **investigate all women of childbearing age** with FBE and ferritin, and **Hb electrophoresis for women from an at-risk group** (see Figure 2).
- Investigation for β-thalassaemia carrier state is usually a multi-step process, with results of FBE, ferritin studies and clinical picture influencing decisions regarding haemoglobinopathy testing and DNA analysis.
- All indications for investigation should be given, including pregnancy, gestation, ethnicity and family history, to assist the laboratory in interpreting test results.

**Management**

- Treatment and management is performed by specialist services.
- Patients with β-thalassaemia major require regular blood transfusions every three to four weeks for their whole life.
- Excess iron is eliminated from the body by iron-chelating agents (eg desferrioxamine, administered by subcutaneous infusion pump), with oral chelating agents now available to supplement or replace desferrioxamine.
- A ‘no added iron’ diet is recommended.
- The majority of complications associated with β-thalassaemia major are due to iron build-up, despite chelation therapy, or marrow expansion.
- Splenectomy may be performed because of enlargement. These patients require the same immunisation as other children and prompt treatment of infections.
- Bone marrow transplantation may cure β-thalassaemia major but has a significant risk of complications and mortality.
- The life expectancy of well-treated, compliant patients is not known but is likely to be normal or near normal.
- Carriers for β-thalassaemia should have folic acid (5 mg) daily throughout all pregnancies.
- Carriers for β-thalassaemia must not have long-term iron treatment to attempt to cure microcytosis, unless they are also iron deficient.

**α-Thalassaemia**

**Clinical features**

- Clinical features of α-thalassaemia can manifest in pregnancy or after birth and include:
  - Hydrops fetalis, resulting from deletions of all four α-globin genes, is fatal in the fetus or neonate.
  - Haemoglobin H (HbH) disease is an intermediate form of α-thalassaemia caused either by deletions or other mutations of three copies of the α-globin genes. It causes life-long anaemia of mild to moderate degree.
  - Carriers for α-thalassaemia are usually asymptomatic but may have a mild hypochromic microcytic anaemia.
Genetics

• α-thalassaemia is caused by decreased or absent production of the α-globin chains.
• Two identical α-globin genes encode the α-globin chains.
• Each individual therefore has four α-globin gene copies: two gene copies inherited from each parent.
• Hydrops fetalis is caused by deletion of all four copies and results in early fetal or neonatal death. In addition, the mother of an affected fetus is at risk of severe early pre-eclampsia, ante-partum or post-partum haemorrhage, and pre-term delivery.
• Haemoglobin H disease (HbH disease) is caused by deletion of three copies of the α-globin genes, which results in the presence of HbH (β₄), an abnormal form of haemoglobin caused by excessive β-globin chains. HbH disease is an intermediate form of α-thalassaemia, which varies in severity. HbH disease can cause life-long anaemia of mild to moderate degree and sometimes requires transfusion support. Medical management is advised.
• Individuals with α-thalassaemia minor have one or two copies of the α-globin genes deleted. This is not clinically significant; however, haemoglobin is often in the low end of the normal range and MCV and MCH may be reduced.
• In general, α-thalassaemia major follows an autosomal recessive pattern of inheritance, but the genetics is complex.

Prevalence

• The carrier state is common in certain ethnic groups. Those who are at increased risk for having α-thalassaemia carrier state (α-thalassaemia minor or trait) include individuals:
  > With an MCH <27pg and/or MCV <80fl.
  > Who are most commonly of Chinese and South East Asian origin but the disorder occurs in many other ethnic groups, including those from Southern European countries, the Middle East, the Indian subcontinent, Pakistan, Africa, the Pacific Islands and New Zealand (Maori), and some Indigenous Australian communities in the Northern Territory and northern Western Australia.
  > With a family history of α-thalassaemia major and/or α-thalassaemia minor.
  > Have a history of severe pre-eclampsia in association with early fetal death.
• Also see ‘Prevalence of haemoglobinopathies in general’ above.

Investigations

• See ‘Investigations of carriers for haemoglobinopathies in general’ above.
• Genetic Services or haematologists can provide advice regarding appropriate testing.

For affected individuals

• FBE usually shows significant anaemia, microcytosis, hypochromia and abnormal red cell morphology, including target cells and fragmented cells.
• Haemoglobinopathy testing demonstrates normal HbA₂ and abnormal haemoglobin electrophoresis. In younger individuals HbH preparation demonstrates presence of varying amounts of HbH.
For potential or identified carriers

- It is considered good practice to investigate all women of childbearing age with FBE, ferritin and Hb electrophoresis for women from an at-risk group (see Figure 2).
- Investigation for α-thalassaemia carrier state is usually a multi-step process, with results of FBE, ferritin studies and Hb electrophoresis and clinical picture influencing decisions regarding further haemoglobinopathy testing and DNA analysis.
- All indications for investigation should be given, including pregnancy, gestation, ethnicity and family history, to assist the laboratory in interpreting test results.
- In couples where both people are carriers for α-thalassaemia or another haemoglobinopathy, referral to a specialist service for information about their risk of having an affected pregnancy should be arranged.

Where an α-thalassaemia carrier state is identified it is essential that the partner be investigated. Testing the partner is an urgent priority if the woman is already pregnant.

Management

- Some individuals with HbH diseases require regular blood transfusion and folic acid.
- Patients should receive regular medical care from their GP.

Sickle cell disease (also known as HbS disease)

Clinical features

The common features include:

- Anaemia
- Failure to thrive
- Repeated infections
- Painful swelling of the hands or feet
- Infarction
- Asplenia
- Abdominal pain
- Chest pain

Genetics

- Haemoglobin contains two α-globin chains and two β-globin chains. Each individual has two copies of the β-globin gene, one from each parent.
- Sickle cell disease is caused by a mutation in both copies of the β-globin genes resulting in changes to the structure of the β-globin chain of haemoglobin, ie haemoglobin variant. This results in red blood cells that form an irreversible sickle shape after repeated cycles of deoxygenation.
- Individuals with sickle cell disease usually have chronic anaemia due to increased destruction of red blood cells.
- They may also experience sickle cell crises due to blockage of blood vessels by these cells, causing bone and chest pain and damage to other organs.
- They usually autosplenectomise within the first ten years of life.
- Individuals with sickle cell disease who have crises require medical management, which may include regular blood transfusions.
- Sickle cell trait (term to describe the carrier state) is caused by a mutation in one copy of the β-globin gene. Carriers are usually healthy. In some very rare instances (eg anaesthesia or long distance air travel), the red blood cells of a carrier can undergo partial sickling.
• Sickle cell disease is an autosomal recessive condition. Carriers have a 50% chance of passing the mutated gene to their children. Couples who are both carriers have a 25% chance of having an affected child. This risk applies for every pregnancy of that partnership.

• Co-inheritance of sickle cell trait (or other haemoglobin variant) and β-thalassaemia minor may result in a form of sickle cell disease. This is known as compound heterozygosity, as the two types of gene mutations are different.

**Prevalence**

• Sickle cell disease is one of the most common inherited conditions of haemoglobin worldwide and is seen in many populations including people from Africa, the Middle East, Southern Europe, India, Pakistan, South America and the Caribbean.

• The WHO estimates that 1 in 500 African-American births and 1 in every 1,000 to 1,400 Hispanic-American births are affected by sickle cell disease, and that 1 in 12 African-American people carry the mutated sickle cell allele.

• In Australia, sickle cell disease has been most commonly seen in individuals of Southern European and Middle Eastern origin (especially Lebanese and Turkish). However, with increasing immigration from sub Saharan Africa and the Indian subcontinent, HbS is becoming more prevalent.

• Individuals who are carriers for sickle cell disease may be clinically and haematologically silent, with normal red cell indices.

• Individuals at increased risk of being a carrier for sickle cell also include those with a family history of sickle cell disease and/or sickle cell carrier state.

• Also see ‘Prevalence of haemoglobinopathies in general’ above.

**Investigations**

• See ‘Investigations of carriers for haemoglobinopathies in general’ above

• FBE and ferritin tests generally do not show abnormalities.

• Haemoglobinopathy testing results are abnormal and indicate sickle cell disease (homozygosity) or sickle cell trait (heterozygosity – sickle cell disease carrier state)

• It is important to identify couples who are both carriers for sickle cell disease or other haemoglobin variants and/or thalassaemia in order to offer information about their risk of having a severely affected child and, where possible, prenatal diagnosis.

• The best time to identify carriers is prior to pregnancy.

Where the sickle cell carrier state is identified it is essential that the partner be investigated. Testing the partner is an urgent priority if the woman is already pregnant.

**Management**

• Sickling of red blood cells can occur in any organ and affect its function.

• Individuals with symptoms of sickle cell crisis should be sent immediately to the emergency department of a hospital for administration of:
  > IV fluids
  > Pain relief
  > Other treatment if indicated

• Patients should receive regular medical care from their GP.

• Women with sickle cell disease who are pregnant should be referred to a specialist centre for management.

• Carriers for sickle cell disease are healthy and are not affected by anaemia. In some very rare instances, (eg anaesthesia), the red blood cells of a carrier can undergo sickling. Anaesthetists should be informed when a patient is a carrier for sickle cell disease.
Other haemoglobinopathies caused by structural change

- Individuals from certain ethnic backgrounds have an increased risk of carrying a globin chain gene mutation causing a structural variant.
- Only a small number of variants capable of causing a severe condition in the homozygote or in compound heterozygotes are encountered in Australia. These include HbS (sickle cell disease), HbC, HbD, HbE, HbO and Hb Lepore.
- Testing for haemoglobin variants requires haemoglobin electrophoresis as it is common for no other haematological abnormality to be present.
- Partners should have FBE and haemoglobinopathy testing to investigate carrier status for β-thalassaemia and/or haemoglobin variants.

Table 2. Examples of states causing clinically significant haemoglobinopathies

<table>
<thead>
<tr>
<th>Haemoglobin types</th>
<th>Disease status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homozygous HbS</td>
<td>Sickle cell disease</td>
</tr>
<tr>
<td>HbS/β-thalassaemia</td>
<td>Sickle cell disease</td>
</tr>
<tr>
<td>HbS/HbC disease</td>
<td>Sickle cell disease</td>
</tr>
<tr>
<td>HbS/HbD</td>
<td>Sickle cell disease of variable severity</td>
</tr>
<tr>
<td>Homozygous HbE</td>
<td>Behaves as a mild β-thalassaemia mutation</td>
</tr>
<tr>
<td>HbE/β-thalassaemia</td>
<td>Mild to severe condition equivalent to β-thalassaemia major</td>
</tr>
<tr>
<td>HbC/β-thalassaemia</td>
<td>Sickle cell disease (mild to severe, depending on causative mutations)</td>
</tr>
<tr>
<td>Homozygous Hb Lepore</td>
<td>β-thalassaemia intermedia (moderate to severe β-thalassaemia)</td>
</tr>
<tr>
<td>Hb Lepore/β-thalassaemia</td>
<td>β-thalassaemia major</td>
</tr>
<tr>
<td>Hb Lepore/HbS</td>
<td>Sickle cell disease of variable severity</td>
</tr>
</tbody>
</table>
Further information


Bibliography


http://www.genetics.com.au


Petrou V, Bowden D, 2005. Suggested protocol for targeted testing of high risk populations. Medical Therapy Unit, Monash Medical Centre, Victoria, Australia (adapted).


http://www.who.int/genomics/public/Maphaemoglobin.pdf


Haemoglobin is an important protein in the blood. Haemoglobin is found in red blood cells and carries oxygen from the lungs to all the tissues.

Various genetic conditions affect haemoglobin, making it less able to carry oxygen, or causing damage to the red blood cell it is in.

The most common problems are thalassaemia (a genetic disorder inherited from both parents resulting in a reduction in the amount of haemoglobin produced by the body) and sickle cell anaemia (a genetic disease in which red blood cells may change shape under certain circumstances; this causes problems when the cells become stuck in blood vessels that carry oxygen and nutrients to individual cells). About 5 in every 100 people throughout the world are carriers for one of these conditions. Haemoglobinopathies are more common in some parts of the world than in others, particularly where malaria is common.

Haemoglobinopathies may be mild or they may be severe. They can cause range of illnesses from slight tiredness, to severe anaemia (not enough red blood cells) needing regular blood transfusions, to episodes of severe pain.

You should consider having a blood test to see if you are a carrier for one of these conditions and possibly see a genetic counsellor if you:

• Have a relative with one of these conditions, or have a relative who is a carrier for one of these conditions
• Have unexplained anaemia or have people in the family with unexplained anaemia
• Have ancestry from where these conditions are common – southern Europe, the Middle East, South-East Asia, Africa, the Indian subcontinent, South America, the Caribbean and the Pacific Islands.

This is particularly important if you are pregnant or could become pregnant.
Contacts and further information

- Your local genetic service, which you can contact through your nearest community health centre, public hospital or health department.
- Thalassaemia Society of Victoria at http://www.tsv.org.au
- National Organization for Rare Disorders at http://www.rarediseases.org
- Australasian Genetic Alliance at http://www.australasiangeneticalliance.org.au
- MyDr at http://www.mydr.com.au
- The Centre for Genetics Education at http://www.genetics.edu.au
- HealthInsite at http://www.healthinsite.com
- MedicineNet at http://www.medicinenet.com
- For other related fact sheets, you can contact the Gene Technology Information Service on free call Australia-wide 1800 631 276 or email gtis-australia@unimelb.edu.au or visit Biotechnology Australia’s website at http://www.biotechnology.gov.au