

Treatments

This chapter provides an overview of all the main questions about HIV treatment—when to start, what to use and how to make it work.

Since treatment information can be complex and changes quickly, we have written this chapter as a general introduction to the major treatment issues that you may face as a person living with HIV. However, as you begin to make treatment decisions, you may want more detailed and current information than this chapter provides. At the end of the chapter, you can find further resources by CATIE and others that provide more in-depth information on the treatment topics covered here.



About the author

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Sooner or later, most people with HIV do have to go on treatment.

Treatment decisions: the pros and cons

Having HIV doesn't necessarily mean you will need to go on anti-HIV treatment, known as highly active antiretroviral therapy (HAART)—at least, not right away. But, sooner or later, most people with HIV do have to go on treatment. The best time to start varies. Since HAART can't cure HIV infection, starting treatment involves a trade-off: when do the benefits of going on treatment outweigh the benefits of staying off? The benefits of successful treatment include:

- **Controlling the virus:** HAART reduces HIV's ability to make copies of itself (see page 131–132). It forces the virus down to extremely low levels and partly protects the body from the ongoing effects of infection and immune system activation.
- **Immune system restoration:** people on HAART usually see significant increases in their CD4+ cell counts. This means a stronger immune system that's better able to fight off infections (see Chapter 9, Monitoring your health).
- **Slowing or reversing disease progression:** as the immune system strengthens, the risk of life-threatening infections drops, and many of the other, less serious symptoms of HIV infection diminish or disappear (see Chapter 12, HIV-related infections and cancers).

If that all seems a bit abstract, let's be blunt. Left untreated, HIV can kill you. Treatment can save your life. We often tiptoe around that frightening fact, but sometimes it's best to look it in the face.

Naturally, when making decisions about treatment, the benefits, or pros have to be weighed against the potential problems, or cons. These include:

- side effects and toxicities, both short term and long term;
- the difficulty of adherence: sticking to a drug schedule for the rest of your life.

An important question for people with HIV is this: when should you start treatment so that you have good health and long-term quality of life? There is no single answer—but that's a far cry from saying nobody knows. The experience of hundreds of thousands of HIV-positive people has been carefully evaluated.

This has given us guidelines to help guide treatment decisions. These guidelines provide answers to many questions, while allowing for more give and take in other areas. They also change as our knowledge grows.

In this chapter, we will walk you through the biggest questions of anti-HIV therapy—the when, what and how of treatment. Since treatment changes rapidly, with new drugs and new information constantly becoming available, this chapter is only meant as a starting point. Treatment decisions will always have to be made with your doctor and healthcare team, using the best and most up-to-date information.

Where do treatment guidelines come from?

Groups of experts from around the world meet regularly to agree on recommendations for the use of HIV treatments. The treatment guidelines are long, comprehensive documents that incorporate evidence from hundreds of studies. They include the most up-to-date answers to treatment questions like when to start, what to take and when to switch. If you have Internet access, you can review the most recent HIV treatment guidelines at these websites:

- www.aidsinfo.nih.gov (U.S. Department of Health and Human Services—DHHS). *Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents.*
- www.cfenet.ubc.ca (British Columbia Centre for Excellence in HIV/AIDS). *Therapeutic guidelines: Antiretroviral therapy for HIV-1-infected adults.*
- www.bhiva.org (British HIV Association). *Treatment of HIV-1 infected adults with antiretroviral therapy.*
- www.eacs.eu (The European AIDS Clinical Society). *Guidelines for the clinical management and treatment of HIV-infected adults in Europe.*
- www.msss.gouv.qc.ca/sujets/prob_sante/itss/index.php?aid=132 (Le ministère de la Santé et des Services sociaux du Québec) *La thérapie antirétrovirale pour les adultes infectés par le VIH – Guide pour les professionnels de la santé du Québec* (available in French only).

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Once you start HAART, you will be taking it for a very long time, probably the rest of your life. Spending the time to think some things through *before* you start can better your chances of success.

Before you start

There are many things to consider before deciding to start HIV treatment. Once you start HAART, you will be taking it for a very long time, probably the rest of your life. Spending the time to think some things through *before* you start can better your chances of success.

First of all, assess your overall health. Have you had any HIV-related illnesses, such as *Pneumocystis pneumonia* (see Chapter 12, HIV-related infections and cancers)? Have you had infections that keep coming back? Have you had ongoing symptoms like chronic fatigue, weight loss, skin problems or diarrhea? If any of these are true, you may not be able to wait—these problems could signal a need to get on treatment right away. See *When to start* on page 130.

Health conditions that are not related to HIV can influence your treatment decisions, leading you to decide to start treatment earlier than you otherwise would have, or to postpone treatment. For example, if you are pregnant, you may need to start treatment to reduce the chance your baby will have HIV. If you're depressed or using recreational drugs or alcohol a lot, you might have trouble sticking to a strict medication schedule. In this case, it may be better for your health to postpone HIV treatment until you have your mental health and/or substance use issues cleared up. Everyone with HIV should have a thorough, head-to-toe checkup and medical history review to catch everything that might be relevant.

Keep track of your CD4+ cell count and your viral load (see Chapter 9, *Monitoring your health*). Unless your CD4+ cell count is already extremely low, it's better to make decisions based on trends rather than the results of a single test. Have your CD4+ cell counts been falling? Is your viral load high or has it recently increased significantly? If so, you might need treatment sooner rather than later.

Consider how you feel about anti-HIV drugs. Some people have strong feelings of scepticism, fear or distaste about taking them. They may feel that taking anti-HIV drugs every day is a constant reminder of living with HIV. It's important to discuss such feelings with your doctor and work through them. If you're looking at each pill thinking, "I don't want to take this," that's a difficult emotional situation to be living with every day—and a set-up for poor adherence and treatment failure.

Think about the practical impact that treatment could have on your life. Consider when and where you might have to take your drugs, such as on vacation, at work, on the street, across the border or out socializing. If there are going to be any issues, it's better to think them through beforehand.

You'll definitely want to consider possible side effects. Not everyone will have significant side effects; for some they may be short-lived, mild or barely noticeable. However, for many others, side effects may be much more severe (see Chapter 11, Side effects and symptoms).

Nobody wants to live with side effects but, realistically, they may be something you have to deal with. Decide where you're willing to draw the line. Remembering that HIV endangers your life, what are you willing to put up with in exchange for that? Side effects vary with specific treatments, so this may mean some practical trade-offs: would you rather risk diarrhea or sleeping poorly? Higher cholesterol or visibly losing fat? With luck, you may not encounter any of these things, but it's important for you to know what side effects you may have and to prepare yourself, emotionally and practically, to deal with them.

Try to learn as much as you can about side effects and how to cope with them before making treatment choices. Chapter 11 (Side effects and symptoms) explains many ways to help prevent or lessen side effects. By considering these issues before starting treatment, you will give yourself the best chance of not just living longer with HIV, but living well.

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Treatment-related definitions

- *Side effects* refers to an unintended reaction to a drug.
- A *drug interaction* occurs when two or more drugs increase or decrease each others' levels in your bloodstream. This may result in side effects, or in the drug becoming ineffective.
- *Drug toxicity* happens when the level of drug in your bloodstream is too high, which may also result in unwanted side effects.

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Deciding when to start drug treatment is often one of the toughest choices a person with HIV has to make.

Even during the phase of HIV disease that we call asymptomatic, HIV is creating an ongoing process of inflammation in our bodies, particularly in the gut, brain and heart, which has a negative effect on our health.

When to start?

Deciding when to start drug treatment is often one of the toughest choices a person with HIV has to make. This decision means choosing the best margin of safety: at what point does your HIV infection pose more risk than treatment does? The answer to that is based on:

- your medical health history (that is, how long you've been infected, your symptoms, co-infections and illnesses);
- your CD4+ cell count;
- your HIV viral load;
- whether you are pregnant or thinking about pregnancy;
- the emerging understanding of the early and ongoing impact of HIV on our body.

Treatment should definitely be started if:

- You have had serious symptoms or illness (symptomatic infection) related to HIV infection, regardless of your CD4+ cell count or anything else, see Chapter 12 (HIV-related infections and cancers). Even if you've recovered, you may be at immediate risk of getting seriously sick again without treatment.
- Your CD4+ cell counts are very low. (As we learn more, guidelines can change on how low CD4+ cell counts can safely fall before starting treatment is recommended. Make sure you consult the most up-to-date information.)
- You are pregnant, to prevent transmitting HIV to your baby. This is regardless of your CD+ cell count or your viral load. Usually once you start anti-HIV drugs, you continue for the rest of your life. In pregnancy, women with HIV may use anti-HIV drugs just during their pregnancy and then stop after the baby is born (see Chapter 15, HIV and women).

Getting on treatment immediately will let your immune system rebuild itself until you're no longer in immediate danger of infections.

If you have not had any HIV-related symptoms (that is, you are asymptomatic), your viral load is low, your CD4+ cell counts are high and your overall health is good, you and your doctor may decide to postpone starting treatment. Your own readiness to start treatment will be crucial as well.

For people who have not experienced serious symptoms or illnesses related to HIV and who have a relatively high CD4+ cell count, expert opinion on the best time to start treatment has swung back and forth. Ongoing studies keep tracking which treatment choices (starting earlier or starting later) lead to the best long-term outcomes. This means weighing the long-term effects of treatment against the effects of having HIV for a long time—something that is not always easy to analyze. As research reveals more about HIV, we are coming to understand that even during the phase of HIV disease that we call asymptomatic, HIV is creating an ongoing process of inflammation in our bodies, particularly in the gut, brain and heart, which has a negative effect on our health.

It's important to get the most up-to-date information, and to discuss the issue of when to start treatment carefully with your doctor. Delaying treatment may call for more frequent testing of viral load and CD4+ cell counts to watch for emerging trends.

Anti-HIV drugs: the building blocks of treatment

Because HIV is a type of virus called a retrovirus, anti-HIV drugs are also called antiretroviral drugs or just antiretrovirals. In order to explain how anti-HIV drugs work, we need to first tell you some information about HIV. When HIV infects a cell in your body, it takes control of that cell (see next page). HIV then forces the cell to make many more copies of the virus. This replication of HIV—called the HIV life cycle—is a step-by-step process, like an assembly line in a factory. Anti-HIV drugs are designed to interfere with different steps in that replication process.

The HIV life cycle and classes of anti-HIV drugs

The viral life cycle is the process by which HIV makes copies of itself. There are four main stages in the viral life cycle:

1. HIV enters a cell;
2. HIV takes control of the cell;

When HIV infects a cell in your body, it takes control of that cell.

HIV then forces the cell to make many more copies of the virus. Anti-HIV drugs are designed to interfere with different steps in the replication process. There are four main stages in the viral life cycle.

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3. HIV becomes part of the infected cell;
4. HIV tricks the infected cell into making copies of itself.

There are several different “classes” (or groups) of anti-HIV drugs: each class works by interfering with a specific step of the cycle.

1. HIV enters a cell Different cells in your body have different molecules or receptors on their surfaces. These molecules identify the cells like fingerprints. CD4+ cells get their name from the CD4 receptors that are sprinkled over their outer surface.

HIV also has certain specific molecules on its outer surface. These proteins fit perfectly onto the CD4 receptors. This allows HIV to attach itself to the cell like a key fitting into a lock.

HIV also needs to lock onto one or more co-receptors besides CD4. Once HIV is attached to both CD4 and the co-receptor, the virus can fuse with the cell and get inside. It's as though there are two locks on the door, and HIV has the key to both of them.

Anti-HIV drugs in the classes called entry inhibitors and fusion inhibitors prevent HIV from getting inside cells.

2. HIV takes control of the cell Two molecules called RNA and DNA are essential for every living thing. These molecules work like master instruction manuals: they tell a living cell how to build everything it needs to build and how to do everything it needs to do. The genes that you were born with are made of DNA that explains how to make everything from your fingernails to your blood cells.

HIV has its own “genes,” made of RNA. RNA is similar to but not exactly the same as the DNA that makes up human genes. Once inside a human cell, HIV has to convert its RNA into DNA before it can do anything else. HIV brings along a molecule called reverse transcriptase, which converts the viral RNA into DNA. After this conversion, the genetic material of the virus matches the genetic material of the cell.

Anti-HIV drugs called reverse transcriptase inhibitors slow down or stop the action of the reverse transcriptase enzyme. There are two classes of anti-

HIV drugs that slow down this enzyme:

- nukes or nucleoside analogue reverse transcriptase inhibitors (also called NRTIs);
- non-nukes or non-nucleoside analogue reverse transcriptase inhibitors (also called NNRTIs).

The nukes were the first drugs approved to treat HIV, and they continue to be a major part of most drug regimens.

The non-nukes were developed later than the nukes. Due to their powerful ability to suppress HIV, they have also become an important part of many treatment combinations.

3. HIV becomes part of the infected cell In the cell's nucleus, genes made of DNA contain all the instructions for the day-to-day running of the cell. The cell follows the instructions that come from this DNA.

HIV takes advantage of this for its own purposes. It inserts its own viral DNA (which was made in the previous step) into the cell's DNA molecules—like adding a few new beads to a necklace.

The virus uses an enzyme called integrase to make this insertion. Anti-HIV drugs in the class called integrase inhibitors can be used to interfere with integrase, preventing the viral DNA from being inserted into the cell's own DNA.

4. HIV tricks the infected cell into making copies of itself At this point, the infected cell can't tell the difference between the viral DNA and its own. It is now programmed to produce new viruses when the cell becomes activated. CD4+ cells can remain infected but inactive for long periods of time. This is one of the challenges to finding a permanent cure for HIV infection. Once the infected CD4+ cell is activated, which happens if it is called upon to respond to an infection, it will start making copies of itself and eventually releasing new virus.

There are still a few steps needed to complete the process of making new virus particles or HIV virions. First, the cell makes long chains of HIV proteins. These long molecules contain all the various pieces of the new HIV virions, but not put together in the proper way. An HIV enzyme called protease then works like scissors to cut these chains into the correct smaller pieces. These newly

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In order to effectively treat HIV you have to take a combination of anti-HIV drugs from different classes.

Such combinations are called highly active antiretroviral therapy or HAART.

There is no single “best” combination of drugs that overshadows all the rest.

The goal is to pick a combination that will work as well as possible for you.

cut pieces are assembled by the cell into new HIV virions. Finally, the new HIV virions leave the infected cell, in a process called budding, and can go on to infect other cells.

Protease inhibitors are the class of anti-HIV drugs that interfere with the action of the HIV enzyme called protease. They prevent the protease enzyme from cutting the long chains of new HIV proteins. This results in defective HIV that cannot infect new cells. Protease inhibitors have a very powerful ability to suppress the virus and are an important part of many drug combinations.

Putting it together: HAART combinations

In order to effectively treat HIV you have to take a combination of anti-HIV drugs from different classes. Such combinations are called highly active antiretroviral therapy or HAART. They are also sometimes called ART (antiretroviral therapy) or CART (combination antiretroviral therapy.)

At present, there are five different classes of drugs approved in most of the world, including Canada:

- nukes;
- non-nukes;
- protease inhibitors;
- entry and fusion inhibitors;
- integrase inhibitors.

Each of these classes inhibits the HIV life cycle differently as described in the section above.

Drug names and the names of drug classes can be wordy and confusing. It does take a little getting used to, but don't let it throw you too much. You may end up sounding like an expert, but if not, don't forget that your treatment won't stop working just because you forget exactly what “reverse transcriptase” means.

Choosing treatment: *what to use?*

There is no single “best” combination of drugs that overshadows all the rest. Instead, there are a number of desirable things to look for. The goal is to pick a combination that will work as well as possible for you; there may be more than

one of these. The most important things to look for in a drug combination are:

- efficacy—how well does it work? A treatment combination should lower viral load as much and as quickly as possible, with the greatest increases in CD4+ cell counts;
- durability—how long has it been proven to work? The effects should be sustained over the longest possible time;
- tolerability—how easy is it to take? Side effects, both short term and long term, should be as tolerable as possible, and the dosing schedule should be easy to live with.

There are other questions to consider, as well. For instance, what are your prospects for treatment choices later on? HIV can develop resistance to drugs, especially if they aren't taken correctly or if the doses are too low because of poor absorption. Could the drugs in your combination lead to resistance patterns that would make effective second- and third-line combinations harder to find? Your doctor will pay great attention to such questions and we'll talk about this issue in the Making it Work section, on page 137. It is also important to know if the drugs in your HAART combination interact with any other drugs you are taking now or may need to take in the foreseeable future. We'll discuss this later on page 138. If you are pregnant or thinking about becoming pregnant, this could also impact your treatment choices.

Given all of these questions, and the dozens of anti-HIV drugs available, the possibilities might seem mind-boggling. Fortunately, that's not quite the case. While new drugs, strategies and combinations are being investigated all the time, there are several preferred combinations that have performed well over years of study. Many alternative combinations are available as well.

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Starting treatment: first-line treatments

First-line treatments refer to the combinations of anti-HIV drugs that are usually taken by people who are starting treatment for the first time. First-line treatments are well studied and have a proven track record for people starting

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Three classes of anti-HIV drugs are most often used in first-line treatments: nukes, non-nukes and protease inhibitors.

HAART. Your doctor will likely perform a drug resistance test to help decide which combination will work best for you. Currently, three classes of anti-HIV drugs are most often used in first-line treatments: nukes, non-nukes and protease inhibitors. The other classes of drugs are generally only used by people who have already taken treatment and/or are resistant to some of the drugs in first-line treatments. However, this may change in the future.

At the time of writing, the standard first-line treatment combinations consist of two nukes, plus either a protease inhibitor or a non-nuke. These are sometimes referred to as protease inhibitor-based and non-nuke-based therapy, respectively.

Protease inhibitor-based therapy

The protease inhibitor/two-nuke combination is the oldest version of HAART, and the one for which we have the most long-term research data. The power of protease inhibitor-based therapy as a treatment combination is well proven. However, most currently available protease inhibitors have possible side effects, and many are subject to a wide range of drug interactions (see page 138).

Protease inhibitor-based combinations almost always include a small dose of ritonavir (Norvir). The ritonavir works to boost the levels of the other protease inhibitors in the combination, without having to take a larger dose. This approach is called boosted protease inhibitor therapy.

For information about the side effects of protease inhibitor-based therapy (see Chapter 11, Side effects and symptoms).

Non-nuke-based therapy

Non-nuke-based regimens use two nukes plus one non-nuke. In clinical trials, protease-inhibitor-based and non-nuke-based combinations have both proven to be very effective and durable (that is, they can keep HIV suppressed for many years).

For information about the side effects of non-nuke-based therapy, see Chapter 11, Side effects and symptoms.

Once-daily therapy

Very few people actually like taking pills. Since effective anti-HIV drugs first became available, there has been a push to find combinations that require fewer pills, fewer times per day—preferably, once-daily drug combinations.

The danger here lies in putting the cart before the horse: more convenient does not necessarily mean better, and any once-daily combination also has to be proven effective and durable. Recently, several such options have become available. For obvious reasons, most people living with HIV greatly prefer these once-daily combinations. There is also evidence that once-daily combinations make adherence easier, and thus may be more effective in the long term.

However, there are some potential drawbacks that may be less obvious. If you are only taking drugs once a day, skipping even one dose means there could be inadequate amounts of the drug in your bloodstream for quite a lengthy period. This could increase the chance of developing drug resistance. The trade-off, therefore, is that while once-daily therapy may be easier, adherence also becomes even more important.

Making it work: aiming for long-term success

Resistance and adherence

No matter which drugs you end up taking, there is one crucial rule: the pills only work when you take them. “Duh,” you say, but remembering to take your pills at the right times every day isn’t always easy. And sticking to your pill-taking schedule (this is called “adherence”) is very important: even missing pills occasionally could sabotage your long-term success in using these anti-HIV drugs.

This may set off all sorts of alarm bells for you. Some people don’t take kindly to being told what to do, even (or especially!) when they’re told it’s “for your own good.” Others may feel that the whole idea of adherence is very challenging or overwhelming and will take some getting used to. But this isn’t just an exercise in finger-wagging—adherence is crucial if the drugs are going to work.

Sticking to your pill-taking schedule (this is called “adherence”) is very important: even missing pills occasionally could sabotage your long-term success in using anti-HIV drugs.

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If the virus keeps making copies of itself while exposed to low drug levels, it will eventually figure out how to make copies of itself even at the proper doses. Then your drugs will no longer work for you.

You'll keep your drug combination working as long as possible by sticking to your regimen as best you can.

Pill-popping schedules and correct doses are designed to keep enough drugs in your bloodstream to keep the virus suppressed. Missing doses means that drug levels may, at least temporarily, drop too low to keep the virus under control and HIV can make more copies that will go on to infect new cells. In the short run, this may not be a disaster—the next drug dose will probably knock the virus back down under control. The real danger is drug resistance. If the virus keeps making copies of itself while exposed to those low drug levels, it will eventually figure out how to make copies of itself even at the proper doses. Then your drugs will no longer work for you. Your viral load will go back up and your CD4+ cell count will start to fall, even if you keep taking the drugs. Then, you'll need to find a new combination that will be effective against the resistant virus. That may not be impossible, but it's trickier than just staying with a combination that already works.

So, that's why you may sometimes feel like you're being lectured about adherence. Missing the occasional dose is not the end of the world (let's face it; there'd be little hope for any of us if that were true). But you'll keep your drug combination working as long as possible by sticking to your combination as best you can.

If you are having difficulties remembering to take your drugs as they were prescribed, it's important to get help. Sometimes people have underlying problems, such as depression or substance use, that may affect their adherence. Dealing with these underlying issues can help to improve adherence. Your doctor and pharmacist may have practical tips to help with adherence, so be sure to discuss this with them before starting your pills, or if you experience any challenges in taking your pills regularly.

If you are at a point in your life, for whatever reason, where you are not able to take your pills regularly and as prescribed, you should take a clear look at exactly what's giving you trouble. Solving adherence problems is a very individual matter. Your pharmacist, clinic nurse or even friends who are also HIV-positive can often help you work out strategies. In spite of the importance of your anti-HIV combination in keeping you healthy, perhaps you are not ready to be taking HAART until you get some things in your life sorted out, like your housing situation or substance use issues. Talk to your doctor and perhaps you

can find a combination that is more “forgiving” and easier for you to take. While it does take some getting used to, drug adherence should eventually become as routine as brushing your teeth.

Drug interactions

A drug interaction occurs when you are taking a combination of drugs and one drug affects how the others are absorbed, broken down, or flushed out of the body. When choosing the drugs that will make up your HAART combination, it's important to look at the possibility of drug interactions. Drug interactions can greatly affect the levels of drugs in the body. Too-high drug levels can lead to increased (sometimes dangerous) side effects. If levels are too low, the drugs will not work properly. With anti-HIV drugs, this can lead to the drug resistance you take such pains to avoid: you don't want your near-perfect adherence sabotaged by an unexpected drug interaction.

Complex drug interactions are just one more reason you need expert medical care. An experienced doctor and pharmacist should be able to plan your treatment so you don't run into this trouble. Your part of the bargain will be to make sure your doctor and pharmacist are aware of everything you're taking—prescription drugs, over-the-counter medications, herbal and nutritional supplements, and even recreational drugs. Most drug interactions can be anticipated and dealt with safely. See CATIE's *A Practical Guide to HAART* for more information.

Changing treatment: after first-line therapy, what next?

Even with the best planning, you may find you have to change your drug combination. Maybe the combination is not working to control HIV (so your viral load doesn't stay undetectable), or maybe it doesn't work for you because of difficulties with adherence (see above).

Your doctor and pharmacist may have practical tips to help with adherence, so be sure to discuss this with them before starting your pills, or if you experience any challenges in taking your pills regularly.

While it does take some getting used to, drug adherence should eventually become as routine as brushing your teeth.

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Even with the best planning, you may find you have to change your drug combination.

If your viral load is still detectable after a reasonable time on therapy (usually about 24 weeks)—or if it bounces back up to consistently measurable levels after being undetectable—that indicates your treatment is not working.

Changing because of side effects

Sometimes your treatments seem to be working just fine: your viral load is staying undetectable, and your CD4+ cell counts are climbing. Yet despite the “good numbers,” you find the side effects are too hard to take, and they are just not going away.

In that case, it’s important to talk to your doctor to find out exactly what is causing the side effects you are experiencing. If you and your doctor determine that your drugs are causing the side effects, you have two options: find some way to control the side effects, or switch off the drug(s) causing them.

Many side effects can be dealt with. See Chapter 11, Side effects and symptoms, for a preliminary discussion of how to manage side effects and symptoms. Depending on the side effect, you might consider seeing a naturopathic doctor or nutritionist. By using an integrated approach to HIV—combining the best available drugs with the remedies that help eliminate side effects and other symptoms—you may be able to stay on your drugs happily instead of miserably.

If nothing works to make the side effects more bearable, then it’s time to talk to your doctor about changing your drugs. Your goal is to find a different combination that’s still effective, while avoiding side effects that make you miserable. It isn’t usually necessary to change all the drugs in your combination. Often, your doctor can pinpoint the drug responsible for the problems you’re experiencing, and change just that one while leaving the others alone.

Changing because of treatment failure

One big reason for changing treatment is treatment failure—that is, your treatment isn’t keeping HIV suppressed. Your viral load will tell you this: on successful treatment, viral load should drop to undetectable and stay that way. If your viral load is still detectable after a reasonable time on therapy (usually about 24 weeks)—or if it bounces back up to consistently measurable levels after being undetectable—that indicates your treatment is not working.

With your doctor, you’ll need to work out why the treatment failed (was it because of drug resistance or adherence problems?) and which drugs you need to go on next. This decision is more challenging than the choice of your

first combination. You and your doctor will have to consider which of the original drugs have failed, and which ones will likely work instead.

Cross-resistance is a challenge here: when HIV becomes resistant to one drug, it may also be resistant to other drugs in the same class, even if you've never taken them. For example, if you're resistant to efavirenz (Sustiva, and also in the combination pill Atripla), you'll likely be resistant to nevirapine (Viramune) as well. Resistance testing can help guide these choices: resistance tests pinpoint which drugs your virus is resistant to, and which ones still have a shot (see Chapter 9, Monitoring your health).

The sooner action is taken to switch off a failing treatment, the better. Cross-resistance can worsen the longer you stay on a failing combination, making it harder to find alternatives.

The sooner action is taken to switch off a failing treatment, the better.

Taking breaks and stopping treatment

One thing everybody wants to know is: once you've started treatment, when can you stop? The reality, since anti-HIV drug treatment does not get rid of or "cure" HIV infection, is that treatment is pretty much ongoing. That is, you generally can't stop.

Many people hoped that "drug holidays"—more technically called structured treatment interruptions—would give people with HIV a break from the ongoing demands and side effects of treatment.

Unfortunately, large and carefully designed studies of treatment interruptions showed surprising and disappointing results. People who took treatment breaks, even at high CD4+ cell counts, had greater risks of serious, even life-threatening, complications. As a result, treatment interruptions are generally not recommended, except in specific circumstances, for instance, severe drug toxicity, or serious complications due to other illnesses or surgical procedures.

Resources

Practical Guides for People Living with HIV

CATIE's practical guide series contains extensive information about HIV treatments. See:

- *A Practical Guide to HAART for People Living with HIV*
- *A Practical Guide to Managing HIV Drug Side Effects*

Plain and Simple Factsheets on Complementary Therapies

Available in multiple languages

In-Depth Factsheets on supplements

Comprehensive information for people living with HIV and their care providers

The Positive Side

Health and wellness magazine contains articles about treatment, such as:

- The importance of being adherent
- Staying on the road to health
- Resistance assistance

Look under *Drug Treatment Strategies* in the e-zine index (www.positiveside.ca)

TreatmentUpdate and CATIE News

News bulletins about cutting-edge developments in HIV research and treatment

Many other relevant resources can be accessed on CATIE's website (www.catie.ca), through the CATIE Ordering Centre (www.orders.catie.ca) or by calling CATIE at 1-800-263-1638.

