Early-capture HIV study allows for characterization of acute infection period

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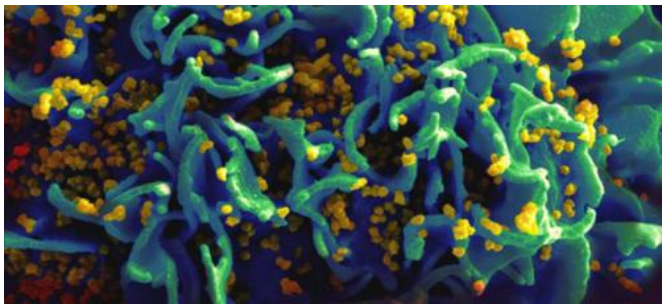

An HIV-infected cell. Credit: NIAID

Acute HIV infection (AHI) contributes significantly to HIV transmission and may be important for intervention strategies seeking to reduce incidence and achieve a functional cure. In a study by the U.S. Military HIV Research Program (MHRP), Walter Reed Army Institute of Research, published in The *New England Journal of Medicine*, scientists enrolled and intensively followed a cohort of high-risk individuals, tracking their HIV status and characterizing the disease through the acute stages of HIV infection.

This landmark study (RV217) is a prospective cohort of individuals from East Africa and Thailand at high risk for HIV infection, who had blood drawn twice weekly for qualitative plasma HIV RNA nucleic acid testing (NAT), a highly sensitive assay that allows for early detection of the virus. This is the first study to characterize the evolution of symptoms and signs prospectively in a large number of persons with acute infection.

"We were able to capture people with HIV infection before they had symptoms and before they had antibodies, which is how a diagnosis of HIV is usually made, and while their viral loads were actually very low," said Dr. Merlin Robb, the study's principal investigator and the Deputy Director of MHRP. "We're able to define the symptoms and signs during the acute interval, and now we're working intensively on evaluating the relationship between the virus and the host immune response."

Early events in HIV infection also appear to impact future course of the disease in individuals. It has been known that the amount of HIV virus in blood increases rapidly during acute infection and then decreases over time. The exact duration and type of human immune responses for controlling the viremia have not been not well defined.

"We find that events that occur in the first 30 days or so of infection are critical, and that is what we refer to as the acute phase," said Robb. Researchers found a correlation between peak viremia, which is the point during acute infection when the amount of virus in the blood is highest, and set-point viremia, which dictates the risk of transmission and long-term disease course. The study showed that viral load set-point is established at resolution of acute viremia, within 18-42 days after infection.

"This indicates that events during acute infection are abrupt and decisive, meaning they play a role in later disease outcomes over many years of HIV infection in the absence of treatment," said Dr. Robb.

RV217 also demonstrated that clinical presentation of HIV infections was less symptomatic than previously believed. The duration and number of symptoms were briefer, milder and fewer than reported previously.

"Our impression from this finding is that most of these people would not have come into a clinic with complaints and would not have been identified as acutely HIV infected," said Dr. Robb. "It changes the way we need to think about identifying people with acute infection."

Interventions during AHI may influence the long-term course of the disease. The present study demonstrates that identifying infected individuals during the observed brief AHI interval is possible, although not yet feasible on a large scale, as it would require scalable NAT diagnostic approaches.

"This study is now being re-purposed to allow us to test promising new interventions at the very earliest period of HIV infection with a view to develop approaches to HIV cure," said Col. Nelson Michael, the MHRP Director and senior author of the paper.

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