

Sensitive testing reveals drug-resistant HIV with possible consequences for treatment

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Drug-resistant HIV at levels too low to be detected by standard tests is not unusual and may contribute to treatment failure, according to research published in *PLoS Medicine*.

Mutations in the AIDS virus commonly occur during treatment, especially if HIV drugs are not taken consistently, and may cause treatments to fail. HIV treatment in developed countries normally includes testing for these mutations, both to select first-line drugs for a given patient and to choose second-line drugs if the virus rebounds from initial treatment. However, tests used by clinical laboratories cannot reliably detect mutant viruses that make up less than about 20% of the virus in a patient's blood.

To investigate the role of resistant virus present at lower levels, Jeffrey Johnson of the Division of HIV/AIDS Prevention Laboratory in the National Center for HIV, STD, and TB Prevention at the US Centers for Disease Control and Prevention and colleagues studied HIV from more than 500 recently infected patients in Canada and the US. Although these individuals had not received anti-HIV drugs, a highly sensitive test developed by the researchers showed that more than 10% carried HIV with common drug-resistance mutations that were not detected using usual tests.

The researchers then studied 316 samples from a separate study of about 1400 patients who were started on their first HIV treatment, which included the drug efavirenz. Before starting treatment, none of these patients had resistance to efavirenz according to standard tests. However, highly sensitive testing showed that 7 of the 95 patients who experienced treatment failure had low levels of HIV with resistance mutations to efavirenz prior to treatment. Of 211 patients whose treatment did not fail, only 2 showed low level resistance prior to treatment.

These data suggest that sensitive testing for

resistance could avert failures in HIV treatment. However, given the small number of cases in this initial study, larger studies are needed to confirm the results.

In an accompanying Perspective, Steven Deeks of the University of California San Francisco, who was uninvolved with the research, discusses "whether assays for the detection of low level variants can or even should be developed for patient management." He notes that although "a sizable proportion of treatment naïve HIV infected individuals harbor a minority population of drug-resistant HIV," many patients with positive results on highly sensitive resistance testing might not go on to experience treatment failure.

Citation: Johnson JA, Li J-F, Wei X, Lipscomb J, Irlbeck D, et al. (2008) Minority HIV-1 drug resistance mutations are present in antiretroviral treatment-naïve populations and associate with reduced treatment efficacy. *PLoS Med* 5(7): e158. doi:10.1371/journal.pmed.0050158

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