Revolutionary gene therapy may offer new life for patients battling chronic sickle cell disease

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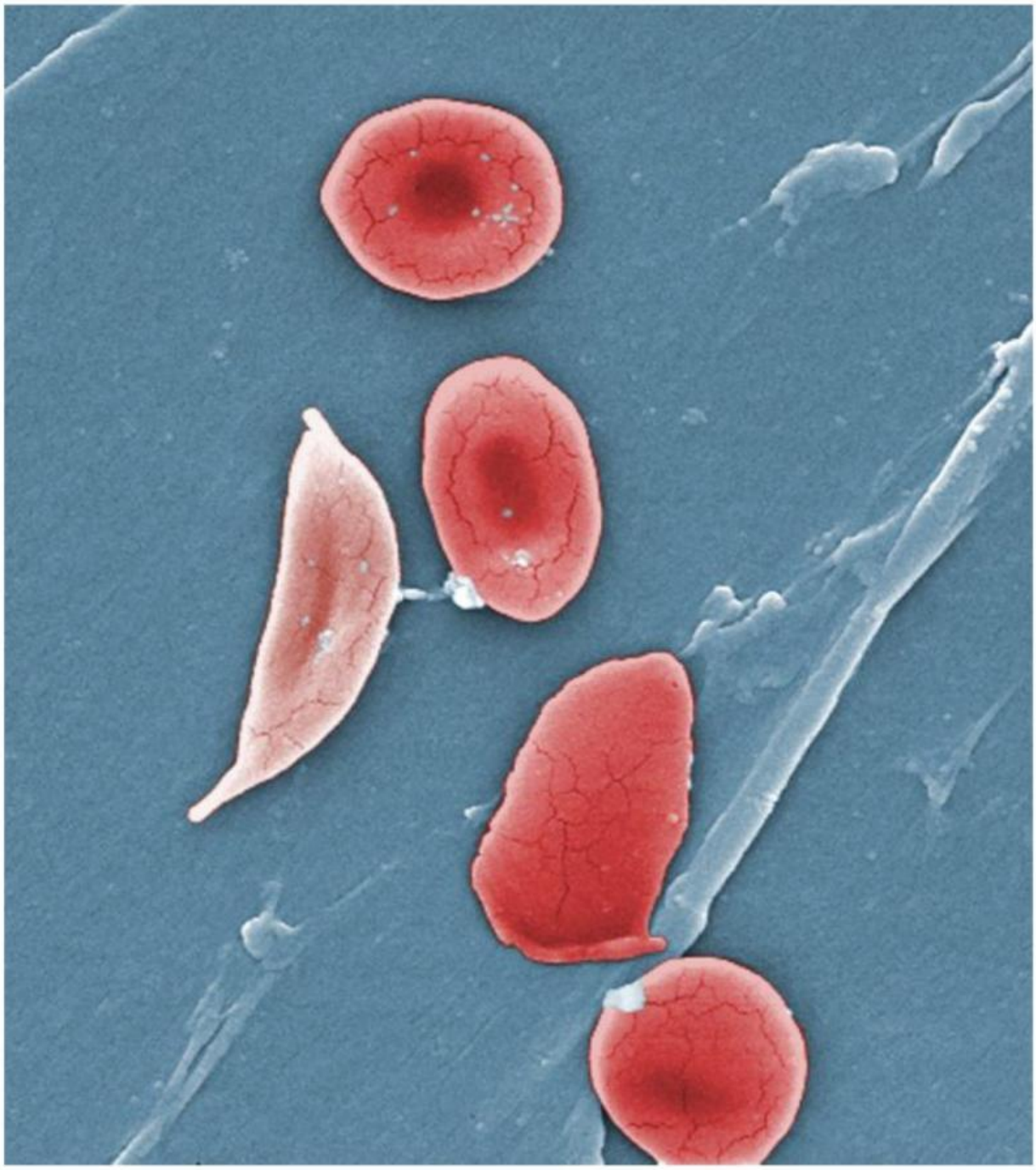

Normal blood cells next to a sickle-blood cell, colored scanning electron microscope image. Credit: Wikipedia/Illustration from Anatomy & Physiology

Lyric Porter wanted her life back. Born with sickle cell disease, she had a fever at age 5 that scarred her lungs and required her to roll an oxygen tank to school. When she was growing up, clogged blood vessels racked her body with stabbing sensations and forced her to be hospitalized again and again.

When she learned of a new experimental treatment at the University of Chicago Medicine to alter her genes and possibly cure her, she decided to take it. The process itself was an ordeal, but more than a year later, at age 27, Porter is feeling better, has more energy and has stayed out of the hospital.

"I had to take the risk," she said. "I wanted a better quality of life. And I lost so many friends who had sickle cell disease."

Now, other patients may benefit from a similar new treatment. Federal regulators recently approved a groundbreaking protocol that has the potential to relieve some of the 100,000 Americans, most of them Black, who suffer from this lifelong disease.

The University of Chicago is one of just nine medical centers nationwide initially approved to offer the therapy, with the University of Illinois at Chicago expected to do so early in 2024.

Sickle cell causes not only debilitating pain, but also anemia, organ damage, strokes and, often, an early death.

The new Casgevy treatment alters patients' genes to produce healthy round red blood cells, rather than the crescent- or sickle-shaped cells that cause the disease.

The treatment, by Vertex Pharmaceuticals Inc., is the first therapy approved by the U.S. Food and Drug Administration to use

CRISPR/Cas9 gene therapy. CRISPR is a revolutionary tool that can cut and remove, add or replace DNA in targeted areas to address different genetic disorders. Its developers won the 2020 Nobel Prize in chemistry.

In the case of sickle cell, the process switches a gene to produce fetal hemoglobin, which in effect replaces and dilutes the defective blood cells.

The treatment is not yet being called a cure because the long-term effects are unknown. But in a trial of 44 patients, all the treatments worked, and 29 patients went two years without any severe blood clotting episodes.

While many patients take hydroxyurea pills to try to manage sickle cell symptoms, the only long-lasting treatment previously had been a stem-cell transplant from a well-matched donor, typically a sibling. But the donation required suppression of the immune system that could cause severe complications. And in Porter's case, she didn't have a full sibling match.

While Porter did not use the Casgevy treatment, she used a similar and effective treatment by Novartis.

Casgevy uses fresh stem cells, whereas the Novartis therapy that Porter underwent in a clinical trial used frozen stem cells, which created delays that led to the Novartis trial being closed, said Dr. James LaBelle, director of the Pediatric Stem Cell and Cellular Therapy Program at the U. of C.'s Comer Children's Hospital.

LaBelle is optimistic in the Casgevy treatment's potential to treat genetic disorders.

"This is the future of medicine in some areas," LaBelle said. "We've

broken this glass ceiling now of using gene therapy to treat complex and debilitating diseases, which is really revolutionary."

Gene therapy is difficult and time-consuming. In Porter's case, it took three years of testing and procedures from the time she volunteered for a clinical trial until she got her treatment. She had stem cells filtered from her blood and sent away for the gene correction, then sent back and reinfused.

In between, as with donor transplants, the patient must undergo high-dose chemotherapy to kill the faulty stem cells. The chemo made Porter sick, and she was hospitalized with an infection. She also still has chronic problems left over from her years with poor blood supply.

The chemo can also cause infertility, so Porter had her eggs frozen for potential future use, a roughly $60,000 procedure that she said was covered by Medicaid.

In the long run, a big advantage to using one's own stem cells rather than a transplant is that it eliminates the need for immune suppression, which should keep patients healthier.

At the University of Illinois at Chicago, Dr. Damiano Rondelli coauthored a study showing how gene therapy helped patients with sickle cell and another blood disease called beta thalessemia. UIC has some 600 sickle patients in what is believed to be one of the largest such programs in the nation.

Rush University Medical Center officials also said they are closely monitoring the rollout of the new therapy and will strongly consider prescribing it once it becomes available.

One major drawback of the Casgevy treatment is its cost, estimated at

$2 million. With millions of sickle cell patients worldwide, many in poor areas of Africa, India and the Middle East, it's likely to have limited availability.

Porter had her treatment costs covered through a clinical trial, though she had to pay some expenses herself. But as with other transplants in the United States, the procedure usually depends on insurance for prior approval.

Most of UIC's sickle cell patients have Medicaid or Medicare, and it remains to be seen how they and other insurers will handle it. Rondelli hopes they will see it as well worth it because it will prevent hospitalizations and treatments that may cost as much or more over time.

Ultimately, Rondelli said, both donated transplants and gene therapy can give patients freedom to live. One donor recipient began searching for a home to buy now that he was finally healthier.

"Patients find a new life they never knew they could have," Rondelli said.

Gene therapy carries unknown long-term effects and potential risks, such as allergic reactions or tissue damage, or some cases of leukemia in the other newly approved treatment for sickle cell, Lyfgenia.

The FDA's Dr. Nicole Verdun said gene therapy holds the promise of delivering more effective treatments, especially for rare diseases where the current treatment options are limited. It's been approved for treating one type of blindness. Eventually, researchers hope gene therapy may be applied to many genetic disorders, from cystic fibrosis to hepatitis B.