

Sickle Cell Disease



Yesterday

- As recently as 1970, the average patient with sickle cell disease (SCD) died in childhood, often of overwhelming infection.
- Approximately 10 percent of children with SCD suffered fatal or debilitating strokes.
- Although the technology for screening newborns for SCD was available, it was not generally used because an early diagnosis offered no advantage.
- Many persons with SCD were burdened with recurrent acute pain episodes and often with chronic pain, limiting their ability to complete schooling and maintain employment.

Today

- Patients with sickle cell anemia live to their mid-50s and patients with a related condition, SC-hemoglobin disease, live to the mid-60s. This remarkable improvement can be attributed, in large part, to NIH research.
- When NIH-supported researchers discovered that a daily dose of penicillin could prevent fatal infections in infants who had SCD, they not only established a new standard of care but also provided an impetus for now universal screening of newborn babies in the US. Today, newborns found to have the disease are given antibiotics until age 5, when another NIH study demonstrated that preventative penicillin can be stopped safely.
- With NIH support, researchers found ways to identify children with SCD who were likely to have strokes and established that regular blood transfusions could reduce stroke risk by 90 percent. A subsequent study showed that, unlike prophylactic penicillin, transfusion therapy must be continued indefinitely to maintain protection from stroke.
- Based on results of an NIH-supported clinical trial in adults, hydroxyurea became the first agent approved by the U.S. Food and Drug Administration (FDA) for prevention of painful sickle cell episodes. Hydroxyurea

increases life expectancy, reduces emergency department visits and hospitalizations, and is cost effective even for gravely ill adult patients. Another study showed hydroxyurea to be safe and effective in children aged 5-15 years. Hydroxyurea is now being tested in even younger children.

Tomorrow

- Although all individuals with SCD have the same molecular defect in the gene for beta-hemoglobin, their symptoms vary greatly. Some experience frequent, debilitating pain crises or develop severe kidney, lung, or brain damage while others have little disability and mild symptoms. The NIH is supporting efforts to detect genetic modifiers associated with SCD severity that would enable early identification of at-risk patients.
- The SCD community now has an array of treatments for improving and prolonging lives of high-risk children. Some of them, such as stem cell transplants, are suitable only for a subset of patients. Many people who could benefit from transplants are not identified until after they have suffered considerable brain, kidney, or liver damage. Advances in research may enable doctors to identify children who are likely to suffer from severe SCD before irreversible organ damage occurs.
- Initially, stem cell transplantation was used to treat only children with SCD. Researchers at the NIH Clinical Center developed a new stem cell transplant regimen that can be used to treat SCD in adult patients. The new regimen, which uses adult stem cells collected from the blood of carefully matched donors without SCD to replace the abnormal red blood cells in people with SCD, offers hope for severely affected adults.
- Some children and adults who have a mild form of SCD produce both the defective (sickle) beta-hemoglobin protein and another form of hemoglobin—fetal hemoglobin—which usually is found only before and shortly after birth. The FDA-approved drug hydroxyurea stimulates production of enough fetal

hemoglobin to prevent major complications in many but not all persons who have SCD. Researchers identified several other compounds that may be more effective than hydroxyurea in reactivating the fetal hemoglobin gene and are conducting clinical trials of other compounds that, if given with hydroxyurea, might improve its effectiveness.

- Other researchers are examining gene-therapy strategies to deliver active fetal hemoglobin genes to red blood cells in animals with SCD. A gene-therapy approach would correct the beta-hemoglobin gene in the bone marrow so that it can produce normal adult hemoglobin.
- In a recent study, NIH-supported researchers demonstrated a technique that can simultaneously silence the sickle hemoglobin gene and increase fetal hemoglobin levels.
- NIH supported researchers are examining the nature and fundamental processes involved in pain episodes in persons with SCD with an eye to developing more effective therapies that will enable patients to lead fuller lives.
- NIH-supported researchers are studying both mild and more severe injury to the brains of persons with SCD due to silent infarcts and overt strokes to develop better approaches to protect healthy brains.
- NIH-supported researchers are studying the nature of damage that occurs to the lungs of persons with SCD, which can cause pulmonary hypertension and other forms of lung disease as patients age.
- The NIH is working closely with other Federal agencies to improve the care of people with SCD and other diseases that affect the hemoglobin protein (hemoglobinopathies). The NIH will link its efforts to advance hemoglobinopathies research with efforts of other agencies to improve disease surveillance, ensure reliable access to care and services, improve health care quality, and facilitate the development of new drugs. For example, the NIH is working with the Centers for Disease Control and Prevention to develop and implement a national surveillance system and biospecimen repository that will provide data to describe the epidemiologic and clinical characteristics of people with SCD, thalassemias, and other hemoglobinopathies. The registry will allow

researchers to determine where patients are, what care they receive, and how their health is affected. Ultimately, the surveillance system will facilitate research and provide policy makers with the information needed to improve access to and quality of care.

- NIH-funded research has led to the development of a number of options to treat or prevent complications of SCD. Because SCD affects only 70,000 – 100,000 persons in the United States, many providers do not have experience treating SCD and are unaware of treatment options. To improve health outcomes in persons with SCD, the NIH is developing evidence-based clinical practice guidelines as a resource for health care providers. Once the guidelines are completed, the NIH plans to disseminate them to health care professionals to ensure that more SCD patients have access to state-of-the-art evidence-based care.

For additional information please contact: Carl Roth, Ph.D., LL.M. rothc@nhlbi.nih.gov ; 301-496-6331.

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<http://www.nhlbi.nih.gov/index.htm>