Treating HIV Very Early Can Shrink Viral Reservoir 100-Fold

Researchers found that during the earliest phases of infection, the reservoir is quite susceptible to antiretroviral treatment.

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When people with HIV begin antiretroviral (ARV) treatment within weeks of infection, their viral reservoirs can be reduced by 99%, a new study has found. Although HIV begins to establish a viral reservoir very soon after infection, during the earliest phases the reservoir remains susceptible to ARVs.

As described in Science Translational Medicine, an international research team of investigators from the University of Montreal Hospital Research Centre and other organizations analyzed blood and tissue samples collected by the U.S. Military HIV Research Program's acute HIV infection cohort. Known as TV254/SEARCH010, the cohort launched a decade ago in partnership with the Thai Red Cross AIDS Research Centre.

The cohort includes people who had contracted HIV no more than two weeks prior, meaning they were in what is known as the Fiebig I or II stages of infection. These individuals were put on ARV treatment immediately.

During Fiebig Stage 0, which lasts about 10 days after infection with HIV, all signs of the virus are undetectable. Stage I begins when a test can detect HIV RNA; it lasts about seven days. Stage II begins when a test picks up the p24 antigen, a viral protein, and lasts about five days. Stage III begins when an ELISA test detects HIV antibodies and lasts about three days. Stage IV begins when a Western blot test is positive or indeterminate and lasts about six days. Stage V begins when a Western blot test is positive but does not detect the integrase p31 antigen and lasts about 70 days. And finally, Stage VI, which lasts indefinitely and indicates chronic infection, begins when the Western blot test detects the p31 antigen.

The authors of the new study looked at samples from 170 people in Thailand who had very recently acquired HIV when they entered the TV254 study. The cohort members had a median age of 27 years old. Ninety-six percent were men. They began ARVs within a median of two days after their diagnosis.

The investigators found that people who started ARV treatment during Fiebig stages I to III

experienced a precipitous decline in the frequency of HIV infection in their cells, such that the reservoir was rendered nearly undetectable throughout the body. The rare infected cells that persisted were largely found in lymphoid tissues.

“The initiation of [ARV treatment, or ART] at this very early stage leads to a drastic decrease in the size of viral reservoirs by clearing large pools of infected cells harbored in gut-associated lymphoid tissues and lymph nodes, which are known to be preferential sites for HIV persistence during ART,” Nicolas Chomont, PhD, a professor at the University of Montreal, said in a press release.

"Although the viral reservoirs from these early treated people are extremely small,” Chomont continued, “the virus is still there, and one might say there is no immediate clinical benefit for now. Nonetheless, since these early treated individuals have viral reservoirs 100 times smaller compared to our control group, we could reasonably think that it will be easier to eradicate these mini reservoirs than the large reservoirs in people who started ART later.”

Those who started ARVs during Fiebig stages IV or V experienced only a slight decline in the frequency of HIV infection in their cells.

To read a press release about the study, click here.

To read the study abstract, click here.

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