

RESISTING RESISTANCE

Created 4 Mar 2010 - 11:53am

HIV is able to replicate in our bodies by attaching itself to the CD4 receptors of key cells in our immune system. It then makes new copies of itself by hijacking our cells' genetic material. And it does this by a series of processes which result in around one billion new HIV particles being produced every day.

These processes rely on specially adapted chemical compounds called enzymes. HIV contains a number of enzymes including reverse transcriptase, protease and integrase. They are all necessary for HIV to replicate. Most HIV drugs work by 'inhibiting' the activity of these enzymes.

There are around 10,000 different points in the genetic material of HIV which may change during replication. Most of the time these changes are insignificant and your drugs will remain active against enough of these different strains to keep HIV under control.

However, sometimes enough changes occur so that your drugs are no longer able to control the [virus](#) [1]A small infective organism which is incapable of reproducing outside a host cell.. HIV is then said to have developed resistance. Note that it is HIV that has changed, not our bodies. It is HIV which has become [resistant](#) [2]HIV which has mutated and is less susceptible to the effects of one or more anti-HIV drugs is said to be resistant..

REDUCING YOUR RISK

Effective treatment reduces the amount of HIV found in your blood so that it can no longer be detected by [viral load](#) [3]A measurement of the quantity of HIV RNA in the blood. Viral load blood test results are expressed as the number of copies (of HIV) per milliliter of blood plasma. tests (generally below 40 or 50 copies of HIV in each millilitre of blood). With sufficient drug maintaining this pressure on HIV the possibility of mutations and thus resistance is very much reduced.

The doses prescribed are designed so that there will be sufficient drug present to do this 24/7. If you lower the dose to the point where HIV is able to replicate, the risk of developing resistance increases.

Many factors influence the amount of HIV drug in your blood. These include:

- The potency of the drugs themselves. Newer HIV drugs generally act more rapidly and more successfully suppress HIV.
- What else you take into your body. With some of the earlier drugs it was recommended we not drink grapefruit juice and, even now, St John's Wort is not recommended. This is because these things include components which interfere with the way HIV drugs are processed ('metabolised') in your body, particularly in the [liver](#) [4]
- The way HIV drugs are metabolised in your body. Men and women process some [antiretrovirals](#) [5]A medication or other substance which is active against retroviruses such as HIV. slightly differently. So do people of different racial backgrounds, body weights and those with other conditions and infections. HIV drugs are trialled taking into account these differences so that in general these factors are not so significant.
- Adherence. The timing and consistency with which you take your HIV drugs is by far the most important factor in determining the amount of drug in your blood. If you consistently take your pills, not missing or skipping doses, at the times prescribed by your doctor, and follow other instructions, your risk of developing resistance is hugely reduced. This is the one most important thing you can do to avoid drug resistance.

WHEN SHOULD YOU CONSIDER RESISTANCE AN ISSUE?

- If you are about to start treatment. In Australia the guidelines for using HIV drugs recommend that people should have a test to determine whether they have drug-resistant HIV when they are first diagnosed, and again when they are about to start treatment. The reason for this is you may have been infected with a strain of HIV which is already resistant to certain HIV drugs. If this is the case then treatment with that drug will almost certainly fail, so a substitute will be offered.
It is estimated that around 5% of HIV strains circulating in the Australian community are resistant to the

nucleoside reverse transcriptase inhibitor ([NRTI](#) [6]) A type of anti-HIV drug that works by inhibiting a stage of the HIV life cycle called reverse transcription. Non-nucleosides work in a similar way, but are chemically different.) class of drugs and around 12% are resistant to nonnucleoside reverse transcriptase inhibitors (NNRTI). Resistance to protease inhibitors (PI) is lower. And resistance to others including entry inhibitors and integrase inhibitors is not currently known. These figures will be different to other HIV strains circulating in other parts of the world. (Antiretroviral guidelines – Australian commentary)

If you have been on antiretroviral treatment but you're 'failing'. Virological failure occurs when your viral load increases or becomes detectable. Most of the time this is simply a 'blip' and your doctor will repeat the test. If virological failure is confirmed then generally this means that the HIV drugs you are taking are not doing their work and it is time to change. The most common cause for this is that your HIV has developed resistance.

HOW TO KNOW IF YOUR HIV IS DRUG RESISTANT?

Resistance is normally identified by having a 'resistance assay' or test
Your doctor will normally consider this if viral load becomes detectable over several tests.

Resistance assays are of two kinds: phenotypic assays which measure the ability of HIV to replicate in differing concentrations of HIV drugs; and genotypic assays which detect drug resistance mutations in the [genes](#) [7] The most basic unit of genetic information. within HIV.

Genotypic assays are normally offered to patients in Australia who are suspected of having HIV drug resistance. They normally need your viral load to be above 1000 copies of HIV per millilitre of blood. A blood sample is sent to the pathology laboratory and generally a result will be available within three weeks. This will show the mutations and provide an indication of whether the HIV you have is sensitive to a range of HIV drugs. With this knowledge your doctor will be able to suggest the most appropriate drug combinations to once again control your HIV.

Resistance is an issue for everyone on HIV treatment but you can reduce your risk by adhering to your medication regimen: by not missing doses, by having your doses on time and by following the other instructions. If you do develop resistance there are lots of options to get you back on track. With good compliance and better drugs, the risk of failing treatment is reducing all the time.

LINKS TO FURTHER READING

- [Aidsmap \(UK\) \(2009\) Adherence & resistance \[booklet\]](#) [8]
- [The Body \(2009\) Guide to HIV Drug Resistance \[booklet\]](#) [9]
- [NAPWA \(2009\) Resistance \(chapter in HIV Tests and Treatments\)](#) [10]

- [Understanding HIV treatments](#)
- [Treating HIV](#)
- [adherence](#)

Links:

- [1] <http://www.napwa.org.au/glossary/term/125>
- [2] <http://www.napwa.org.au/glossary/term/109>
- [3] <http://www.napwa.org.au/glossary/term/416>
- [4] <http://www.napwa.org.au/glossary/term/102>
- [5] <http://www.napwa.org.au/glossary/term/122>
- [6] <http://www.napwa.org.au/glossary/term/104>
- [7] <http://www.napwa.org.au/glossary/term/126>
- [8] <http://www.aidsmap.com/files/file1003808.pdf>
- [9] <http://www.thebody.com/multidrug/pdfs/resistance.pdf>

[10] <http://www.napwa.org.au/resource/hiv-tests-and-treatments/antiviral-treatments/resistance>