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New data suggests HIV superinfection rate comparable to initial HIV infection

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HIV superinfection, when a person with HIV could acquire a second, new strain of HIV, may occur as often as initial HIV infection in the general population in Uganda, a study suggests.

Since researchers demonstrated more than a decade ago that a person infected with HIV could subsequently acquire a second, new strain of HIV, there has been little agreement in the scientific community as to how often HIV superinfection occurs. Previous studies have found HIV superinfection to be relatively frequent among individuals who engaged in high-risk behaviors, but the rate of superinfection in general populations remained unclear. The new study, supported in part by the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health, offers some evidence about the likelihood.

In light of the study's findings, the authors say post-test counseling for individuals newly diagnosed with HIV infection should emphasize the risk of HIV superinfection and the possible health implications of continuing practices that put them at risk for HIV. Studies of the rate of new cases, or annual incidence rates, of HIV superinfection, including those conducted in the United States, estimate 4 percent incidence among highly sexually active people diagnosed with HIV infection.

"This study indicates that HIV superinfection may be more common than was previously thought," said NIAID Director Anthony S. Fauci, M.D. "These findings have implications for public health strategies to

prevent new infections and efforts to develop an HIV vaccine. In addition, they are important because HIV superinfection can accelerate disease progression and the development of drug resistance, even in individuals who were previously controlling their HIV infection."

The study, published online in the *Journal of Infectious Diseases*, was led by Thomas C. Quinn, M.D., and Andrew D. Redd, Ph.D., of NIAID's Laboratory of Immunoregulation, and Maria J. Wawer, M.D., Ph.D., formerly of the Johns Hopkins University Bloomberg School of Public Health, Baltimore, and now with Columbia University Mailman School of Public Health, New York City. Their collaborators included researchers at NIAID's Rocky Mountain Laboratories, Hamilton, Mont., the Rakai Health Sciences Program in Kalisizo, Uganda, and Makerere University in Kampala, Uganda.

The blood samples examined in the study were from the ongoing NIH-supported Rakai Community Cohort Study (RCCS), a community-based open study of heterosexual men and women ages 15 to 49 years old in rural Rakai District, Uganda. Since 1994, researchers working with the RCCS have been annually conducting interviews and collecting blood samples from approximately 14,000 consenting individuals in 50 Ugandan villages to better understand HIV infection and its risk factors and to develop potential preventive measures.

"Previous studies of HIV superinfection have focused on individuals exposed to the virus through high-risk sexual activity or intravenous drug use," said lead author Dr. Redd. "We wanted to determine the rate of HIV superinfection among a broader, general population using a novel technique sensitive enough to detect even the lowest levels of circulating HIV strains."

Using an advanced high-throughput genetic screening method called next-generation ultra-deep sequencing, the scientists examined blood samples

from RCCS participants who became HIV infected. The screening was designed to detect differences in the distinctly positioned and relatively restricted p24 and gp41 genes of the virus and could detect a virus that represented as little as 1 percent of the total viruses circulating in the blood if it were of a different HIV subtype, or genetically related subgroup.

The researchers tested two blood samples. The first samples were taken at initial HIV diagnosis between 1998 and 2004, and the second samples were taken at least a year later, before the infected individuals began antiretroviral therapy. The samples were analyzed to find examples where the initial infecting strain did not cluster with viral strains found at a later time, thus confirming HIV superinfection. The rate of superinfection was then compared with an estimated overall HIV incidence rate for the entire population of initially HIV-negative individuals during the same time period.

Of the samples tested from 149 HIV-infected people, the scientists found seven cases of HIV superinfection, all detected in the gp41 region of the virus. Of these cases, four individuals were initially infected and then later superinfected with different strains of HIV subtype D, the most common viral subtype found in Rakai. The other three were initially infected with subtype D and superinfected with a different HIV subtype, subtype A. These findings suggest a rate of superinfection of 1.44 per 100 people annually. The investigators were surprised to find that the rate of superinfection was comparable to the current estimated annual rate of new, initial HIV infections in the Rakai cohort, or 1.15 infections per 100 people per year. HIV superinfection had been thought to be less common than initial infection.

"Our findings suggest that HIV vaccine strategies designed to recreate the natural immune response to HIV may be insufficient to protect an individual from infection," Dr. Redd noted. "However, the data also

provide an interesting new population to explore since it is possible that some individuals will be protected from superinfection. Determining what controls superinfection could lead to new avenues for vaccine research."

More information: "The Rates of HIV Superinfection and Primary HIV Incidence in a General Population in Rakai, Uganda," was written by Andrew D. Redd, Caroline E. Mullis, David Serwadda, Xiangrong Kong, Craig Martens, Stacy M. Ricklefs, Aaron A. R. Tobian, Changchang Xiao, Mary K. Grabowski, Fred Nalugoda, Godfrey Kigozi, Oliver Laeyendecker, Joseph Kagaayi, Nelson Sewankambo, Ronald H. Gray, Stephen F. Porcella, Maria J. Wawer and Thomas C. Quinn.

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