AIDS InfoNet **www.aidsinfonet.org** **Fact Sheet Number 126**

HIV RESISTANCE TESTING

WHAT IS RESISTANCE?

HIV is "resistant" to a drug if it keeps multiplying rapidly while you are taking the drug. Changes (mutations) in the virus cause resistance.

HIV mutates almost every time a new copy is made. Not every mutation causes resistance. The "wild type" virus is the most common form of HIV. Anything different from the wild type is considered a mutation.

An antiretroviral drug (ARV) won't control a virus that is resistant to it. It can "escape" from the drug. If you keep taking the drug, the resistant virus will multiply the fastest. This is called "selective pressure."

If you stop taking medications, there is no selective pressure. The wild type virus will multiply the fastest. Although tests may not detect any drug resistance, it might come back if you re-start the same drugs.

Resistance testing helps health care providers make better treatment decisions for their patients.

HOW DOES RESISTANCE DEVELOP?

HIV usually becomes resistant when it is not totally controlled by drugs someone is taking. However, more people are getting infected with HIV that is already resistant to one or more ARVs.

The more that HIV multiplies, the more mutations show up. These mutations happen by accident. The virus doesn't "figure out" which mutations will resist medications.

Just one mutation can make HIV resistant to some drugs. This is true for 3TC (Epivir) and the non-nucleoside reverse transcriptase inhibitors (NNRTIs). However, HIV has to go through a series of mutations to develop resistance to other drugs, including most protease inhibitors.

The best way to prevent resistance is to control HIV by taking strong ARVs. **If you miss doses of your medications, HIV will multiply more easily. More mutations will occur. Some of them could cause resistance.**

If you have to stop taking **any ARV, talk to your health care provider. You may have to stop some drugs sooner than others.** If you stop taking drugs while the virus is under control, you should be able to use them again.

TYPES OF RESISTANCE

There are three types of resistance:

- **Clinical resistance:** HIV multiplies rapidly in your body even though you're taking ARVs.
- **Phenotypic resistance:** HIV multiplies in a test tube when ARVs are added.
- **Genotypic resistance:** The genetic code of HIV has mutations that are linked to drug resistance.

Clinical resistance shows up as a higher viral load, lower CD4 count, or opportunistic infections (see Fact Sheet 500). Laboratory tests can measure phenotypic and genotypic resistance.

PHENOTYPIC TESTING

A sample of HIV is grown in the laboratory. A dose of one ARV is added. The growth rate of the HIV is compared to the rate of wild type virus. If the sample grows more than normal, it is resistant to the medication.

Phenotypic resistance is reported as "fold" resistance. If the test sample grows twenty times as much as normal, it has "20-fold resistance."

Phenotypic tests cost about $800. It used to take over a month to get the results. New phenotypic tests are somewhat quicker.

GENOTYPIC TESTING

The genetic code of the sample virus is compared to the wild type. The code is a long chain of molecules called nucleotides. Each group of three nucleotides, called a "codon," defines a particular amino acid used to build a new virus.

Mutations are described by a combination of letters and numbers, for example K103N. The first letter (K) is the code for the amino acid in the wild type virus. The number (103) identifies the position of the codon. The second letter (N) is the code for the "changed" amino acid in the mutant sample.

Genotypic testing costs about $250. Results come back in about two weeks.

VIRTUAL PHENOTYPE

This test is really a method of interpreting genotypic test results. First, genotypic testing is done on the sample. Phenotypic test results for other virus samples with a similar genotypic pattern are taken from a database. These matched samples tell you how the virus is likely to behave. The virtual phenotype is faster and less expensive than a phenotypic test.

CROSS-RESISTANCE

Sometimes a mutant version of HIV is resistant to more than one drug. When this happens, the drugs are called "cross-resistant." For example, most HIV that is resistant to nevirapine (Viramune) is also resistant to efavirenz (Sustiva). This means that nevirapine and efavirenz are cross-resistant.

Cross-resistance is important when you change medications. You need to choose new drugs that are not cross-resistant to drugs you've already taken.

We do not totally understand cross-resistance. However, many drugs are at least partly cross-resistant. As HIV develops more mutations, it gets harder to control. **Take every dose** of your ARVs according to instructions. This reduces the risk of resistance and cross-resistance. It saves the most options for changing medications in the future.

PROBLEMS WITH RESISTANCE TESTING

Resistance tests are not available everywhere. They are expensive. However, they are becoming more common, faster, and cheaper.

The tests aren't good at detecting "minority" mutations (less than 20% of the virus population). Also, they work better when the viral load is higher. If your viral load is very low, the tests might not work. Tests usually cannot be run if the patient's viral load is less than 500 to 1,000 copies per ml.

Test results can be difficult to understand. Drugs that should work according to the tests sometimes don't work, and vice versa. Sometimes genotypic and phenotypic tests give conflicting results for the same patient. Some mutations can "reverse" or reduce resistance to some medications.

Despite these problems, many researchers believe that resistance testing should be a normal part of HIV treatment. More physicians will probably use resistance testing before choosing someone's first ARVs to see if they were infected by drug-resistant virus.

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