

Three steps closer to the cure

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'The field is moving fast,' says Sharon Lewin, from Monash University, one of our co-chairs at the next World AIDS Conference in Melbourne in 2014.

'While we don't have a cure currently, we do have a better understanding of what we need to do.'

VIRAL LATENCY

One of the things that makes HIV so difficult to cure is the way it can integrate itself into resting T-cells in reservoirs like lymph tissue, bone marrow and the spleen.

In these places, the [virus](#) [1]A small infective organism which is incapable of reproducing outside a host cell. becomes latent (or sleeps) but if these cells are activated, HIV is released into the bloodstream and resumes viral production.

Several cure approaches being studied at the moment involve activating resting cells to flush the virus out of hiding, making it vulnerable to antiretroviral drugs and the natural immune response.

One international study — which Professor Lewin's team has been [recruiting](#) [2]The act of signing up participants into a study. Generally this process involves evaluating a participant with respect to the eligibility criteria of the study and going through the informed consent process. for in Melbourne — is testing whether a chemotherapy drug called vorinostat, a 'histone deacetylase inhibitor', can disrupt this HIV latency in people who are on ART.

US lead researcher of the University of North Carolina, David Margolis, described how his team collected resting CD4 cells from eight people who had fully suppressed [viral load](#) [3]A measurement of the quantity of HIV RNA in the blood. Viral load blood test results are expressed as the number of copies (of HIV) per milliliter of blood plasma.

His experiment demonstrated that it is possible for us to target and wake up these sleeping cells and that histone deacetylase inhibitors work as a class to do the job.

The next step is to figure out how to apply this procedure to all latent CD4 cells in the body while protecting new cells from infection.

STEM CELL TRANSPLANTS

Another exciting development was reported by Timothy Henrich, an infectious disease physician from Boston, who described how two men who underwent stem cell transplants to treat lymphoma now appear to be free of HIV.

Unlike the widely reported case of Timothy Brown, the Berlin patient, these men received transplants from donor cells that were not missing CCR5 co-receptors; and they also received milder chemotherapy and no whole-body radiation. So, unlike Brown, this less toxic regimen enabled them to remain on antiretroviral drugs.

Over time, the transplanted donor cells replaced the recipients' own lymphocytes, and their HIV viral load became undetectable using even the most sensitive tests.

As for HIV-DNA inside cells in blood samples, the researchers noted that genetic material was detected in the months following stem cell transplantation. While HIV antibodies are still detectable in both patients, HIV-DNA became undetectable by day 200 in one patient and day 300 in the other.

Are these patients cured of their HIV infection? While Henrich suggested the data are encouraging, noting the 'substantial and sustained reduction in the HIV reservoir' and that the 'declining HIV specific antibody levels provide further evidence for minimal persistence of HIV antigen' are important findings, some key pieces of the

puzzle are still missing.

Unlike Brown, who has remained off HIV treatment for more than five years and has produced tissue samples lacking HIV, the two patients under Henrich's care have not stopped taking ART and do not yet have tissue samples available. These are necessary, Henrich explained, 'to fully assess the extent of HIV reservoir reduction after stem cell transplantation.'

'We're being very careful to refer to our patients as not being functionally cured,' added Daniel Kuritzes, MD, a Harvard Medical School researcher who has been working alongside Henrich.

Although the donor cells were not missing CCR5 co-receptors, researchers explained that replacing the old cells apparently got rid of a reservoir of latent HIV, and continued ART protected new cells from infection.

'It's a form of pre-exposure prophylaxis (PrEP) on the cellular level,' they said.

VISCONTI [COHORT](#) [4]In epidemiology, a group of individuals with some characteristics in common. A cohort study is a special kind of clinical trial which looks at a treatment or treatment strategy in a cohort of people.

In the third study, Charline Bacchus and Asier Saez-Ciron from France looked at a group of 14 people — dubbed the VISCONTI cohort — who started treatment very early, on average within 40 days after they became HIV positive.

An analysis of this group showed that after being on ART for a median of three years and then stopping treatment, they have all been able to control HIV for up to six years on their own.

Like 'elite controllers' who can suppress HIV without treatment, the VISCONTI cohort all show small and decreasing viral reservoirs without being on ART. However, unlike elite controllers they all started off with much higher viral loads. They also have different HLA genetic patterns and their viral reservoirs are largely made up of short-lived T-cells, while long-lived cells that could harbour virus for many years contributed very little, the researchers explained.

A small proportion of people with HIV — perhaps 5 to 15% — may be able to control the virus over the long term off therapy if they start treatment very early.

'These results suggest that antiretroviral treatment should be started very early after infection,' said Charline Bacchus.

Scientists are continuing to study the immune characteristics of this group for clues as to why they do not need prolonged medication.

NEXT STEPS

Importantly, participants in the vorinostat and stem-cell studies remained on antiretroviral therapy, and only a treatment interruption will show whether they are able to achieve a functional cure.

And unlike the Berlin patient, who required intensive and risky procedures to save his life, most HIV positive people who are suitable candidates for [experimental](#) [5](Of a drug) Not licensed for use in humans, or as a treatment for a particular condition. Experimental drugs are studied in clinical trials to determine their safety and efficacy, and are sometimes made available via Special Access Schemes prior to their approval. cure approaches are on ART and are often in overall good health. Taking such people off HIV treatment to see what will happen raises new ethical concerns.

IAS president-elect Françoise Barré-Sinoussi says that the Towards an HIV Cure initiative has established an [ethics](#) [6](In clinical trials) The process of determining that a proposed clinical trial conforms to a wide range of moral, scientific and ethical standards, to ensure that participants in the trial are not abused, mistreated or unfairly

taken advantage of. Before a clinical trial can go ahead, it must be given approval via an independent ethics process. working group to address these issues.

When asked when a cure might be expected, her colleague Steven Deeks offered a sobering but realistic perspective.

'The barriers to a cure are far greater than barriers to antiretroviral therapy [in the late 1980s]. I think we will discover a bunch of hits, none will be curative alone, and eventually they'll move into [combination therapy](#) [7] Highly Active AntiRetroviral Therapy ??? aggressive treatment of HIV infection using several different drugs together.. Unless we get very lucky this is going to take well over a decade.'

Content for this article was condensed from various sources, particularly those on www.AIDSmap.com [8]

- [Defeating HIV](#)
- [HIV research](#)

Links:

[1] <http://napwa.org.au/glossary/term/125>

[2] <http://napwa.org.au/glossary/term/489>

[3] <http://napwa.org.au/glossary/term/416>

[4] <http://napwa.org.au/glossary/term/477>

[5] <http://napwa.org.au/glossary/term/491>

[6] <http://napwa.org.au/glossary/term/498>

[7] <http://napwa.org.au/glossary/term/96>

[8] <http://www.AIDSmap.com>