

German Man Free of HIV Nearly 10 Years After Stem Cell Transplant

The Düsseldorf Patient received his transplant in 2013, but his doctors were cautious about declaring a cure.

February 20, 2023 By [Liz Highleyman](#)

A German man who received a transplant of HIV-resistant stem cells to treat leukemia has no detectable HIV more than four years after stopping antiretroviral treatment, according to a report today in [Nature Medicine](#). After nearly a decade, his doctors are finally ready to declare that he's cured.

The Düsseldorf Patient appears to be either the second or third person who has eliminated HIV after the procedure—depending on whether the clock starts with the transplant itself or the treatment interruption—but his case has not gotten extensive media coverage like the other four cases reported to date. The man, named Marc, [was interviewed by the Dutch newspaper NRC in 2021](#), but he has received little attention in the English-language press.

The man, now 53, was diagnosed with acute myeloid leukemia in 2011, soon after he started antiretroviral treatment. On Valentine's Day in 2013, he received a stem cell transplant from an unrelated donor with two copies of a rare genetic mutation called CCR5-delta32, which deletes receptors that most strains of HIV use to enter CD4 T cells. In effect, the donor cells give the recipient a new HIV-resistant immune system.

"From the outset, the aim was to treat both the leukemia and the HIV," Guido Kobbe, MD, of Düsseldorf University Hospital, who performed the transplant, said in a media statement.

To prepare for the transplant, the man received reduced-intensity conditioning chemotherapy to make room for the new cells. Afterwards, he experienced mild but persistent graft-versus-host disease, where the donor cells attack the recipient's body.

After more than five years with undetectable HIV, the man and his medical team decided to undertake a closely monitored antiretroviral treatment interruption in November 2018. Since then, they have tested his blood using ultrasensitive assays and examined his peripheral immune cells and gut and lymph node tissue. Although they did see "sporadic traces" of HIV DNA, they found no evidence of HIV capable of replicating. Further, the man has low-level immune activation and

waning HIV-specific antibody and T-cell responses, suggesting a lack of ongoing virus production.

“Following our intensive research, we can now confirm that it is fundamentally possible to prevent the replication of HIV on a sustainable basis by combining two key methods,” said lead study author Björn Jensen, MD. “On the one hand, we have the extensive depletion of the virus reservoir in long-lived immune cells, and on the other hand, the transfer of HIV resistance from the donor immune system to the recipient, ensuring that the virus has no chance to spread again.”

The Düsseldorf Patient is proud of his team who succeeded in curing him of both HIV and leukemia. “On Valentine’s Day this year, I celebrated the tenth anniversary of my bone marrow transplant in a big way,” he said in a statement. “My bone marrow donor was present as a guest of honor.”

Other Stem Cell Cures

So far, only a handful of people have been cured of HIV after stem cell transplants. The first, [Timothy Ray Brown](#), known as the Berlin Patient, received two transplants to treat leukemia in 2006. His doctor, Gero Hütter, MD, came up with the idea to use cells from a donor with a double CCR5-delta32 mutation, speculating that it might cure both cancer and HIV.

Brown first underwent intensive conditioning chemotherapy and radiation to prepare for the transplant. Afterwards, he developed near-fatal graft-versus-host disease. As described in a poster at the 2008 Conference on Retroviruses and Opportunistic Infections (CROI), Brown stopped antiretroviral treatment at the time of his first transplant, but his viral load did not rebound. Researchers extensively tested his blood, gut and other tissues, finding no evidence of functional HIV anywhere in his body. At the time of [his death in September 2020](#), due to a recurrence of leukemia, he had been free of HIV for more than 13 years.

The second man, Adam Castillejo, known as the London Patient ([featured in POZ’s June 2022 issue](#)), underwent a stem cell transplant in 2016 to treat Hodgkin lymphoma, receiving cells from a donor with the same double mutation. As researchers first reported at CROI 2019, he stopped antiretroviral treatment in September 2017, and he has now been HIV-free for more than five years.

At CROI 2022, researchers described [the New York Patient](#), a middle-aged woman with leukemia who in 2017 received a combination of umbilical cord blood cells with the CCR5-delta32 mutation and partially matched adult stem cells from a relative. She stopped antiretroviral therapy three years after the transplant, and at last report she was still free of HIV.

Finally, at last summer’s International AIDS Conference, researchers described the [City of Hope Patient](#), who is older and has been living with HIV longer than the other people cured with stem cell transplants. In 2019, at age 63, he received a transplant from an unrelated donor with the same double mutation. He stopped antiretroviral therapy about two years later and remains free of HIV.

Clues to a Cure

Researchers are still trying to figure out why these people were cured after stem cell transplants while other attempts have failed. Using stem cells from donors with a double CCR5-delta32 mutation appears to be a key to success. At CROI 2012, researchers reported that [two HIV-positive men in Boston](#) who received stem cell transplants from donors without the mutation initially looked like they might be cured, but their HIV eventually came back.

Having a donor with the mutation might not be enough, however. A poster at this year's CROI describes what is thought to be the first known case of HIV rebound in a person who received a stem cell transplant from a donor with a double CCR5-delta32 mutation. In this case, a 67-year-old individual who had no detectable HIV 15 months after the transplant tried a treatment interruption, but HIV came back eight weeks later. These findings indicate that HIV that uses CCR5 receptors "can persist and perpetually spread" even more than a year after a clinically successful double CCR5-delta32 stem cell transplant, Paul Rubinstein, MD, of the University of Illinois at Chicago, and colleagues concluded.

Some experts have suggested that the intensity of pretransplant conditioning chemotherapy or the severity of the posttransplant graft-versus-host reaction might play a role in eliminating HIV. But the five patients cured to date received different conditioning regimens and some experienced mild or no graft-versus-host disease.

Even if the remaining mysteries are solved, stem cell transplants are far too risky for people who do not need them to treat life-threatening cancer. What's more, the procedure is medically intensive and costly and likely would be impossible to scale up to treat the millions of people living with HIV worldwide.

The Düsseldorf Patient now aims to support fundraising for research so there can also be HIV cures without a bone marrow transplant. "In my case, it was necessary because of the leukemia, but it really is a very rocky road," he said.

These cases offer clues that could help researchers develop more widely applicable approaches to achieve a functional cure, or long-term remission without antiretroviral therapy. For example, gene editing technologies such as CRISPR could be used to snip out genes encoding CCR5 receptors, making a person's own immune cells resistant to HIV.

"Expansion of this approach to introduce the CCR5-delta32 mutation into wild-type stem cell grafts using gene therapy in combination with new reservoir reduction strategies may hold the promise of an HIV-1 cure outside of life-threatening hematological malignancies," the study authors wrote.

[Editor's note: This article was updated on February 21, 2023, to add details about the CROI poster]

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