

Special Report: An end to AIDS?



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(Reuters) - For his doctors, Timothy Ray Brown was a shot in the dark. An HIV-positive American who was cured by a unique type of bone marrow transplant, the man known as "the Berlin patient" has become an icon of what scientists hope could be the next phase of the AIDS pandemic: its end.

Dramatic scientific advances since HIV was first discovered 30 years ago this week mean the virus is no longer a death sentence. Thanks to tests that detect HIV early, new antiretroviral AIDS drugs that can control the virus for decades, and a range of ways to stop it being spread, 33.3 million people around the world are learning to live with HIV.

People like Vuyiseka Dubula, an HIV-positive AIDS activist and mother in Cape Town, South Africa, can expect relatively normal, full lives. "I'm not thinking about death at all," she says. "I'm taking my treatment and I'm living my life."

Nonetheless, on the 30th birthday of HIV, the global scientific community is setting out with renewed vigor to try to kill it. The drive is partly about science, and partly about money. Treating HIV patients with lifelong courses of sophisticated drugs is becoming unaffordable.

Caring for HIV patients in developing countries alone already costs around \$13 billion a year and that could treble over the next 20 years.

In tough economic times, the need to find a cure has become even more urgent, says Francoise Barre Sinoussi, who won a Nobel prize for her work in identifying Human Immunodeficiency Virus (HIV). "We have to think about the long term, including a strategy to find a cure," she says. "We have to keep on searching until we find one."

The Berlin patient is proof they could. His case has injected new energy into a field where people for years believed talk of a cure was irresponsible.

THE CURE THAT WORKED

Timothy Ray Brown was living in Berlin when besides being HIV-positive, he had a relapse of leukemia. He was dying. In 2007, his doctor, Gero Huetter, made a radical suggestion: a bone marrow transplant using cells from a donor with a rare genetic mutation, known as CCR5 delta 32. Scientists had known for a few years that people with this gene mutation had proved resistant to HIV.

"We really didn't know when we started this project what would happen," Huetter, an oncologist and haematologist who now works at the University of Heidelberg in southern [Germany](#), told Reuters. The treatment could well have finished Brown off. Instead he remains the only human ever to be cured of AIDS. "He has no replicating virus and he isn't taking any medication. And he will now probably never have any problems with HIV," says Huetter. Brown has since moved to San Francisco.

Most experts say it is inconceivable Brown's treatment could be a way of curing all patients. The procedure was expensive, complex and risky. To do this in others, exact match donors would have to be found in the tiny proportion of people -- most of them of northern European descent -- who have the mutation that makes them resistant to the virus.

Dr Robert Gallo, of the Institute of Virology at the University of Maryland, puts it bluntly. "It's not practical and it can kill people," he said last year.

Sinoussi is more expansive. "It's clearly unrealistic to think that this medically heavy, extremely costly, barely reproducible approach could be replicated and scaled-up ... but from a scientist's point of view, it has shown at least that a cure is possible," she says.

The International AIDS Society will this month formally add the aim of finding a cure to its HIV strategy of prevention, treatment and care.

A group of scientist-activists is also launching a global working group to draw up a scientific plan of attack and persuade governments and research institutions to commit more funds. Money is starting to flow. The U.S. National Institutes of Health is asking for proposals for an \$8.5 million collaborative research grant to search for a cure, and the Foundation for AIDS Research, or amfAR, has just announced its first round of four grants to research groups "to develop strategies for eradicating HIV infection."

THE COST OF TREATMENT

Until recently, people in HIV and AIDS circles feared that to direct funds toward the search for a cure risked detracting from the fight to get HIV-positive people treated. Even today, only just over five million of the 12 million or so people who need the drugs actually get them.

HIV first surfaced in 1981, when scientists at the U.S. Centers for Disease Control and Prevention discovered it was the cause of acquired immunodeficiency syndrome (AIDS). An article in the CDC's Morbidity and Mortality Weekly Report of that June referred to "five young men, all active homosexuals" from Los Angeles as the first documented cases. "That was the summer of '81. For the world it was the beginning of the era of HIV/AIDS, even though we didn't know it was HIV then," says Anthony Fauci, director of the U.S. National Institute of Allergy and Infectious Diseases, who has made AIDS research his life's work.

In the subsequent three decades, the disease ignorantly branded "the gay plague" has become one of the most vicious pandemics in human history. Transmitted in semen, blood and breast milk, HIV has devastated poorer regions, particularly sub-Saharan Africa, where the vast majority of HIV-positive people live. As more tests and treatment have become available, the number of new infections has been falling. But for every two with HIV who get a chance to start on AIDS drugs, five more join the "newly infected" list. United Nations data show that despite an array of potential prevention measures -- from male circumcision to sophisticated vaginal or anal microbicide gels -- more than 7,100 new people catch the virus every day.

Treatment costs per patient can range from around \$150 a year in poor countries, where drugs are available as cheap generics, to more than \$20,000 a year in the United States.

The overall sums are huge. A recent study as part of a non-governmental campaign called AIDS2031 suggests that low and middle-income countries will need \$35 billion a year to properly address the pandemic by 2031. That's almost three times the current level of around \$13 billion a year. Add in the costs of treatment in rich countries and experts estimate the costs of HIV 20 years from now will reach \$50 to \$60 billion a year.

"It's clear that we have to look at another possible way of managing of the epidemic beyond just treating everyone forever," says Sharon Lewin, a leading HIV doctor and researcher from Monash University in Melbourne, [Australia](#).

In some ways, we have been here before. Early AIDS drugs such as AZT came to market in the late 1980s, but within a decade they were overtaken by powerful cocktail treatments known as HAART, or highly active antiretroviral treatment. HAART had a dramatic effect -- rapidly driving the virus out of patients' blood and prompting some to say a cure was just around the corner.

But then scientists discovered HIV could lie low in pools or reservoirs of latent infection that even powerful drugs could not reach. Talk of a cure all but died out.

"Scientifically we had no means to say we were on the way to finding a cure," says Bertrand Audoin, executive director of the Geneva-based International AIDS Society. "Scientists ... don't want to make any more false promises. They didn't want to talk about a cure again because it really wasn't anywhere on the horizon."

GENE THERAPY

The ultimate goal would allow patients to stop taking AIDS drugs, knocking a hole in a \$12 billion-a-year market dominated by Californian drugmaker Gilead and the likes of Pfizer, GlaxoSmithKline and Merck.

It's unlikely to happen anytime soon, but Brown's case has opened the door to new ideas. "What it proved was that if you make someone's cells resistant to HIV...then all the last bits of HIV, that hang around for a long time in patients on treatment, did in fact decay and disappear," says Lewin.

Now scientists working on mimicking the effect of the Berlin patient's transplant have had some success. One experimental technique uses gene therapy to take out certain cells, make them resistant to HIV and then put them back into patients in the hope they will survive and spread.

At an HIV conference in Boston earlier this year, American researchers presented data on six patients who had large numbers of white blood cells known as CD4 cells removed, manipulated to knock out the existing CCR5 gene, and then replaced.

"It works like scissors and cuts a piece of genetic information out of the DNA, and then closes the gap," says Huetter. "Then every cell arising from this mother cell has this same mutation."

Early results showed the mutated cells managed to survive inside the bodies of the patients at low levels, remaining present for more than three months in five. "This was a proof of concept," says Lewin. Another potential avenue is a small group of patients known as "elite controllers", who despite being infected with HIV are able to keep it under control simply with their own immune systems. Researchers hope these patients could one day be the clue to developing a successful HIV/AIDS vaccine or functional cure.

Scientists are also exploring ways to "wake up" HIV cells and kill them. As discovered in the late 1990s, HIV has a way of getting deep into the immune system itself -- into what are known as resting memory T-cells -- and going to sleep there. Hidden away, it effectively avoids drugs and the body's own immune response.

"Once it goes to sleep in a cell it can stay there forever, which is really the main reason why we can't cure HIV with current drugs," says Lewin. Her team in Melbourne and another group in the United States are about to start the first human trials using a drug called SAHA or vorinostat, made by Merck and currently used in cancer treatment, which has shown promise in being able to wake up dormant HIV.

WHAT ABOUT PREVENTION?

As scientists begin to talk up a cure, the old question of whether that's the right goal has re-emerged. Seth Berkley, a medical epidemiologist and head of the U.S.-based International AIDS Vaccine Initiative (IAVI) is concerned.

"From a science point of view, it's a fabulous thing to do. It's a great target and a lot of science will be learned. But from a public health point of view, the primary thing you need to do is stop the flow of new infections," says Berkley. "We need a prevention revolution. That is absolutely critical."

Vuyiseka Dubula agrees. The South African activist finds talk of a cure for HIV distracting, almost disconcerting. "This research might not yield results soon, and even when it does, access to that cure is still going to be a big issue," she says. "So in the meantime, while we don't have the answer on whether HIV can be cured or not, we need to save lives."

(Additional reporting by [Julie Steenhuisen](#) in Chicago, editing by Sara Ledwith and [Simon Robinson](#))