Sickle Cell Disease

WHAT IS SICKLE CELL DISEASE?

Sickle cell disease (SCD) is an inherited disorder of the red blood cells (RBCs). Sickle cell anemia is the most common type of SCD. RBCs carry oxygen throughout the body via hemoglobin, a protein comprised of 4 subunits that each has an iron-containing heme group. RBCs are round and elastic so they can move through small blood cells and capillaries. With SCD, defective hemoglobin (aka hemoglobin S) replaces normal hemoglobin (aka hemoglobin A). Over time, this causes many RBCs to become rigid and sickle-shaped and die earlier than normal RBCs, leading to a constant shortage.

SYMPTOMS AND COMPLICATIONS

Faulty hemoglobin leads to the common symptoms of anemia (e.g., fatigue, shortness of breath) due to the shortage of RBCs and inadequate amount of oxygen being transported around the body by hemoglobin. The sickled RBCs also become sticky, which, when coupled with their rigidness, leads to clogged small blood vessels and capillaries, blocking blood flow.[1] This results in more serious symptoms such as chronic pain, chest pain, infections, headaches and stroke. Severe or long-lasting anemia can damage the heart, brain, lungs, kidney, spleen and other organs, and, in very severe cases, can lead to death.[2]

90-120 days

Time it takes for normal red blood cells to die

10-20 days

Time it takes for red blood cells affected by sickle cell disease to die

TRANSMISSION

SCD is an inherited autosomal recessive pattern, meaning copies of the gene from both parents have mutations, which results in the homozygous disease phenotype (HbSS). People with sickle cell trait (i.e., only one gene with a mutation, or HbS) usually do not experience symptoms but can pass the trait to their children. Other abnormal hemoglobin genes can also be passed to HbS offspring resulting in varying disease severity (e.g., HbSX or beta thalassemia).

Symptoms of Sickle Cell Disease

Early symptoms related with lack of oxygen: fatigue, shortness of breath

Later symptoms related to clogged blood vessels: chronic pain, chest pain, infections, headaches and stroke

Later symptoms related to severe or long-lasting anemia: organ damage and death

DIAGNOSIS AND TREATMENT

To prevent complications, early diagnosis and treatment of SCD are very important. SCD is most often found at birth during routine newborn screening tests but can also be diagnosed within the first few weeks of pregnancy using amniotic fluid or placental tissue. In the US, all state governments require testing for SCD as part of their newborn screening programs.[3]

Data current as of February 24, 2020

SCD can be diagnosed with simple blood tests such as the use of a blood film to look for sickling, complete blood count or hemoglobin electrophoresis with HPLC confirmation.

Common strategies to treat symptoms of SCD include antibiotics for infections, pain-relieving medications and hydroxyurea to stimulate fetal hemoglobin production. Blood transfusions are commonly used to treat worsening anemia and other sickle cell complications. Currently, the only cure for SCA is bone marrow or stem cell transplant. However, these treatments are very risky and can have serious side effects, including death. In addition, the donor and recipient must be an exact match. However, more novel treatments including nitric oxide, hemoglobin-boosting drugs, gene therapy and monoclonal antibodies are currently under development for SCD.

CURRENT SITUATION, EPIDEMIOLOGY AND WHAT'S NEXT

There are >300,000 SCD births globally per year, and with an incidence of 0.05%, the global SCD prevalence is estimated to reach ~400,000 by 2050. Sub-Saharan Africa has 70% of new global SCD (HbSS) births, while the following 3 countries account for 90% of the world's SCD population: Nigeria, the Democratic Republic of the Congo and India.[4] In the US, SCD affects 70,000-80,000 individuals. While the highest prevalence in the US is among African Americans (1 in 500), Hispanic Americans carry a burden of 1 in 1,000-1,400.

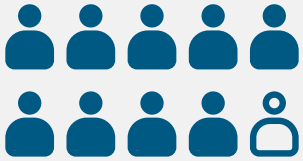
While the sickle cell trait (HbS) provides a survival advantage against malaria-related fatalities in endemic regions, the disease burden of malaria on individuals with HbSS can be high. Thus, governments and foundations have launched global initiatives to promote continued research into SCD diagnostics and treatments, while biopharma continues to translate R&D into commercial products. There are currently >120 clinical trials for SCD recruiting or ongoing worldwide.

>300,000

SCD births occur globally each year

~400,000

SCD prevalence expected globally by 2050



90%

of the world's SCD population lives in Nigeria, the Democratic Republic of the Congo and India

1 "Sickle Cell Anemia," Cleveland Clinic website.
2 Sickle Cell Disease: Symptoms, Diagnosis, Treatment and Recent Developments," NIH Medline Plus, 5(4), 2011, p. 18.
3 Rees D, et al. Lancet, 2010, 376: PP. 2018-2031.
4 DeBaun M, et al. UpToDate, August 8, 2019.

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