

“Unprecedented” Transmission of Highly Drug-Resistant HIV in France

Researchers are surprised and concerned that a strain of HIV that is so broadly resistant to treatment even has the capacity to transmit.

September 12, 2020 By [Benjamin Ryan](#)

French researchers are concerned after identifying a young man in France who contracted a strain of HIV that has superlatively extensive [resistance to antiretroviral \(ARV\) treatment](#) for the virus.

Typically, the more that HIV mutates and develops resistance to a broad range of ARVs, the less “fit” it becomes—meaning it does not replicate or transmit as effectively. Consequently, there has been little documented transmission of such highly resistant strains throughout the history of ARV treatment.

So the discovery of this new transmission, which investigators described as an “unprecedented event” in a letter in *The Lancet*, is a worrisome surprise. The letter’s authors indicated that the strain is even more drug resistant than one famously identified in New York City in 2004.

The discovery of that strain gave rise to what proved to be quite unjustified public panic. There was pervasive concern that an especially virulent strain of “super HIV” would start transmitting widely. The doomsday phenomenon never came to pass.

In their *Lancet* letter, Stéphanie Raymond, PhD, of the University Hospital of Toulouse, and colleagues noted that less than 0.1% of HIV transmissions involve a strain that is resistant to at least three classes of ARVs.

The new case concerns a 23-year-old French man who has sex with men and who was diagnosed with HIV in September 2019. He had tested negative for the virus through an ELISA test the previous June. Tests suggested that he had contracted the virus perhaps a month before he tested positive.

At the time of his diagnosis, the man had a viral load of about 126,000, and a CD4 count of 821. He had not taken pre-exposure prophylaxis (PrEP).

A genetic analysis of his virus indicated that it belonged to the subtype B strain of HIV-1. His particular strain had resistance to all available nucleoside/nucleotide reverse transcriptase

inhibitors, non-nucleoside reverse transcriptase inhibitors and protease inhibitors. The virus was also resistant to almost all integrase inhibitors, the drugs in the newest main class of ARVs; however, it had only low-level resistance to dolutegravir (sold individually under the brand name Tivicay) and bictegravir (included in the Biktarvy combination tablet).

This strain of HIV was what's known as CCR5 tropic, meaning that it attaches to the CCR5 coreceptor on CD4 cells when establishing an infection in the cell. This is relevant to the effort to find an effective ARV treatment because the drug Selzentry (maraviroc) works by blocking that particular coreceptor.

Especially as people live with HIV over the course of many years, their viral population may diversify such that at least some of it becomes CXCR4 tropic, meaning it attaches to the coreceptor of that name on CD4 cells. There is no approved ARV that blocks that coreceptor.

The investigators also identified a 54-year-old French man who had been living with HIV for decades and had a strain of the virus that was genetically related to the one that the 23-year-old contracted. However, the investigators were not able to establish a direct history of how the virus might have transmitted from the older man to the younger one. This suggests that the virus had likely transmitted through intermediary individuals.

The older individual, who was also a man who has sex with men, was diagnosed with HIV in 1995. He had experienced a long history of ARV regimens failing. In July 2019, he had a viral load of 316,000 and a CD4 count of 205, despite the fact that he was on an ARV regimen including Truvada (tenofovir disoproxil fumarate/emtricitabine), ritonavir-boosted Prezista (darunavir) and Tivicay.

His viral strain was primarily CCR5 tropic, but he also had variants that were CXCR4 tropic.

Clinicians planned to treat the 23-year-old man with drugs that target the virus's entry into cells, including Trogarzo (ibalizumab), Rukobia (fostemsavir), Selzentry and Fuzeon (enfuvirtide) plus 50 milligrams of Tivicay twice daily. They planned to give the 54-year-old man the same regimen without Selzentry, considering that the drug's effectiveness would be compromised by the man's CXCR4-tropic viral variants.

The investigators noted that in the famous 2004 case in New York City, the virus of the individual in question did not have resistance to the protease inhibitor Aptivus (tipranavir) or integrase inhibitors, which at that point in history were still in clinical trials. The first integrase inhibitor was approved in 2007.

Noting that the 23-year-old's viral load tended to decrease after he was diagnosed, the investigators asserted that longer follow-up studies are needed to assess his viral variant's fitness.

"An epidemiological surveillance network of virologists, clinicians and local actors of prevention should prevent the diffusion of this extensively drug-resistant HIV-1 strain," the researchers concluded. "New antiretroviral drug classes are needed to open alternative therapeutic avenues

for such strains.”

To read the Lancet letter, [click here](#).

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