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An end to AIDS?

> **Dramatic scientific advances mean having HIV is no longer a death sentence**

KATE KELLAND

LONDON: 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 vigour 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 US\$13 billion (RM39 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.

Brown was living in Berlin when besides being HIV-positive, he had a relapse of leukaemia. 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.

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," he 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.

"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 false promises. They didn't want to talk about a cure because it really wasn't anywhere on the horizon."

The ultimate goal would allow patients to stop taking AIDS drugs.

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.

Scientists are also exploring ways to "wake up" HIV cells and kill them. As discovered in the late 90s, 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 US are about to start the first human trials using a drug called SAHA or vorinostat, currently used in cancer treatment, which has shown promise in being able to wake up dormant HIV. - Reuters

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