Curing HIV and AIDS means clearing HIV from the body. The virus replicates by inserting its genetic code into CD4 cells, an important part of the immune system. Antiretroviral drugs (ARVs) interfere with this replication process, which is why they are very effective at reducing the amount of HIV in a person’s body to low levels.

However, existing treatments cannot completely remove HIV from the body. Even if someone takes ARVs for many years, HIV will still be hiding in various parts of their body, known as ‘viral reservoirs’. If treatment stops or is interrupted, HIV can re-establish itself by leaking out of these reservoirs.

Researchers talk about two different types of cure for HIV. One is called a ‘sterilising cure’, in which the virus is completely eradicated from the body. They also talk about a ‘functional cure’, where HIV remains in the body but is kept under control by treatment.1

How close are we to a ‘functional cure’ for HIV?

A lot of cure research has been focussed on the idea of a ‘functional cure’. A functional cure means HIV is not eradicated from the body (as it still survives in the viral reservoirs) but removes HIV from the blood and prevents negative effects like progression to AIDS, or transmission to others.

The most well-known case of a potential functional cure occurred in a man called Timothy Brown, also known as the ‘Berlin Patient’. In 2008, he had a bone marrow transplant to treat leukaemia that also seemed to have cured his HIV. However, the procedure is not an option for most people with HIV as it is very dangerous. It is only really an option for patients living with HIV who need a bone marrow transplant for other reasons.2

There has been more success with treating people very soon after they become infected with HIV. In a 2012 study, 14 French people living with HIV known as the ‘Visconti cohort’, started taking ARVs very soon after they became infected. After three years of medication, they stopped taking ARVs, which would normally result in the HIV infection re-emerging. They remained with low levels
of virus in their systems for an average of seven years.3

Case study: Early treatment for new-born babies living with HIV

The potential benefits of early ARV treatment has also been seen in two new-born babies. In March 2014, it was reported that a nine-month-old baby born in California with HIV may have been functionally cured as a result of ARVs that doctors administered just four hours after birth.

Similarly, in March 2013, researchers announced that a Mississippi baby born with HIV and given high doses of three ARVs shortly after delivery still appeared to be functionally cured two years on.4 But progress towards a functional cure took a significant blow in July 2014, when detectable levels of HIV were found in the Mississippi baby.5

Most recently in July 2015, researchers announced that a French teenager who was infected with HIV at birth was still in good health 12 years after she last took ARVs. However, it is not yet known why she has fared better than the Visconti cohort or the Mississippi baby. Moreover, some scientists say that in all of these cases it is still unknown whether they could have controlled the virus on their own if they had never been treated.6

Many have pointed out the similarities between HIV and cancer, in that it is impossible in both cases to definitely prove they have been removed from the body. This has led some to suggest that in the HIV field, ‘remission’ should be used to describe the absence of HIV (viral replication) when someone is not on treatment instead of ‘cure’ to avoid confusion.7

"I am personally convinced that remission is achievable. When? I don't know. But it is feasible. We have 'proof of concept'. We have the famous Visconti patients, treated very early on. Now it is more than 10 years since they stopped their treatment and they are still doing very well, most of them." - Francoise Barre-Sinoussi, virologist and Director of the Regulation of Retroviral Infections, Institut Pasteur 8

Flushing HIV out of its hiding places

Many researchers believe that the best hope for curing HIV infection lies in combining antiretroviral treatment with drugs that flush HIV from its hiding places. The idea is to force the dormant, infected cells to become active so that the body's own immune system or ARVs can destroy the last remnants of the virus. This approach is called 'shock and kill'.9

There have been a number of attempts to employ this technique. Most recently, in July 2015, researchers at the University of California, United States of America (USA) announced that a compound called PEP005 in the anti-cancer drug Picato, is effective at waking up dormant HIV. The researchers also tested other compounds capable of reactivating dormant HIV. They found that a substance called JQ1, when used in combination with Picato, boosts the activation of HIV more than seven-fold.10

Satya Dandekar, lead author of the study said:

"We are excited to have identified an outstanding candidate for HIV reactivation and eradication that is already approved and is being used in patients." 11

In another study published in the same journal, researchers at the Free University of Brussels reported that they had found two more drug combinations that are effective at flushing HIV out of its hiding places.12
However, so far, these drug combinations have only been shown to work on infected tissue and blood samples in the laboratory, not in people living with HIV. Moreover, these drug combinations have only been approved to prevent cancer in sun-damaged skin. Clinical trials are needed to prove that the drugs are safe and effective for people living with HIV.13

What about a vaccine?

A vaccine to prevent HIV infection remains an important, but challenging priority for researchers. The history of smallpox and polio shows that when highly effective, affordable vaccines are available, mass vaccination programmes can eradicate infectious diseases.

To be effective, a vaccine would require a substance that teaches the immune system how to create protective immune responses against HIV. While scientists have discovered a great deal about the immune system’s response to HIV in over 30 years of research, they have not yet identified a fully effective substance.

The development of a vaccine to prevent HIV infection is especially challenging because:

- the diversity of HIV subtypes and the frequency with which the virus mutates means that a vaccine would need to prevent infection from multiple strains. But in general, antibodies are not effective against multiple strains
- HIV attacks and uses the same CD4 cells that are needed for an effective immune response.

The most exciting recent progress in vaccine research concerns the Thai RV144 trial, which reported its results in 2009. Individuals who received a vaccine were 31% less likely to become infected with HIV than people who received a placebo.14

Individuals received two vaccines with different modes of action; a ‘prime’ vaccine called ALVAC and a ‘boost’ vaccine that was modelled on the gp120 protein on the outer surface of HIV. Several groups of researchers are now trying to refine and improve this approach.15

Vaccine researchers are also excited by the discovery that some individuals living with HIV produce antibodies that work against multiple strains of HIV. These are called ‘broadly neutralising antibodies’ (bnAbs). Researchers are attempting to manufacture bnAbs to see whether they could protect HIV-negative people from infection.16

Other cure research

Antibodies

All people living with HIV naturally respond to the virus by producing antibodies. While most people's antibodies are unable to kill HIV, the immune systems of a small minority produce broadly neutralising antibodies (bnAbs), which can kill or neutralise a wide range of HIV strains.17

In 2014, one study detailed how a research team found and identified these antibodies in a South African woman before cloning them in a laboratory. Despite providing hope for gene therapy in other people, these antibodies were unable to destroy the HIV virus within her own body because the virus mutates too quickly. She is currently on ART.18

Abdool Karim, one of the scientists working on the study said:

“When a person develops broadly neutralising antibodies it actually has no benefit to the individual who develops it; [they are] not able to neutralise their own virus.” 19

Gene therapy

Gene therapy has also been explored as a potential option for eliminating HIV infection. This
involves injecting genetically modified white blood cells into people living with HIV to build their resistance to the virus.

1% of people naturally produce bnAbs that make them resistant to the most common strains of HIV. In 2014, 12 people living with HIV were given these genetically modified CD4 cells.20

At the start of the trial, all of the patients were on ART but were taken off treatment after they received the modified cells. As expected, the HIV levels in their bodies began to rise but as the modified cells multiplied and circulated, they pushed levels of the virus back down.21

However, the number of modified cells fell over time, halving roughly once a year. The trial has been running since 2009 and all of the participants are now back on treatment.22 A 2015 study that used a similar technique in mice reported an 80% to 95% decrease in HIV levels.23

Most recently, researchers reported success in using this technique to remove HIV genes completely from infected cells. Once the virus was gone, the cells continued to function normally with no signs of damage, and appeared to be protected from reinfection. So far, this technique has only been used on cells in the laboratory.24

Despite promising trials, it isn’t yet clear whether gene therapy could be an effective treatment for HIV.

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