Sickle Cell Disease (SCD)

A common hereditary blood disorder that leads to serious complications in many patients, including chronic iron overload in patients receiving blood transfusions

What is SCD?	Sickle cell disease (SCD) is a hereditary blood disorder characterized by sickle-shaped red blood cells. SCD occurs when a person carries at least one sickle cell gene from one parent.[1] There are many forms of SCD, which range in clinical severity from asymptomatic to life threatening.[1,2] Sickle cell anemia, the severe form of the disease, occurs when individuals carry two copies of the sickle cell gene, one from each parent.[2] Stroke is one of the most devastating effects of SCD and is responsible for many deaths, especially in children.[3,4] Many children affected by SCD born in developing countries die undiagnosed because they have little or no access to medical treatment.[5] Many others affected by SCD die later from the complications of the disease and from consequences of chronic iron overload due to blood transfusions.[3] With proper treatment, the life expectancy of patients with SCD significantly increases to an average of 48 years.[6]
Prevalence and cause of SCD	The World Health Organization estimates that about 275,000 babies are born annually with SCD.[5] Although SCD occurs predominantly in individuals of African descent, sickle cell disorders are also prevalent throughout the Mediterranean, Middle East and parts of India, the Caribbean, and South and Central America. In parts of Africa and India, the prevalence of the sickle cell trait is as high as 30 percent.[7] In SCD, red blood cells contain an abnormal form of hemoglobin, the oxygen-binding part of the red blood cells that stores most of the body's iron.[8] Due to this abnormality, red blood cells do not receive enough oxygen and adopt a sickle shape. This structural variation leads to the obstruction of blood vessels, reduced blood flow to vital organs and a weakened immune system.[8]
Symptoms and clinical complications of SCD	Symptoms of SCD, include:[9] • Fatigue • Shortness of breath • Headache and dizziness • Cold feet and hands • Pale skin and jaundice (yellowing of the skin or eyes) • "Sickle cell crisis," an acute pain resulting from blocked blood vessels Complications of SCD include:[9] • Stroke (sickle cell anemia patients have a 50 percent risk of experiencing a stroke or blood vessel disorder by age 14)[10] • Swelling of the hands and feet, especially in small children • Spleen damage and increased risk of infections • Pulmonary complications • Eye problems, including blindness • Acute chest syndrome

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Diagnosis of SCD	In the past, SCD was diagnosed in young children who developed painful swelling of the feet and hands, a consequence of blood vessel blockage.[8] In the developed world, the disease is now commonly detected during routine newborn genetic screening.[6] Patient quality of life and life expectancy can be greatly improved by simple medical care, such as early diagnosis, patient education, access to antimalarials/antibiotics and access to hospital treatment.[5] However, in many regions of the world, these measures are not available, and treatment and pain management remain inadequate.[5,11]
Treatment of SCD	SCD cannot be cured. By early childhood, patients with SCD often suffer from persistent infections, pain, stroke and other severe complications. In their teens, patients' chronic anemia usually worsens and organ damage can occur.[12] Current treatments only manage disease complications and include: o **Blood transfusion therapy**, which increases the amount of normal-shaped cells, helping restore normal blood flow and reduce serious complications such as stroke.[6] o **Hydroxyurea drug administration**, which increases the amount of fetal hemoglobin and reduces the sickling of the red blood cell.[13] Hydroxyurea is used to reduce pain, episodes of acute chest syndrome, and the need for hospitalization and transfusions,[13] although it has not been proven to prevent the incidence of stroke.[14] o **Bone marrow transplantation,** which replaces malformed bone marrow cells with healthy donor cells, allowing the body to produce healthy bone marrow following transplantation in some cases.[6] This is an effective treatment for SCD, although access to donors is limited and the disease recurs in 10 percent of patients.[6]
Iron overload due to blood transfusions in SCD	Undergoing regular blood transfusions can lead to iron accumulation because the body has no mechanism to remove the excess iron.[15] Chronic iron overload occurs when the body's limited iron storage capacities are exceeded, and can be seen after only 10 to 20 transfusions.[16] Excess iron is deposited into organs, increasing the risk of liver, cardiac and other complications, and reducing patient survival rates.[3] Accurate assessment of iron in the body is essential for managing SCD and administering treatment. Iron levels in the body can be measured using two methods:[17,18] • **Serum ferritin (SF)**: A noninvasive and inexpensive blood test that allows for frequent monitoring. SF tests are an indirect measurement of iron burden and can require several tests or combinations with other indicators of iron overload to increase accuracy. • **Liver iron concentration (LIC):** A more accurate measurement of iron levels that assesses tissues in the liver, the main site of body iron storage. Testing can be done via biopsy, magnetic resonance imaging (MRI), or a superconducting quantum interference device (SQUID).

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