

Resistance

Once in your body, HIV replicates, making many new copies of itself very quickly. Each new generation of virus has small differences in structure. These are known as mutations. Many of these mutations are in the parts of the virus that are targeted by anti-HIV drugs and they can lead to the emergence of HIV strains which are less sensitive to treatment.

When you start your antiretroviral therapy, strains of virus that are highly sensitive to the drugs disappear quickly. However, other strains may reproduce in spite of the treatment: these are the so-called resistant viruses. Over time the amount of drug-sensitive virus will fall and the level of resistant virus will rise.

It is worth noting that in Europe and North America, more than 10% of new infections involve viral strains resistant to one or more anti-HIV drugs and that resistant viruses can become predominant within months of infection, limiting treatment options.

Minimizing the risk of resistance

It is very important you take your anti-HIV treatment exactly as prescribed, being strict with doses, taking it on time and following any food restrictions. If you take less medication than prescribed, the amount of the drug in your blood will fall, which gives the virus an opportunity to replicate and increases the risk of resistance developing.

Starting treatment with three or more anti-HIV drugs, as is current practice, prevents or at very least delays the emergence of resistance, because viruses resistant to one drug can be controlled by the other drugs in your regimen.

Several studies suggest that the risk of viral load rising again is linked to the lowest viral load (called the 'nadir') reached at the beginning of treatment. The lower the nadir viral load, the lower the risk of a rise in viral load and therefore the lower the risk of developing resistance. People whose viral load drops to undetectable levels (below 40-50 copies/ml, depending on the test) have a much lower risk of developing resistance. However, it can still emerge in the long term.

Adding or changing a single drug, in a drug regimen that is failing to suppress viral load, may lead to the emergence of resistance, since the impact of a single drug may not be enough to block the virus replication. In this case experts advise that where possible, you should change to a completely new combination of anti-HIV drugs.

Furthermore, if you stay on the same drugs when your viral load is starting to rise, it may lead to the emergence of resistance. This is because resistance to some drugs develops progressively. The more resistance mutations the virus has, the less sensitive it will be to drugs. However, resistance emerges at different rates. For instance, resistance to 3TC (lamivudine, EpiVir® and as part of Combivir® and Trizivir®), nevirapine (Viramune®) and efavirenz (Sustiva® and as part of Atripla®) emerges quickly.

Nevertheless, for some people whose viral loads remain high or have a blip when using an anti-HIV regimen, CD4 counts may continue to rise and the progression of the infection may be blocked, although there is not any clear explanation for this. Resistance is one of the reasons for an increased viral load, but not the only one.

Cross-resistance

Antiretroviral drugs belong to different classes or families, depending on their mechanism of action against HIV. A single mutation in the virus (i.e. a change in its structure), or a set of mutations, can generate resistance to several drugs from the same class. This means that once the virus develops resistance to one drug, it may also be resistant to other drugs from the same family, even if you haven't taken them. For instance, if HIV becomes resistant to a drug from the class of non-nucleoside reverse transcriptase inhibitors (NNRTIs), it can also be resistant to all drugs from this family. This is called cross-resistance. Again, continuing with a regimen that is failing to suppress your viral load to undetectable levels can lead to cross-resistance.

Resistance tests

Resistance tests have been developed with the aim of detecting which antiretroviral agents an individual's virus is resistant to and to what extent. Tests should be taken soon after HIV is first diagnosed, and again when starting treatment or whenever you need to change a regimen, to help guide the choice of drugs. Results should be included in your medical records (see *InfoVIHTal #47 Resistance tests*).