Viral Blips Linked to Higher Viral Load and Later HIV Treatment Initiation

In theory, if HIV is given more time to establish a reservoir, this will fuel viral blips after individuals start antiretrovirals

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People who start HIV treatment during the acute, or very early, phase of infection are more likely to experience viral blips—transient, low-level elevations of viral load—if they had a high viral load or were in a later stage of acute infection at the time of treatment initiation.

Publishing their findings in Clinical Infectious Diseases, a research team led by Trevor A. Crowell, MD, PhD, of the U.S. Military HIV Research Program at the Walter Reed Army Institute of Research in Silver Spring, Maryland, analyzed data on 326 members of the ongoing RV254/SEARCH010 cohort in Thailand who started HIV treatment while acutely infected.

The participants enrolled in the cohort between May 2009 and May 2017. They all achieved a fully suppressed viral load of less than 20 and continued on antiretrovirals (ARVs) for at least one year. They received viral load testing upon enrollment in the study, then at weeks 2, 4, 8 and 12 and then every 12 weeks thereafter.

The study defined a blip as a viral load of 20 to 999 bookended by a pair of viral loads of less than 20, provided the individual did not change ARVs during this time.

The cohort members were monitored for a median of 2.4 years after achieving a fully suppressed viral load. They had a median age of 26 years old. A total of 305 (93.6%) of them were men who have sex with men.

Fifty-five (16.9%) of the participants experienced 69 blips between them, for a rate of 8.2 blips per 100 cumulative years of follow-up. The median time between the first undetectable viral load and a viral blip was 60 weeks.

Those who experienced blips, compared with those who did not, had a lower CD4 count (a median of 308 versus 379) and a higher viral load at treatment initiation (a median 3.9 million versus 630,000) and were more likely to be in later stages of acute infection when starting ARVs. The two groups did not differ by age, likely mode of HIV acquisition, education, HIV subtype or first ARV regimen.

To differentiate different phases of acute infection, the researchers relied on the six Fiebig stages. During Fiebig Stage 0, all signs of the virus are undetectable. This period lasts for about 10 days. Stage I begins when a test can detect HIV RNA and lasts for about seven days. Stage II begins when a test picks up 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 and indicates nonacute, or chronic infection, begins when the Western blot test does detect the p31 antigen.

The new study's lowest viral blip rate, of zero, was seen among those who started HIV treatment during the Fiebig I stage. The rate was highest, at 15.9 blips per 100 cumulative years of follow-up, among those who started ARVs during the Fiebig V stage.

The median viral load during all 69 viral blips in the study was 33. Sixteen (23.2%) of the blips involved a viral load greater than 50, including four (5.8%) that were greater than 100; none was greater than 200. There was no significant association between the magnitude of the viral load elevation and which Fiebig stage individuals were in upon starting ARVs. Nor was there a link between the length of viral suppression prior to a blip and the viral load magnitude.

After adjusting the data to account for various differences between the participants, the study authors found that having a viral load greater than 1 million at treatment initiation, compared with having a lower viral load at that time, was associated with 4.39-fold more viral blips during follow-up. Compared with starting ARVs during Fiebig I or II, starting treatment during Fiebig III or IV was associated with 1.87-fold more blips and starting during Fiebig I was associated with 4.2-fold more blips.

The study authors theorized that those who started HIV treatment during later phases of acute infection had effectively given the virus more time to establish a viral reservoir. In turn, a larger reservoir was more likely to drive viral blips during treatment.

"The clinical implications of this remain uncertain," the authors wrote. "Further research is needed."

Current guidelines call for people diagnosed with HIV to start treatment as soon as possible, but in practice, very few people are diagnosed during these earliest stages of infection.

To read the study abstract, click here.
