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Finding a Cure for HIV

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Although a few people appear to have been cured of HIV under special circumstances, there is currently no general cure for this virus. See our fact sheet on <u>HIV Cure-Related Research Strategies</u> for information on what scientists are trying to do to develop such a cure. The current fact sheet provides information on different kinds of cures, challenges to developing them and what the research means for women.

What Does "Cure" Mean?

It may seem fairly simple. Depending on whom you talk to, a cure for people living with <u>HIV</u> can be defined as:

- Living without treatment
- Not transmitting HIV to others
- No longer having any virus in the body

There are several terms currently used in HIV cure-related research. All of them assume that a person no longer needs to take today's HIV drugs, at least for long periods of time:

- Eradication or complete elimination getting rid of all virus from all locations in the body; sometimes referred to as "complete cure"
- Durable antiretroviral (ART)-free control HIV may still be in the body, but it is not active; the body is not fully rid of HIV, but the virus cannot affect one's health and cannot be transmitted to others; also sometimes called "functional cure"
- Remission a term borrowed from the cancer field, it means that HIV is not active in the body; there is no guarantee of lifelong control of the virus, and it suggests the need for continued monitoring (to make sure HIV is still inactive)

Why Is It Taking So Long to Find a Cure?

For those living with HIV, it may seem like it is taking scientists forever to find a cure for the virus. Considering how many drugs are out there to treat HIV, surely, they would have found a way to knock the virus out once and for all, right?

Unfortunately, several factors contribute to why it is taking so long to find a cure. The first set of these is more about the research to find a cure than the virus itself. It includes limitations on our global capacity to study HIV in laboratories, to fund cure research, and even to find willing study participants.

HIV-specific factors

There are also several factors specific to HIV and how it acts in the body that contribute to the time it is taking to find a cure. First, HIV produces proteins specifically designed to defeat our natural immune responses. Secondly, HIV not only exists in several different strains, but also mutates (makes changes in its genetic code) so quickly that it can bypass our immune system's attacks and develop <u>drug resistance</u>.

HIV "hides" from our <u>immune system</u> by inserting its genetic material into our own genes. Its genetic material (DNA) can hide in our bodies in inactive infected cells that our immune system does not recognize (viral reservoirs; <u>more details below</u>). HIV can also remain where the immune system has limited access, such as in the brain and in certain important parts of our lymph nodes.

Current HIV drugs cannot remove HIV's DNA from these cells or directly clear infected cells, but they do keep the virus from reproducing in large amounts. To provide a cure, we would need to understand where these viral reservoirs are located, how they form, and how to get rid of them.

HIV reservoirs

HIV persists in the body by forming *reservoirs*. HIV reservoirs refer to a collection of inactive, "resting," or latent HIV-infected cells. HIV may not be in the bloodstream, but it can still hide in reservoirs. At some point, HIV may re-activate, return to the bloodstream, and infect other cells. One cure for HIV would be eliminating all HIV in the reservoirs so that this cannot happen.

There are several known reservoirs in the body, including immune cells in the gut, lymphoid tissue, blood, the brain, the genital tract, and in bone marrow. It is unclear when reservoirs are established, but recent research suggests that it could be as early as 24 hours after initial infection.

Research also suggests that the earlier a person receives HIV treatment, the smaller the size of their reservoirs may be. Early treatment may also prevent reservoirs from forming in some areas of the body. It is important to keep the reservoir size small because people with larger reservoirs experience greater and more persistent immune activation.

Keeping the immune system constantly activated or "turned on" can lead to fatigue and chronic inflammation. Chronic inflammation in people living with HIV is thought to be responsible for several conditions usually seen at <u>older ages</u> in people not living with HIV, including <u>heart disease</u>, <u>bone loss</u>, kidney disease, and certain non-AIDS-related <u>cancers</u>.

Because some current cure strategies aim to knock out HIV reservoirs, these strategies may work better in people who <u>start HIV treatment</u> very early and have fewer or smaller reservoirs that need to be eliminated.

The Mississippi Child

It is clear that early treatment of HIV is not a cure for HIV. A patient known as the "Mississippi child," for example, acquired HIV at birth and started taking HIV drugs only 30 hours after birth. The child took HIV drugs for 18 months, then stopped. It was thought that the infant was cured of HIV, since she had no detectable HIV in her bloodstream for more than two years without HIV treatment. However, at four years old, the child had a detectable viral load and showed a decrease in her CD4 count. The case of the Mississippi child, while not a story of a successful HIV cure, does show that early HIV treatment can reduce the reservoirs for a period of time in which HIV drugs may not be needed.

Cure-Related Research and Women Living with HIV

Globally, women represent approximately 51 percent of all people living with HIV; however, very few women have ever participated in HIV cure research. It is important to many researchers to be sure that when the time comes for an HIV cure, women will have an opportunity to benefit.

In the early days of the HIV epidemic, people living with HIV joined clinical trials of HIV drugs that could help them and others in their communities stay alive. In the case of HIV cure studies, people living with HIV are asked to participate to advance science so that someday other people living with HIV can be cured – but participants now will not get these clinical benefits. In fact, being part of cure research could

even expose them to health risks, because some cure studies may require participants to stop taking their HIV drugs (known as "analytical treatment interruptions" or ATIs) for some period of time during the study. During this time, participants are no longer considered "virally suppressed" and could possibly transmit HIV to sexual partners. As a result, there are additional considerations for sexual partners of people who participate in ATI studies to minimize the risk of HIV transmission during the treatment interruption, including offering pre-exposure prophylaxis (PrEP) and other options for HIV prevention.

In 2020, a group of US researchers studied whether or not people living with HIV would be willing to participate in HIV cure studies based on potential risks and benefits. The researcher group included people living with HIV and community organizations like The Well Project that represent them. Survey participants were much more diverse than in past studies. The researchers found differences in preferences and reasons for participating based on gender – which would not have been found if women (cisgender and transgender) had not been included in the study.

For example, cis and trans women were less likely than cis men to want to try a new HIV cure strategy over their daily HIV drugs. In general, a majority of people in the study were unlikely to switch to an HIV cure method if there were even a very small increase in the risk of transmitting HIV to a partner. Especially in the era of <u>Undetectable Equals Untransmittable</u> (U=U), when being on effective HIV drugs makes transmission to a sexual partner impossible, fear of interrupting HIV treatment and transmitting HIV remains one of the most important factors that could keep people living with HIV from participating in cure research. Another study conducted by a diverse group of researchers found that it will be important to pay attention to power dynamics between partners – including concerns around <u>disclosure</u> or potential intimate partner <u>violence</u> – when women (or their partners) participate in cure research involving ATIs.

The features that led cis and trans women to be interested in joining a clinical trial were different than for cis men. They included supports like regular nurse visits, being paid, help with transportation to the study location, and having a meal while there. In one ongoing study in an area of South Africa where rates of poverty, unemployment, and HIV are extremely high, researchers have worked with community members to develop an empowerment program for young sexually active women that has been successful in providing life and job skills training as well as HIV prevention support. Women take weekly blood tests and, when HIV cases do occur, participants have immediate access to HIV drugs while scientists are able to study immune responses very soon after HIV acquisition. This information will be valuable in developing cure strategies.

It is extremely important for women living with HIV to be involved at every level of research into a cure for HIV – including designing studies. When a diverse range of people that will be affected by a drug or process being studied are included in figuring out how the study will be carried out, every aspect of the study will be more useful, successful, and safe.

Where Are We Now?

In some ways, the search for a cure for HIV and an end to the pandemic resembles the fight against cancer. A few decades ago, HIV infection was almost always fatal. Then we began to find therapies that could slow disease progression. Now, there are multiple antiretroviral therapies that can be used to treat HIV. People who are living with HIV and taking HIV drugs can live long, healthy lives – in many cases as long as those who are not living with HIV.

While we do not yet have a cure, scientists are both cautious and optimistic. Researchers have been humbled by events that appeared to be advancements and were not. Nevertheless, we know so much more about HIV than we did in the past, we continue to expand upon that knowledge, and we have several good leads. Perhaps most important, we have determination and hope.

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Additional Resources

Select the links below for additional material related to Finding a Cure for HIV.

- Is There a Cure for HIV and AIDS? (Be in the Know)
- <u>Are Scientists Getting Closer to an HIV Cure? (TheBody.com)</u>
- An HIV Cure May Work Differently for Women and Men (aidsmap)
- <u>#Cure (POZ)</u>
- What Does the 'New York Patient' Mean for Everyone Else Who's Living With HIV? ...
- <u>HIV Cure Research Strategy for Women: Where Are We? (Positively Aware)</u>
- <u>There's a Second Woman Whose Immune System Seems to Have Cured Her HIV. What Do...</u>
- FRESH Cohort (Ragon Institute, Massachusetts General Hospital)
- With HIV Cure Research on the Horizon, Exploring Ethical Questions in Advance (...
- Countdown to a Cure (amfAR; video)
- How a Select Few People Have Been Cured of HIV (PBS)
- <u>Cure (AVAC)</u>
- HIV Cure Research Lacks Diversity From the Earliest Stages, Scientists Warn (Th...



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