

So you want to take a break...

Know the risks of stopping treatment

by Dr. Mona Loutfy

Yes, you're thankful that there are now effective drugs to treat HIV. And yes, you know that they're extending your life and keeping you relatively healthy. But there may come a time when taking antiretrovirals seems so limiting, or side effects sap your energy so much that you just want to stop. Can you? Is it possible to take a break from treatment without letting the virus run rampant? There are no guarantees, but the answer seems to be, under some very narrow circumstances, a cautious yes.

People living with HIV often grow frustrated with the difficult drug regimens needed to keep the disease in check, especially if they've been on treatment for several years. The idea of taking a break becomes especially appealing for people suffering from side effects. These are the unfortunate backlash of very effective highly active antiretroviral therapy — (HAART) that can help keep viral levels low and CD4 counts high.

Is it safe?

The most important factor when considering treatment interruption is safety. The last thing anyone living with HIV wants is to make changes that will cause their viral loads to rise and CD4 counts to drop. Early research seemed to find some advantages in treatment interruptions, but more recent studies counter the theory that treatment interruptions are beneficial. It is clear that when antiretroviral drugs are stopped, a rapid and brisk re-emergence of HIV-1 occurs; similar to when a person is first infected, called acute retroviral syndrome (ARS). In some cases, this can lead to symptoms similar to those you can get when first infected with HIV, followed by an



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abrupt fall in CD4 count and the development of opportunistic infections. Also, depending on how the treatment is stopped, HIV can become resistant to antiretrovirals, making them unable to keep viral loads low after you resume treatment.

When not to stop

If you're receiving HAART immediately after being infected with HIV, you should not stop therapy until your doctor deems it safe. Treatment at this stage of infection can help to develop and preserve a strong immune response against HIV. Yet the long-term clinical benefits of this approach are not proven. There are some major risks to interruptions, including the development of drug resistant mutations and uncontrolled viral loads, and no proven benefits.

When to consider

Some people living with HIV can consider a treatment interruption without too much risk, but there are always pros and cons associated with the decision. The most important issue here is your nadir CD4 count, which is the lowest CD4 value you've had. This will be the guiding factor in whether you can interrupt treatment without becoming sick or jeopardizing the effectiveness of future drug therapy.

Chronic, controlled infection

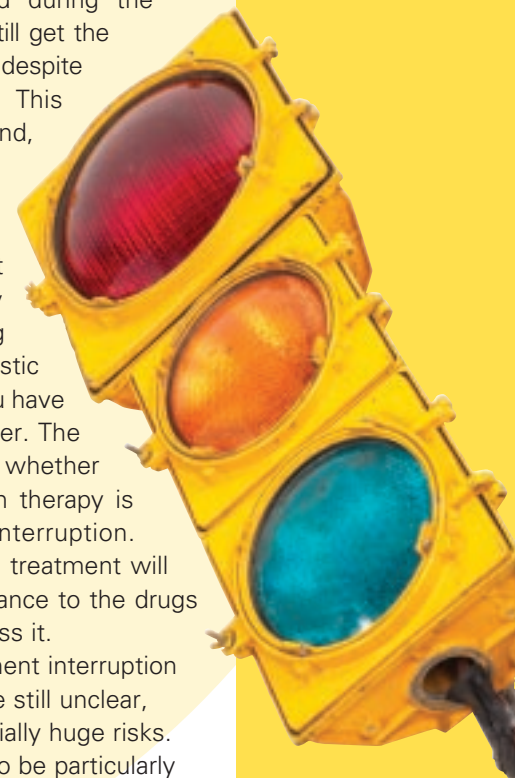
If your viral load has been undetectable (less than 50 copies/mL) for over a year, and your nadir CD4 was 350 or more, you may be able to interrupt treatment without negative consequences and benefit from a break from drugs and their side effects. You could also consider interrupting therapy if your

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nadir was between 200 and 350 but this should be done cautiously, due to an increased risk of developing opportunistic infections. In some people, immune function is maintained during the interruption, meaning that they still get the benefits of antiretroviral therapy despite decreased exposure to drugs. This brings relief from side effects and, in theory, might also decrease long-term toxicity associated with the drug regimen.

However, it's also possible that your CD4 count will fall rapidly after you stop treatment, leaving you vulnerable to an opportunistic infection. This is more likely if you have a nadir CD4 count of 200 or lower. The other important consideration is whether HIV can be re-suppressed when therapy is resumed after a treatment interruption. There's a chance that a break in treatment will allow the virus to develop resistance to the drugs that once worked well to suppress it.

While the benefits of a treatment interruption in chronic controlled infection are still unclear, there are well-known and potentially huge risks. Treatment interruptions appear to be particularly problematic with drugs like efavirenz (Sustiva®) or nevirapine (Viramune®) because they have longer half-lives (take longer to break down in the body)



and lower genetic barriers to resistance, meaning the chance of becoming resistant to these treatments is higher than with other drugs.

Warnings

If your viral load is currently well controlled but you had a CD4 count of less than 200 at any time in the past, a treatment interruption is very risky and your doctor will likely advise against it. Your CD4 count could fall abruptly and leave you open to opportunistic infections.

If your CD4 count has always been above 200, your doctor will be able to help you weigh the risks and benefits and come up with a plan to stop treatment as safely as possible and monitor you carefully while you're off treatment. Drugs with longer half-lives, such as NNRTIs (Non-nucleoside

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reverse transcriptase inhibitors), should be stopped earlier than others. During the interruption, it's very important to have your CD4 count, and possibly also your viral load, measured regularly to be sure your CD4 counts don't fall too quickly. You'll also want to stay in close touch with your healthcare team and alert them immediately to any changes in your health.

Virologic failure with multidrug resistance

Virologic failure is when your meds are either failing to bring your viral load down to undetectable levels, or are allowing viral load rebounds, meaning the viral load becomes consistently detectable again after being undetectable. Multidrug resistance is when HIV has mutated and become resistant to the action of a number of different antiretrovirals (ARV). This means your meds are no longer working as well to fight off HIV. People with both virologic failure and multidrug resistance may consider taking a break from treatment.

A treatment interruption may allow the ARV-resistant HIV to revert to "wild-type" HIV, the original strain that first entered the body. This original "wild type" HIV mutated to become ARV-resistant, but in the absence of antiretrovirals, the wild-type virus may become stronger than the mutation and replace the ARV-resistant virus. An early study showed that ARVs to which you were previously resistant may start working again when you resume therapy and allow for better control of HIV. However, other reports including one large study showed this didn't work and may even be dangerous. CD4 cell counts may drop quickly during the treatment interruption, and the response to the next regimen is likely to be short-lived. So when your current treatment is failing, it might be better to start a new regimen as soon as possible, rather than taking a break.

The main benefit of a treatment interruption is that it gives a break from treatment and allows people to recover from side effects. However, there's always the risk that CD4 count will fall abruptly after stopping therapy, especially if you had a low nadir CD4 count (200 or less). This could result in the development of an opportunistic infection.

Anyone contemplating a treatment interruption should consult their doctor about the potential risks and benefits, and plan the interruption carefully.

Take the long view

When considering a treatment interruption, you must question whether the temporary benefits — no more pill-taking at intervals throughout the day, a break from side effects and dietary restrictions — outweigh the potential risks. The dangers associated with stopping treatment are numerous and potentially life-threatening. Your virus could become resistant to ARVs and thus limit your future treatment options. Your CD4 count could drop so low that you start developing opportunistic infections. The latest strategy being studied is CD4-driven interruptions, where people living with HIV are taking breaks when their CD4 is higher than 500 and resuming treatment when it reaches 350. Don't make up your mind before discussing it with your doctor and healthcare team. Talk to other people living with HIV who've tried treatment interruptions. Many AIDS Service Organizations (listed on pages 8-9) can offer additional treatment information as well as suggestions on how to deal with the side effects that might be contributing to your decision. Before you take this kind of break, look at the alternatives and be sure you're not paying too high a price for a brief respite. **R**

