Very Early HIV Treatment May Preserve Key Immune Responses to Virus

Researchers compared the immune systems of South African women who started treatment at different points postinfection.

June 4, 2019 By Benjamin Ryan

Treating HIV very soon after infection may preserve key facets of the natural immune response to the virus that otherwise would have been compromised by leaving the infection untreated for longer.

Shortly after infection, HIV spurs the body to launch a massive response based in CD8 “killer” immune cells. This will bring down what is typically a very high initial viral load. However, over time, this immune response becomes exhausted and dysfunctional, permitting the virus to rebound and sustain a lifelong infection.

Early HIV infection is divided into six phases called the Fiebig Stages. Prior to Fiebig Stage I, an individual is so recently infected that he or she is undetectable for all signs of the virus. This period lasts for about 10 days. Stage I begins with the presence of detectable HIV RNA and lasts for about seven days. Stage II begins with the presence of the p24 antigen, a viral protein, and lasts for 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 for about six days. Stage V begins when a Western blot test is positive but does not detect the integrase p31 antigen and lasts for about 70 days. And finally, Stage VI, which lasts indefinitely, begins when the Western blot test does detect the p31 antigen.

Publishing their findings in Science Translational Medicine, researchers from the longitudinal FRESH study enrolled South African women who were 18 to 23 years old at enrollment. The women are seen twice weekly and receive testing each time with an assay that can detect acute (very recent) HIV infection as it looks for viral RNA.

The current paper is an analysis of the immune responses over time of certain women who tested positive for HIV during the study. This included 12 women whose infections were identified during Fiebig Stages I or II and who did not start antiretroviral (ARV) treatment until their CD4s declined to 350 or below per South African treatment guidelines at the time. Twenty-six women tested positive during Fiebig Stages I or II and started ARVs within 24 to 48 hours. Eight women’s infections were identified during Fiebig Stages III, IV or V and were started on ARVs within 24 to 48

hours.

The study authors found that the women who received ARV treatment during those very early stages of infection—Fiebig Stages I through V—compared with those who delayed treatment, demonstrated a much less intense initial HIV-specific CD8 response to the virus. However, as time progressed, those in the early treatment group maintained the functionality of their CD8 response to HIV, while those who received delayed treatment did not. Such very early treatment fostered the maturation of CD8 cells such that these individuals' immune systems maintained HIV-specific memory. Early treatment also spurred robust HIV-specific responses from CD4 cells.

"The results have implications for HIV vaccine development, as this kind of functional immunity to HIV is what we would need from a vaccine," Bruce Walker, MD, the director of the Ragon Institute of Massachusetts General Hospital, the Massachusetts Institute of Technology and Harvard Medical School and the senior author of the report, said in a press release."We now need to see whether these [immune] responses [among those treated early] can control HIV in the absence of ongoing [ARV] treatment or if we can further augment their immune responses."

There are indeed documented cases of individuals with HIV who started ARVs very soon after infection and who later went off treatment and have sustained a controlled viral load for years.

That said, in the most famous case of such sustained posttreatment control of the virus, that of "the Mississippi Child," the girl did experience viral rebound after 27 months off ARVs and was put back on treatment.

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

To read the study, click here.
