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News: Briefing

Stem-cell transplant wipes out HIV

But the treatment is too risky to help most who are infected with the virus.

Heidi Ledford

A man may have been cured of both HIV and leukaemia after receiving a stem-cell transplant from a donor who is genetically resistant to HIV.

About two years after the procedure, there is still no sign of the virus, even though the patient no longer takes antiretroviral drugs. *Nature News* takes a look at the promises and limitations of the experimental treatment.

Haven't we heard about this before?

The German physicians announced their **finding** in November 2008. Since then, the results have been peer reviewed and are now published in the *New England Journal of Medicine*¹.

What did the physicians actually do?

They essentially did what they would do for any leukaemia patient who was not responding adequately to chemotherapy: they searched donor registries for bone-marrow donors who were a match for their patient, and prepared to perform a transplant.

But haematologist Gero Hütter of the Charité Universitätsmedizin in Berlin took the search for a donor one step further. Hütter does not specialize in HIV cases but when he realized that his patient would need a transplant, he remembered a paper he had read more than a decade earlier about HIV resistance in people who carry a specific genetic mutation.

The mutation is a short deletion in the *CCR5* gene. The gene encodes a receptor that HIV uses to enter immune cells called CD4⁺ T cells. About 1% of the European population carries the *CCR5* mutation in both copies of the *CCR5* gene, making such people much less likely to contract the virus. If Hütter could replace his patient's immune cells with cells that lacked the *CCR5* receptor, his patient might be less susceptible to HIV infection.

The patient had 80 matches in the bone-marrow registries of the German Bone Marrow Donor Center, and Hütter reasoned that one of those matches might also carry *CCR5* mutations. Donor number 61 turned out to be the one, and in February 2007, the transplant was performed.

Can we really learn anything from an experiment performed in only one patient?

Even though the technique has only been applied in one patient, the results are valuable, says James Riley, an HIV researcher at the University of Pennsylvania in Philadelphia. "Of all the 'n=1' experiments out there, this is a good one," he says. "It's a tremendous proof of principle that if you can make the majority of your cells resistant to infection, you can really stop the virus."

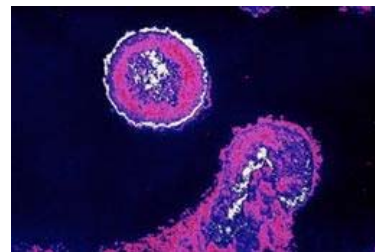
Meanwhile, Hütter says that a different team of physicians intends to perform the same procedure in another HIV-positive patient with leukaemia. So in a few years, the experiment may reach n=2.

Was the patient cured?

That remains unclear. Although the patient has gone about two years without a relapse, it is still possible that the virus will make a comeback. The virus could be lurking in cells that doctors have not been able to test — such as cells in the brain or heart.

In addition, there is another strain of HIV that does not use *CCR5* receptors to invade cells. This strain does not typically show up in patients with functioning immune systems, but it is still possible that this form of HIV could eventually proliferate in this patient.

What is clear is that this is not a treatment most HIV-positive people would want to receive. The risks involved with a bone-marrow transplant far outweigh those that come with years of antiretroviral drug therapy, even considering the troublesome side effects of these drugs. Before receiving the transplant, recipients are "conditioned" with drugs and radiation to destroy their own blood-producing stem cells. The procedure leaves them vulnerable to infection, and there is also the possibility that their bodies will eventually reject the transplant.



Bone marrow stem-cells may have cured one man of HIV.

Getty

Instead of risking a transplant, couldn't you just use a drug to block CCR5?

You could. One CCR5 inhibitor, called maraviroc, is made by the pharmaceutical company Pfizer and is approved for use in the United States and Europe. Other companies are busy developing additional CCR5-targeting drugs.

Unfortunately, maraviroc does not completely prevent the virus from binding to CCR5, and it can only be used in combination with other antiretrovirals. "Basically HIV can find its way around the drug and still use CCR5," says Riley, who adds that the virus might outcompete the inhibitor, or may be able to bind to a different region of CCR5 than the drug.

Others are trying gene-therapy approaches to prevent CCR5 from being made at all. For example, Riley has been collaborating with Sangamo BioSciences, a biotechnology company based in Richmond, California, to determine whether the company's technique for snipping out targeted genes could be used to delete the CCR5 gene. Sangamo announced last week that it has launched a Phase I clinical trial that will involve removing a sample of the participant's T cells, deleting the CCR5 gene, and then infusing the cells back into the patient. The trial is a first step towards ascertaining the safety of the technique — not its efficacy — and participants will not be conditioned to destroy their unmodified T cells.

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References

1. Hütter, G. *et al. N. Engl. J. Med.* **360**, 692–698 (2009).

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Stem-cell transplant wipes out HIV , it is a big achievement, which may help people to fight with HIV. <http://www.tradestead.com>

Posted by: **abby g** | 11 Feb, 2009

I really appreciate the experiment cos' I believe it all starts with ONE! And the other aspects discussed in the article are encouraging. As you mentioned that transplanting is basically not possible in all patients, looking for CCR5 blockers is a better option. I work with HIV positives and this news enhances my hope. Thanks

Posted by: **Karuna Devi** | 12 Feb, 2009

This achievement is a reminder especially for some sectors of the society, that believe stem cell research should be avoided, they should change their preconceptions.

Posted by: **Daniel Collucci** | 12 Feb, 2009

This guy's life was pretty dismal; he had both Leukaemia and HIV. He goes into the operating room and then wakes up, cured of both illnesses. This guy must feel like he won both the lottery and the Nobel prize in a single day. Congrats to science and the patient.

Posted by: **Bill Noderer** | 12 Feb, 2009

Hey Daniel Colluci, News Flash: These are bone marrow stem cells, NOT embryonic stem cells. No aborted babies were used in this procedure. I'll keep my preconceptions right where they are.

Posted by: **Caleb F** | 12 Feb, 2009

Great news. N=1 may also be very important for this finding as new ray of hope for HIV. Of course more numbers will be further needed.-Vivek Rai (CUMC, NY).

Posted by: **Vivek Rai** | 13 Feb, 2009

While the CD4+ T cells receptors being the entrance for HIV, but does CCR5 mutation cause any compromisation in immune system?

Posted by: **Thierry Bogaert** | 13 Feb, 2009

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