Sickle cell disease

Sickle cell disease is a group of disorders that affects hemoglobin, the molecule in red blood cells that delivers oxygen to cells throughout the body. People with this disorder have atypical hemoglobin molecules called hemoglobin S, which can distort red blood cells into a sickle, or crescent, shape.

Signs and symptoms of sickle cell disease usually begin in early childhood. Characteristic features of this disorder include a low number of red blood cells (anemia), repeated infections, and periodic episodes of pain. The severity of symptoms varies from person to person. Some people have mild symptoms, while others are frequently hospitalized for more serious complications.

The signs and symptoms of sickle cell disease are caused by the sickling of red blood cells. When red blood cells sickle, they break down prematurely, which can lead to anemia. Anemia can cause shortness of breath, fatigue, and delayed growth and development in children. The rapid breakdown of red blood cells may also cause yellowing of the eyes and skin, which are signs of jaundice. Painful episodes can occur when sickled red blood cells, which are stiff and inflexible, get stuck in small blood vessels. These episodes deprive tissues and organs of oxygen-rich blood and can lead to organ damage, especially in the lungs, kidneys, spleen, and brain. A particularly serious complication of sickle cell disease is high blood pressure in the blood vessels that supply the lungs (pulmonary hypertension). Pulmonary hypertension occurs in about one-third of adults with sickle cell disease and can lead to heart failure.

Frequency

Sickle cell disease affects millions of people worldwide. It is most common among people whose ancestors come from Africa; Mediterranean countries such as Greece, Turkey, and Italy; the Arabian Peninsula; India; and Spanish-speaking regions in South America, Central America, and parts of the Caribbean.

Sickle cell disease is the most common inherited blood disorder in the United States, affecting 70,000 to 80,000 Americans. The disease is estimated to occur in 1 in 500 African Americans and 1 in 1,000 to 1,400 Hispanic Americans.

Genetic Changes

Mutations in the *HBB* gene cause sickle cell disease.

Hemoglobin consists of four protein subunits, typically, two subunits called alpha-globin and two subunits called beta-globin. The *HBB* gene provides instructions for making beta-globin. Various versions of beta-globin result from different mutations in the *HBB* gene. One particular *HBB* gene mutation produces an abnormal version of beta-globin

known as hemoglobin S (HbS). Other mutations in the *HBB* gene lead to additional abnormal versions of beta-globin such as hemoglobin C (HbC) and hemoglobin E (HbE). *HBB* gene mutations can also result in an unusually low level of beta-globin; this abnormality is called beta thalassemia.

In people with sickle cell disease, at least one of the beta-globin subunits in hemoglobin is replaced with hemoglobin S. In sickle cell anemia, which is a common form of sickle cell disease, hemoglobin S replaces both beta-globin subunits in hemoglobin. In other types of sickle cell disease, just one beta-globin subunit in hemoglobin is replaced with hemoglobin S. The other beta-globin subunit is replaced with a different abnormal variant, such as hemoglobin C. For example, people with sickle-hemoglobin C (HbSC) disease have hemoglobin molecules with hemoglobin S and hemoglobin C instead of beta-globin. If mutations that produce hemoglobin S and beta thalassemia occur together, individuals have hemoglobin S-beta thalassemia (HbSBetaThal) disease.

Abnormal versions of beta-globin can distort red blood cells into a sickle shape. The sickle-shaped red blood cells die prematurely, which can lead to anemia. Sometimes the inflexible, sickle-shaped cells get stuck in small blood vessels and can cause serious medical complications.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- HbS disease
- Hemoglobin S Disease
- SCD
- Sickle cell disorders
- Sickling disorder due to hemoglobin S

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: FS
  https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/HbSS_FS.pdf
- ACT Sheet: FSA
  https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/Hb_Sbeta_plus_thal_FSA.pdf
- ACT Sheet: FSC
  https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/Hb_SC_FSC.pdf

Genetic Testing

- Genetic Testing Registry: Hb SS disease
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0002895/

Other Diagnosis and Management Resources

- Baby's First Test: S, Beta-Thalassemia
  http://www.babysfirsttest.org/newborn-screening/conditions/s-beta-thalassemia
- Baby's First Test: S, C Disease
  http://www.babysfirsttest.org/newborn-screening/conditions/s-c-disease
- Baby's First Test: Sickle Cell Anemia
  http://www.babysfirsttest.org/newborn-screening/conditions/sickle-cell-anemia
- GeneReview: Sickle Cell Disease
  https://www.ncbi.nlm.nih.gov/books/NBK1377
- Genomics Education Programme (UK)
  https://www.genomicseducation.hee.nhs.uk/resources/genetic-conditions-factsheets/item/86-sickle-cell-anaemia/
- Howard University Hospital Center for Sickle Cell Disease
  http://huhealthcare.com/healthcare/hospital/specialty-services/sickle-cell-disease-center/disease-information
- MedlinePlus Encyclopedia: Sickle Cell Anemia
  https://medlineplus.gov/ency/article/000527.htm
- MedlinePlus Encyclopedia: Sickle Cell Test
  https://medlineplus.gov/ency/article/003666.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Sickle Cell Anemia
  https://medlineplus.gov/ency/article/000527.htm
- Encyclopedia: Sickle Cell Test
  https://medlineplus.gov/ency/article/003666.htm
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html
- Health Topic: Sickle Cell Disease
  https://medlineplus.gov/sicklecelldisease.html

Genetic and Rare Diseases Information Center

- Sickle cell anemia
  https://rarediseases.info.nih.gov/diseases/8614/sickle-cell-anemia

Additional NIH Resources

- GeneEd
  https://geneed.nlm.nih.gov/topic_subtopic.php?tid=142&sid=149
- National Heart, Lung, and Blood Institute
  https://www.nhlbi.nih.gov/health-topics/sickle-cell-disease
- National Human Genome Research Institute
  https://www.genome.gov/10001219/learning-about-sickle-cell-disease/
- National Library of Medicine: Changing the Face of Medicine
  https://cfmedicine.nlm.nih.gov/activities/sickle_cell.html

Educational Resources

- About Sickle Cell Disease
  http://www.sicklecellinfo.net/
- Action Medical Research for Children (UK)
  https://www.action.org.uk/category/sickle-cell-anaemia-children
- Disease InfoSearch: Sickle cell anemia
  http://www.diseaseinfosearch.org/Sickle+cell+anemia/6589
- Genetic Science Learning Center, University of Utah
  http://learn.genetics.utah.edu/content/disorders/singlegene/
- Genetics Education Materials for School Success (GEMSS)
  https://www.gemssforschools.org/conditions/sickle-cell-disease/default
- Illinois Department of Public Health
  http://www.idph.state.il.us/HealthWellness/fs/sickle.htm

- Information Center for Sickle Cell and Thalassemic Disorders
  http://sickle.bwh.harvard.edu/menu_sickle.html
- MalaCards: sickle cell disease
  http://www.malacards.org/card/sickle_cell_disease
- Merck Manual of Medical Information, Second Home Edition
  https://www.merckmanuals.com/home/blood-disorders/anemia/sickle-cell-disease
- Michigan Department of Community Health
  http://www.michigan.gov/documents/sicklecell_79213_7.pdf
- My46 Trait Profile
  https://www.my46.org/trait-document?trait=Sickle%20cell%20disease&type=profile
- Nemours Foundation
  http://kidshealth.org/en/parents/sickle-cell-anemia.html
- Orphanet: Sickle cell anemia
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=232
- Swedish National Board of Health and Welfare
  http://www.socialstyrelsen.se/rarediseases/sicklecellanaemia
- University of Rochester Medical Center
  https://www.urmc.rochester.edu/encyclopedia/content.aspx?ContentTypeID=85&ContentID=P00101
- Virginia Department of Health
  http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet_SICKLE-CELL-ANEMIA_English.pdf
- Washington State Department of Health: Hemoglobin S Fact Sheet
  https://www.doh.wa.gov/Portals/1/Documents/5220/HbSFactSheet.pdf
- Your Genes Your Health from Cold Spring Harbor Laboratory
  http://www.ygyh.org/sickle/whatisit.htm

Patient Support and Advocacy Resources

- American Sickle Cell Anemia Association
  http://www.ascaa.org/index.php
- March of Dimes
  https://www.marchofdimes.org/baby/sickle-cell-disease-and-your-baby.aspx
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/sickle-cell-disease/
- Sickle Cell Disease Association of America
  http://www.sicklecelldisease.org
- The Sickle Cell Information Center
  http://scinfo.org/

GeneReviews

- Sickle Cell Disease
  https://www.ncbi.nlm.nih.gov/books/NBK1377

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22sickle+cell+anemia%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Anemia,+Sickle+Cell%5BMAJR%5D%29+AND+%28sickle+cell+anemia%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- SICKLE CELL ANEMIA
  http://omim.org/entry/603903

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