

U.S. NEWS

ALS Patients, Defying Odds

Researchers study those who seem to show improvement for clues and treatments

By AMY DOCKSER MARCUS

Richard Bedlack has treated more than 2,000 patients with ALS, the neurological condition known as Lou Gehrig's disease. Almost without exception, his patients get worse over time and eventually die.

Now, Dr. Bedlack, head of Duke University's ALS clinic, is focusing on a different kind of patient: someone who seems to be getting better.

ALS, or amyotrophic lateral sclerosis, progressively robs people of the ability to move their muscles and is fatal, usually within two to five years.

But in a small number of cases—Dr. Bedlack says he has verified 23 so far—patients report unexpectedly regaining lost motor functions for at least a year. Some attribute their improvement to supplements or experimental therapies, but acknowledge they can't be certain why they started to improve.

Dr. Bedlack believes that studying these so-called "ALS reversals" and trying to determine what, if anything, separates these individuals from the overwhelming majority of others may lead to new understanding of the disease and, potentially, new therapies.

The effort to study people who seem to defy medical odds isn't limited to ALS. The Resilience Project, started in 2014, is examining genomes of healthy individuals, trying to find people who aren't sick despite having gene mutations that should cause disease.

For over a decade, a research consortium has followed "elite controllers," people infected with HIV who somehow naturally control the virus without anti-retroviral medications and don't develop AIDS. Studies of patients by the International HIV Controllers Consortium and other groups helped identify a genetic signature associated with controllers, and experimental therapies are being tested.

"At the beginning, HIV was this incredible black box," says Bruce Walker, director of the Ragon Institute of MGH, MIT and Harvard, which operates the HIV study. "The difficult thing is, how do you turn other people into elite controllers?"

Dr. Bedlack says he would like to do the same for ALS.

Earlier this year, researchers, including Dr. Bedlack, published a paper in *Neurology* based on a database of more than 10,000 patients stripped of any identifiable information who are taking part in clinical trials for ALS treatments.

The researchers found a



So-called ALS reversals include Michael McDuff, above, who couldn't dress or feed himself in 2013 but now can swallow again and has gained weight, and Kim Cherry, below, whose function has dramatically improved since his low point in 2012.



small subset—less than 1% of patients in the database—they consider ALS reversals, who had significant improvement and regained lost function for a year or more.

Even if the numbers of patients are small, "I think they are worth studying," says Merit Cudkowicz, director of the ALS clinic at Massachusetts General Hospital in Boston and one of the authors of the *Neurology* paper.

Dr. Bedlack says a number of theories may explain ALS reversals. Perhaps, he says, these patients didn't really have ALS but an unknown mimic syndrome. They might

have genetic traits that help resist the disease. An environmental factor that helped drive the disease could be removed, he says, or an unusual treatment the patient tried worked.

To study the phenomenon, Dr. Bedlack is running two programs. For his Study of ALS Reversals, he is collecting verified cases of reversals. When he hears of a case, Dr. Bedlack gets in touch with the patient. He asks to review medical records and speak to the doctor. This summer he will start collecting blood samples of verified cases to be used for whole genome sequencing and testing for any unusual antibodies.

One participant, Kim Cherry of Boise, Idaho, was diagnosed with ALS in 2011. His low point was in 2012, but his function has since sharply improved. The 68-year-old says he tried a variety of approaches, including treatment in a hyperbaric oxygen tank and a gluten-free diet. He thinks his reversal may be due to a combination of factors. "ALS is a puzzle," says his wife, Kay Cherry.

In cases where an unusual treatment seems to be involved, Dr. Bedlack's second program—Replication of ALS Reversals—is trying to reproduce the reversal using the patient's regimen. The first such trial, based on Michael McDuff, a 64-year-old former machinist from Westport, Mass., has enrolled 16 patients and is expected to enroll 34 more. Participants in the trial will report updates to PatientsLikeMe, a company that aggregates and analyzes health data.

Mr. McDuff says he first noticed weakness in his arms in 2010 and was diagnosed with ALS. By spring 2013, he couldn't dress or feed himself. At the suggestion of a friend, he started taking a supplement called lunasin—a protein claimed to have potential health benefits.

After three months, Mr. McDuff and his wife noticed improvements. Today, Mr. McDuff can swallow again and has gained weight. He is the first to say he isn't cured. But now, "I have a better quality of life," he says.