What You Need to Know About HIV Drug Resistance

Taking medications consistently is the best way to avoid resistance mutations.

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Effective antiretroviral therapy has made the fight against HIV much easier, but treatment still involves challenges, including drug resistance. When resistance occurs, medications can stop working, leading to disease progression and raising the risk for HIV transmission. What's more, some mutations confer cross-resistance to related drugs, limiting future treatment options.

Fortunately, modern antiretrovirals are more potent, so the virus is not able to defeat them as easily. But it's still important to take your HIV medications as directed and to receive recommended monitoring tests to ensure your treatment is working.

Drug resistance refers to HIV's ability to continue multiplying in the presence of drugs that usually disable it. This occurs when the virus develops mutations, or changes in its genetic code. These changes alter HIV proteins, including the reverse transcriptase, protease and integrase enzymes the virus uses to replicate. Certain antiretroviral classes have a higher barrier to resistance, meaning HIV must mutate more to compromise their effectiveness.

In some cases, people acquire a strain of HIV that already has resistance mutations. In other cases, they initially have nonresistant, or "wild type," virus that later develops these mutations. This is most likely to happen if a person doesn't always take their antiretrovirals on schedule. Missing doses can lead to low drug levels, which allows the virus to replicate and accumulate mutations.

Resistance can also occur when HIV meds are not properly absorbed, resulting in drug levels that are too low to fully control the virus. Certain drugs, for example, must be taken with food or on an empty stomach to be fully absorbed. Drug interactions can interfere with absorption too.

Finally, resistance mutations can evolve if a person uses only one drug that is active against the virus, known as monotherapy. Combining drugs that target different steps of the HIV life cycle

makes it harder for the virus to overcome the meds. Some people who used less potent antiretrovirals one at a time early in the epidemic have multidrug-resistant HIV, making it harder to construct a fully suppressive regimen.

A viral load test often gives the first indication of drug resistance. If your HIV RNA level does not drop soon after starting therapy or if it starts going up while on treatment, this may be due to resistance.

Resistance testing can help determine whether HIV is no longer susceptible to your medications. Tests may also be done before starting treatment or when switching to a new regimen to help determine which drugs are most likely to work well. Genotypic tests examine HIV's genetic sequence to see whether it contains known resistance mutations, while phenotypic tests show whether HIV in a blood sample can still replicate when exposed to drugs in a laboratory.

People living with HIV can take steps to reduce the likelihood of drug resistance. Start treatment with a potent combination regimen, which offers the best chance of fully suppressing the virus. When switching meds, pick a potent new regimen that is well tolerated and easy to use. Take your medications exactly as prescribed, which usually means every day. Tell your health care provider if you struggle with adherence—some meds are more forgiving of occasional missed doses. Get regular monitoring tests to ensure that your treatment is working.

Today's antiretrovirals are very effective if taken consistently. Most people starting treatment for the first time can find a regimen that keeps their viral load suppressed over the long term, which minimizes the risk of resistance. Putting together an effective regimen is more challenging for treatment-experienced people, but most can still get their HIV under control with modern meds.

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