FINALLY!

Big News About Sickle Cell Disease

New hope is on the horizon for those living with this excruciating illness.

BY FRIEDA WILEY

SICKLE CELL DISEASE (SCD) is a genetic disorder that affects about 100,000 Americans, predominantly people of sub-Saharan ancestry (though also people with Southern European, Hispanic, Saudi Arabian, or South Asian backgrounds). In SCD, the body's normally disc-shaped red blood cells stiffen and take on a warped C shape, like the sickles used by farmers. Clumps of distorted cells can get stuck in blood vessels, reducing the flow of blood—and the oxygen it carries—to organs. People with SCD frequently develop anemia (which is why the disease is commonly known as sickle cell anemia). They're also prone to fatigue, swelling in the hands and feet, bacterial infections, strokes, and unpredictable attacks of horrifying pain called sickle cell crises. Symptoms usually start around 5 or 6 months of age.

Despite the misery sickle cell disease causes patients and their families, it hasn't received much research investment. "Compared with other rare diseases, SCD research has been disproportionately funded," says Beverley Francis-Gibson, president of the Sickle Cell Disease Association of America. Francis-Gibson points to cystic fibrosis (CF), also a rare inherited disease that reduces life expectancy. In the U.S., CF occurs in 1 in every 2,500 to 3,500 white babies, while SCD affects 1 in every 365 black babies. According to a 2018 study in the journal *Blood,* average annual funding from the National Institutes of Health between 2008 and 2016 was 3.4 times greater per person with CF than with SCD; between 2013 and 2016, private foundation funding was 971 times greater for CF than for SCD. No drugs were approved for sickle cell disease between 2010 and 2013, while five were approved for cystic fibrosis.

But now there's some optimistic news about SCD: Late in 2019, the FDA approved two promising new drugs.

For years, the only medicine for SCD has been hydroxyurea, an anticancer drug that can reduce mortality and decrease the rate of sickle cell pain episodes by 45 percent, says John J. Strouse, MD, PhD, associate professor of medicine and pediatrics at Duke University School of Medicine. Each of the new drugs can be taken in addition to hydroxyurea to provide more comprehensive treatment, Strouse says. Adakveo, delivered via monthly injection by a healthcare professional, can reduce the frequency of a common, painful complication that occurs when blood vessels are obstructed by sickled cells. Even more groundbreaking, Oxbryta, a daily pill, is the first SCD treatment that addresses the root cause of the disease: It inhibits the process by which blood cells become deformed. Unfortunately, neither medication is approved for children, and, like most new drugs, they're not yet available as generics and are therefore extremely expensive (as much as $100,000 per year). But roughly 30 sickle cell drugs are now in late-stage clinical trials, which means even more options should be available in the next few years.

There is no cure for SCD; today the average life expectancy in the U.S. is around 50 years.

Thanks to recent breakthroughs in gene therapy and new insights into cell biology, there's been an increase in funding for SCD research, says George Daley, MD, PhD, the dean of Harvard Medical School. One exciting venture at the Dana-Farber/Boston Children's Cancer and Blood Disorders Center targets fetal hemoglobin, a sickle cell–resistant form of hemoglobin found only in newborns; the idea is to keep this healthy hemoglobin active beyond infancy. And the NIH recently announced a joint partnership with the Bill and Melinda Gates Foundation in which both organizations will invest a collective total of at least $200 million over four years to fund research and development of gene therapies for SCD as well as HIV. The NIH is also exploring the process of modifying SCD patients' blood-forming stem cells with gene therapy and then returning them to the patients via a bone marrow transplant. Says Daley, "These advancements present the very real opportunity for development of potentially curative therapies." And in the field of sickle cell research, that's saying a lot.