How do we know HIV causes AIDS?

Antiretroviral treatment that halts HIV replication can prevent or reverse immune deficiency.

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Four decades into the epidemic, skeptics still periodically question whether HIV is really the cause of AIDS, or acquired immune deficiency syndrome.

Early in the epidemic in the 1980s, as AIDS ravaged the gay community, several potential causes were suggested. Some, for example, hypothesized that the use of recreational drugs—including inhaled nitrites, or poppers—or frequent anal sex might harm the immune system. In fact, the condition was so closely associated with gay men that it was initially dubbed Gay-Related Immune Deficiency (GRID).

But before long, it became clear that people other than gay men were succumbing to AIDS, including people who inject drugs, blood transfusion recipients, people with hemophilia who required frequent administration of blood products and health care workers accidentally exposed to blood during medical procedures. This suggested that the condition was caused by a blood-borne pathogen. Sex partners who had no risk factors themselves developed AIDS, suggesting that the pathogen was transmitted in semen and vaginal fluid—and using condoms could prevent transmission. Babies born to women with AIDS often became sick too, demonstrating mother-to-child transmission. Today, in many countries, a majority of people living with HIV are not gay men.

In 1983 and 1984, researchers from France and the United States independently identified the virus that causes AIDS, which would come to be known as HIV, or human immunodeficiency virus. HIV was isolated from people with all stages of disease, even before they developed severe symptoms. What's more, non-human primate studies showed that monkeys exposed to a closely related virus (SIV) developed AIDS.

HIV infects immune cells, primarily CD4 helper T-cells. As the virus replicates, it kills these cells and, over time, depletion of CD4 cells leaves people severely immunocompromised and prone to a wide range of opportunistic infections and cancers. Of note, some people are born with inherited immune deficiency and others develop immune system problems for a variety of reasons (for example, blood cancers or use of immunosuppressive medications), but AIDS refers specifically to immune deficiency caused by HIV.

Perhaps the most persuasive evidence that HIV causes AIDS is the fact that antiretroviral drugs that stop viral replication can prevent immune suppression. People who start treatment early do

not develop serious immune deficiency, and for people who are already immunocompromised when they start treatment, antiretroviral therapy halts HIV replication and allows their CD4 cells to recover.

Some people who don't believe HIV causes AIDS are also skeptical about antiretroviral medications. In particular, some claim that AZT (zidovudine or Retrovir) is a poison that caused many deaths attributed to AIDS. AZT, a nucleoside analog previously tested as cancer chemotherapy, has harsh side effects, especially at the high doses initially used. Modern antiretrovirals, however, are safe and well tolerated.

While a single antiretroviral alone can inhibit HIV replication temporarily, the virus develops drug resistance as it mutates, which can make treatment stop working. Today, we know that a combination regimen containing at least two medications that work in different ways is necessary for sustained viral suppression.

People who start treatment promptly using a modern combination regimen can have a normal life expectancy. Plus, we now know that HIV-positive people on treatment with an undetectable viral load do not transmit the virus during sex, and preventive use of antiretrovirals—known as pre-exposure prophylaxis (PrEP)—is highly protective for HIV-negative people.
