



# HIV Resistance Testing

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## WHAT IS HIV DRUG RESISTANCE?

HIV medications work by preventing the virus from replicating (making copies of itself). When a particular strain of HIV is able to make copies of itself, even in the presence of a particular [antiretroviral medicine \(ARV\)](#), we say that it is drug resistant.

HIV drug resistance is caused by changes in the genetic structure of HIV that affect the ability of drugs to block the replication of the virus. Every time the virus makes a copy of itself, changes (mutations) occur that may cause drug resistance. All current ARVs, including newer classes, are at risk of becoming partly or fully inactive because of the emergence of drug-resistant virus strains. If not prevented, HIV drug resistance can jeopardize the efficacy of ARVs, resulting in increased numbers of HIV infections and HIV-associated complications and deaths.

HIV drug resistance isn't an all-or-nothing condition. People with HIV may have one or several drug-resistant mutations that make them less sensitive to one or more ARVs. For example, if someone has protease mutations, their HIV is resistant to [protease inhibitors \(PIs\)](#), meaning that a drug like [darunavir \(Prezista\)](#) may not work for them. Someone with [nucleoside reverse transcriptase inhibitor \(NRTI\)](#) mutations may be resistant to a drug like [emtricitabine \(Emtriva\)](#).

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

## HOW DOES HIV DRUG RESISTANCE DEVELOP?

**Transmitted HIV drug resistance** occurs when a person who has never been on treatment before acquires a strain of HIV that is already resistant to one or more HIV drugs. Transmitted drug resistance, as the name implies, occurs when a strain of HIV with drug-resistant mutations gets transmitted from a person with HIV to an HIV-negative person. The prevalence of transmitted drug resistance is estimated to be between 12-24% among people with HIV in the U.S.

**Pre-treatment HIV drug resistance** can occur before treatment is started. This may occur if a person is exposed to HIV medications before they become infected with HIV. For instance, if a [pregnant person](#) is taking drugs for prevention of [perinatal transmission](#) or if a person is taking [pre-exposure prophylaxis \(PrEP\)](#), and then that person becomes infected with HIV, it is theoretically possible for that person to develop drug-resistance. Remember, however, that it is rare for drug resistant mutations to develop from a person taking PrEP.

**Acquired HIV drug resistance** can happen when a person has HIV that is replicating even though they are taking one or more ARVs. HIV can mutate around that medication. This will result in HIV being resistant to the

medications and those medications now being ineffective. In most studies, more than 70-80% of people with virologic failure develop acquired HIV drug resistance. (Keep in mind that once a person becomes [virally suppressed](#), these drug resistant mutations are no longer an issue.)

Just one mutation can make HIV resistant to some drugs. This is true for [lamivudine \(Epivir\)](#) 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 PIs.

## **HOW DO YOU PREVENT HIV DRUG RESISTANCE?**

People with HIV can prevent drug resistance by remaining on treatment and [adhering](#) to their medication regimens. With current [antiretroviral treatment \(ART\)](#) regimens, adherence commonly means taking medications once a day or every 1-2 months for long acting injectable medications.

To avoid the development of ARV resistance, it is recommended that individuals with HIV be treated with a combination of drugs that are from two different classes of ARVs. This is known as highly active antiretroviral therapy or HAART. There are many different ARVs approved by the U.S. Food and Drug Administration (FDA).

In general, if you forget to take a dose, take your medication as soon as you realize you've missed the dose. However, if it's almost time for your next dose, just wait until your next dose and continue your regular routine. Most important, do not take a double dose; you cannot make up for a missed dose that way. Although it's important to take your HIV medications every day, you likely will not develop drug resistance from missing just one medication dose.

## **WHAT IS HIV DRUG RESISTANCE TESTING?**

HIV drug resistance testing is used to help select a drug regimen that will likely be effective in treating your HIV infection. The test is used to determine whether the HIV strain infecting you is resistant to one or more ARVs. Testing analyzes the genes of the virus to detect the presence of one or more mutations that are associated with ARV resistance.

When you are first diagnosed, HIV drug resistance testing is used to determine whether the HIV strain you have is already resistant to one or more drugs. The information is used to identify and select the ARVs that will likely be effective.

HIV drug resistance testing may also be used after you begin treatment to help determine the cause of drug treatment failure. Treatment failure is identified when your HIV [viral load](#) does not decrease or begins to increase despite treatment. In this case, your treatment will likely be changed. Results of drug resistance testing may help you and your healthcare provider select a different drug regimen that may be effective in suppressing the virus. Testing is used to identify resistance to ARVs in classes such as:

- [Protease inhibitors \(PIs\)](#)
- [Nucleoside reverse transcriptase inhibitors \(NRTIs\)](#)
- [Integrase inhibitors](#)

There are two types of resistance tests: genotype testing and phenotype testing.

**Genotype tests** look for drug resistance mutations in relevant genes of the virus. Most genotype tests

involve looking at the reverse transcriptase (RT), protease (PR), and integrase (IN) genes to see whether there are mutations that are known to be associated with drug resistance. These genes are essential for HIV to take over cells and replicate, so these are the same genes that the different classes of drugs take action against to stop HIV from replicating. For example, two drug classes are known as protease inhibitors and integrase inhibitors, because they inhibit the protease and integrase genes.

Genotypic testing is the preferred method for people having problems with their first or second treatment regimen.

**Phenotype tests** measure the ability of the virus to replicate in different concentrations of ARVs. A sample of HIV is grown in the laboratory and a dose of one or more ARVs is added. If the sample grows more than normal, it is resistant to the medication. This test is typically done in individuals who have been on treatment and who have more complicated drug resistance patterns.

Phenotypic testing is the preferred method for people with known or suspected resistance, especially to protease inhibitors.

### **WHAT IS 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.

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.

### **HOW DO YOU KNOW IF YOU HAVE DEVELOPED HIV DRUG RESISTANCE?**

HIV drug-resistance testing is recommended at entry into care for people with HIV to guide selection of the initial ART regimen. However, ART initiation should not be delayed while awaiting resistance testing results; the regimen can be modified once results are reported.

It's important for your healthcare provider to know if you have or develop any drug resistance mutations, which is why it's important for you to complete and follow-up with clinical and lab monitoring plans.

If you're already on treatment, and you suddenly experience a detectable viral load, that doesn't automatically mean your treatment regimen is failing or that you have drug resistance. This may be just a viral load blip and continuing to take your HIV medications will bring your viral load back to undetectable. You and your healthcare provider will make a decision based on your viral load and specific case.

In general, HIV drug resistance testing is recommended at the following times:

- If your viral load goes above 1,000 copies/mL.
- If your viral load goes above 500 copies/mL, but remains below 1,000 copies/mL, drug resistance

- testing may not be successful, but is still worth considering.
- If your treatment regimen is not lowering your viral load as quickly as it should.

## **THE BOTTOM LINE**

Mutations in the genetic material of HIV may make some strains of the virus resistant to medications used to treat it. In people with HIV, drug resistance testing is used to determine whether the strain causing the infection is resistant to one or more ARVs.

People living with HIV should be tested when first diagnosed with HIV and immediately prior to the start of ART. In addition, drug resistance testing is performed during ART whenever the viral load does not decrease or begins to rise steadily.

## **MORE INFORMATION**

HIV.gov: [Drug Resistance Testing Guidelines](#)

HIVinfo.NIH.gov: [FDA-Approved HIV Medicines](#)

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