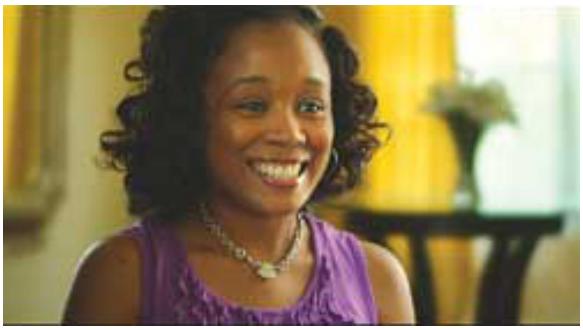
Progress in Heart, Lung, and Blood Research

Reducing the Burden of Sickle Cell Disease

Meeting 26-year old Tiffany McCoy, a bubbly and happy mother, you would never know that she has a serious disease. She is one of about 100,000 Americans with sickle cell disease. Her life, like that of many others with sickle cell disease, has been immeasurably improved because of research supported by the National Institutes of Health (NIH).

Sickle cell disease is an inherited condition that affects the ability of red blood cells to travel throughout the body, and shortens the lifespan of the cells. Red blood cells are generally smooth and round so they readily move through the body's small blood vessels, but the red blood cells in patients with sickle cell disease often assume a rigid "C" or sickle shape that causes them to stick in the small blood vessels, where they block the normal flow of blood and starve vital tissues and organs of life-giving oxygen. A minor genetic change produces a form of hemoglobin, the protein in red blood cells that picks up oxygen in the lungs and delivers it to the tissues, which leads to shape changes and shortened survival of red blood cells.

People with sickle cell disease can experience life-threatening infections, extreme fatigue, and pain so debilitating that they must visit an emergency room to obtain relief through treatment with powerful prescription narcotics. Forty years ago, almost 15 percent of children born with sickle cell disease died before the age of 2, and many more died in their teens. Today, however, the life expectancy for people with sickle cell disease has dramatically increased, and the health problems they experience are less severe because of new treatments that have been developed with NIH support. The NIH has supported research on sickle cell disease since the founding in 1948 of what is now the National Heart, Lung, and Blood Institute (NHLBI).



Tiffany McCoy, a person who lives with sickle cell disease

In the 1960s, scientists noted that bacterial infections caused the majority of deaths among children with sickle cell disease. Both children and adults who have sickle cell disease get infections easily and have a hard time fighting them because of damage to the spleen. However, NHLBI-funded clinical research showed in 1986 that daily doses of penicillin begun shortly after birth could help children stave off the infections and stay alive. In fact, the NHLBI stopped the trial early because the evidence of benefit was so compelling, with children in the penicillin treatment group having an 84 percent lower infection rate than those who were in the comparison group.

The dramatic effectiveness of penicillin therapy led states to begin testing newborns for sickle cell disease. Instituting mandatory blood tests at birth enabled hospitals to identify newborns with sickle cell disease and ensure proper follow-up care. Now, most children born with sickle cell disease live into their 40s, 50s, and beyond.

Unfortunately, infections are not the only health problem associated with sickle cell disease. Some children born with the disease are also prone to suffer strokes caused by the lodging of sickled blood cells in the small blood vessels in the brain. NHLBI-funded research improved their lives

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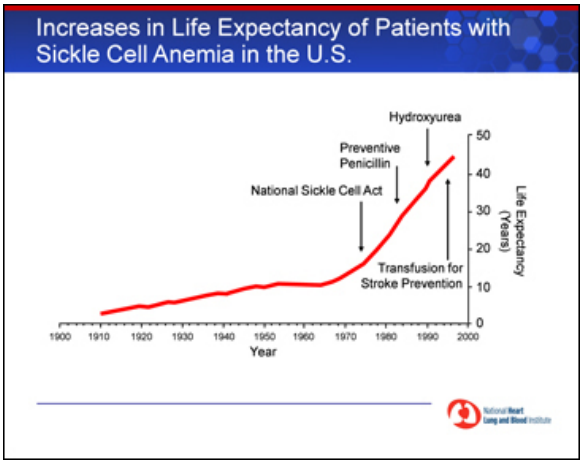
as well by developing a noninvasive test to identify those children who are at risk of stroke, and by showing that periodic blood transfusions are highly effective in lowering their stroke risk.

One approach that has been shown to be effective in reducing the chronic health problems experienced by sickle cell patients is to treat them with a drug that stimulates the formation of red blood cells that contain fetal hemoglobin, an oxygen-carrying molecule in red blood cells that normally is produced only before and shortly after birth. Red cells with a mixture of fetal and sickle hemoglobin are far less likely to undergo shape changes, are destroyed less rapidly, and cause fewer problems. NHLBI-funded clinical research published in 1985 showed that hydroxyurea, a drug that increases levels of fetal hemoglobin, could be used to treat sickle cell disease. Hydroxyurea therapy, now approved for use in adult sickle cell patients, can markedly reduce the frequency of severe pain episodes, hospitalizations, lung damage, and blood transfusions.

Hydroxyurea therapy could help many more people with sickle cell disease, but not all who might benefit are currently receiving the drug. Advice on how to treat sickle cell disease, including the use of hydroxyurea, will be highlighted in an upcoming NHLBI-sponsored, evidence-based set of guidelines about managing sickle cell disease that will be widely distributed.

To date, NIH-funded basic and clinical research on sickle cell disease has transformed a malady once fatal in childhood into a chronic, often manageable condition. Yet a widely available cure would be even better, and recent research results appear to be moving us closer to that goal.

For example, bone marrow transplantation has cured some patients with sickle cell disease. Bone marrow transplantation entails serious risk and is limited in its applicability by the availability of qualified donors, so new approaches are being tried to lower the risk and increase the availability of donors. In December 2009, NIH researchers used a specialized, partial blood stem-cell transplant to treat ten adults with severe sickle cell disease and cured nine of them. Scientists are now perfecting the partial transplant procedure and hope to be able to offer it soon to more people.



Because sickle cell disease most commonly affects people of African, Hispanic, Mediterranean, and Middle Eastern descent, developing effective treatments that will have a global impact – reducing the burden of disease in those populations whether they live in the United States or elsewhere in the world.

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