

This fact sheet describes sickle cell disease and includes the symptoms, cause and any treatment or testing which is available.

In summary

- Sickle cell disease is a group of common inherited red blood cell conditions where the red blood cells form a sickle, or crescent shape
- It is caused by a specific change in the beta globin gene known as Haemoglobin S that codes for the oxygen carrying protein haemoglobin in our red blood cells
- 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, lethargy, pale skin (pallor) and delayed growth and development in children. The sickled red blood cells can also cause periodic episodes of pain in the extremities of the body 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 susceptible to 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 must be faulty.

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.

What does it mean to be a genetic carrier?

Being a genetic carrier for sickle cell disease is quite common in different ethnicities, and may be as high as 1 in 12 in certain populations.

- Being a genetic carrier for sickle cell disease is not like being a carrier of an infectious virus such as hepatitis where the hepatitis virus is carried in the body
- Genetic carriers for sickle cell disease do not carry sickle cell disease in their bodies and cannot pass it on to others like a virus. They can however, pass the faulty gene on to their children as described above.

There is a high proportion of sickle cell genetic carriers found in countries where the mosquito-borne disease malaria is more common. Being a genetic carrier for sickle cell disease is believed to provide some natural protection against severe forms of malaria.

Many children used to die from malaria, and it was noted that children who were sickle cell genetic carriers were more likely to survive the disease and, in turn, pass on their genetic carrier status to their children. Hence, there are now many genetic carriers for sickle cell disease in areas where malaria is (or was) more common.

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

- 1 chance in 4 (25% chance) that they will have a child who inherits both copies of the recessive gene mutation from his/her parents. In this case, no working gene product will be produced and their child will be affected by sickle cell disease
- 1 chance in 4 (25% chance) that their child will inherit both copies of the working gene and will be unaffected by sickle cell disease and not a genetic carrier

1 chance in 2 (2 chances in 4 or 50% chance) that their child will inherit the recessive gene mutation and the working copy of the gene from the parents and he/she 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 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 chance in 2 (2 chances in 4 or 50% chance) that they will have a child who inherits both copies of the working gene from his/her parents. In this case, the child will be unaffected by sickle cell disease
- 1 chance in 2 (2 chances in 4 or 50% chance) that their child will inherit the recessive gene mutation and the working copy of the gene from the parents and he/she will be an unaffected genetic carrier for sickle cell disease.

Our body is made up of millions of cells, and in each cell there are instructions, called genes, that make all the necessary structural components and chemicals for the body to function. These genes are packaged onto little 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. Sometimes, a gene may have a variation in the instruction that causes the gene to no longer function properly. This variation is called a **mutation** or **pathogenic variant**, and means that the product produced by the gene, called a protein, is impaired or even absent.

Gene mutations may be inherited from a parent, or occur for the first time in an individual. Once you have a gene mutation however, it may be passed on to future generations. This is referred to as genetic inheritance.

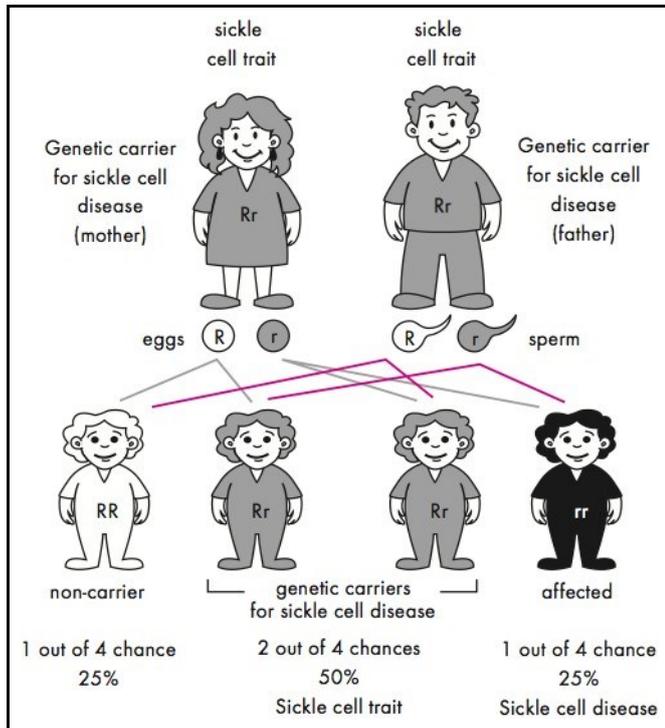


Figure 44.1: Autosomal recessive inheritance where both parents are carriers of Haemoglobin S in the beta globin gene on chromosome 11. There is one chance in four of having a child with sickle cell disease. The faulty Haemoglobin S is represented by 'r'; the working copy by 'R'.

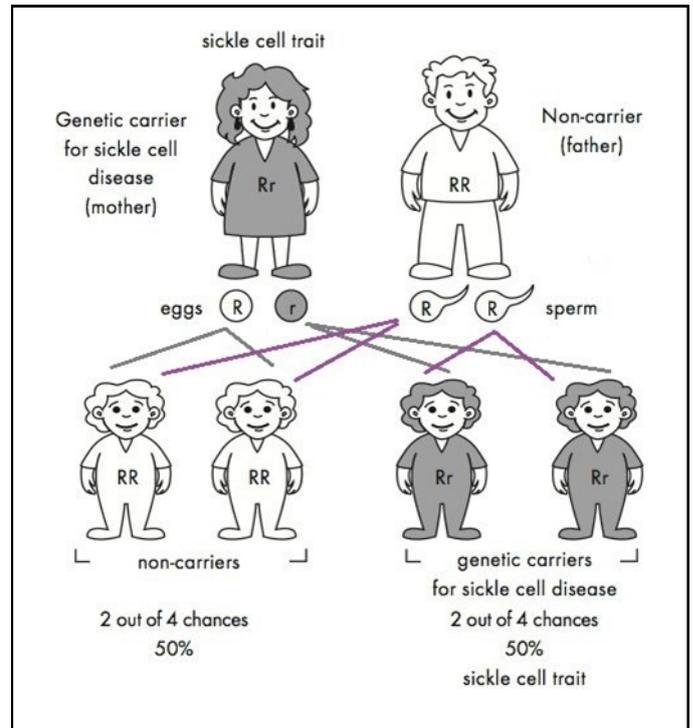


Figure 44.2: Where only one parent is a carrier of Haemoglobin S in the beta globin gene on chromosome 11, there is no chance of having a child with sickle cell disease. The faulty Haemoglobin S is represented by 'r'; the correct copy by R.

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 produced inside the red blood cell is structurally different. Another common red blood cell condition is **thalassaemia**, where the amount of haemoglobin produced is reduced, leading to red blood cells that are 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.

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 chance in 4 (25%) that the baby will inherit both genetic mutations and be a carrier for sickle cell disease and beta thalassaemia. As both sickle cell disease and beta thalassaemia involve variations in the same beta globin gene, the baby will not have any normal production of the beta globin gene and will develop sign and symptoms of both beta thalassaemia and sickle cell disease. This is sometimes known as **Sickle-Beta Thalassaemia**. Like sickle cell disease, 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 in order to have an affected child.

IS THERE ANY TESTING AVAILABLE FOR SICKLE CELL DISEASE?

People who are affected with sickle cell disease have chronic anaemia and this may be detected 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 exclude genetic carrier status. Genetic testing of the beta globin gene to look for Haemoglobin S may be performed to 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 may be performed through specialised blood tests through your family doctor, or genetic testing may be offered.

Prenatal testing and PGD

For couples who are both known genetic carriers for sickle cell disease, testing may be available during a pregnancy to determine whether the baby will be unaffected, affected or a genetic carrier for sickle cell disease. It may also be possible to undergo **pre-implantation genetic diagnosis** (PGD) screening for sickle cell disease on an embryo created using in vitro fertilisation (IVF). These options are best discussed and considered before pregnancy, when possible, in order to ensure all possible risks, benefits and outcomes to be explored.