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# Hemoglobinopathies: Sickle Cell Disease (HbSS, HbSC or HbS/ $\beta$ -Thalassemia)

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## What is Sickle Cell Disease?

Sickle cell disease is an inherited form of anemia. Under certain conditions, the red blood cells acquire a crescent, or 'sickle' shape and break down (hemolyse) more quickly than usual. This sickling occurs because the hemoglobin within the red blood cells is defective (denoted HbS for hemoglobin "sickle").

## What causes the disease?

Hemoglobin, the substance that carries the oxygen in the blood, is made up of building blocks called  $\beta$ -globin chains and  $\alpha$ -globin chains. A specific defect in the  $\beta$ -globin component causes the physical structure of hemoglobin associated with HbS. Another specific defect in  $\beta$ -globin causes another structural variant, hemoglobin C (HbC). Other mutations in the  $\beta$ -globin gene can cause other structural variations of hemoglobin or can cause a deficiency in the amount of  $\beta$ -globin being produced. These types of mutations are referred to as  $\beta$ -thalassemia mutations.

Individuals can also have the combination of HbS and another  $\beta$ -globin variant - HbSC or HbS/ $\beta$ -thalassemia, for example. These individuals have a sickling disorder, as described below, but tend to have slightly milder features than in HbSS.

## What is its incidence?

Although sickle cell disease and thalassemia occurs in all ethnic groups, it is more common in certain populations, such as the African, Mediterranean, Middle Eastern, and Asian communities – in parts of the world in which malaria is endemic. Carriers for sickle cell disease and thalassemia are less susceptible to malarial infection, which explains their prevalence in these parts of the world. The incidence of sickle cell disease has been reported as high as 1 in 400 in individuals from the Caribbeans and parts of Africa.

## What are the clinical features of the disease?

Sickling of the red blood cells means that they can block blood vessels, causing painful crises. Tissue ischemia and, subsequently, organ dysfunction can also occur. Splenic sequestration and acute chest crises can be life threatening. There is also an increased risk for stroke if blood vessels in the brain become blocked. Increased hemolysis results in anemia and jaundice. Children with sickle cell disease are more susceptible to infection and sepsis, and may have some growth delays. There is a wide range of variation in the severity of symptoms in sickle cell disease.

## How is the diagnosis confirmed?

The diagnosis of sickle cell disease and sickle cell variants can be confirmed by testing a blood sample using a variety of methods, including high-performance liquid chromatography (HPLC), isoelectric focusing (IEF) and hemoglobin electrophoresis. Genetic testing to look for mutations in the  $\beta$ -globin gene can also assist in confirming the diagnosis. Diagnostic testing is arranged by specialists at your regional treatment centre.

## What is the treatment of the disease?

Prophylactic antibiotic and immunizations are used, and certain vitamins and medications such as folic acid and hydroxyurea may be considered. In some situations, blood transfusions may be suggested. Pain management is an important feature of treatment for sickle cell disease. Children who experience several episodes of splenic sequestration may require splenectomy. Bone marrow transplantation is the only curative form of treatment.

## What is the outcome of treatment?

Early treatment to prevent the complications of SCD improves prognosis and affected children are likely to be indistinguishable from other children the same age.

## Can a family have more than one child with SCD?

Sickle cell disease is inherited as an autosomal recessive disease. Mutations in the gene for  $\beta$ -globin produce the defective hemoglobin S. A child with 'classic' sickle cell disease has HbSS – one HbS from each parent. A child with HbSC has HbS from one parent and HbC from the other. Similarly, a child with HbS/ $\beta$ -thalassemia has inherited HbS from one parent and  $\beta$ -thalassemia trait from the other parent.

The parents of a child who has one of these sickling disorders are assumed to be carriers of  $\beta$ -globin variants and have a 1 in 4 chance, in each pregnancy, of having another child with the same condition. Prenatal testing for SCD and  $\beta$ -globin variants can be done as early as 10-12 weeks of pregnancy. Genetic counselling to discuss the benefits of prenatal testing options in more detail is recommended.

Carriers are those who receive a sickle gene from one parent and a normal gene from the other- a condition called sickle cell trait. People with sickle cell trait are healthy and, except under very unusual conditions, do not have symptoms of a sickling disorder.

## Resources

<http://www.sicklecellontario.com/>

[http://www.sicklecelldisease.org/about\\_scd/index.phtml](http://www.sicklecelldisease.org/about_scd/index.phtml)

[http://www.marchofdimes.com/professionals/14332\\_1221.asp](http://www.marchofdimes.com/professionals/14332_1221.asp)