The adaptability of pathogens

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Drug-resistant HIV viruses can spread rapidly. This is the conclusion of a study conducted as part of the SWISS HIV Cohort Study, which is supported by the SNSF. Only the continuous introduction of new drugs can stop the virus from getting the upper hand.

The adaptability of pathogens is a great challenge to modern medicine, particularly the growing bacterial resistance to antibiotics. But other pathogens also possess the ability to adapt and render drugs powerless. A new study, conducted as part of the SWISS HIV Cohort Study, now shows how drug resistance can spread if it is not hindered by the continuous introduction of new drugs.

"Modern therapies can practically stop HIV viruses from replicating in the bodies of patients," says Huldrych Günthard, President of the HIV Cohort Study and Professor of Infectious Diseases at the University Hospital Zurich. "On the basis of this, fewer drug-resistant viruses should occur and be transmitted than a few years ago." However, studies have shown that this is not necessarily the case: the number of drug-resistant viruses that have been transmitted from one patient to another has remained stable.

New drugs offer respite

To explain this seeming paradox, Günthard and his colleagues have examined the viral resistances that have occurred in the HIV Cohort between 1998 and 2012. According to their recently published study, the proportion of patients with transmitted resistant viruses comes to about

10% for the entire period, but the transmission rate fluctuated considerably. Two opposing developments have contributed to these fluctuations, explains Günthard: when a new class of drugs entered the market, the transmission rate of resistant viruses dropped significantly for a period. This happened in 2000 after approval of the so-called "boosted protease inhibitors" and in 2009 when "integrase inhibitors" started to be used. But in both cases, the rate of transmission gradually climbed back up after the initial drop. "This shows how important a constant supply of new drugs is," explains Günthard.

Varying patterns of transmission

The researchers were also able to show how different the transmission patterns of individual types of resistant viruses can be. Worldwide, there are over 100 significant known mutations which lead to a resistance of the HI virus to one or more drugs. One frequently occurring mutation named M184V is transmitted mainly by HIV patients who receive drug therapy. In the case of two different but also frequently occurring mutations (L90M and K103N), patients who do not receive drug treatment seem to be the preferred host.

"This is probably the result of differing fitness costs of the mutations," says Günthard. M184V mutations quickly revert to their "un-mutated" state in untreated patients because the mutation limits viral replication; as a result, M184V viruses multiply above all in treated patients, who can can transmit them to other persons. On the other hand, L90M and K103N can also multiply in the absence of drugs, which means that untreated patients can propagate these two types of resistance. According to Günthard, these results exemplify that the spread of viral resistances is even more complex than previously assumed.

More information: "Assessing the paradox between transmitted and acquired HIV-1 drug resistance in the Swiss HIV Cohort Study from

1998 to 2012," Wan-Lin Yang, Roger Kouyos, Alexandra U Scherrer, Jürg Böni, Cyril Shah, Sabine Yerly, Thomas Klimkait, Vincent Aubert, Hansjakob Furrer, Manuel Battegay, Matthias Cavassini, Enos Bernasconi, Pietro Vernazza, Leonhard Held, Bruno Ledergerber, Huldych F. Günthard, and the Swiss HIV Cohort Study (SHCS), *Journal of Infectious Diseases* DOI: 10.1093/infdis/jiv012