

because you asked

Slow rising CD4s

“My viral load is undetectable, but my CD4 count is rising incredibly slowly. Is this normal?”

Dr Alex Klein responds: Your question is a good one. The answer, as you might expect, is not straightforward.

Antiretroviral (ARV) drugs attack the HIV virus, which destroys CD4 cells. These drugs don't directly affect the number of CD4 cells in your blood, but by suppressing viral replication, they do give your body a chance to rebuild. How long that will take varies from one person to the next, but if you stay on your medication and maintain an **undetectable viral load**, your CD4 count will continue to gradually increase. After years of therapy, CD4 counts and other “markers” of immune strength return to normal in many individuals.

There are lots of reasons why your CD4 cells may be taking a little longer to get there. If your CD4 count was very low when you started treatment, your recovery will be slower. The duration of infection is another factor: the longer you've been infected with HIV, the longer it will take to rebuild your CD4 stores. Older people tend to recover CD4 cells more slowly. Other infections, such as hepatitis and chronic liver or kidney disease may also delay the body's rebuilding process.

Ironically, some ARVs can have negative effects on your CD4 levels. AZT (Retrovir®, also found in Combivir® and Trizivir®) can suppress the bone marrow, which is where new CD4 cells are made. The combination of ddI (Videx®) and tenofovir (Viread®, also found in Atripla™ and Truvada®) has been known to significantly reduce the anticipated CD4 response in some people (even if the viral load is undetectable), particularly in individuals who have low numbers to begin with.

Staying healthy and eating well are also important for helping your immune system recover. Not getting enough rest or using recreational drugs, especially crystal methamphetamine, can have a profound negative impact. You should also review the non-HIV specific medications you are taking with your doctor to see if any of them could be playing a role.

Several medications that increase CD4 levels are currently in clinical trials. An important study of interleukin-2 (the SILCAAT trial), for example, has just closed and the results should be available in the near future. Although not yet available in the clinic, we may see it as a treatment soon.

The most important message I can relay is that you shouldn't be discouraged by your apparent slow response. It's certainly important to achieve a level above about 200 cells/mm³, which is the threshold at which risk of opportunistic infections become high. More is always better, but even a few CD4 cells can make the difference between staying healthy and getting sick.

Switching back

“If I decide to go off one of my ARV medications because of side effects, can I still go back to it later if I want or need to?”

Dr. Marianne Harris responds: That depends on the type of side effect you're referring to. Some side effects will always come back if you restart the same medication and can be very serious the second time around. This is the case with allergic reactions such as abacavir (Ziagen®) hypersensitivity and severe rash or liver problems with nevirapine (Viramune®). If these occur, you should never go back on that medication again, including “fixed dose combination pills” that contain it. Abacavir, for example, is available not only alone as Ziagen®, but is also in Kivexa® (with 3TC) and Trizivir® (with AZT and 3TC). All of these medications must be avoided if you are diagnosed with a hypersensitivity to abacavir, as the next reaction can be severe and even fatal.

On the other hand, some side effects are more variable and may be related to other factors, such as the other medications you were taking at the same time. So if you take the same medication again later, the side effects may be less severe or not happen at all. For example, nausea, diarrhea and other gastrointestinal (GI) side effects can occur with PIs, especially ritonavir (Norvir®). These may be more bothersome with some PIs (e.g. Kaletra® [lopinavir/ritonavir]) and less with others (e.g. Reyataz® [atazanavir/ritonavir] or Prezista™ [darunavir/ritonavir]).

Dr. Alex Klein is an HIV primary care physician in private practice and a family practitioner at Mount Sinai Hospital in Toronto.

Dr. Mark Hull is an Infectious Diseases specialist at the University of British Columbia. He's currently working as a Postdoctoral Fellow with the Canadian HIV Clinical Trials Network at the BC Centre for Excellence in HIV/AIDS.

Dr. Marianne Harris is a family doctor who currently works with the AIDS Research Program at the Immunodeficiency Clinic in St. Paul's Hospital, Vancouver.

Also, GI symptoms might be worse if you're taking your PI with other meds also known to cause GI upset, such as AZT (Retrovir®) or ddI (Videx®, Videx EC®). If you take the same PI again with newer ARVs such as Truvada® (tenofovir/FTC) or Kivexa® (abacavir/3TC), your GI problems may not be as bad.

If the side effect that leads you to stop your medication is lipodystrophy, less is known about whether it's likely to recur if you take the same medication again. It probably will, again depending on which other medications you are taking with it. Luckily some of the newer ARVs are less likely to cause lipodystrophy than the older ones, so you may have more options the next time around.

People often think that if they stop taking a drug, it will no longer work if they ever decide to go back to it. But if the medication in question was effective and no resistance developed, there's no reason why you can't go back to it if you want or need to.

Hope for Hep C

"I'm co-infected with hepatitis C and have heard that the treatment is very difficult. Are there any new drugs on the horizon?"

Dr. Mark Hull responds: Let me first say that you're not alone. We estimate that at least 20% of Canadians living with HIV are co-infected with hepatitis C (HCV).

About 5-10% of co-infected individuals will clear the HCV infection on their own.

The rest must have a series of tests (including liver enzyme tests or a liver biopsy) to determine if treatment would be appropriate for them. The standard drug regimen for those who are treated is a combination of pegylated interferon and ribavirin, two antiviral agents with activity against HCV.

Pegylated interferon is given by injection every week, while ribavirin is a pill that you have to take every day. Therapy usually lasts between 24 and 48 weeks, based on the **genotype**, or strain of HCV you're infected with.

The success of treatment ranges from 29-62%, depending, in large part, on the underlying HCV genotype. Side effects include flu-like symptoms (joint aches, muscle pains, fevers and headaches), dry skin, itchiness and rashes. More serious side effects include bone



marrow suppression, which can cause anemia, low platelets or low white cell count. Pegylated interferon has also been linked to depression, which can sometimes be severe.

For all these reasons, there's lots of interest in developing new treatments for HCV. These include:

- **Protease and polymerase inhibitors:** medications that target the proteins HCV needs to replicate. One of the most promising is a compound known as telaprevir (or VX-950). In people infected with HCV (but not HIV), the triple combination of pegylated interferon, ribavirin and telaprevir was more successful than standard treatment, with response rates of 61-65%. The next round of clinical trials is now being planned.
- **New formulations of interferon** that would allow the drug to be given less often may significantly reduce the number of side effects.
- **Nitazoxanide:** an antibiotic that seems to work against HCV. So far, a small trial has shown that adding nitazoxanide to standard therapy made it more effective against HCV genotype 4.

New therapies are still several years away and when they do become available, they will probably be used in combination with pegylated interferon and ribavirin. Delaying treatment in the hopes of being able to avoid this therapy is probably not a good idea at this stage. Talk to your doctor about the likelihood your treatment will be successful and your personal risk of side effects. **R**

Is there something
you need to know?
Please send your questions to:
relay@parkpub.com

9

