National Institutes of Health

Fact Sheet — *Sickle Cell Disease*

Thirty Years Ago

- 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.

Today

Today, patients with sickle cell anemia live to their mid-40s 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 widespread neonatal screening. Today, newborns found to have the disease are given antibiotics until age 5, when prophylaxis can be stopped safely (as demonstrated by another NIH study).
- 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 the case with 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 cheaper than standard care for even the most ill of adult patients. Another study showed hydroxyurea to be safe and effective in children aged 5-15 years, and it is now being tested in even younger children.
- NIH investigators recently found that almost one-third of adults with SCD develop pulmonary hypertension. Pulmonary hypertension in SCD leads to a 10-fold greater risk of death. An NIH-funded clinical trial will determine whether sildenafil (an FDA-approved therapy for other forms of pulmonary hypertension) benefits SCD patients.

Tomorrow

The NIH is poised to make major discoveries to enable clinicians to *predict* which infants born with SCD are at greatest risk of disabling or life-threatening complications, *personalize* therapies according to an individual's risk profile, and *preempt* devastating complications so that people who have SCD can enjoy healthy, productive lives.

- *Predictive medicine – Identifying people who will experience severe SCD.* 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 committed to supporting efforts to detect genetic modifiers associated with SCD severity (e.g., frequent painful crises, high risk of stroke or kidney failure) that would enable early identification of at-risk patients.
- *Personalized medicine – Applying predictive medicine to health care decisions.* Like the screening technologies developed decades ago, predictive medicine will only be useful if therapies can be offered based on the findings. The SCD community now has an array of treatments for improving and prolonging lives of high-risk children. Some of them (e.g., stem cell transplants), however, are so risky that

they are suitable only for the most severely affected patients. Unfortunately, people who could benefit from transplants are not identified until *after* they have suffered considerable brain, kidney, or liver damage. Advances in predictive medicine may enable doctors to identify children who are likely to suffer from severe SCD *before* irreversible organ damage occurs.

- *Preemptive medicine – Replacing defective beta-hemoglobin.* 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 in infants. The FDA-approved drug hydroxyurea stimulates production of enough fetal hemoglobin to prevent major complications in many who have SCD. Unfortunately, hydroxyurea does not work in approximately 25 percent of patients, and it has been associated with serious side effects. Researchers identified several other compounds that may be more effective than hydroxyurea in reactivating the fetal hemoglobin gene. They also are conducting clinical trials of other compounds that, if given in conjunction with hydroxyurea, might improve its effectiveness. Other researchers are conducting preclinical studies examining gene-therapy strategies to deliver active fetal hemoglobin genes to red blood cells. An alternative gene-therapy approach would correct the beta-hemoglobin gene and, in conjunction with stem cell therapies, insert it into 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.