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HIV persists in the gut despite long-term HIV therapy

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Even with effective anti-HIV therapies, doctors still have not been able to eradicate the virus from infected individuals who are receiving such treatments, largely because of the persistence of HIV in hideouts known as viral reservoirs. One important reservoir is the gut, where HIV causes much of its damage due to the large number of HIV target cells that reside there. These cells, known as CD4+ T cells, are largely contained in lymph nodes and patches of lymphocytes that collectively are called gut-associated lymphoid tissue, or GALT.

Because of the importance of the gut to HIV disease, scientists hoped that long-term treatment with antiretroviral drugs could eradicate HIV from the GALT. A new NIAID study, published online by The Journal of Infectious Diseases, has found that this goal seems unlikely with current antiretroviral drugs.

Tae-Wook Chun, Ph.D., of the NIAID Laboratory of Immunoregulation (LIR), Anthony S. Fauci, M.D., LIR chief and NIAID director, and their colleagues intensively studied eight patients receiving effective antiretroviral therapy for up to 9.9 years. In each of these of these individuals, therapy had consistently kept their blood levels of HIV at undetectable levels.

Sensitive tests, however, detected the persistence of HIV as well as lowered CD4+ T cell levels in the GALT that did not completely rebound in response to therapy. Levels of virus were higher in the GALT than in immune cells in the blood, where HIV also was consistently

found. In addition, the scientists found evidence of cross infection between the GALT and the lymphocytes in the blood, suggesting that one reason the virus persists in the blood is because of ongoing cycles of replication in the GALT. The authors conclude that any possibility of further lowering or eliminating viral reservoirs likely will require more powerful drug regimens to stop the low levels of ongoing viral replication originating in the GALT. The development of such regimens is an important goal of NIAID-supported research.

A second study from the Fauci laboratory, conducted by Susan Moir, Ph.D., and her colleagues and also published online by The Journal of Infectious Diseases provides additional insights into the effects of antiretroviral therapy on the HIV disease process.

In most HIV-infected individuals, the virus replicates at high levels and CD4+ T-cell numbers decline. These two factors also strongly affect B cells, the cells of the immune system that make antibodies and help protect against infection.

Dr. Moir and her colleagues demonstrated that prior to treatment with antiretroviral therapy, B-cell numbers in the blood of HIV-infected individuals who have been infected for several years are low, and the B cells also include several dysfunctional subsets. After one year of effective treatment with antiretroviral therapy, B-cell numbers returned to normal, and several of the dysfunctional subsets also normalized. However, those B-cells that provide long-term protection against infection--so-called memory B cells--did not return to normal levels.

Dr. Moir notes that these findings strengthen the notion that while antiretroviral therapy improves many aspects of immune function in HIV-infected individuals, important deficiencies remain, especially in individuals who wait several years before initiating therapy. More studies are needed to determine whether early initiation of antiretroviral therapy

helps restore the immune system more completely.

Source: National Institute of Allergy and Infectious Diseases