Superinfection Impacts Laboratory, Not Clinical Measures of HIV Progression

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HIV-1 superinfection, the reinfection of a previously infected patient with a second HIV variant, has been documented in several prior studies. Previous observations that increased viral diversity is linked to more rapid disease progression and that superinfection may increase a patient's steady state viral load suggest that superinfection may accelerate a patient's progression to AIDS (Sagar *et al*., 2003). However, studies of the repercussions of superinfection on clinical disease progression have been limited. In a recent study published in *AIDS*, Drs. Keshet Ronen and Julie Overbaugh (Human Biology Division) and an international team of collaborators from Seattle and Kenya demonstrate that superinfection accelerates laboratory based measures of HIV disease but it does not significantly impact clinical progression to disease.

The researchers assembled the largest prospective cohort study of superinfection to date to determine the effect of superinfection on disease progression, identifying 21 superinfected patients within a cohort of 146 HIV-infected Kenyan women. Interestingly, women that ultimately became superinfected initially had a lower viral initial load than singly infected patients (-0.45 $\log_{10}$ copies/mL, P=0.05). However, the viral load in superinfected women increased faster (+0.009 $\log_{10}$ copies/mL/month, P=0.0008), and they also showed a trend toward faster CD4+ lymphocyte decline than singly infected individuals (P=0.06). The researchers next evaluated the impact of superinfection on an individual's disease progression. They found a borderline association for higher viral loads in patients after superinfection relative to their viral loads pre-superinfection (+0.21 $\log_{10}$ HIV copies/mL, P=0.09). Despite these changes to laboratory measures of disease progression, the researchers did not detect any significant differences in the time to clinical progression events including CD4+ counts <200 cells/μL, initiation of antiretroviral therapy, or death.

"Our findings have implications on two fronts. First, the observation that individuals who went on to acquire superinfection had lower viral load in initial infection suggests that properties of their immune response, or the virus they were initially infected with, may predispose them to another HIV infection. We are now investigating what these predisposing factors are, since they may shed light on how to prevent infection. Second, our findings suggest that a second infection leads to increased viral replication. We also hope to understand what mediates that, to help us understand the factors that determine viral fitness and replication," said Dr. Keshet Ronen.

Ronen K, Richardson BA, Graham SM, Jaoko W, Mandaliya K, Mcclelland RS, Overbaugh J. 2014. HIV-1 superinfection is associated with an accelerated viral load increase but has a limited impact on disease progression. *AIDS* Epub ahead of print, doi: 10.1097/QAD.0000000000000422

See also: Sagar M, Lavreys L, Baeten JM, Richardson BA, Mandaliya K, Chohan BH, Kreiss JK, Overbaugh J. 2003. Infection with multiple human immunodeficiency virus type 1 variants is associated with faster disease progression. *J Virol* 12921-6.

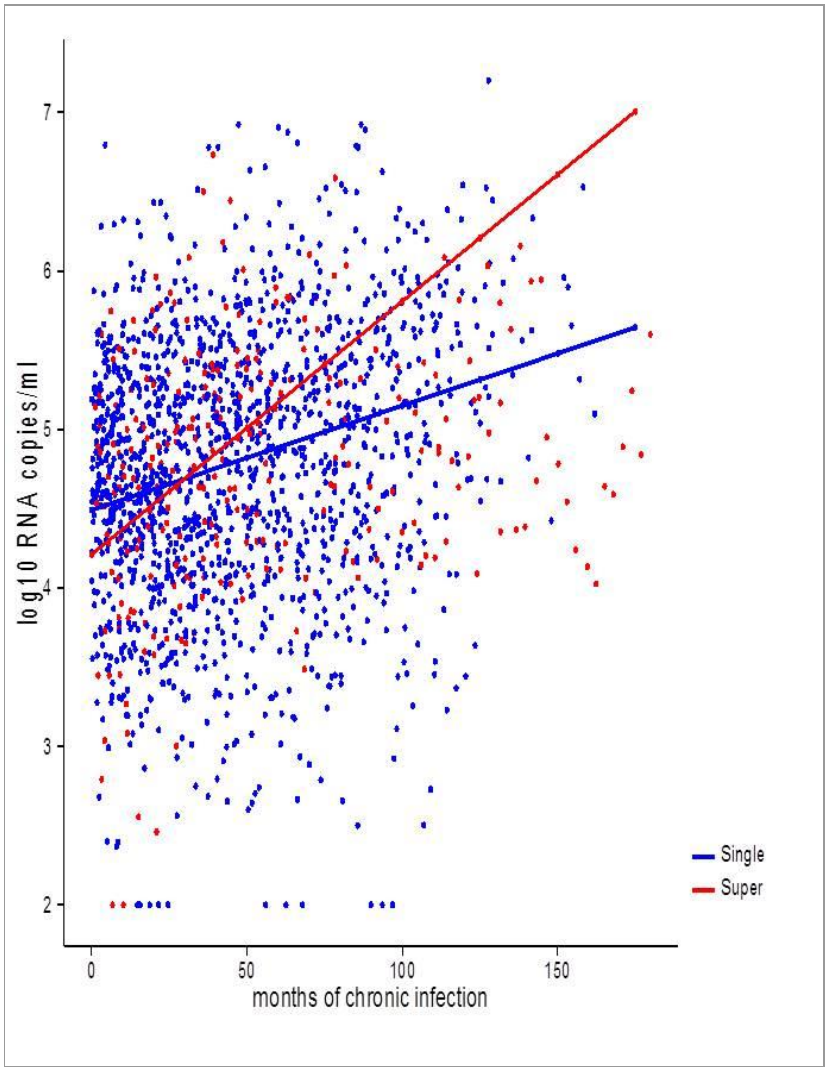

Image courtesy Dr. Keshet Ronen

Superinfected women (red) have faster viral load increases over time than singly infected women (blue).