Fact sheet **44**

SICKLE CELL DISEASE

This fact sheet talks about sickle cell disease and includes details of the symptoms, causes and any treatments or testing available.

IN SUMMARY

- Sickle cell disease is a group of common inherited conditions where the red blood cells form a sickle, or crescent shape
- It is caused by specific changes in the beta globin gene (*HBB*) known as Haemoglobin S. This gene codes for a protein called beta globin, which makes up part of the haemoglobin in our red blood cells, responsible for carrying oxygen to the organs of the body
- Sickle cell disease is inherited in an autosomal recessive pattern and genetic carriers for sickle cell disease usually do not have any symptoms.

WHAT IS SICKLE CELL DISEASE?

Sickle cell disease is a group of common inherited red blood cell conditions where the red blood cells form a sickle or crescent shape. The sickling of red blood cells causes the cells to break down prematurely, reducing the number of red blood cells in the body. This leads to chronic anaemia sometimes referred to as **sickle cell anaemia** and may cause tiredness, pale skin (pallor) and delayed growth and development in children. The sickled red blood cells can also cause episodes of pain in the extremities of the body such as hands and feet as the inflexible shaped cells get caught in the small blood vessels. These painful episodes may result in bone and chest pain, repeated bacterial infections and can lead to organ damage. People with sickle cell disease are more likely to get pulmonary hypertension (high blood pressure in the arteries to the lungs), which may lead to heart failure.

Sickle cell disease is more common in people whose ancestry is from Africa, and is also seen in people from the Middle East, Mediterranean, Central Asia and Southern America.

WHAT CAUSES SICKLE CELL DISEASE?

Inside our red blood cells there are proteins called haemoglobin, whose job is to transport oxygen from the lungs to all parts of the body. Haemoglobin is what gives our red blood cells their red colour and is made up of four chains, two alpha globin chains and two beta globin chains. A specific variation in the beta globin gene that codes for the beta globin chain causes the characteristic sickle shape seen in sickle cell disease. This variation is called **Haemoglobin S**.

HOW IS SICKLE CELL DISEASE INHERITED?

Sickle cell disease follows a pattern of autosomal recessive inheritance. Autosomal refers to the fact that the beta globin gene is located on the numbered chromosome 11, and therefore affects males and females equally. Recessive means that, in order to develop signs and symptoms of the condition, both copies of the beta globin gene are not working.

People who have one copy of Haemoglobin S and one working copy of the beta globin gene are known as **genetic carriers** for sickle cell disease (or Haemoglobin S), and are sometimes referred to as having **sickle cell trait**. Genetic carriers for sickle cell disease are generally healthy, although they may show signs of mild anaemia.

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If a couple are both genetic carriers for sickle cell disease (*Figure 44.1*), in every pregnancy there is:

- 1 in 4 (25%) chance that they will have a child who inherits both copies of the recessive gene variant from their parents. In this case, no working gene product will be made and their child will have sickle cell disease
- 1 in 4 (25%) chance that their child will inherit both copies of the working gene and will not have sickle cell disease and not be a genetic carrier
- 1 in 2 (50%) chance that their child will inherit the recessive gene variant and the working copy of the gene from the parents and they will be an unaffected genetic carrier for sickle cell disease, just like the parents.

If only one parent is found to be a genetic carrier for sickle cell disease (*Figure 44.2*) in every pregnancy there is no chance that the couple will have a baby affected with sickle cell disease:

- 1 in 2 (50%) chance that they will have a child who inherits both copies of the working gene from the parents. In this case, the child will not have sickle cell disease
- 1 in 2 (50%) chance that their child will inherit the recessive gene variant and the working copy of the gene from the parents and they will be an unaffected genetic carrier for sickle cell disease.

SICKLE CELL DISEASE AND OTHER RED BLOOD CELL CONDITIONS

Sickle cell disease is part of a group of red blood cell conditions known as haemoglobinopathies, where the haemoglobin inside the red blood cell is put together differently. Another common red blood cell condition is thalassaemia, where the amount of haemoglobin made is reduced. This causes red blood cells to be smaller and paler than usual. There are two main types of thalassaemia, alpha thalassaemia caused by variations in the alpha globin genes, and beta thalassaemia caused by variations in the beta globin gene. The Haemoglobin S variation that causes sickle cell disease is found in the same beta globin gene that can cause beta thalassaemia.

Our body is made up of billions of cells, and in each cell there are instructions, called genes, that make all the necessary structural components and chemicals for the body to work properly. These genes are packaged onto long strands known as chromosomes.

We all have 46 chromosomes arranged into 23 pairs. One copy of each pair is inherited from our mother and the other from our father. The first 22 chromosome pairs are numbered and are known as autosomal chromosomes. The 23rd pair is made up of the sex chromosomes called X and Y. Males have an X and a Y chromosome and females have two copies of the X chromosome.

Since all our chromosomes come in pairs, all our genes also come in pairs. The genes provide the instructions for proteins, which are the building blocks of the cells that make up our body. Although we all have variation in our genes, sometimes this can affect how our bodies grow and develop. Generally, gene variations that have no impact on our health are called benign variants or polymorphisms. These variants tend to be more common in people. Less commonly, variations can change the gene so that it sends a different message. These changes may mean that the gene does not work properly or works in a different way that is harmful. A variation in a gene that causes a health or developmental condition is called a pathogenic variant or mutation.

Gene variants may be inherited from a parent, or happen for the first time in a person. Once you have a gene variant, however, it may be passed on to future generations. This is referred to as genetic inheritance.

Figure 44.1:
Autosomal recessive inheritance where both parents are carriers of Haemoglobin S in the beta globin gene on chromosome 11. There is one chance in four of having a child with sickle cell disease. The non-working Haemoglobin S is represented by 'r'; the working copy by 'R'.

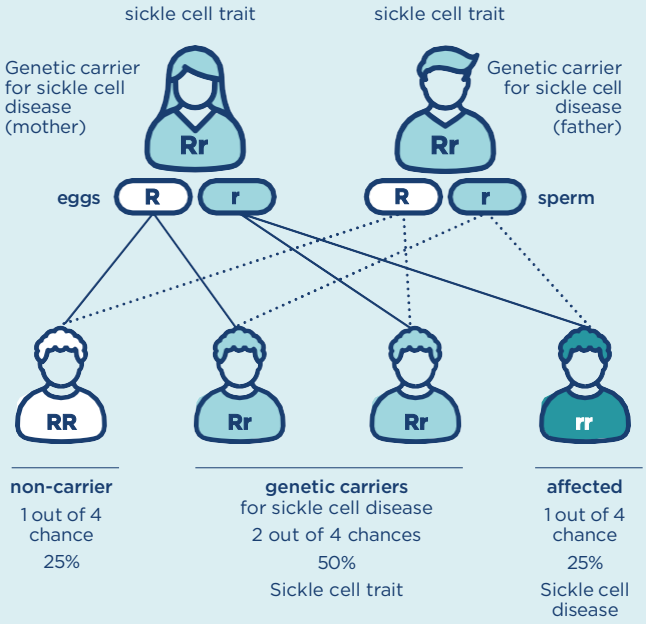
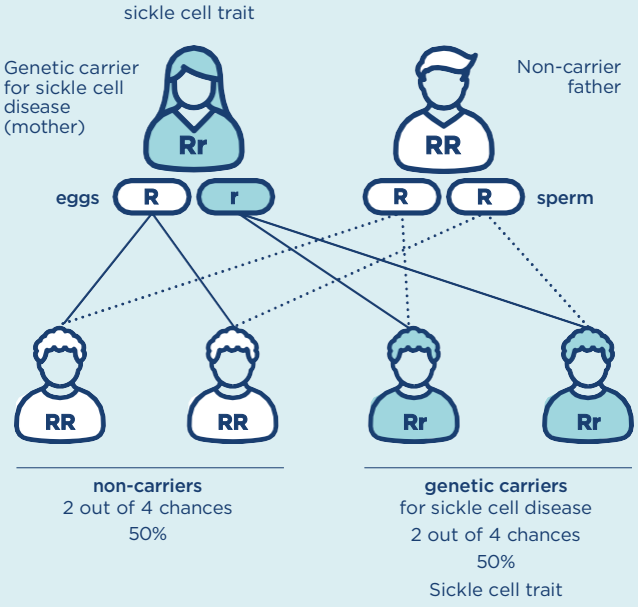


Figure 44.2:
Where only one parent is a carrier of Haemoglobin S in the beta globin gene on chromosome 11, there is no chance of having a child with sickle cell disease. The non-working Haemoglobin S is represented by 'r'; the correct copy by R.



What happens if a sickle cell disease carrier and a beta thalassaemia carrier have a family?

It is possible that one parent may be a genetic carrier for sickle cell disease and the other parent is a genetic carrier for beta thalassaemia.

There is a 1 in 4 (25%) chance that the baby will inherit both genetic variants. As both sickle cell disease and beta thalassaemia involve variations in the same beta globin gene, the baby will have two non-working copies of this gene and not make the protein properly. They will develop signs and symptoms of a condition sometimes called **Sickle-Beta Thalassaemia**. Sickle-beta thalassaemia follows a pattern of autosomal recessive inheritance where both parents must be either a genetic carrier for Haemoglobin S or another beta globin gene variation for there to be a chance of having a child with Sickle-Beta thalassaemia.

IS THERE ANY TESTING AVAILABLE FOR SICKLE CELL DISEASE?

People who have sickle cell disease have chronic anaemia. This may be found out through specialised blood tests through your family doctor. These blood tests may also identify genetic carriers for sickle cell disease, although an ordinary full blood count alone cannot rule out genetic carrier status. Genetic testing of the beta globin gene to look for Haemoglobin S may confirm a diagnosis of sickle cell disease, or to confirm the genetic carrier status of a person.

Testing for carrier status

When a person is identified as a genetic carrier for sickle cell disease, their first degree relatives (parents, children, brothers and sisters) all have a 1 chance in 2 (50%) of also being a genetic carrier. Screening by specialised blood tests or genetic testing may be offered by your health professional.

Planning a pregnancy

For couples who are both known genetic carriers for sickle cell disease and/or beta thalassaemia, testing may be available during a pregnancy. This will work out whether the baby will be unaffected, affected or a genetic carrier for sickle cell disease or beta thalassaemia.

Genetic testing in a pregnancy for a haemaglobinopathy is optional and should be talked about in full with your doctor, midwife or genetic counsellor. It may also be possible to have pre-implantation genetic diagnosis (PGD) to look for a haemoglobinopathy in an embryo made using in vitro fertilisation (IVF).

Reproductive genetic carrier screening is also available for couples who are planning pregnancy, or are in early pregnancy. This may include genetic screening for haemoglobinopathies, amongst other recessive genetic conditions.

More support and information is available for individuals and families through support organisations including Genetic Alliance Australia.