

→ Mark your confusion.

→ Purposefully annotate the article (1-2 mature, thoughtful responses per page to what the author is saying)

→ Write a 250+ word response to the article.

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H.I.V. Is Reported Cured in a Second Patient, a Milestone in the Global AIDS Epidemic

By Apoorva Mandavilli for *The New York Times*, 03-04-19

Scientists have long tried to duplicate the procedure that led to the first long-term remission 12 years ago. With the so-called London patient, they seem to have succeeded.

For just the second time since the global epidemic began, a patient appears to have been cured of infection with H.I.V., the virus that causes AIDS.

The news comes nearly 12 years to the day after the first patient known to be cured, a feat that researchers have long tried, and failed, to duplicate. The surprise success now confirms that a cure for H.I.V. infection is possible, if difficult, researchers said.

The investigators are to publish their report on Tuesday in the journal *Nature* and to present some of the details at the Conference on Retroviruses and Opportunistic Infections in Seattle.

Publicly, the scientists are describing the case as a long-term remission. In interviews, most experts are calling it a cure, with the caveat that it is hard to know how to define the word when there are only two known instances.

Both milestones resulted from bone-marrow transplants given to infected patients. But the transplants were intended to treat cancer in the patients, not H.I.V.

Bone-marrow transplantation is unlikely to be a realistic treatment option in the near future. Powerful drugs are now available to control H.I.V. infection, while the transplants are risky, with harsh side effects that can last for years.

But rearming the body with immune cells similarly modified to resist H.I.V. might well succeed as a practical treatment, experts said.

“This will inspire people that cure is not a dream,” said Dr. Annemarie Wensing, a virologist at the University Medical Center Utrecht in the Netherlands. “It’s reachable.”

Dr. Wensing is co-leader of IciStem, a consortium of European scientists studying stem cell transplants to treat H.I.V. infection. The consortium is supported by AMFAR, the American AIDS research organization.

The new patient has chosen to remain anonymous, and the scientists referred to him only as the “London patient.”

“I feel a sense of responsibility to help the doctors understand how it happened so they can develop the science,” he told *The New York Times* in an email.

Learning that he could be cured of both cancer and H.I.V. infection was “surreal” and “overwhelming,” he added. “I never thought that there would be a cure during my lifetime.”

At the same conference in 2007, a German doctor described the first such cure in the “Berlin patient,” later identified as Timothy Ray Brown, 52, who now lives in Palm Springs, Calif.

That news, displayed on a poster at the back of a conference room, initially gained little attention. Once it became clear that Mr. Brown was cured, scientists set out to duplicate his result with other cancer patients infected with H.I.V.

In case after case, the virus came roaring back, often around nine months after the patients stopped taking antiretroviral drugs, or else the patients died of cancer. The failures left scientists wondering whether Mr. Brown’s cure would remain a fluke.

Mr. Brown had had leukemia, and after chemotherapy failed to stop it, needed two bone-marrow transplants.

The transplants were from a donor with a mutation in a protein called CCR5, which rests on the surface of certain immune cells. H.I.V. uses the protein to enter those cells but cannot latch on to the mutated version.

Mr. Brown was given harsh immunosuppressive drugs of a kind that are no longer used, and suffered intense complications for months after the transplant. He was placed in an induced coma at one point and nearly died.

“He was really beaten up by the whole procedure,” said Dr. Steven Deeks, an AIDS expert at the University of California, San Francisco, who has treated Mr. Brown. “And so we’ve always wondered whether all that conditioning, a massive amount of destruction to his immune system, explained why Timothy was cured but no one else.”

The London patient has answered that question: A near-death experience is not required for the procedure to work.

He had Hodgkin’s lymphoma and received a bone-marrow transplant from a donor with the CCR5 mutation in May 2016. He, too, received immunosuppressive drugs, but the treatment was much less intense, in line with current standards for transplant patients.

He quit taking anti-H.I.V. drugs in September 2017, making him the first patient since Mr. Brown known to remain virus-free for more than a year after stopping.

“I think this does change the game a little bit,” said Dr. Ravindra Gupta, a virologist at University College London who presented the findings at the Seattle meeting. “Everybody believed after the Berlin patient that you needed to nearly die basically to cure H.I.V., but now maybe you don’t.”

Although the London patient was not as ill as Mr. Brown had been after the transplant, the procedure worked about as well: The transplant destroyed the cancer without harmful side effects. The transplanted immune cells, now resistant to H.I.V., seem to have fully replaced his vulnerable cells.

Most people with the H.I.V.-resistant mutation, called delta 32, are of Northern European descent. IciStem maintains a database of about 22,000 such donors.

So far, its scientists are tracking 38 H.I.V.-infected people who have received bone-marrow transplants, including six from donors without the mutation.

The London patient is 36 on this list. Another one, number 19 on the list and referred to as the “Düsseldorf patient,” has been off anti-H.I.V. drugs for four months. Details of that case will be presented at the Seattle conference later this week.

The consortium’s scientists have repeatedly analyzed the London patient’s blood for signs of the virus. They saw a weak indication of continued infection in one of 24 tests, but say this may be the result of contamination in the sample.

The most sensitive test did not find any circulating virus. Antibodies to H.I.V. were still present in his blood, but their levels declined over time, in a trajectory similar to that seen in Mr. Brown.

None of this guarantees that the London patient is forever out of the woods, but the similarities to Mr. Brown’s recovery offer reason for optimism, Dr. Gupta said.

“In a way, the only person to compare with directly is the Berlin patient,” he said. “That’s kind of the only standard we have at the moment.”

Most experts who know the details agree that the new case seems like a legitimate cure, but some are uncertain of its relevance for AIDS treatment overall.

“I’m not sure what this tells us,” said Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases. “It was done with Timothy Ray Brown, and now here’s another case — ok, so now what? Now where do we go with it?”

One possibility, said Dr. Deeks and others, is to develop gene-therapy approaches to knock out CCR5 on immune cells or their predecessor stem cells. Resistant to H.I.V. infection, these modified cells should eventually clear the body of the virus.

(CCR5 is the protein that He Jiankui, a scientist in China, claimed to have modified with gene editing in at least two children, in an attempt to make them resistant to H.I.V. — an experiment that set off international condemnation.)

Several companies are pursuing gene therapies but have not yet been successful. The modification must target the right number of cells, in the right place — only the bone marrow, for example, and not the brain — and tweak only the genes directing production of CCR5.

“There are a number of levels of precision that must be reached,” said Dr. Mike McCune, a senior adviser on global health to the Bill and Melinda Gates Foundation. “There are also concerns that you might do something untoward, and if so you might wish to have a kill switch.”

Several teams are working on all of these obstacles, Dr. McCune said. Eventually, they may be able to develop a viral delivery system that, when injected into the body, seeks out all CCR5 receptors and deletes them, or even a donor stem cell that is resistant to H.I.V. but could be given to any patient.

“These are dreams, right? Things on the drawing table,” Dr. McCune said. “These dreams are motivated by cases like this — it helps us to imagine what might be done in the future.”

One important caveat to any such approach is that the patient would still be vulnerable to a form of H.I.V. called X4, which employs a different protein, CXCR4, to enter cells.

“This is only going to work if someone has a virus that really only uses CCR5 for entry — and that’s actually probably about 50 percent of the people who are living with H.I.V., if not less,” said Dr. Timothy J. Henrich, an AIDS specialist at the University of California, San Francisco.

Even if a person harbors only a small number of X4 viruses, they may multiply in the absence of competition from their viral cousins. There is at least one reported case of an individual who got a transplant from a delta 32 donor but later rebounded with the X4 virus. (As a precaution against X4, Mr. Brown is taking a daily pill to prevent H.I.V. infection.)

Mr. Brown says he is hopeful that the London patient’s cure proves as durable as his own. “If something has happened once in medical science, it can happen again,” Mr. Brown said. “I’ve been waiting for company for a long time.”

Response option(s):

- What new ideas or perspectives or facts about curing HIV does this article give you? Explain your responses to these.
- Does this case make you optimistic or cynical about finding a widespread cure for HIV? Why? Support your perspective with details from the article.
- Pick any passage and respond to it.