

A Practical Guide to
HIV Drug Treatment

for People Living with HIV



Canada's source for
HIV and hepatitis C
information

A Practical Guide to
HIV Drug Treatment

for People Living with HIV

(formerly *A Practical Guide to HAART*)

Second Edition, 2011

© 2011, CATIE (Canadian AIDS Treatment Information Exchange). All rights reserved.

ISBN 978-0-9784654-9-0

CATIE would like to thank the following people for working with us to help produce this guide. Their time and knowledge were invaluable and much appreciated.

Lead Author (2011 edition)

Derek Thaczuk

Authors (previous editions)

Lark Lands

Deirdre Maclean

Editors

Sean Hosein

Debbie Koenig

David McLay, PhD

RonniLyn Pustil

Tim Rogers, PhD

Translation

Alain Boutilier

Jocelyne Demers-Owoka

Christiane Devaud

Design and Layout

Raymond Helkio

Illustration

Moe Asem

Beverly Deutsch

Don Short

Reviewers

Jonathan Angel, MD

Mara Brotman

Brian Cornelson, MD

Laurie Edmiston

Melissa Egan

Marianne Harris, MD

Patrice Junod, MD

Laurette Lévy

Stephen Shafran, MD

Darien Taylor



Contact CATIE

By telephone

1-800-263-1638

416-203-7122

By fax

416-203-8284

By e-mail

info@catie.ca

On the web

www.catie.ca

www.hepCinfo.ca

By mail

555 Richmond St. W.

Suite 505

Toronto ON M5V 3B1

Canada

CATIE thanks the many people living with HIV who contributed their stories, wisdom and advice to this guide.

Production of this guide has been made possible through financial contributions from the Public Health Agency of Canada, Bristol-Myers Squibb Canada and ViiV Healthcare in partnership with Shire Canada.

About CATIE

CATIE is Canada's source for up-to-date, unbiased information about HIV and hepatitis C. We connect people living with HIV or hepatitis C, at-risk communities, healthcare providers and community organizations with the knowledge, resources and expertise to reduce transmission and improve quality of life.

Permission to Reproduce

This document is copyrighted. It may be reprinted and distributed in its entirety for non-commercial purposes without prior permission, but permission must be obtained to edit its content. The following credit must appear on any reprint: *This information was provided by CATIE. For more information, contact CATIE at 1-800-263-1638 or www.catie.ca.*

Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV-related illness and the treatments in question.

CATIE (Canadian AIDS Treatment Information Exchange) in good faith provides information resources to help people living with HIV/AIDS who wish to manage their own healthcare in partnership with their care providers. Information accessed through or published or provided by CATIE, however, is not to be considered medical advice. We do not recommend or advocate particular treatments and we urge users to consult as broad a range of sources as possible. We strongly urge users to consult with a qualified medical practitioner prior to undertaking any decision, use or action of a medical nature.

We do not guarantee the accuracy or completeness of any information accessed through or published or provided by CATIE. Users relying on this information do so entirely at their own risk. Neither CATIE nor the Public Health Agency of Canada nor any of their employees, directors, officers or volunteers may be held liable for damages of any kind that may result from the use or misuse of any such information. The views expressed herein or in any article or publication accessed or published or provided by CATIE are solely those of the authors and do not reflect the policies or opinions of CATIE or the views of the Public Health Agency of Canada.

Contents

A Practical Guide to

HIV Drug Treatment

for People Living with HIV

Getting Started • 1

How to Use This Guide • 2

Living with HIV, Living with Treatment: The Capsule Version • 4

HIV and AIDS: The Basics • 7

The Immune System • 8

Outside the body

Inside the body

Immune cells

What Does HIV Do to You? • 11

HIV and the immune system

The phases of untreated HIV infection

Primary infection

Chronic infection

Stopping the slide

Monitoring Your Health • 17

Monitoring symptoms

CD4 count

CD4 percentage

Viral load

Other tests

Factors that may affect test results

Tracking your lab results

Personal Health Record

Treating HIV • 29

There's More to Health than ART: Holistic Health • 30

Good nutrition

Exercise

Complementary therapies

Program the mind for healing

Dealing with depression and drug use

Working with Your Doctor • 35

Beyond your doc

HIV Treatment • 38

What is ART?

What do antiretroviral drugs do?

Do I have to take antiretroviral drugs at all?

Can I still infect other people if I am taking antiretroviral drugs?

How do we know which treatments are "best"?

When to Start • 42

Some people need to start as soon as possible

If possible, everyone should start treatment before their CD4 counts fall below 350 cells

For CD4 counts above 350 cells, you should consider starting treatment

Summary of when to start treatment

Preparing to Start Treatment • 46

ART Start Checklist

Choosing a Drug Combination • 50

Building a combination

First combinations

Which combination is best for you?

Choosing the Best Combination for Me • 57

Once You've Started • 59

How to Tell if Your Treatment Is Working • 60

Making Your Treatment Work Long-Term • 61

How to keep your treatment working ... and why you don't want it to fail

Making sure your drugs play well together

Stopping treatment?

Changing Treatment • 67

After your first combination

Changing medications due to treatment failure

Changing medications due to side effects

What Next? • 73

Living with HIV and ART Over the Long Haul • 74

The Future of HIV Drug Treatment • 76

The End ... But Not Really • 77

Appendices: Antiretroviral Drugs, Drug Combinations and Drug Resistance • 79

Appendix A: The Viral Life Cycle and Antiretroviral Drugs • 80

Appendix B: Antiretroviral Drugs Available in Canada • 83

Appendix C: Building a Treatment Combination • 85

Appendix D: First Combinations • 88

Appendix E: Drug Resistance and Resistance Testing • 91

Getting Started

This first part of the guide includes two short sections to help get you started:

- ◎ **How to Use This Guide** gives you a quick sketch of how the guide is laid out and some tips on how you might want to use it.
- ◎ **Living with HIV, Living with Treatment: The Capsule Version** is a super-quick summary of what's in the guide. The points we touch on here get talked about at greater length throughout this practical guide.

How to Use This Guide

In a Capsule

- This guide is meant to be a practical source of information about drug treatment for HIV. It should not replace your doctor's advice but may help you to ask the right questions.
- We will look at when it's best to start treatment, how to choose between drugs, and how to make sure your treatment is working for you.
- Since drug treatments and guidelines are constantly changing, we will try to stick to the more general issues and questions about treatment. You should always get the most up-to-date facts about specific drugs and treatment.

Throughout the guide you will find the voices of people living with HIV in boxes like this one. They share their experiences with HIV treatment and offer advice on how to live well with HIV.

Welcome to the second edition of *A Practical Guide to HIV Drug Treatment* (formerly *A Practical Guide to HAART*), published by CATIE (the Canadian AIDS Treatment Information Exchange). Thanks to advances in HIV treatment, prospects for people living with HIV and AIDS are better than ever before. However, all the treatment options now available make for many decisions—a process that HIV-positive people often find confusing and sometimes stressful. Pill charts keep getting bigger, medical words are everywhere, and a lot of people feel like they don't know where to start.

In this guide, we hope to help you understand the following:

- how HIV can make you sick
- how to monitor your health
- how to decide when you need to start treatment
- what your treatment options are
- how to approach these decisions as confidently as you can

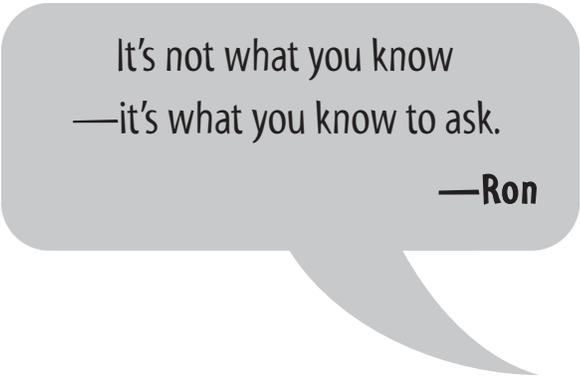
As the title says, this publication is meant to be a practical guide. Feel free to use it any way that suits you. If you have only recently been diagnosed as HIV-positive, or if you want a refresher on the basics, you may want to start right at the beginning. If you've been positive for some time and you know a lot already, please skip straight to the parts you want to know more about.

In this guide, we tackle the big questions like “Do I have to go on treatment at all?,” “When should I start?” and “Which drugs are best?” Of course, the answers to these questions change with time, as new treatments and new information become available. However, a lot of the underlying issues—the benefits and challenges of treatment, factors to consider when you're making decisions, questions to ask your doctor—stay largely the same. We've tried to focus on those issues that don't change as quickly.

We've also tried to make this practical guide work with other CATIE publications and resources, including our indispensable *Managing Your Health: a guide for people living with HIV*. *Managing Your Health* covers a lot of ground, including some of the issues discussed here. While you may notice many similarities between the two publications, this practical guide provides more detailed information about HIV treatment.

For the most up-to-date information on specific drugs and treatments, there is a lot more “stuff” out there you can refer to. CATIE produces *CATIE News* and *TreatmentUpdate*, two publications that provide timely reporting on the latest developments in HIV treatment. We also maintain a set of up-to-date fact sheets with extensive information on different anti-HIV drugs and treatment topics—you can find these on the CATIE website at www.catie.ca. (We provide links to many other reputable online sources of HIV treatment information as well.) You can email or call CATIE with any questions, and we’ll do our best to answer them. Get in touch with us at info@catie.ca or 1-800-263-1638. Most importantly, don’t forget that none of this information can replace the advice of your doctor.

You can also use this guide as a bit of a workbook. We know it’s easy to remember things until the moment you’re in your doctor’s office, then ... Poof! Your mind goes blank. So we’ve included a few simple tools: charts you can use to keep track of your health information, checklists of questions and concerns that you can take with you when you visit your doctor, and questions to ask yourself when you’re trying to make decisions.



It’s not what you know
—it’s what you know to ask.

—Ron

Living with HIV, Living with Treatment: The Capsule Version

In a Capsule

- HIV is a virus that weakens your body's defences against infections and cancers.
- There is no cure for HIV infection yet. However, with the right treatment and care, many people with HIV are now living long and well and may live nearly normal lifespans.
- You can do many things to stay healthy if you are HIV-positive, such as seeing a doctor regularly, eating healthy food, getting enough rest, exercising, starting HIV treatment at the right time and using appropriate complementary therapies.
- Anti-HIV drugs have to be taken in combination. You and your doctor will choose the best combination for you.
- Your CD4 count—a measure of the strength of your body's defence system—will affect your treatment decisions. If your CD4 count falls very low, your risk of certain infections becomes very high. You can prevent this by starting treatment *before* your CD4 count falls too low and *before* you get sick from HIV.
- Anti-HIV drug treatments need to be taken every day as directed and may cause side effects and other challenges. Most people find they can deal with these challenges.
- If one combination of anti-HIV drugs does not succeed in controlling HIV or if the side effects or pill-taking schedule are unmanageable, you and your doctor may need to try another combination of drugs.

Human immunodeficiency virus, or **HIV**, is a virus that slowly weakens the immune system—your body's defence against infections and some cancers. If you have HIV for a long time without treating it, your immune system can become too weak to fight off certain serious—even fatal—illnesses. At this time, there is no cure for HIV infection, and there is no vaccine that can reliably protect people from getting the virus. However, there are now dozens of treatments for fighting HIV. When used properly, these treatments can help you stay healthy and well.

Living well with HIV does not begin and end with drug treatment. Taking care of your general well-being—by eating well, getting plenty of rest and exercising regularly—can go a long way toward keeping you healthy, and there are countless other ways you may find to better your health. CATIE publishes practical guides on nutrition, herbal therapies and complementary therapies; we hope you'll read these and find them useful. In this guide, we're discussing the biggest weapon against HIV: the drug treatments known as **antiretroviral therapy (ART)**.

Treatments have improved a lot since the "early days" of HIV medications in the late 1980s and early 1990s. New treatments have completely changed the prospects for people with HIV. To be blunt, in all but the rarest cases, HIV infection used to lead to illness and death. But by taking HIV treatment, most people with HIV are now able to control, or "suppress," the virus, strengthen their immune systems and fight off infections. Many experts now predict that with proper treatment and care, most people with HIV should be able to live nearly as long as HIV-negative people.

There are now dozens of anti-HIV drugs, also known as **antiretroviral drugs**, available in Canada. These drugs have to be taken in combination to fight HIV effectively. Sooner or later, most people with HIV have to tackle two questions: (1) When should I start HIV drug treatment? and (2) Which combination should I take?

The best time to start treatment is *before* you get sick from HIV and before you are at high risk of getting sick. You and your doctor will keep an eye on your symptoms and your blood tests, especially key numbers like your **CD4 count**. You should start treatment before your CD4 count falls too low (as we discuss in detail starting on page 42).

Deciding which combination of antiretroviral drugs to take may seem complicated, but most people can choose from a few simple and effective “preferred” combinations (see page 50). It’s an individual decision that will likely depend on many factors, including the state of your health, your personal preferences and which treatments you have taken in the past.

Of course, treatment can have its downsides. Antiretroviral drugs can cause side effects and long-term complications, which can range from minor to serious. However, advances in treatment mean that many people are able to choose treatments with fewer side effects.

The success of your treatment depends on continuing to take the drugs exactly as directed every day—this is called **adherence**. Many people find they can deal with the side effects and adhere to their recommended pill-taking schedule, especially if they’ve had time to prepare.

Sometimes, treatment doesn’t work: it may not be able to control the HIV in a person’s body, or the side effects or number of pills may be too much to bear. Most people are able to find an alternate combination if the first one does not work out. However, second, third or later combinations need to be chosen carefully. We talk more about changing treatment later in the guide (page 67).

This guide is intended to guide you through what we know (and don’t know) about HIV treatment. We hope it gives you enough information to make you feel more confident about discussing your treatment decisions with your doctor.

My advice is: Gather information, become knowledgeable, and know what HIV is, what it does and what’s out there in terms of support. The more you know about yourself and the virus, the better you can manage your own health and stand strong and positive . . . You don’t have to do that alone. Get connected, build a support network and learn how to speak to your doctor.

—Jane

HIV and AIDS: The Basics

In this part of the guide, we go over some of the “basics” of HIV—what your immune system is, what CD4 cells are, what HIV infection does and how to fight it.

- ◎ **The Immune System** describes how your body fights infection with the help of vital cells called CD4 cells.
- ◎ **What Does HIV Do to You?** explains how untreated HIV gradually destroys CD4 cells and weakens the immune system. HIV treatment can stop HIV from attacking the immune system, allowing the immune system to repair itself and keep you healthy.
- ◎ **Monitoring Your Health** talks about how you can track the strength of your immune system, the activity of the virus in your body, and your overall health.

The Immune System

In a Capsule

- ⦿ Your immune system is your body's defence against infections and cancers.
- ⦿ The immune system has many components, including the skin, mucous membranes and white blood cells.
- ⦿ There are many types of white blood cells. Each type plays a different role in fighting infections.
- ⦿ A CD4 cell is a type of white blood cell that is especially important to the immune system. HIV infects and destroys CD4 cells.



The immune system is the body's defence against disease. It protects the body from disease-causing germs, such as bacteria, viruses, fungi and parasites, as well as cancerous cells.

Normally, the immune system can tell the difference between what belongs in your body and what doesn't. It "remembers" previous encounters with disease-causing germs (for example, the virus that caused the measles you had as a child) and knows how to defend against these threats. It also learns how to respond to invaders it hasn't seen before, by developing specific defences against them.

Outside the body

The **skin** is your immune system's first line of defence. It provides a physical barrier that keeps bacteria and viruses from getting inside the body. HIV, for instance, cannot be transmitted through healthy, unbroken skin.

However, HIV and other organisms can be transmitted through the body's **mucous membranes**. These are the wet linings of body cavities and other organs, such as the vagina, rectum and urethra (the "pee hole" in the penis or the vulva). These tissues don't have to be damaged or bleeding to be infected: HIV can infect cells in the lining of the vagina, rectum and penis even if the tissues are healthy.

Inside the body

When disease-causing germs get into the body, the internal part of the immune system comes into play. Its job is to recognize intruders and either destroy them or suppress them so they won't cause harm. The immune system includes white blood cells, lymph nodes and body tissues, such as the tonsils and insides of the intestines. The immune system also includes other components, such as the bone marrow, the thymus, the spleen and the appendix. All of these play different roles in fighting infections.

The **lymphatic system** is especially important in people with HIV. The lymphatic system is made up of vessels that branch out into all parts of the body, similar to the veins, arteries and capillaries that carry blood. Instead of blood, lymphatic vessels carry a clear, watery fluid, called *lymph*, which carries foreign material away from your body's cells. The lymphatic

vessels pass through **lymph nodes** and tissues. Inside these nodes and tissues, cells of the immune system trap, filter and destroy foreign material, including bacteria, viruses and other microbes.

There are 500 to 1,000 lymph nodes and tissues scattered throughout the body. Large groups of lymph nodes are found in the neck, armpits and groin, but the largest concentration is in your abdomen. Sometimes when you have an infection, you can feel what people call “swollen glands” in some of these areas. These swellings are your lymph nodes responding to unwanted germs.

Each lymph node is densely packed with millions of immune cells that identify and destroy the microbes that cause disease. These infection-fighting cells are known as *white blood cells*, or *leukocytes*, and they are the key players in the response of your immune system.

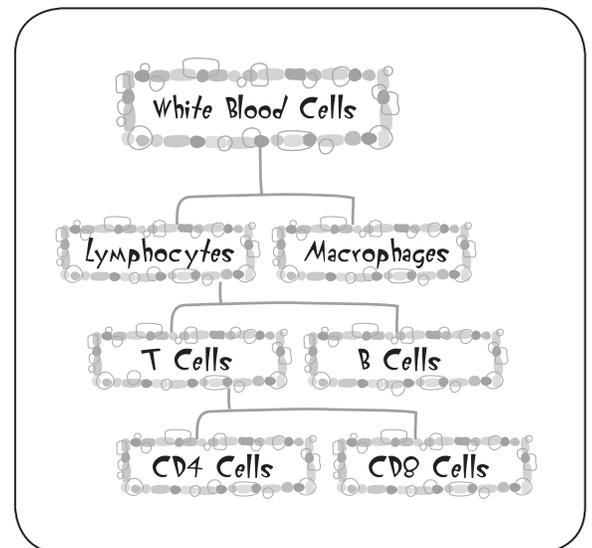
Immune cells

There are many different kinds of white blood cells. Don't worry too much if you can't keep them all apart. Although CD4 cells are very important for HIV-positive people, the other types of white blood cells will rarely come up during your doctor's visits. If you're interested, this list should give you a quick sense of what's what.

Leukocytes are the biggest group, including all types of white blood cells. (*Leuko* means white and *cytes* means cells.)

Lymphocytes are a kind of leukocyte, which include the *T cells*. T cells are identified by molecules, called *receptors*, on their surfaces. T cells with different kinds of receptors carry out different functions.

One particular kind of T cell, the **CD4 cell**, is especially important for people with HIV. CD4 cells are named after a protein called CD4, which they carry on their surface like a fingerprint. CD4 cells lead the attack against infections. They release chemical messengers called *cytokines* that stimulate other immune cells to make antibodies or to destroy infected cells. CD4 cells are sometimes compared to the quarterbacks of a football team or the conductors of an orchestra, because they direct the response of your body's immune system.



A partial lineage of white blood cells.

I used to pretend to coax my CD4 cells down to a cut on my fingertip by rubbing my finger and saying words of encouragement. It was my way of reminding myself that my CD4 cells are still there to help keep me healthy.

—André

CD8 cells are T cells that have a protein called CD8 on their surface. When CD8 cells recognize a specific infection, such as HIV, they can develop into what are often referred to as killer T cells or CTLs (cytotoxic T lymphocytes). These killer T cells seek out and kill other cells that are already infected or cancerous.

B cells are lymphocytes that make and release *antibodies*. An antibody is a type of protein that can lock on to bacteria or viruses. When an antibody locks on to a germ, it acts as a signal for other immune cells to destroy the invader. Each B cell is programmed to make one specific antibody. For example, one B cell will make the antibody that blocks measles viruses, while another makes antibodies to the bacteria that cause pneumonia. Although the immune system produces antibodies against HIV, these antibodies don't protect the body from HIV infection.

Macrophages are immune cells that perform many functions, such as warning the immune system of invading microbes and helping to attack and destroy HIV-infected cells and cancerous cells.

Dendritic cells help alert the rest of the immune system to invading germs and help magnify the immune system's response to germs.

Natural killer cells are lymphocytes that help prevent the spread of infection by killing infected cells. (They kill cancerous cells too.) Natural killer cells also help direct the production of other immune cells. They may contribute substantially to the body's efforts to control HIV.

What Does HIV Do to You?

HIV and the immune system

Your immune system is supposed to protect you from viruses and other infections. Why, then, doesn't it protect you from HIV? The answer is complicated, but essentially, it's because HIV destroys CD4 cells, which direct the response of the immune system. This destruction of CD4 cells (and a number of other processes that we are gradually learning more about) prevents the immune system from working properly.

Eventually, if HIV infection is left untreated, your immune system becomes too damaged to defend against life-threatening infections and cancers. The number of CD4 cells in your bloodstream—your CD4 count—is one of the most important measures of immune strength for people with HIV.

In the past, we painted a fairly straightforward picture of HIV infection: HIV infects and destroys CD4 cells, causing CD4 counts to drop as a result. We now realize that this description of events is oversimplified. It's true that HIV infects and kills CD4 cells directly. However, HIV causes much of its damage in more roundabout ways. The immune system's efforts to fight the virus throw it into a state of *immune activation*, or *inflammation*. Over time, prolonged inflammation can increase a person's risk of heart attacks and lead to other damage, as we'll discuss further in the section on chronic infection (see page 13).

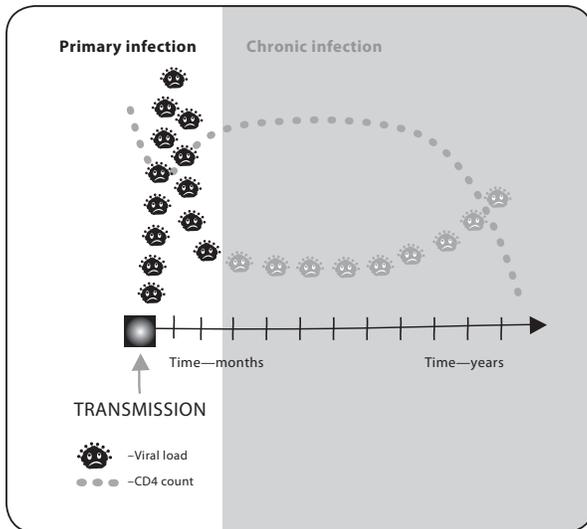
The phases of untreated HIV infection

When HIV infection is not treated with antiretroviral drugs, the course of disease generally moves through several phases. In **primary infection** (also called **acute** infection), HIV establishes itself throughout the body. Within a few weeks or months, the immune system develops antibodies against the virus—a process known as **seroconversion**. The infection then enters a **chronic** phase. During this phase, a person may have no symptoms at all, only mild symptoms or severe symptoms. If left untreated, HIV infection eventually progresses until the immune system is too weak to defend against life-threatening infections and cancers. This stage is called **AIDS**.

In a Capsule

- ⦿ HIV destroys CD4 cells—the very cells that are most critical to the immune system.
- ⦿ If HIV is left untreated, the number of CD4 cells decreases over time and the immune system becomes weaker. Eventually, the immune system becomes too weak to fight off certain serious infections.
- ⦿ Ongoing HIV infection also causes inflammation, which may increase your risk of heart attack, stroke, kidney damage and other long-term health complications.
- ⦿ Following an acute phase, when the virus is establishing itself in the body, HIV becomes a chronic infection. With proper care and treatment, people with chronic HIV infection can remain healthy for many years without ever developing AIDS.

However, the course of HIV infection is not a one-way street. In addition to preventing life-threatening illnesses from developing, anti-HIV drugs can halt the progress of disease and allow the immune system to rebuild itself, even in people who have very serious disease.



During the first stage of HIV infection, the viral load is high and the CD4 count drops. Once the body produces HIV antibodies (seroconversion), the viral load falls and the CD4 count returns to a more normal level.

Primary infection

During the first stage of HIV infection, called primary or acute infection, the virus makes its way from the point of infection—usually the genital tissues or the bloodstream—to the lymph nodes. This process takes a few days. Once HIV is inside the lymph nodes, it very quickly *replicates* (makes copies of itself) and releases new virus into the bloodstream. This burst of rapid HIV activity usually lasts for two to three months.

During primary infection, the amount of HIV in the blood (the **viral load**) is very high. This makes people very infectious during primary infection, a time when many people are not even aware that they are infected. They may have no or very few symptoms, and standard HIV tests may not detect HIV infection at this early stage.

During this time, there is usually a sharp but only temporary drop in the number of CD4 cells. The body also begins to produce large numbers of CD8 cells. These CD8 cells produce natural substances that help shut down or destroy HIV-infected cells, thus helping to reduce the amount of virus in the blood.

Some people experience flu-like symptoms two to 12 weeks after they are first infected with HIV. These can include one or more of the following:

- fever
- sore throat
- unexpected tiredness or lack of energy
- swollen lymph nodes
- aching joints and muscles
- skin rash

However, many people have no symptoms of any kind when they are first infected.

As the immune system learns to recognize and fight HIV, it starts to make **antibodies** to HIV. This process, known as seroconversion, usually occurs within one to three months of infection. Seroconversion is important because the best test we have to know whether you have been infected with HIV is the **HIV antibody test**. This test does not look specifically for HIV; instead, it looks for the antibodies that your immune system produces in response to HIV infection.

While the HIV antibody test is very good at detecting HIV, it may not give an accurate result until several weeks after infection. (The exact amount of time depends on the specific test being used.) This is because seroconversion needs to occur before the test can detect HIV antibodies in the blood sample and produce a positive result. Before seroconversion, an antibody test will produce a “false negative” result—in other words, it will incorrectly show that someone is HIV-negative.

There are newer HIV tests that look for the presence of the virus, not for antibodies. These tests are able to detect infection earlier—as soon as two weeks after infection. Even when these newer tests are used, they are generally followed up by an HIV antibody test to confirm the result.

Seroconversion indicates that the immune system has learned to partially—but not completely—control the infection. At this time, the very high levels of virus in the blood fall somewhat and the CD4 count returns to a more normal level. This signals the beginning of the next phase of infection—the chronic phase.

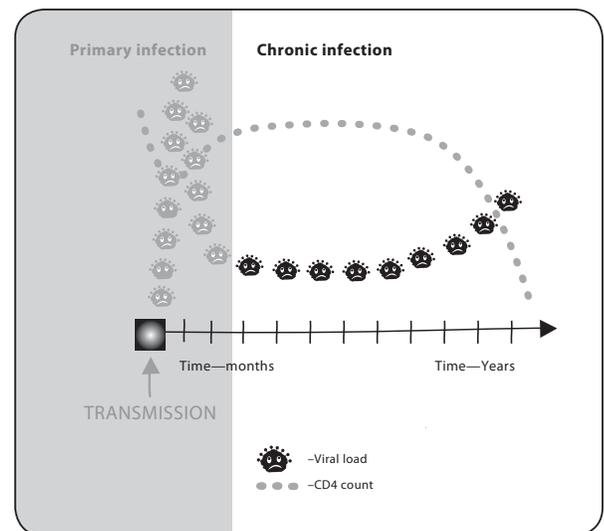
Chronic infection

After primary infection and seroconversion, HIV infection enters a chronic, or long-term, phase. During this time, the virus continues to replicate, even though there may be no obvious signs or symptoms of infection. As this phase progresses, CD4 counts gradually fall (although they may remain steady for many years) and symptoms tend to worsen. Although the specifics can vary widely between individuals, untreated chronic HIV infection generally progresses from being symptom-free (**asymptomatic**) to **symptomatic** and, finally, to a stage in which life-threatening infections are likely.

Asymptomatic infection

Asymptomatic means “without symptoms.” Many people with HIV may have few or no signs or symptoms of the disease for up to 10 years. During this period, the only evidence of HIV infection may come from lab tests: measurable levels of HIV in the blood and a lower-than-normal CD4 count.

However, even when there are no apparent signs or symptoms of HIV, the virus may be damaging the body in less obvious ways. While your body is actively fighting an infection, such as HIV, immune cells produce high levels of messenger molecules called *cytokines*, which signal other immune cells to go into action. This “switched-on” state causes **immune activation**, or **inflammation**.



After the body starts producing HIV antibodies, HIV infection begins a phase of chronic infection. If left untreated, the level of HIV in the blood eventually increases and the CD4 count drops.

Most infections only last a limited time, after which most immune cells return to their normal “resting” or “switched-off” state. Chronic HIV infection, however, throws the immune system into a persistent state of inflammation. This can be harmful in several ways. First of all, HIV most easily infects activated CD4 cells, so an activated immune system gives the virus more cells to infect.

Prolonged immune activation also reduces the lifespan of CD4 cells and possibly other immune cells. It may slowly damage blood vessels, increasing a person’s risk of cardiovascular disease (heart attack and stroke). It may hasten the pace of liver injury in people who have viral hepatitis and may damage the bones, kidneys and other parts of the body.

Most people living with untreated HIV will eventually develop more obvious symptoms. A few lucky individuals continue to have normal CD4 counts and no symptoms for much longer—perhaps throughout their normal lifespans. These rare individuals are called *long-term non-progressors*, or *elite controllers*. On the other hand, in some people, HIV may progress much faster, causing symptoms and significant decreases in CD4 cells within only a few years.

Symptomatic infection

As time passes, untreated HIV gradually causes increasing damage and the body’s defences weaken. At some point, symptoms of HIV infection begin to appear. These can vary widely between individuals, both in the time they take to develop and in the kinds of problems that occur. Some of the more common symptoms include chronic fatigue, unexpected weight loss, diarrhea, fever, night sweats and skin problems.

This stage is associated with the development of HIV-related infections, such as the fungal infection *candidiasis*, which causes thrush when in the mouth or throat and vaginal candidiasis when in the vagina. Usually (although not always), the first infections and symptoms to appear are not serious or life-threatening. They serve as warning signs that the immune system is significantly damaged and that HIV disease will continue to worsen unless the HIV infection is treated.

Life-threatening infections and AIDS

If the immune system becomes damaged enough, it leaves HIV-positive people vulnerable to infections that a healthy immune system could easily control. In general, these infections can be very serious or life-threatening. They are sometimes called **opportunistic infections**.

Some of these, like oral fungal infections, can be relatively minor and easy to treat (although even oral fungal infections can become very serious in people whose immune systems are weak). Other opportunistic infections that can also lead to serious complications and can be fatal if the immune system is weak include PCP (*Pneumocystis pneumonia*), MAC (*Mycobacterium avium* complex), toxo (*Toxoplasmosis gondii*), tuberculosis and CMV (cytomegalovirus). Certain types of cancer, such as lymphoma, are also more common in people with HIV.

The risk of life-threatening infections is usually closely tied to the CD4 count: a person's risk of developing many opportunistic infections increases when their CD4 count drops below 200 cells. For a person whose CD4 count is this low, medication to prevent and treat opportunistic infections is crucial.

The term **AIDS** describes the most serious stage of HIV infection, when the immune system is severely damaged and life-threatening infections have set in. AIDS stands for acquired immune deficiency syndrome:

- *Acquired* means that the condition is not inherited—you acquire (get) it at some point in your life.
- *Immune deficiency* is a weakness in your immune system.
- *Syndrome* is a combination of symptoms and/or diseases.

In Canada, AIDS is diagnosed when a person with HIV develops one or more "AIDS-defining" opportunistic infections or cancers.

HIV does not have to lead to AIDS

Fortunately, HIV infection does not necessarily lead to AIDS. Antiretroviral drugs can slow down or halt the effects of the virus on the immune system. Even people who have had serious AIDS-defining illnesses can usually recover and stay healthy with proper care. This is good news because the word *AIDS* is scary. It harkens back to the time when the progression of HIV disease was all but inevitable: people got HIV, then developed AIDS, and then died. Things have changed a great deal since then. For people with HIV who get proper care, see their doctor several times a year, take their medicines as directed and stay healthy, AIDS is no longer a concern.

The words we use to describe HIV have changed to reflect this new reality. The medical problems resulting from HIV infection are now often referred to as *HIV disease* or *chronic HIV infection*. These terms can be used to describe anyone's condition, whether or not they are being treated and regardless of whether they have been diagnosed with AIDS.

I was diagnosed in the hospital. I was really sick and didn't know what was going on. Then they did an HIV test and I tested positive. I was in really bad shape. My CD4 count was 33 and my viral load was half a million. I had pneumonia (PCP).

—Ken

Stopping the slide

As we mentioned, there is no longer any reason that HIV infection should inevitably lead to severe illness or death. Proper treatment can prevent HIV from causing serious illnesses. Treatment can also help people to get better and stay healthy even if they have already become sick with HIV-related infections.

In addition to treatment, there are many other factors that also affect the speed at which HIV disease progresses. These include the following:

- age
- the strength of the virus you are infected with
- how strongly your immune system responds to the virus
- nutrition
- smoking
- use of street drugs
- mental state and stress level (and how well stress is handled)
- other infections, such as hepatitis B or C

Some of these factors are not controllable, but others are. You may not be able to change your age (we wish!), but you can do something about how well you eat and whether you smoke or use street drugs. (See page 30 for some health hints.)

Unfortunately, some people don't find out that they are HIV-positive until they have had the virus for many years. Their diagnosis may come as a result of a serious HIV-related illness that takes them by surprise. Even so, infections can usually be treated. Most people who develop a serious HIV-related illness and are not taking antiretroviral drugs should begin treatment as soon as possible, to strengthen the immune system so that it can fight off the illness as well as prevent future infections.

People who test positive while they are still physically healthy have one big advantage: they know what to look out for. By getting regular thorough health checkups and routine lab tests, you and your doctor can spot any changes or warning signs and deal with them before they become bigger problems.

Monitoring Your Health

As a person living with HIV, you will likely have regular visits with your doctor to monitor your health. When you meet with your doctor, you will be able to discuss any new symptoms or problems you may be experiencing, and your doctor may do a physical exam to follow up on specific issues. You will also get blood drawn at the lab every couple of months. Your blood will be tested for several things. Two of the most important blood tests will be done to measure your **CD4 count** and your **viral load**. Many other routine tests can spot potential health issues even if there are no noticeable symptoms.

Monitoring symptoms

Every time you see your doctor, tell him or her how you have been feeling, especially if you have noticed any new or unusual symptoms. This could include fever or night sweats, diarrhea or upset stomach, headaches, rashes, a persistent cough, trouble breathing or anything that seems unusual. Your doctor will probably follow up with some questions. Take your time and answer honestly. It can be difficult to judge what's worth mentioning, but err on the side of caution. Not every little ache and pain is serious, but let your doctor know about anything persistent or anything that seems out of the ordinary. Better to spend an extra minute or two than to miss something important.

Any symptoms you're noticing may or may not be HIV-related—but the first step is to get them out in the open so you can find out what's causing them. This also includes changes in your mood, mental health and behaviour: if you've been feeling down or depressed or acting in ways you don't normally, say so.

CD4 count

Your CD4 count is the single most important measure of how strong your immune system is—that is, how well you are able to fight off infections. This, in turn, tells you whether you should start treatment sooner or later.

Generally, you should be getting your CD4 count checked every three to six months. It may make sense to check it more often if you've been stressed or sick. CD4 counts are measured in *cells per cubic millimetre* (cells/mm³—a cubic millimetre is about the size of a pinhead). CD4 counts generally drop as HIV does more damage to your immune system. If your CD4 count falls too low, the risk of serious opportunistic infections increases. However,

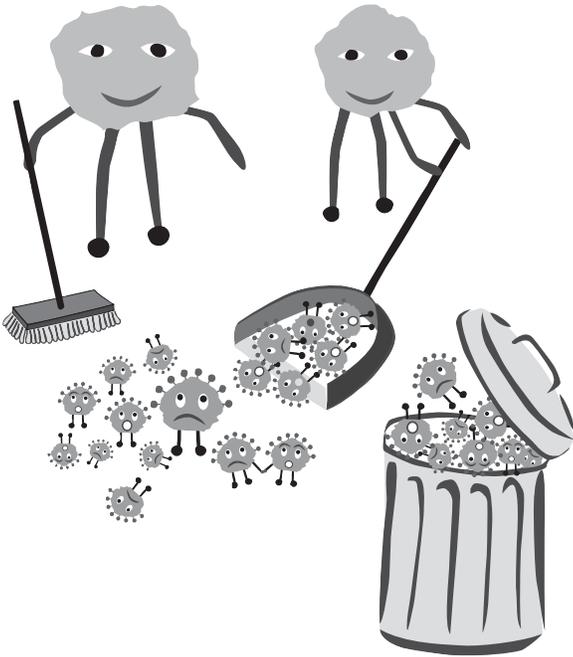
In a Capsule

- ⦿ Regular visits to your doctor are important for monitoring your health.
- ⦿ You and your doctor will likely discuss any new symptoms or problems you may be experiencing. From time to time, you will also have a physical exam.
- ⦿ Your doctor will order blood tests to monitor your CD4 count, viral load and overall health.
- ⦿ Your CD4 count gauges the strength of your immune system and helps determine the best time to start treatment.
- ⦿ Your viral load measures the amount of HIV in your blood and is used to determine whether your treatment is working.

My GP [general practitioner] is a compassionate doctor who spends extra time listening and talking to me, as he knows I've struggled with depression. He's there to help and support me.

—Randy

even lower-than-normal counts may still be “high enough”—that is, high enough to keep you healthy, without significant danger of serious infections.



- A normal CD4 count in healthy HIV-negative people is generally between 500 and 1,500 cells, depending on the lab where the blood is assessed. However, there is a lot of variation—even a “normal” count could be above or below this range.
- With CD4 counts above 500 cells, your immune system is still strong enough to fight off most infections. (In other words, try not to stress too much if your count is below “normal”—that is, below that of an HIV-negative person. The important question: is it high enough to keep you healthy?)
- CD4 counts below 500 cells deserve attention: they indicate that your immune system is becoming weakened. At the high end of this range, the risk of infection is still relatively small, but the risk becomes greater with lower counts.
- A CD4 count below 200 cells indicates that your immune system is very weak and that you are at risk of serious life-threatening infections.

In most HIV-positive people who are not on treatment, the CD4 count declines by an average of 50 to 100 cells each year. Declines in CD4 counts merit more attention if they fall faster than they have in the past or if they put you at greater risk of illness. As counts fall farther below 500 cells, the need to start HIV treatment becomes more pressing.

CD4 percentage

The number of CD4 cells can also be reported as a percentage of the total number of lymphocytes. The normal range is from 32% to 50%.

While your CD4 count can fluctuate a fair amount, the CD4 percentage does not normally vary as much. Looking at both of these numbers may give you and your doctor a better picture of the state of your immune system. If your absolute CD4 *count* takes a dip, but your CD4 *percentage* stays the same, you may not need to be as concerned about the decrease in count—it’s probably due to an overall variation in your white blood cells rather than an HIV-related drop in your CD4 cells.

If, however, your CD4 count and percentage both decline at the same time, that's probably worthy of attention. If your CD4 percentage falls below 20%, you may be at risk for *Pneumocystis pneumonia* (PCP). If your CD4 percentage falls below 15%, you are probably at risk for other opportunistic infections as well.

Viral load

Your viral load is the amount of HIV in your blood. Viral load tests measure the amount of HIV in a sample of blood. The results are reported as the number of copies of HIV genetic material (called RNA) in a millilitre of blood (copies/ml—a millilitre is about the size of a small bean). The standard tests in Canada can measure levels as low as 40 to 50 copies/ml. Below this level, your virus is considered *undetectable*. (There are more sensitive viral load tests, but these are used only in specialized laboratories and in some clinical trials.) Without treatment, a person's viral load can be as high as millions of copies/ml.

An "undetectable" viral load does not mean that HIV has been wiped out. It only means that the amount of HIV in your blood is too low to measure using routinely available tests. If you stop taking your treatment or if the HIV in your body becomes resistant to your antiretroviral drugs, your viral load will once again become detectable (that is, greater than 40 or 50 copies/ml).

If you are not on HIV treatment, the results of your viral load test will give you a rough indication of how fast you can expect your CD4 count to decline. In general, CD4 counts tend to decline faster in individuals with higher viral loads who are not on HIV treatment, and they stay stable longer in people with lower viral loads. However, this varies among individuals.

If you are on HIV treatment, your viral load is the most important measure of whether or not your treatment is working. The main goal of treatment is to reach an undetectable viral load within three to six months of starting treatment (although it might take longer if your viral load was very high to begin with). After your viral load becomes undetectable, the goal is to keep it that way.

If you are on treatment and your previously undetectable viral load becomes measurable, this indicates that the drug combination you are taking may no longer be fully suppressing the HIV. This may be a temporary "blip" and your viral load may go back to being undetectable the next time you test it (especially if it only rose to a very low level). These blips can occur every now and then in people on successful treatment, especially after vaccinations and temporary infections like the flu. However, if you are on treatment and

My CD4 count was around 1,200 for years. The first drop was about a year ago, to about 300. My viral load has always been around 120,000, but it spiraled up to 500,000. Last June I started [antiretroviral medications] and it's been great. I've had no side effects.

—Maggie

two or more tests in a row show a detectable viral load, then you and your doctor need to figure out why this might be happening. It could be due to any of the following factors:

- your body not absorbing the drugs properly
- not taking your drugs as directed
- your virus being resistant to one or more of the drugs you are taking
- interactions between antiretroviral drugs and other medicines, supplements and substances you are taking

It may be time to consider a treatment change. See page 67 for a full discussion of how to handle such “treatment failure.”

Other tests

Whether or not you are on treatment, you will likely be having “blood work” done regularly. Regular lab analysis of your blood can screen for many possible problems.

Your **complete blood count (CBC)** will probably be measured at each visit. The CBC checks all the major types of blood cells, including infection-fighting white cells, oxygen-carrying red cells and the platelets responsible for blood clotting. If any of these are present in abnormal numbers (too low or too high), this can alert you and your doctor to possible problems to keep a close eye on or investigate further.

Although CD4 and CD8 cells are especially important for people with HIV, your CBC may also include a detailed look at other kinds of immune cells, such as your total white blood cells, lymphocytes and neutrophils (see page 9).

Several different blood tests are used to track your **liver health**. Various types of liver damage or impaired function can affect your levels of liver enzymes. These liver enzymes include *AST* (aspartate aminotransferase), *ALT* (alanine aminotransferase), *AP* (alkaline phosphatase), *GGT* (gamma-glutamyltranspeptidase), a waste product called *bilirubin*, and a protein called *albumin*. Abnormal levels of any of these substances should alert you and your doctor that something (perhaps viral hepatitis, alcohol, recreational or prescription drugs) may be stressing or damaging your liver.

Your **kidney health** can be monitored by blood tests that measure your levels of *urea* and *creatinine*. Abnormally high levels could suggest that your kidneys are not functioning normally. Urine tests (*urinalysis*) can also check for things that should not be present in the urine, such as blood, protein, glucose (sugar) and white blood cells.

Blood sugar, or *blood glucose*, tests are an important part of monitoring the health of HIV-positive people. Some people on HIV treatment have high blood sugar levels, which should be carefully monitored. Abnormally high levels (called *diabetes* in the most severe cases) can lead to many health problems if not treated.

Blood fat, or **lipid**, levels are an important measure of your *cardiovascular* health—the health of your heart and arteries. High levels of cholesterol, especially the “bad” cholesterol (low-density lipoprotein, or *LDL*) can lead to heart disease and hardening of the arteries. Antiretroviral medications can raise the levels of “bad” cholesterol and another type of fat called *triglycerides*. Blood tests can also measure your “good” cholesterol (high-density lipoprotein, or *HDL*), which is good for your heart health and helps to clear “bad” cholesterol from the bloodstream.

Many experts and advocates believe that people with HIV should get **bone scans** regularly, due to an increased risk of thinning of the bones (*osteopenia* and *osteoporosis*).

Factors that may affect test results

Many of your lab results, such as your CD4 count, can vary over the course of a day or if done at different labs, and can be affected by many other factors as well. It’s best to have your tests done at the same time of day, at the same lab, and (if you’re premenopausal) at the same time during the menstrual cycle. You may want to always be tested first thing in the morning, before eating or exercising. (Many labs require blood to be drawn for CD4 counts and viral load tests in the morning, anyway.) Some tests have to be done on an empty stomach—in particular, blood sugar and lipid levels. Just make sure you follow any specific instructions for the tests you’re doing.

Getting a vaccination (such as the flu shot) or fighting off an infection (such as a cold or the flu, especially if you have a fever) can temporarily raise your viral load and lower your CD4 count. In these cases, it may make sense to delay your blood tests for a couple of weeks. Anything else unusual that has gone on around the time of your blood tests—such as drinking more alcohol, sleeping less or being more stressed than usual—may affect your results.

In general, if any single CD4 count or viral load measurement seems out of line, a repeat test will reveal whether the difference is a new trend or just a “one-off.” The overall trends in your results are more important than any single result.

I decided to take my doctor’s advice and get a bone scan to check for early-stage bone loss, which is common in both men and women with HIV as we age. Now I’m supplementing regularly with calcium, to protect against further bone loss.

—Darlen

Tracking your lab results

Starting on the next page, we've included a set of sheets you can use to keep track of your lab results, medications, symptoms and other key pieces of health information. There are also tools available online that can help you keep track of other lab results or graph them over time. Here are a couple you can try:

- AIDSmeds—Graph My Labs!
<http://www.aidsmeds.com/graphs>
- The Body—My Health Tracker
<https://secure.thebody.com/tracker>

Personal Health Record

(Photocopy this page and give to a friend in case of emergency.)

Name _____	Date of birth _____
Home address _____	Email address _____
_____	Home phone number _____
_____	Work phone number _____
_____	Cell phone number _____

Health card number _____

Private health insurance information: _____

Age _____ **Weight** _____ **Height** _____ **Blood type** _____

Date of HIV diagnosis _____	Allergies and drug sensitivities _____
Other medical conditions _____	_____
_____	_____
_____	_____

Family history (for example, has a family member ever had diabetes, heart disease, cancer, etc?)			
Condition	Family member (relation)	Condition	Family member (relation)
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____

Healthcare providers		
Specialty	Name	Contact information
Family doctor	_____	_____
_____	_____	_____
HIV specialist	_____	_____
_____	_____	_____
Pharmacy	_____	_____
_____	_____	_____

In case of emergency, contact:

Name _____ **Relationship** _____ **Phone** _____

Personal Health Record

History of anti-HIV drugs (keep this list current)

Anti-HIV drug	Dosing schedule	Special instructions	Date started	Date stopped	Reason for stopping

History of other drugs and/or therapies (keep this list current)

Name of drug or therapy	Dose (if applicable)	Special instructions	Date started	Date stopped	Reason for stopping

History of significant medical events, such as hospitalization, serious illness, surgery (keep this list current)

Date	Description of event	Notes

Personal Health Record

Monitoring tests (fill in this chart with the results of each viral load test, CD4 test and any other tests you want to monitor, such as cholesterol or triglyceride levels)

Date of test											
Viral load											
CD4 cell count											

Record of symptoms and side effects

Describe symptom/side effect	When did it occur and how long did it last?	How was it treated?	Notes

Notes for visit to doctor

(Photocopy this page and use for each visit)

Changes in my health since the last visit (for example, new symptoms, illnesses, etc.)

Difficulties or challenges with my treatment and/or care

Questions for my doctor

Things I need from my doctor (for example, prescription refill, referral)

Action plan

Resources

Monitoring your health—online learning module covering CD4 counts, viral load and other tests used to track your health

HIV Viral Load Testing—informative brochure on the viral load test and how it fits into your treatment plan

In-depth Fact Sheets on AIDS-related infections and cancers and HIV transmission

The Positive Side—health and wellness magazine for people with HIV, featuring such articles as:

- “Top 9 Reasons to Call Your Doctor Immediately”
- “Me and My Liver” (liver health)
- “Here’s Looking at You, Kidneys” (kidney health)
- “Better Living through Rehab” (regaining health after illness)

Look in the e-zine index for more (www.positiveside.ca).

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

Notes

Treating HIV

In this section, we tackle the why, when and how of HIV treatment. Along with questions like “When should I start?” we also suggest some ways you can prepare for HIV treatment.

- ⦿ Drug treatment is just one important part of an overall plan for staying healthy, as you’ll learn in **There’s More to Health than ART**. Looking after every aspect of your health—physical, mental, emotional, sexual and spiritual—is just as important.
- ⦿ **Working with Your Doctor** is about building a good relationship with your doctor and the other members of your healthcare team.
- ⦿ We then begin our journey into the world of **HIV Treatment**. Antiretroviral drugs are used to slow the damage HIV does to the body. These drugs must be chosen carefully and used correctly.
- ⦿ Most people with HIV eventually have to start taking HIV treatment. The main goal is to start treatment early enough to avoid HIV-related health problems. **When to Start** looks at what’s involved in this decision.
- ⦿ Before you start treatment, it can be helpful to work through your feelings about taking antiretroviral medications and some of the practical issues involved. **Preparing to Start Treatment** includes some tools to help you do this.
- ⦿ In **Choosing a Drug Combination**, we let you know that although there are many antiretroviral drugs and many possible combinations, most people are able to start with one of a few “preferred” drug combinations. You may have to choose certain drugs and avoid others, based on your health conditions and other factors.

There's More to Health than ART: Holistic Health

In a Capsule

- ⦿ There is far more to living a healthy life with HIV than simply taking antiretroviral drugs. Being healthy means being healthy physically, mentally, emotionally and sexually.
- ⦿ Simply eating well and getting enough exercise and sleep can make a great difference to your health and well-being. So can maintaining a healthy weight and not smoking.
- ⦿ There are many other ways you may be able to better your health and quality of life.

When you are living with HIV, staying healthy does not begin and end with antiretroviral drugs. Of course, they're a crucial part of treatment. But sometimes it's easy to get so wrapped up in treatment questions that we lose sight of the bigger picture. A more "holistic" approach means looking at that big picture—your body, mind and spirit as a whole.

A few basics—such as healthy food, rest and exercise, and attention to your mental and sexual health—can go a long way toward keeping you well. They can build a strong, healthy foundation that puts you in the best position to deal with a chronic illness and to succeed on treatment when it becomes necessary. All of these things should be part of a lifelong plan for living with HIV, whether you are currently on drug treatment or not.

Good nutrition

You are what you eat, and eating right is especially important for people with HIV. The nutritional needs of people with HIV are greater because the body needs to work harder to deal with the ongoing infection of the virus. HIV can also lead to a shortage of important nutrients, even during the early stages of HIV disease and even while CD4 counts are still high. These shortages can speed up the progression of HIV disease and can cause many symptoms of their own. Since virtually every known nutrient is important for some aspect of the immune response, it makes sense to maintain a healthy diet.

So what does that mean in practical terms? First, it means eating what's good for you as often as you can. This includes a balanced diet with a variety of foods. Here are some simple tips to build your daily menus:

- Have 7 servings of colourful fruits and vegetables each day.
- Add 6 to 8 servings of grains (choose unrefined complex carbohydrates, such as brown rice and whole-grain breads, crackers and pasta).
- Combine with 2 to 3 servings of milk products (such as milk, yogurt, kefir) and/or alternatives (such as soy or almond milk).

- Serve with 2 to 3 servings of meat (red meat, poultry, fish) and/or meat alternatives (such as eggs, legumes, tofu, nuts).
- Sprinkle lightly with 2 to 3 tablespoons of fats and oils. Choose “good” kinds of fats (monounsaturated fats, like olive oil and canola oil) over partially hydrogenated oils and “trans” fats.
- Enjoy with lots of healthful liquids (water, juices, herbal teas and the like; not chemical- and sugar-loaded junk drinks).

Also, make sure the food you eat and the water you drink are safe! People with weakened immune systems are more vulnerable to illness from food that has become contaminated by bacteria. This is especially important when you are travelling.

Make sure you take appropriate nutritional supplements. Having the right levels of nutrients can help slow the progression of HIV, improve long-term survival, and reduce or eliminate many symptoms and drug side effects (such as fatigue, skin problems, neuropathy, diarrhea and digestive problems). Start with a multivitamin/mineral formula that provides basic micronutrients (like vitamins A, B and D₃, minerals and trace minerals), as well as antioxidants (such as vitamins E and C, alpha-lipoic acid, N-acetyl-cysteine, selenium, mixed carotenoids and coenzyme Q₁₀).

CATIE's *Practical Guide to Nutrition* covers, in detail, the nutritional needs of people with HIV. Find it online at www.catie.ca or order your free copy through the CATIE Ordering Centre, available at www.catie.ca or 1-800-263-1638.

Exercise

Not everyone can run a marathon, but people with HIV can benefit from many kinds of exercise. In addition to strengthening your immune system, regular exercise can help you maintain muscle, keep your heart and lungs healthy, manage your stress and fight depression. Start with a moderate amount of exercise that involves aerobic activity (such as walking, rowing, swimming, running, skating or some other heart-pumping exercise) as well as resistance training (muscle-building exercises like weight-lifting). You might be able to combine them in one exercise.

I like to eat well. I'd like to eat better, but unfortunately the cost of 'better' is much more expensive. I try the best I can. I try to get things I can afford: a bit of lettuce, a tomato, broccoli. I take multivitamins.

—Robyn



Working out makes me feel alive. The gym gives me an opportunity to interact with people; it gives me something to look forward to. Both my doctors said hiring a trainer and working out is the smartest thing I ever did. It makes me feel like I'm winning.

—Joe

When I wake up in the morning I do a smudge—a Native ritual that cleanses the energy around you. You burn some sage in a shell—it has a very sweet smell. I learned this from the First Nations people in Canada. This ritual helps me with my depression and to maintain a positive mood. It makes me understand that yesterday is gone and I can start a new day.

—Minneh

Complementary therapies

The term *complementary therapies* describes a wide range of practices. Perhaps the simplest definition is anything that isn't considered part of conventional Western medicine (by which we mean the care you typically get at doctors' offices, HIV clinics and hospitals). Complementary therapies are generally used in addition to, not instead of, conventional Western medicine. The two complement each other, and you can use both as you see fit. You might also hear the term *complementary and alternative medicine* (or CAM) to describe these practices.

Complementary therapies include many different kinds of therapy, from aromatherapy to yoga, herbal remedies to homeopathy. Some, like massage and other forms of touch therapy, are largely focused on your physical body. But even a physical therapy like massage can have profound effects on your mental and emotional state, relaxing you and dispelling stress. Many other complementary therapies are intended to help you heal not just physically, but mentally, emotionally and spiritually as well.

CATIE's *Practical Guide to Complementary Therapies* and *Practical Guide to Herbal Therapies* explore these topics in more depth. Find them online at www.catie.ca or order your free copy through the CATIE Ordering Centre, available at www.catie.ca or 1-800-263-1638.

Program the mind for healing

The mind has an amazing power to boost the body's ability to heal, and the power of hope is one of the best tools you can have for long-term survival. Anything that helps lower stress and create feelings of hope and a positive outlook—including yoga, meditation, positive thinking, affirmations, massage, support groups and absolutely anything else that helps you thrive—can be a powerful aid.

Dealing with depression and drug use

From time to time, everyone experiences short periods of feeling down or "blue." However, some people feel a sense of sadness and helplessness they cannot shake. These are often accompanied by low energy, problems sleeping, eating or concentrating; and, in extreme cases, wanting to harm yourself or commit suicide.

This condition, called **depression**, is common among people with HIV, and many people with HIV feel depressed at some point during their lives. Like other emotional problems, depression limits a person's quality of life and may interfere with the immune system's ability to fight HIV. Also, people often find it harder to stick to any kind of routine if they are depressed. For example, they might find it hard to take medication on schedule or stick to other important routines—even eating and sleeping properly.

Depression is not always just about feeling sad. It can also cause irritability, agitation and restlessness. Some people with depression lose their appetite and lose weight while others eat excessive amounts of food and gain weight. So if you are depressed, or even if your moods just don't seem right and aren't getting better, talk to a doctor or counsellor.

You can get help. The good news is that most people who are depressed can feel better with appropriate care and treatment. It is important to seek support so that the problem can be identified and treated.

I don't consider myself a victim.
I know I have a place in the universe and HIV is one of the pieces in my life, not all of it. I'm finally at peace with HIV. It's doing its thing, I'm doing my thing—we can live together.

—Devan



In caring for a friend who was a crystal meth addict, I fell to temptation and became wired to meth myself. This went on for about a year. My friend has been gone now for 14 months and I am clean. Getting away from the meth was not easy, but I made it through with the support of family and friends.

—Damien

Alcohol and recreational or street drugs are a part of many people's lives. Some people simply enjoy a few drinks, or shake off their day-to-day stresses by partying it up on weekends. But alcohol and drug use can sometimes be a problem, especially if they affect how you take care of yourself, like if they cause you to skip doses of antiretroviral drugs, take sexual risks you later regret, spend money that you need for other things, and neglect your health in other ways. Street drugs may also interact with other medications you're taking, which can cause serious problems in some cases (see page 63). This is something you should discuss with your doctor and pharmacist.

The stress and challenges of being HIV-positive may lead some people to use more drugs and alcohol. Drug use may be a way of coping, but in the end, may only make it harder to deal with the actual issues. Drug or alcohol use can also become an addiction—something you are physically or psychologically unable to stop without professional help.

If you do use alcohol and/or street drugs, hopefully you feel able to talk about it honestly and openly with your doctor. (If not, try to find a counsellor who you *can* talk to. Many AIDS service organizations make referrals.) If drugs or alcohol start to interfere with your mental or physical health, your social life or finances, or if people close to you express concern, it may be time to take an honest look at your use. Help is available; don't be afraid to ask for it if you think you need it.

Quitting smoking is one of the best things someone with HIV can do for their health. You probably know that smoking can cause lung cancer and other kinds of cancer and lung disease and can greatly increase a person's risk of heart attack and stroke. Having HIV makes smoking even more hazardous to your health. If you smoke cigarettes, you should do everything you can to stop. Your doctor can help you.

Working with Your Doctor

Your doctor, and your relationship with your doctor, will play a crucial part in your care. You will likely see your doctor regularly, and together you will chart the course of your HIV treatment and care. Because you'll be working closely together, try to find someone who is knowledgeable and who you can trust and be open with.

Some people see a **general practitioner** (GP) or family physician who has experience in HIV and can treat their HIV infection along with other medical problems they may be experiencing. Others see a **specialist** in infectious diseases or immunology to treat their HIV, while their GP deals with problems that are not related to their HIV.

Ideally, you will want to choose a doctor who is experienced in treating HIV and who takes the time to stay up-to-date on all the latest information. In larger cities, it's possible to find a family physician with expertise in treating people with HIV. Unfortunately, in some parts of Canada, it is difficult to find a doctor knowledgeable about HIV care. In this case, try to find a doctor who is willing to work with you to learn about HIV. Your local AIDS service organization may be able to suggest a doctor in your area who has some experience caring for people with HIV. CATIE can also provide information for you and your healthcare team. Give us a call at 1-800-263-1638 or visit us online at www.catie.ca to find out how we can help.

If you have the option of choosing between doctors, consider interviewing them and asking them about everything that's important to you. You definitely want a doctor with whom you feel comfortable and are able to talk freely, and one who will answer your questions respectfully.

After you find your doctor, remember to keep the lines of communication open. Communication works best when there is mutual respect. You want your doctor to respect you, so it makes sense that you approach the relationship with respect too. Here are some other suggestions for working with your doctor:

- There are several things you can do between visits: keep track of the symptoms or side effects you experience, write down questions you have for your doctor, and keep note of things you need to ask during your next visit. The Personal Health Record (page 23) has spaces for all of these issues and more.

In a Capsule

- Your doctor is your most important healthcare provider, but there are many other people who can help you, from nurses to pharmacists to counsellors.
- Do your best to find a doctor who has experience in caring for people with HIV.
- Good communication is essential for a good relationship with your doctor. We suggest a few tips and tricks that may help.

I first met my new doctor when my original GP, who had lots of experience with HIV, unfortunately passed away. I was his first patient with HIV. In that meeting, he said, "It sounds like you'll be a challenge to work with, but I'm up for it." And he has been.

—Randy

My traditional healer has helped me understand more about my illness by applying it to an Aboriginal context and relating HIV to the medicine wheel teachings. When I combined Western medicine with traditional healing, I stopped getting the side effects.

—Rod

- When meeting with your doctor, remember that there are no stupid questions. If there is something you don't understand, say so. If your doctor is confusing you with medical jargon, ask her or him to explain things in terms you can understand.
- When any treatment is recommended, ask for a clear explanation of why it's being recommended, exactly what it will involve, what kind of results you can expect, what any possible side effects might be, and if there are alternatives to consider. This will likely work best if you can make your doctor feel that you are asking because you would like as much information as possible, so they know you want to work together and are not challenging them or being hostile.
- Because the amount of information your doctor gives you may sometimes seem overwhelming, you may want to bring along a family member, partner or friend who can help remember or record what the doctor is saying. You could also bring a notepad and pen to jot down notes—or even a tape recorder or an MP3 player with a “record” function. Most doctors don't object to that; just ask them first.
- Your doctor may not have enough time to answer all your questions in a single visit. If so, don't skip anything; make another appointment or ask your doctor if it's possible to make a longer appointment the next time.

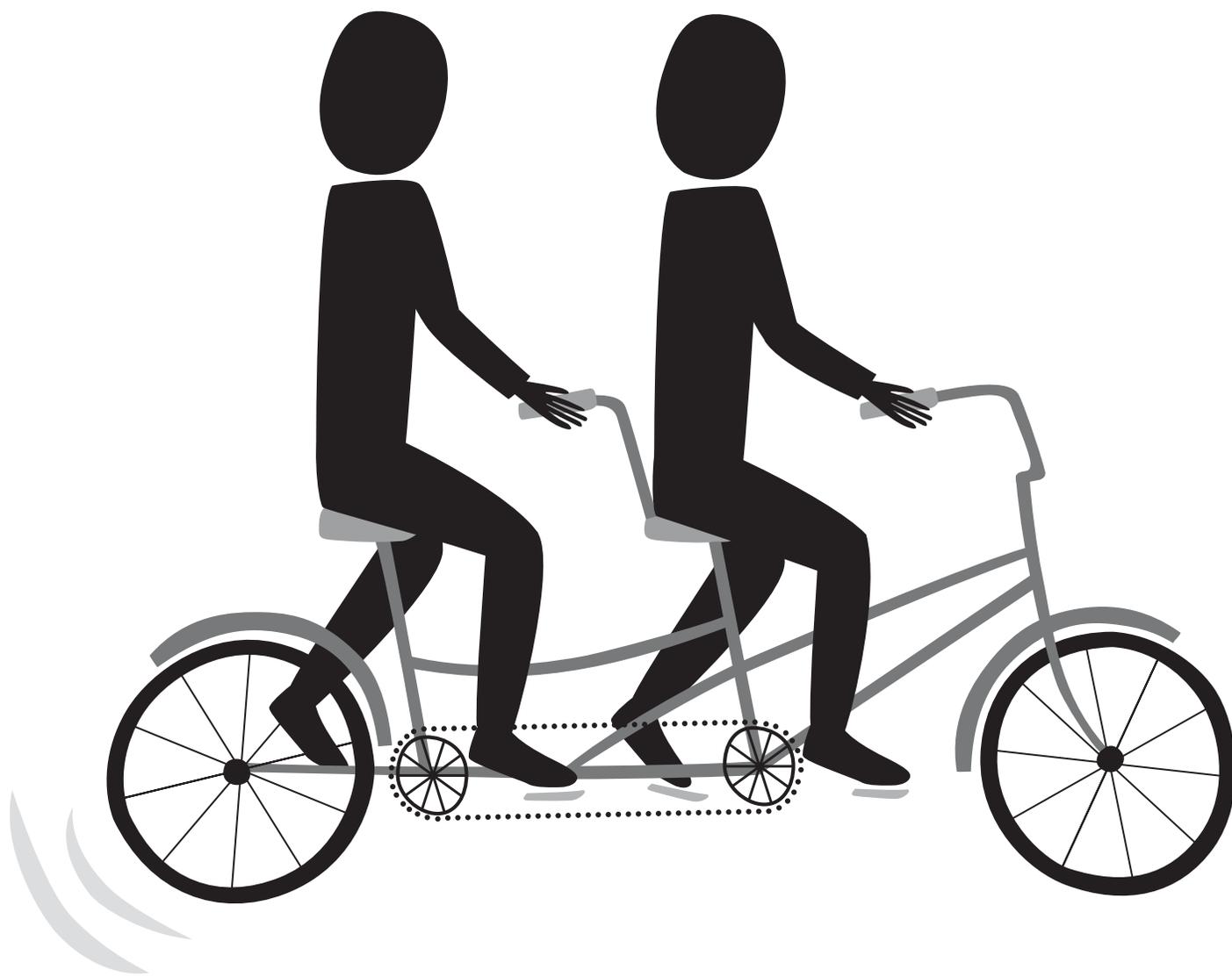
Beyond your doc

Your healthcare team doesn't end with your doctor. Your clinic may have **nurses** on staff, as well as other professionals, like **social workers** and **counsellors**. These people all have valuable skills to contribute to your care and can often give advice on practical matters, like covering drug costs or taking your medications. What's more, they may have more time to talk to you. For example, your nurse may be able to answer a quick question when your doctor is swamped.

You will also be seeing a **pharmacist** whenever you go to pick up your medications. Because pharmacists are generally more available than doctors, many people with HIV rely on their pharmacists for information about HIV and their treatment. Pharmacists can help you keep track of your drugs and avoid allergies or interactions between drugs. To avoid drug interactions, it's best to get them all from a single drugstore, especially if you are filling prescriptions from more than one doctor.

Pharmacists can also provide useful suggestions on how to take your drugs regularly without missing doses. Pharmacists can also help you get your drugs paid for by government programs and insurance companies.

Find out what these health professionals have to offer so that you can get the most out of your team. If a lot of people are involved in your care, make sure important details don't slip through the cracks. The **Personal Health Record** back on page 23 can help you keep track of important information about your healthcare team and your treatments.



HIV Treatment

In a Capsule

- ⦿ Unfortunately, there is currently no cure for HIV infection. However, HIV treatment can significantly reduce HIV's ability to make copies of itself and dramatically slow HIV disease, allowing the immune system to recover.
- ⦿ HIV treatment usually consists of a combination of three or more antiretroviral medications.
- ⦿ Most HIV-positive people have to start treatment at some point. The best time to start depends on your CD4 count and other factors that you and your doctor will discuss.
- ⦿ Guidelines for the best use of antiretroviral medications have been developed by experts and are constantly being updated based on the latest evidence.
- ⦿ Guidelines are not rules. Your doctor may recommend a combination of anti-HIV drugs that are not listed as “preferred” treatment in guidelines.

What is ART?

There is no cure for HIV infection—at least, not yet. However, there are medications for treating HIV, called **antiretroviral drugs**. When used properly, these medications can all but stop HIV from replicating, allowing your immune system to retain (or rebuild) its strength and keep you healthy.

HIV treatment means taking an appropriate combination of antiretroviral drugs—usually at least three. These drug combinations go by the fancy names ART (antiretroviral therapy) or HAART (highly active antiretroviral therapy), but you can call it whatever you like—your meds, your combo, whatever works for you. We’re going with the term antiretroviral drugs in this guide because sometimes we like to be just a bit fancy.

What do antiretroviral drugs do?

As long as HIV is left untreated, it continues to infect CD4 cells and other types of cells inside your body. It uses these cells to make millions of copies of itself, which then infect other cells, and so on. This process, called **viral replication**, eventually damages your immune system, lowers your CD4 count and leaves you vulnerable to serious diseases.

The goal of antiretroviral drugs is to block this replication process. How do they do this? There are several different groups, or *classes*, of drugs. Each class of drugs attacks the virus in a different way. In the appendices, we talk at length about each of the antiretroviral drug classes, the specific drugs in each class, and how each one works to stop the virus. Generally, drug combinations include drugs from different classes, so as to fight the virus in several different ways.

Viral replication slows down dramatically soon after you begin taking antiretroviral drugs. Essentially, the “assembly line” for building new virus slows to a crawl and very little new virus gets produced from that point onward. Since very few viruses are now being created, the overall amount of HIV in your body—your viral load—gradually drops. Most people’s viral loads fall to undetectable levels within several months of starting treatment.

“Suppressing” HIV in this way allows your immune system to rebuild itself and become stronger. Your CD4 count should rise, the risk of serious infections should drop, and many of the other symptoms of HIV infection should diminish or disappear. Your immune system will also “calm down” because it is no longer constantly fighting HIV—we’re beginning to realize all the health benefits this can have (see page 42).

Remember, though: there is still no cure for HIV infection, and an “undetectable” viral load in the blood does not mean that the virus is gone. When a person first becomes infected with HIV, the virus quickly finds its way inside long-lived cells deep inside the immune system and certain organs such as the brain. Antiretroviral drugs sometimes have difficulty penetrating the brain and some other organs, and HIV can replicate there at very low levels. Despite scientists’ best efforts, they have not yet found a way to eliminate this “reservoir” of stored virus. This means that, at present, HIV is a lifelong infection and HIV treatment is a lifelong commitment.

Do I have to take antiretroviral drugs at all?

Most people with HIV probably wonder: Do I have to take antiretroviral drugs at all? The short answer is yes. To put it bluntly, HIV can kill you if it’s left untreated. We sometimes overlook the basic fact that antiretroviral drugs save lives. It’s completely understandable to feel hesitant about treatment, given its potential side effects and the demands of taking pills every day. Just remember that, in the long run, *not* going on treatment is almost always worse. This isn’t just opinion—it has been proven repeatedly in clinical research and in real life. Indeed, the benefits of modern antiretroviral treatment greatly outweigh the risks for the vast majority of HIV-positive people.

Less than one percent of people with HIV seem able to live with the virus for decades without suffering serious harm. These lucky few (so-called “long-term non-progressors”) may have some genetic advantage that helps their bodies control the virus on their own. However, most HIV-positive people will eventually develop more serious disease if their HIV is left untreated. So, for most people, the question isn’t *whether* to start ART, but *when*.

Can I still infect other people if I am taking antiretroviral drugs?

Yes, it’s still possible to transmit HIV during sex even if you are taking antiretroviral drugs. Some experts have pointed out that people with HIV who are on treatment and who have

Since 1989—the year I was diagnosed with HIV—I’ve taken it upon myself to learn about biological sciences and medicine through the lens of HIV disease. Even if I sometimes end up slogging through science I quite frankly don’t understand, learning all that I can about HIV disease has still given me a sense of power and control over my own healthcare.

—Wayne

It is difficult to see this information [about the effect of treatment on risk of transmission] as a clear go-ahead to abandon condoms.

—Darren

undetectable viral loads have a very low risk of transmitting HIV to other people through unprotected sex. However, this depends on many factors. For example, if one partner has a sexually transmitted infection (STI), such as gonorrhea, syphilis or herpes, this increases the chance of transmitting HIV during unprotected sex—and people are not always aware that they have an STI.

The risk of transmission also depends on viral load—not just in the blood, but in sexual fluids (pre-cum, semen, and vaginal or anal fluids). Significant levels of HIV can be present in these fluids, even in people whose viral load is undetectable in their blood. Even in the blood, viral load can vary from one test to the next. People whose viral load is usually undetectable can have short-lived increases, or “blips,” of detectable viral load.

So, while it’s true that treatment may reduce the chances of transmitting HIV in some circumstances, there are many uncertainties involved. It’s unwise to think of HIV drug treatment as a replacement for safer sex.

How do we know which treatments are “best”?

HIV treatment involves many decisions. Two of the most pressing are *when* and *what*, or more precisely: When is the best time to start treatment? and What drugs should I take? The answers to these and other questions come from studies called **clinical trials**. In these studies, two or more groups of otherwise-similar patients are given different treatments, and the outcomes are compared. (For more information about clinical trials, see *Clinical trials: what you need to know*, available at www.hivnet.ubc.ca or through the CATIE Ordering Centre.)

Information from clinical trials is rendered into practical recommendations in **treatment guidelines**. These documents summarize the clinical information we have on key issues, such as when is the best time to start, what are the best combinations to use, how to detect and manage side effects, and so on.

Groups of HIV medical experts in the U. S., Canada, the European Union and elsewhere have produced treatment guidelines. Both British Columbia and Quebec produce their own HIV treatment guidelines, and many doctors in Canada refer to the U.S. guidelines called the *DHHS guidelines*. While in agreement on many points, guidelines may differ as to specific recommendations, such as when to start treatment and which drugs are considered best for first-time use.

Guidelines are not inflexible rules: they change often as new drugs, new technologies and new information become available. Finally, authoritative as they are, they are still *only guidelines*—for doctors to consult and use in combination with their own experience to guide their practice.

For most people with HIV, one of the most important questions is: When is it best to start treatment? We explore this question in the next section.

When to Start

In a Capsule

- To decide when the best time is for you to start treatment, you and your doctor will need to consider your CD4 count and your readiness to start, among other factors.
- People who have very low CD4 counts or have already had any serious HIV-related illness should start treatment as soon as possible.
- People who have had other conditions that put them at risk should start treatment.
- Pregnant women should start treatment to reduce the risk of HIV being transmitted to their baby.
- People with higher CD4 counts can monitor their counts and periodically weigh the benefits and challenges of starting treatment.

Almost everyone with HIV has to start treatment at some point. Deciding on the best time to start involves several factors, including the strength of your immune system, as indicated by your CD4 count. It also depends on other medical conditions or factors in your life, and especially on your readiness to start treatment. Starting treatment is a long-term commitment. In working through this important decision, you will want to factor in both the benefits and challenges of treatment.

Benefits: HIV treatment stops the replication of HIV, which decreases your viral load and allows your immune system to maintain or rebuild itself. A stronger immune system can help keep you healthy and better able to fight off infections. Many people report that after starting treatment, many of their nagging health problems—like tiredness or ongoing skin rashes—were resolved. Starting treatment made them feel healthier. There is also a growing body of evidence that treatment can help stave off some of the long-term problems that affect people with untreated HIV disease—like heart attacks, cancer, and liver and kidney problems. Finally, being on HIV treatment can reduce the risk of HIV passing to others during sex, and so some people also consider taking treatment to reduce the risk of transmission.

Challenges: The decision to start treatment means a commitment to the challenges, inconveniences and possible side effects of taking pills on a regular and ongoing basis. It's important to take antiretroviral medications as directed and to miss as few doses as you possibly can. Too many missed doses, and your treatment can stop working permanently. Antiretroviral drugs can also cause side effects and long-term toxicities, which can range from minor to severe. In the best cases, people have very few problems with their treatment. Many others have either manageable side effects or side effects that go away on their own in time. However, some people experience more serious side effects. Fortunately, treatments have improved considerably since the first antiretroviral drugs. Current combinations have fewer and more tolerable side effects, and require fewer pills and less-frequent dosing.

One thing is for certain: when to start treatment is *your* decision. No matter what your situation, your feelings and your questions about treatment, discuss them with your doctor and make sure the answers make sense to you. At the end of the day, you're the one who has to take the pills, and you shouldn't start until you're ready to make the commitment to succeed.

Some people need to start as soon as possible

People in the following groups should begin treatment as soon as possible. For some people, this may mean beginning treatment right after their HIV diagnosis.

- Most people who have had a **serious HIV-related illness** should start taking treatment as soon as possible. Any active disease is likely to worsen if left untreated. In cases of serious illness, starting HIV treatment could be life-saving. Even if the immune system has been severely damaged, it can usually rebuild itself, though this may take time.
- People with a **CD4 count below 200 cells** should also start treatment as soon as possible. If your CD4 count is below 200 cells, you are at immediate risk of serious HIV-related illness, even if you are feeling perfectly fine. At this stage, serious illnesses could develop at any time. Beginning treatment immediately can increase your CD4 count and decrease this risk. In addition to taking antiretroviral drugs, you may also need to start taking medications to lower the risk of getting certain infections; you'll be able to stop these medications (but not the antiretroviral drugs) once your CD4 count has risen to safer levels.
- **Pregnant women** should start taking antiretroviral drugs to minimize the risk of passing HIV to their fetus and, later, to their baby. Your doctor may recommend specific anti-HIV medications if you are pregnant or planning to become pregnant. After giving birth, you and your doctor will decide whether or not you should continue treatment for your own health.

If possible, everyone should start treatment before their CD4 counts fall below 350 cells

The lower your CD4 count, the more seriously you should think about starting treatment. Experts agree that people with a CD4 count below 350 cells should start treatment. If your CD4 count is below 200 cells, you are at increased risk of life-threatening infections and should start HIV treatment immediately. If your CD4 count is above 200 cells but below 350 cells, leaving HIV untreated still puts you at a significantly higher risk of serious illness and death. This has been confirmed by several studies. If your CD4 count is in this range, your doctor will likely suggest you start treatment.

My doctor really wanted me to take the medications, but I didn't want to start until I was really sick. I'm not a pill person. I was worried about taking them because I have a few friends who have gotten sick from side effects. But my CD4 count was getting low, so I agreed to start meds a little while ago. I feel fantastic. Now, with the meds, I have more energy.

—Deanna

For CD4 counts above 350 cells, you should consider starting treatment

HIV-positive people with CD4 counts higher than 350 cells should consider starting treatment if they:

- are older than 55 years
- are at high risk of cardiovascular disease
- are thinking about becoming pregnant
- have a rapidly falling CD4 count (dropping by more than 100 cells per year)
- have a high viral load (usually 100,000 copies or more)
- are co-infected with hepatitis B, hepatitis C or tuberculosis
- have suffered kidney damage due to HIV

People in any of these situations may benefit from starting treatment rather than waiting until their CD4 counts decline further.

If you do not have any of the conditions listed above and your CD4 counts are above 350 cells, you are not at immediate danger of significant problems due to your HIV infection. However, the higher your CD4 count, the better your body can fight infections. Indeed, **CD4 counts above 500 cells** are comparable to CD4 counts found in HIV-negative people, so many people with HIV who have CD4 counts above 500 cells decide to delay treatment and continue to monitor their health.

The closer your CD4 count gets to 350 cells, the more you and your doctor will likely consider starting treatment. If your **CD4 count is between 350 and 500 cells**, you may choose to begin treatment. If you do not begin treatment, you and your doctor will likely monitor your health more closely. This will include regular lab tests, such as blood tests to measure your CD4 count, to watch for any new trends.

If you want to have a baby and are **planning to become pregnant**, you should discuss your HIV treatment options with your doctor. By discussing pregnancy plans with your doctor, you can decide on a treatment strategy before becoming pregnant and dramatically reduce the risk of HIV passing to your fetus.

For HIV-positive people with CD4 counts above 350 cells, there may be another argument for starting treatment, based on our growing understanding of the long-term consequences of HIV infection. Untreated HIV infection results in ongoing inflammation that puts people with HIV at risk of cardiovascular disease (heart attack and stroke), cancer, bone and kidney problems, and possibly other health conditions. Because antiretroviral drugs help to reduce inflammation and growing

evidence shows that being on treatment can reduce the risk of these problems, some experts suggest that people with CD4 counts above 350 cells but below 500 cells should consider starting treatment.

However, to say that treatment always reduces these risks may be oversimplifying the matter. Certain antiretroviral medications can raise the risk of heart disease. Some medications also appear to contribute to bone mineral loss. Researchers are still investigating this complex topic of long-term risk, to better identify who is most likely to benefit from starting treatment earlier.

Finally, as we discussed earlier on page 39, successful antiretroviral treatment might reduce your chances of transmitting HIV to a sexual partner. This has led some experts to suggest that many new infections can be prevented by diagnosing and treating as many HIV-positive people as possible—a concept called “treatment as prevention.”

How this affects your decision about when to start treatment is, of course, another question. As we mentioned, treatment does not guarantee that you cannot infect anyone else, and it is *not* a substitute for practising safer sex. There are many uncertainties, and you may want to discuss this issue with your doctor or an infectious disease specialist. Your personal medical condition, including the factors we’ve discussed in the previous pages, is still the most important consideration when it comes to starting HIV treatment.

It’s worth repeating this: Guidelines change to keep up with the latest research. Base your treatment decisions on the most up-to-date information. CATIE can help you get the information you need. Give us a call at 1-800-263-1638 or visit us online at www.catie.ca.

Summary of when to start treatment

CD4 count and physical condition	Recommendation
CD4 count below 200 cells or any significant symptoms or conditions related to HIV infection	Start treatment immediately
CD4 count below 350 cells	Start treatment
CD4 count above 350 cells	Consider starting treatment
Women who are pregnant or considering becoming pregnant (with any CD4 count)	Start treatment immediately if pregnant; consider starting treatment before pregnancy

Preparing to Start Treatment

In a Capsule

- ⦿ Starting treatment can cause some people to feel anxious.
- ⦿ Before you take your first dose, you may want to think through some practical issues as well as your feelings and attitudes about treatment.
- ⦿ We've included some helpful tools you can use to help you prepare.

For me, the biggest part of HIV is losing control of life. When I was told I had to start meds, I didn't feel that sick, and so I didn't feel in control because I wasn't even aware of the problem. The control came back when I learned my options.

—Daniel

Before starting treatment, there are many issues—both medical and non-medical—that you may want to consider.

- **What does HIV treatment mean to you?** Treatment can mean different things to different people. Thinking about treatment may make you all too aware of having HIV, just when it finally seemed like a smaller part of your life. You may perceive the need to start treatment as a sign that your health has deteriorated and it is time to take action. Maybe you feel concerned about the future, about the impact of the drugs on your body, your lifestyle and your long-term health. It can be difficult to adjust to taking medications every day; don't be afraid to ask for help (from your doctor or an AIDS service organization) if you think you need it.
- **How do you feel about taking antiretroviral drugs?** You may think of treatment as a positive step that you're taking to improve your health. Or, like some people, you may have strong feelings of skepticism or fear about starting treatment. It is very important to discuss your feelings with your doctor and work through them before you start taking medications.
- **Will you be able to take medication on a regular, ongoing basis?** To keep your drug combination working, you must consistently stick to your pill-taking schedule. Skipping doses can lead to drug resistance, which will cause your treatment to stop working and will limit your future treatment options (see Appendix E). To avoid this, you must be ready to make a firm commitment to taking the drugs as directed.
- **Have you thought about the ways your pill-taking schedule may affect your daily life?** Taking medication on a daily basis will have an effect—sometimes dramatic, sometimes not—on your life and your lifestyle. Some drugs need to be taken only once a day, while others must be taken twice a day. Although most drugs can be taken either with or without food, a couple of them must be taken on an empty stomach. Think about your daily routine, and whether you'll have to make any changes to accommodate your pill-taking schedule.

- **What about work and social situations?** Do your family, friends, co-workers or roommates know your HIV status? Could taking meds or having them around your home or workplace reveal your status to anyone? If this could be a problem, think about how you might be able to avoid this: for instance, maybe you can time your doses so you take them at home instead of at work.
- **Do you know the possible short-term and long-term side effects of the antiretroviral drugs you will be taking?** Side effects don't affect everyone the same way—for some people, they may be mild or barely noticeable. However, for others, side effects can be much more severe and interfere with daily life. Look at the most likely side effects for the different drugs you're considering. Do you find yourself more worried by the prospect of some side effects than others? Ask your doctor about ways you might be able to minimize some of these side effects.
- **Will you be able to deal with the side effects in your day-to-day life?** If reaching your workplace requires a long commute with no possibility of bathroom stops, medications that cause diarrhea might be particularly difficult for you. Try to learn as much as you can about side effects and how to cope with them before starting treatment. There may be quite a bit you can do. (For more information, see CATIE's *Practical Guide to HIV Drug Side Effects*, available online at www.catie.ca or call 1-800-263-1638 to order your free copy.)
- **How will you pay for treatment?** Antiretroviral drugs are expensive. Some people with HIV have private insurance, often through their job, that can cover some or all of the costs of antiretroviral drugs. Many others must rely on provincial or territorial assistance programs to cover their prescription drug costs. Talk to your doctor and your pharmacist about this issue. Most people with HIV are able to get most or all of their drug costs covered, but this may involve some extra paperwork. It's best to sort this out before you start treatment.

By considering these issues before starting treatment, you will give yourself the best chance of living well with HIV, not just longer. Discuss any concerns you may have with your doctor. Your doctor may then be able to recommend a combination of medications that is best suited for you.

Know your lifestyle and habits and don't be afraid to talk about them with your doctor. This could help identify the treatment that will best fit your life. And don't lose sight of why you are taking HIV treatment. The pleasures of the days and years to come make the little hassles worthwhile.

—Ken

ART Start Checklist

These are some of the issues that might come up when you start taking HIV treatment. Think about how these might affect your feelings about treatment and your willingness to start. Don't let this list scare you—you won't have to face every issue on it. But it may help you decide which possibilities you would or would not be willing to risk.

	This would be a huge problem for me.	This would be a challenge, and I would need some help to manage it.	This would be a bit of a problem for me, but I could handle it.	I would be OK with this.
What if I had to take some doses with food?				
What if I had to take some doses on an empty stomach?				
How do I feel about taking pills every single day?				
What if I had to take pills once a day?				
What if I had to take pills twice a day?				
What if each dose meant taking more than one pill at a time?				
What if I found myself out of the house without my pills and had to go home to take them on time?				
What if other people, such as my family or co-workers, found my pills or saw me taking them?				
Is there a pharmacy where I would feel comfortable going to have my prescriptions filled and to ask questions?				
What if my drugs cause side effects such as ...				
... diarrhea?				
... nausea (feeling sick to my stomach) or vomiting?				
... poor sleep or wild dreams?				
... skin rash?				
... jaundice (yellowing of the skin or whites of the eyes)?				
... a visibly thinning face or a visible buildup of fat in my belly or elsewhere (lipodystrophy)?				
... high cholesterol levels that could lead to cardiovascular disease in the future?				

Some other questions you may want to think about:

- How do I feel about HIV treatment? Does it feel like a positive step to take for my own health or something I am being forced to do?

- Would being on HIV treatment make me feel like I have more or less control over my health? What would help me feel more in control?

- What are my biggest fears and concerns about starting treatment? What are my biggest hopes?

- Do I have people I can go to with practical concerns and questions about HIV treatment?

- Do I have drug coverage that will handle most or all of my drug costs? If not, how can I get financial support?

Choosing a Drug Combination

In a Capsule

- An effective combination of antiretroviral drugs keeps a person's viral load undetectable, is easy to take and has few side effects and long-term toxicities.
- Out of the large number of possible drug combinations, a few are preferred as first-time combinations.
- Personal circumstances (such as pregnancy, CD4 count or cardiovascular disease) may narrow your options.
- If you have several good options to choose from, your choice may then depend on comparing the potential side effects of the medications, the number of pills you would have to take, and how often you would have to take them.

The ideal treatment for HIV is one that:

- effectively suppresses the virus—that is, quickly reduces your viral load to an undetectable level and keeps it there as long as possible
- restores your CD4 counts
- has minimal side effects and long-term toxicities
- is easy to take (few pills with an easy schedule)

A single antiretroviral drug is not powerful enough to suppress HIV on its own; it has to be taken in combination with other antiretroviral drugs. Years of experience with dozens of different drug combinations has given us a huge amount of information on each combo, including overall survival rates, how it affects viral load and CD4 count, its side effects and long-term toxicities.

This leads us to suggest one more goal for the “ideal” combo: it should be easy to choose. The number of anti-HIV drugs, and the number of possible ways of combining them, is growing all the time. Fortunately, we know which combinations are best to start with. Earlier (on page 40), we described how expert panels assemble the information from clinical trials into treatment guidelines. Guidelines usually rank drug combinations, often using terms such as *preferred*, *alternate*, and *acceptable*. A drug combination's ranking indicates how well it rates in terms of several criteria, including how well it suppresses viral load over the long term, the ease of its pill-taking schedule, and its risk of major side effects or toxicity.

This ranking system can help differentiate the multitude of possible combinations. It is meant to guide, not to replace, decisions made by you and your doctor. A so-called “alternate” combination is not necessarily “second best.” It may turn out to be the best choice for you.

In the end, the ranking system aims to make the selection process much simpler. Rather than sifting through a bewildering number of possible options, HIV-positive people and their doctors can usually choose between a tried-and-tested few, especially for first combinations.

Building a combination

Antiretroviral drug combinations are built using drugs from different groups, or “classes.” Each class of anti-HIV drugs attacks HIV in a different way. Researchers have discovered that it takes three different drugs from at least two classes to effectively suppress HIV. Clinical trials have taught us that an effective combination includes a “backbone” of two drugs from one class plus a third drug from another class.

If you want to know more about the different drugs in a combination or the theory behind how combinations are chosen, check out the appendices at the back of the guide.

- Appendix A shows how HIV replicates and how the different drug classes block the virus.
- Appendix B lists the antiretroviral drugs that are currently available in each class.
- Appendix C explains the theory behind combination treatment and describes how to build a combination.
- Appendix D lists drug combinations you might start with and some of the advantages and disadvantages of each combination.
- Appendix E explains drug resistance and resistance testing.

In this discussion of choosing a first combination, we will start by presenting the first-time combinations recommended at the time we published this guide. In the rest of this section, we’ll concentrate on the factors to consider and the questions to ask when considering a new treatment combo. These will always be relevant even as the specific options vary over time.

First combinations

Choosing your first combination is such an important topic that we think it is worthwhile to present the current information on recommended choices, even though recommendations may change over time. Knowing the currently preferred combinations will help you and your doctor make the best choice. You can contact CATIE (at 1-800-263-1638 or www.catie.ca) for the most up-to-date information.

A word about drug names before we start. Prescription drugs have two names: a common name, which describes the active ingredient in the drug, and a brand name, which is used to market the drug. (Brand names are always capitalized.) Antiretroviral drugs can be even more complicated because they are sometimes called by a three-letter abbreviation.

I never really chose my meds; it was the doctor who did the choosing. . . Basically, she left the room, wrote out the prescription and put it in my hand. I wasn't even given any options. I didn't ask questions—I figured the doctor knows what she's doing. I think I put too much faith in the doctor. There could be something out there that's better for me, but nobody's ever given me the chance to talk about it.

—Gord

Also, some pills contain more than one drug. In this guide, we mention the common and brand names of each drug the first time we talk about it. After that, we use the most common name. If it all gets too confusing, Appendix B lists all the common and brand names of antiretroviral drugs currently available in Canada.

At the time this guide was published, most HIV treatment guidelines recommended the following first-time combinations:

- efavirenz (Sustiva) plus Truvada (tenofovir + FTC)—also available together in one pill, called Atripla
- atazanavir (Reyataz) with a small dose of ritonavir (Norvir), plus Truvada
- darunavir (Prezista) with a small dose of ritonavir (Norvir), plus Truvada
- for pregnancy, Kaletra (lopinavir-ritonavir) plus Combivir (AZT + 3TC)

Some guidelines also recommend the following first-time combinations:

- Kaletra (lopinavir-ritonavir) plus Truvada
- fosamprenavir (Telzir) or saquinavir (Invirase) plus Truvada
- raltegravir (Isentress) plus Truvada
- any of the combinations listed above, with Kivexa (abacavir + 3TC) instead of Truvada

You can find more information about these drugs in the appendices (or in up-to-date fact sheets from CATIE or other sources).

Remember, that while these are the recommended combinations, this does not mean that other combinations are not as effective or that another combination may not be the best one for you. In the next section, we talk about some issues to consider as you and your doctor choose your drug combination. (Appendix D covers some more of the reasons why you might choose one combination over another.)

Which combination is best for you?

Although choice can be a good thing, it can also be frustrating: “How should I know which to choose?” is a common complaint among HIV-positive people trying to pick a treatment combo. However, some of those decisions may already be made for you. Depending on your medical situation, some drugs may not be allowed or some may be more suitable than others.

Here are some of the most important things to consider. You may not know whether these apply to you, but you can use this list to bring up topics with your doctor.

Pre-existing resistance

Drug-resistant forms of HIV can sometimes be transmitted from person to person. Therefore, you may already be **resistant** to some medications even if you have not taken them before. Guidelines recommend that all HIV-positive people have a resistance test done before they start treatment. Resistance testing is not perfect, but it can identify specific drugs that may not work for you. This allows you and your doctor to choose other drugs that are more likely to work. (See the discussion of drug resistance in Appendix E.)

Hypersensitivity

You may be allergic, or **hypersensitive**, to certain drugs. For example, many people are hypersensitive to abacavir (Ziagen, also found in Kivexa and Trizivir). A simple blood test, done before you start treatment, can determine whether you're likely to have a potentially dangerous *hypersensitivity reaction* to abacavir (see the CATIE Fact Sheet on "Abacavir Hypersensitivity Screening" if you want more information on this subject). If so, you can cross it off your list of choices. You may also be hypersensitive to other antiretroviral drugs, so ask your doctor about the signs of a hypersensitivity reaction so that you can seek medical help should you react to a drug. There are no tests for any medication other than abacavir that will indicate a possible reaction.

Other medical conditions

- If you are **pregnant or thinking about having a baby**, you should not take efavirenz (Sustiva) because of concerns about its possible effects on the fetus. Many other antiretrovirals have proven safe for use during pregnancy.
- If your **CD4 count** is above a certain level, nevirapine (Viramune) is much more likely to cause liver toxicity. Nevirapine is not recommended in these cases.
- Certain drugs can raise cholesterol levels or otherwise put you at increased risk for **cardiovascular disease**. This may be acceptable if your cardiovascular risk is low to begin with. However, if you have risk factors for cardiovascular disease—such as smoking, obesity, high cholesterol or a family history of stroke or heart disease—it may be better to avoid these drugs.

Your doctor and pharmacist should know [about drug interactions]. But, you have to tell them about all the drugs you're taking if you want them to help you. The same goes for your doctor when it's time to talk about street or recreational drugs.

—Chantale

Certain drugs may not be recommended if you have **hepatitis B or C** or other **liver problems, kidney damage, tuberculosis, depression** or other **mental and emotional health** issues.

Drug interactions

As we discuss more fully later on (see page 63), antiretroviral medications can sometimes interfere with other drugs you are taking, or vice versa. For instance, if you are taking methadone, the dose may need to be increased if you also take nevirapine (Viramune) or certain protease inhibitors; otherwise, you'll get less methadone in your system than you're expecting and you could go into withdrawal.

Although adjusting the dose of the drug may take care of any potential interactions, another option is to choose antiretroviral medications that do not interact with other drugs you take. Your doctor or pharmacist will know more about this.

Drug dosing and "pill burden"

Antiretroviral medications today are much easier to take than they were in the past. All first-time combinations are taken just once or twice a day, and the total number of pills that need to be taken each day is relatively small. Part of the reason for this is that *co-formulations* are now available. A co-formulation consists of two or more medications in a single pill. In the case of Atripla, three drugs are combined in a single once-daily tablet.

For obvious reasons, many people with HIV prefer these simplified regimens. They find that taking fewer pills makes it easier to take them consistently. However, there is one caution with once-daily drugs: skipping even one dose could leave you with inadequate drug levels in the bloodstream for a lengthy period. This increases your chance of developing drug resistance. Some drugs are more "forgiving" of missed doses; this is something you should discuss with your doctor.



Side effects

For many people, side effects are the biggest factor in choosing between treatments. When considering side effects, there are a few things to keep in mind. For one thing, nobody experiences all the side effects listed for any given drug. Lists of possible side effects are enough to put anyone off—you wonder how you could even make it through the first day. Remember that these lists include just about all of the symptoms experienced by anyone who took the drug during clinical trials.

Side effects are somewhat “luck of the draw.” We know, from experience, which side effects a given drug is *likely* to cause—but that doesn’t mean they will happen to everyone who takes it. On the other hand, certain side effects are quite rare, but that rarity isn’t much comfort to the people who actually get them.

When considering the side effects of a drug, you may want to ask the following questions:

- How **severe** are the side effects? And how **common** are they? Many antiretroviral drugs have the potential to cause serious reactions, although these are usually in a small percentage of the people who take them. With the help of your doctor, consider the severity of the side effects and the chance of them happening. Then you can decide how willing you are to try the drug.
- How **persistent** are the side effects? Many drugs can cause side effects that are less severe but quite unpleasant nonetheless. Ask whether these occur sooner or later, and how long they are likely to last. Sometimes drugs can cause side effects (such as nausea or itchy skin rash) that last for a little while, perhaps a few weeks, and then go away on their own. Is that something you can get through? Or are the problems likely to continue?
- How **manageable** are the side effects? It may be possible to lessen or manage some of the side effects—for instance, Imodium for diarrhea, or aspirin for headaches. Other side effects may be much more difficult to deal with. Consider how you might deal with problems if they do occur, and ask other people with HIV, your doctor or pharmacist for advice.

When deciding on my first combination, I was lucky because I had several options. I was worried about changes to my body and I wanted something that was simple to take ... At the beginning, I had weird dreams and my mood changed. Those side effects come back from time to time, but mostly I'm happy with my choice.

—Ladidee

Drug insurance

Antiretroviral drugs are expensive, so most people with HIV rely on drug insurance plans—either private plans or provincial or territorial plans—to cover their drug costs. Which drugs are eligible for coverage varies with the plan. If you have private insurance, contact your insurer to find out which antiretroviral drugs are covered under your plan and what are the terms of coverage.

Provinces and territories have lists called *formularies* that include all the drugs covered under their plan. Most antiretroviral drugs are covered on most provincial and territorial formularies. However, there may be special conditions or restrictions—for instance, certain drugs may not be covered unless you have tried other drugs first. As well, it may take some time for a newly approved drug to be included on a formulary.

There may be ways you can get financial assistance even if the drugs are not covered by your private, provincial or territorial plan, so don't despair. Your doctor, pharmacist or local AIDS organization can give you more information about getting coverage for HIV drug treatment. You can also check out CATIE's webpage "Access to HIV Drugs," available at www.catie.ca/eng/Publications/drugaccess/drugaccessIndex.shtml.

This is not necessarily a complete list, but it covers most of the major things to consider when choosing a drug combination. At first glance, it may seem that this complicates the decision-making process beyond all hope! But it should help to do the opposite: by eliminating drugs that might be poor choices, you should end up with a more manageable "short list" to pick from.

Choosing the Best Combination for Me

Here are some questions to consider when choosing a drug combination. You may not know all the answers, so you might want to look at this list with your doctor.

- Are there any medications I should avoid because...
 - ... I am resistant to them?
 - ... I am hypersensitive (allergic) to them?
 - ... I am pregnant or want to get pregnant?
 - ... of possible risks to my liver or kidneys?
 - ... of possible risks to my cardiovascular health?
 - ... of depression or other mental health conditions?
 - ... they could interact with other medications I am taking?
- How many pills would I be taking, and how many times a day?
- How forgiving of skipped doses is this combination?
- What are the possible side effects, and how prepared am I to risk them?
- Are the drugs I'm considering covered by my drug insurance program?

To help answer some of these questions, here is a table that lists some factors that might affect your treatment options. (Again, don't hesitate to discuss these with your doctor.)



	Yes	No	Not sure
I am pregnant or thinking of having a baby.			
My LDL ("bad") cholesterol levels are high.			
I smoke.			
I have diabetes.			
I have other risk factors for heart disease (other people in my family have had heart disease, I am overweight, or I have high blood pressure).			
I have chronic hepatitis B, hepatitis C or other liver problems.			
My kidneys are not working as well as they should.			
I suffer from depression, anxiety or other mental health issues.			
I have a drug dependence or I am taking methadone.			

Resources

Managing Your Health—a guide for people living with HIV

Practical Guides for People Living with HIV—CATIE’s practical guide series contains extensive information about a holistic approach to treating HIV. See:

- *A Practical Guide to Nutrition*
- *A Practical Guide to Complementary Therapies*
- *A Practical Guide to Herbal Therapies*

In-depth Fact Sheets on antiretroviral drugs and supplements

Federal, Provincial and Territorial Drug Access Programs—information about drug coverage and benefit programs in Canada can be accessed on CATIE’s website at www.catie.ca/eng/Publications/drugaccess/drugaccessIndex.shtml

The Positive Side—health and wellness magazine for people living with HIV, with articles such as:

- “Patients Are from Venus, Doctors Are from Mars” (building a good relationship with your doctor)
- “The Pharmacist List” (reasons to get to know your pharmacist)

- “As the Wheel Turns—the HIV/AIDS medicine wheel”
- “On the Road to Health” (starting treatment)
- “How Did You Choose Your Meds?” (personal experiences)
- “Sex, Drugs and Viral Load” (HIV treatment, viral load and sex)

Look in the e-zine index for more (www.positiveside.ca).

These and many other relevant resources can be accessed on CATIE’s website (www.catie.ca) or by calling CATIE at 1-800-263-1638.

Other websites with reliable information on HIV treatment:

- www.aidsmap.com
- www.aidsmeds.com
- www.hivandhepatitis.com
- www.thebody.com

Notes

Once You've Started

In this part of the guide we talk about some of the things to keep track of to make sure your treatment is working—and what you may need to do if it isn't.

- ◎ Once you've started treatment, you and your doctor will monitor your viral load to make sure your treatment is working.
- ◎ Together, you will also watch for side effects and toxicities. These might cause noticeable symptoms, such as a severe rash or flu-like symptoms, or may only show up in your blood tests. We cover these issues in **How to Tell if Your Treatment Is Working**.
- ◎ **Making Your Treatment Work Long-Term** explains why taking your medications as prescribed and watching out for drug interactions are important for ensuring that your treatment continues to work.
- ◎ **Changing Treatment** explores the two most common reasons for changing a drug combination: either it stops working and HIV becomes active again or you just can't live with the side effects or some other aspect of the treatment.

How to Tell if Your Treatment Is Working

In a Capsule

- If your treatment is successful,
 - your viral load should drop to an undetectable level and stay there;
 - your CD4 count should increase, although you may not see dramatic increases immediately;
 - the side effects should be manageable; and
 - you should be able to follow your pill-taking schedule.
- If your viral load does not drop, your CD4 count does not increase, the side effects you experience are unmanageable or you cannot stick to your pill-taking schedule, you and your doctor will need to assess why your combination is not working.

My CD4 cells have gone up from 300 to 1,100. My health has improved tremendously.

—Hazra

Once you've started your treatment, you'll want to evaluate two things: how well the treatment is doing its job, and how well you're dealing with the treatment.

The first question—how well your treatment is working—depends on test results. Successful treatment should accomplish two things: it should bring down your viral load to an undetectable level and it should increase your CD4 count. Depending on how high your viral load was to start with, it should become undetectable, usually within three to four months. A viral load that doesn't become undetectable immediately isn't necessarily cause for alarm: ask your doctor how long it could take in your case. If your viral load is still detectable after several months, you and your doctor will need to look at why this is. Your virus may be resistant to one or more of the drugs, a drug interaction may have escaped notice, or you may be having trouble sticking to your pill-taking schedule.

Once your viral load becomes undetectable, it should stay there. Some people, however, do see occasional blips in their viral load. (A "blip" is when your viral load becomes detectable at a very low level on one test and then becomes undetectable again on the next test.) Among other reasons, "blips" may occur if you're fighting an infection or have recently been vaccinated. If your viral load becomes detectable, your doctor will probably measure it again. A single blip may not be cause for alarm, but two detectable measurements in a row are probably a sign that your treatment is no longer working (see page 68).

Increases in CD4 counts don't usually happen as quickly as drops in viral load, so don't worry too much if your CD4 count doesn't skyrocket the way you had hoped. Once HIV is successfully suppressed, your immune system should rally. Unfortunately, people who have started treatment with low CD4 counts are likely to see the most modest increases in counts.

If the results of your viral load and CD4 tests show that your treatment is working, an equally important question is: How are you doing? Has your health improved? How are the side effects? Are you managing to take your pills as prescribed every day?

Let's look at some of the common issues that may arise once you've started taking antiretroviral medications.

Making Your Treatment Work Long-Term

How to keep your treatment working . . . and why you don't want it to fail

Regardless of the particular drugs you're taking, **your drugs will 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 is very important because these drugs leave the body very quickly. You need to have a certain amount of antiretroviral drugs in your blood to keep the virus suppressed. The goal of your pill-taking schedule is to ensure that the drug levels in your blood stay above that level. Missing doses leads to drug levels that drop too low to control the virus.

Worse yet, those low drug levels can lead to **drug resistance.** (We talk about *how* this can happen in Appendix E.) Bottom line: If you develop resistance to a drug, the drug won't work for you again—ever. It's possible that you and your doctor will be able to find something else, but it's better to keep your current treatment working than it is to burn through your options.

Your doctor and pharmacist may have practical tips to help you adhere to your pill-taking schedule, so be sure to discuss this with them before starting your treatment. Here are a few tips and tricks that some people have found useful:

- Many doctors and pharmacists recommend practicing with jellybeans, Smarties or mints for a couple of weeks before starting the real treatment. It may sound silly, but if you find yourself forgetting jellybeans, that flags a problem you can address *before* you start taking the real pills.
- Every week, divide your pills into your doses for each day. Use plastic pill boxes (sometimes called “dosettes”) with separate compartments for storing each day's supply of pills. Some pharmacies will package your pills in bubble-packs according to your daily dosing schedule.
- If remembering to take your dose on time is difficult, wear a watch with an alarm, set the alarm on your cell phone, or carry a small medication “beeper” (talk to your pharmacist about getting one) as a reminder. This can be particularly useful when you are travelling.

In a Capsule

- ⦿ Taking all your pills as prescribed (adherence) is crucial to the long-term success of your treatment.
- ⦿ While adhering to your medication schedule can sometimes be challenging, there are many tips and tricks you can try to make it easier.
- ⦿ Being aware of possible interactions between all the drugs you're taking—including antiretroviral drugs, other medications, over-the-counter products, herbs and supplements, street drugs and even some foods—will help ensure that your drugs work well together.
- ⦿ Evidence has shown that stopping and starting HIV treatment is harmful; for now, HIV treatment is a lifelong commitment.

Talk to your doctor and find a regimen that works for your schedule. If you can't find a regimen that suits your lifestyle, there will always be adherence problems.

—Troy

Adjust the meds to your life; don't adjust your life to the meds.

—Daniel

(Most medications still work even if you don't take them at exactly the same time each day. Talk to your pharmacist or doctor to find out how much wiggle room you have.)

- Try to fit your pill-taking schedule into your everyday routine. Keep your medications where you'll be reminded to take them—near your bed, in a kitchen cupboard you open frequently, or somewhere else that's safe and where you will be likely to see them and remember to take them.
- Ask your nurse or pharmacist for directions on how to store your pills—some may need to be refrigerated. Check the expiry date on the bottles from time to time.
- To avoid running short of meds, keep a small supply of medication in places you frequently visit—at your family's or partner's house, at your workplace—as long as you're not concerned about people accidentally finding them. If you're going on a trip, pack the number of pills you'll need for the time you will be away plus a few extra doses in case your plans change.

If you are having trouble taking your drugs as they were prescribed, don't be afraid to get help. Or maybe you're dealing with depression or substance use—issues that will affect more than just your adherence to your HIV treatment. It's important to acknowledge and deal with those issues as well.

If all the tricks in the world don't help you stick to your pill-taking schedule, you and your doctor may need to consider switching to a new combination. It will be important to figure out what the problem was the first time around, so it doesn't get repeated. For example:

- Did you have trouble with a twice-daily regimen because of a busy schedule? If so, a once-a-day regimen might be the answer.
- Was it a specific side effect that led you to skip doses? There may be ways to manage the side effect, or there may be other drugs that are less likely to cause the problem.
- Are you OK until the weekend rolls around, and then it's party time? A bit of strategic thinking might help you stick to the plan even if you're partying—or you might need to look at your alcohol or drug use and see if it's causing problems.

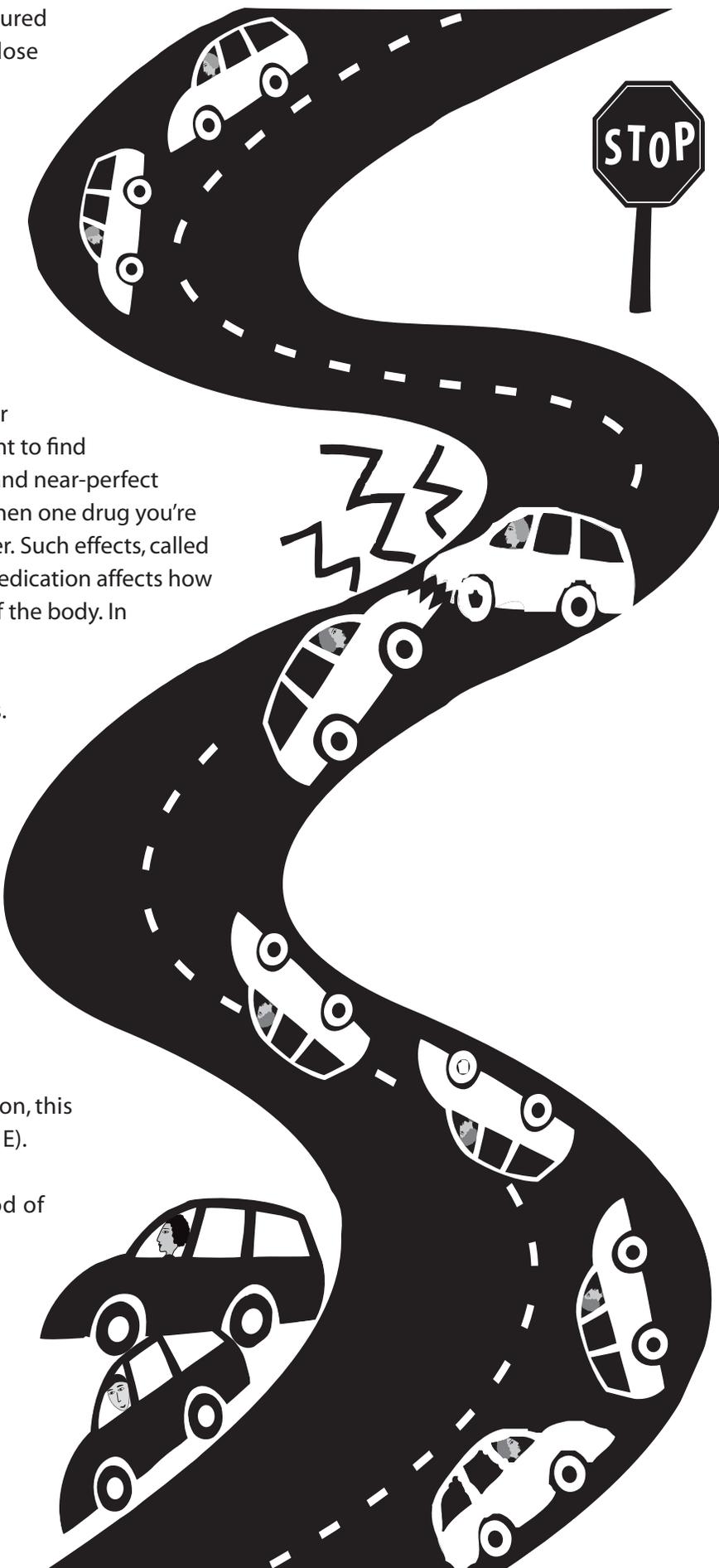
You may sometimes feel you're being lectured about adherence. Missing an occasional dose is not the end of the world, so don't panic if you fall asleep too early, get caught at work without a dose, or just plain forget once in a while. Do the best you can: you'll keep your drug combination working as long as possible, and do yourself the most good in the long run.

Making sure your drugs play well together

You're taking great pains to make sure your treatment works as planned. You don't want to find that it has failed despite your best efforts and near-perfect adherence. This can sometimes happen when one drug you're taking has an unintended effect on another. Such effects, called **drug interactions**, can occur when one medication affects how another is absorbed, used or flushed out of the body. In some cases, this can be a problem.

Drug interactions can have several effects. One is that one drug can slow down the breakdown of another drug in the body. This can increase the level of the drug in the body, which might improve its efficacy but could also lead to more intense side effects or even toxicity. A drug interaction can also have the opposite effect: sometimes one drug will speed up the breakdown of another. In that case, the second drug's effectiveness may be diminished. If the affected drug is an antiretroviral medication, this can lead to viral resistance (see Appendix E).

Interactions can also affect the likelihood of **side effects**. If two drugs tend to cause the same type of side effect, using them together may increase the chances that a serious side effect will occur. For example, a couple of older drugs—ddl and d4T—have a tendency to cause peripheral neuropathy (nerve damage that affects the hands and feet). Combining these drugs increases a person's risk of neuropathy, so ddl and d4T should not be used in the



same combination. (Fortunately, these two drugs are rarely prescribed in Canada, alone or together, since many more tolerable drugs are now available.)

Drug interactions are not always obvious. They can take various forms: some occur immediately after you first combine the drugs, and others do not cause any noticeable problem for weeks or longer.

There are no foolproof ways to prevent all possible drug interactions. Most studies have only looked at the interactions between two drugs at a time, and many people take far more than that. Add the possibility of interactions between multiple drugs and foods and herbs and you get the picture—it's complicated! However, there are several steps you can take to try to ensure that it is safe to combine all the things you're taking:

- Make sure that your doctor and your pharmacist are aware of every single thing you're taking—prescription drugs, over-the-counter drugs, street drugs, herbal and nutritional supplements, or anything else. You can do a “brown bag” checkup—put all your medications and supplements in a bag and let your doctor take a look. If you know your medical visits are too rushed for this, make a special appointment and request the extra time.
- Your pharmacist can help you avoid drug interactions. Your pharmacist is often the best-informed member of your healthcare team when it comes to this topic. Also, they can usually make the time to review your prescriptions, especially if you request it. Most pharmacies now have computer programs that can warn of any potential drug interactions if they have a complete list of all agents being taken.
- Possible drug interactions can get overlooked if you have more than one doctor or use more than one pharmacy. If you have more than one doctor writing prescriptions for you, let each one know about everything you are taking. If at all possible, use the same pharmacy for all your prescriptions.
- You don't need to check interactions at every single visit—just when your treatment changes. Reassess your list every time you are prescribed a new medication or decide to add a herb, supplement or over-the-counter product. You may want to do that brown-bag thing again.

- Lastly, you can do some checking on your own with a great web resource available at www.aidsmeds.com. From the homepage, click on “My Cool Tools,” then “Check My Meds.” From here, you can key in all the drugs, nutritional and herbal supplements, and various foods (such as grapefruit or raw garlic, both known to cause certain interactions) that you are taking. Then click on “Check Interactions” to find out about any possible interactions.

In some cases, there are drugs that absolutely cannot be used together and the only solution is to stop taking one of them. In other cases, it may be possible to use certain drugs together provided you make certain adjustments (for example, change the time when you take them).

Stopping treatment?

To put it plainly: to the best of our knowledge, HIV treatment is a lifelong necessity. This is because HIV can stay inside infected cells of the body for a very long time. It only takes a few infected cells to restart the whole process of HIV replication once treatment is stopped—just as it only takes a few remaining coals to restart a fire that you had “almost” put out.

What about taking breaks? It’s not hard to think of the advantages—fewer pills, lower cost, fewer side effects and a general break from the constant pill-taking. Some people have tried taking “drug holidays”—occasional breaks from their treatment. We know that such drug holidays are not a good idea, due to the risk of drug resistance (see Appendix E).

Several large clinical trials have looked at the outcomes of planned or “structured” treatment interruptions, in which people went off their antiretroviral drugs for a specific length of time or based on their CD4 counts. The idea was that as long as CD4 counts were above a certain level, it might be safe to go off treatment without becoming ill. Unfortunately, and to many people’s surprise, these treatment interruptions proved to be more harmful than helpful for many people living with HIV. In one large clinical trial, people who interrupted their treatment were nearly three times more likely to die or develop serious infections than people who stayed on treatment continuously. The people who took breaks from their treatment were more likely to experience many different kinds of serious health problems, including cancer, life-threatening infections, heart attack, stroke, kidney damage and liver damage.

I decided to stop taking meds altogether. I told my doctor and he advised me not to, but I wanted some life back. I eventually realized that if I didn’t take my meds, I would die. It took me three months to decide that I wanted to live, and I went back on meds.

—Paul

While treatment interruptions may not necessarily be harmful for everyone on treatment—for instance, they may be relatively safe for people with higher CD4 counts—they are generally not recommended due to the possible risks. Anyone considering an interruption in their treatment should discuss the issue with their doctor very carefully before stopping any of their medications. A careful plan of how to stop all the drugs in your combination is needed to ensure that drug resistance does not develop.

Changing Treatment

After your first combination

Even if you have planned your HIV treatment carefully and stuck to your medication schedule perfectly, you may have to change your drug combination. This could be for one of two main reasons:

- Sometimes even a carefully chosen combination doesn't succeed in controlling HIV—your viral load does not drop to an undetectable level or it does drop but then climbs back up to consistently detectable levels. In either case, you need to find a new combination that can effectively control the virus.
- You can't stand some aspect of the treatment—the side effects, the number of pills you have to take or how often you have to take them—even though your CD4 count and viral load may look great on paper. In this case, you need to find another combination that not only works but that you can live with.

The two situations are similar in some ways, but quite different in others. In both cases you've gone to a lot of trouble to make what you thought was the best choice. You've relied on "the experts"—your doctor, the researchers who make the treatment guidelines, and yes, even guides like this one. After putting all that effort into picking your first combination, it may be very frustrating to feel like it hasn't worked out and you're going "back to the drawing board."

Those kinds of frustrations are understandable, but don't despair. Changing your treatment does not mean starting all over again from square one. You have already gathered a lot of information and done a lot of thinking about which drugs are best suited for you. Not all of that is going to change; you can put the same knowledge to use the second time around. Finding an effective combination that you can tolerate may take a bit of trial and error at first, but most HIV-positive people are able to do it. (Read Appendix C for information on the drugs you can consider when changing your HIV treatment.)

In a Capsule

- ⦿ You may have to change your drug combination if it does not keep your viral load undetectable.
- ⦿ You may have to change your combination if you can't tolerate its side effects or adhere to the prescribed pill-taking schedule.
- ⦿ In either case, the new combination must be chosen carefully.

You will work closely with your doctor to make any changes to your treatment. Don't stop any medications without talking it over with your doctor first; suddenly stopping any drug might have consequences you don't expect, including HIV developing drug resistance. There may be a "right way" and a "wrong way" to make the changes you're considering.

Changing medications due to treatment failure

As previously discussed, your viral load is the best way to know whether your current drug combination is working. If your treatment is successful, your viral load should drop to an undetectable level and stay there (apart from occasional, short-lived blips up to a detectable level).

If your viral load remains detectable after several months on your first combination of antiretroviral drugs, this means your treatment isn't working. You and your doctor will have to do some detective work to find out why. The most common reason is missing too many doses of medication. It could also be because the dosage of one of the drugs is not quite right, and a simple change (the number of pills you take, how often you take them or perhaps what you take them with) will correct the problem—or it might be time to change your drug combination.

If you've been on treatment for awhile with an undetectable viral load, and then your viral load becomes detectable and stays that way, it's likely that your treatment has stopped working and it's time to switch to a new combination.

When a drug combination cannot suppress the HIV, this is called **treatment failure**. If your treatment fails to suppress the virus, you and your doctor will have to determine: (a) whether you are missing too many doses of your medications, and (b) whether your virus has developed resistance to one or more of the drugs in your combination. If blood tests show that you have drug-resistant virus, you and your doctor will need to pick a new combination, one that has the highest chance of controlling the virus in your body. For your next combination to be effective, you will need to identify which drugs are no longer working and replace them with drugs that will work against the virus.

The important thing is to make sure that your new combination has as many effective medications as necessary. If an effective new drug is combined with others that are ineffective, the virus will probably become resistant to the new drug fairly quickly, and the potential effect of the new drug will be wasted. Ideally, the new combination should contain three fully effective drugs.

If your treatment is not working, you may not need to scrap your whole combination: some of the drugs you're taking may still be effective. Resistance tests (see Appendix E) can detect changes in the virus, which predict which drugs are most likely to work and which ones won't. Some expert "judgment calls" may also be required, as tests are not always able to detect viral resistance. With this information, a doctor who is knowledgeable about HIV drug resistance should be able to suggest new treatment combinations.

Finding new combinations after a treatment failure is generally easier at first and becomes more challenging as more treatments fail, since each failure leaves you with fewer options to choose from. HIV that has become resistant to one or more drugs may also be **cross-resistant** to other drugs in the same class, even if you have not taken those other drugs before. If you have already used several antiretroviral drugs and your virus has become resistant or cross-resistant to many, you may need to:

- Choose drugs from newer classes that you have not been exposed to yet. You may have virus that is cross-resistant to many drugs in the classes you have already tried. A drug from a different class has the best chance of being effective.
- Resort to drugs that may cause more side effects or have less-appealing pill-taking schedules.
- Go beyond the usual three-drug combination. Resistance isn't all or nothing—if your virus is only partially resistant to a drug, you may be able to get some benefit from it as long as you combine it with enough other drugs. The more drugs your virus is resistant to, the more you may have to rely on this "pile on more" approach. The expert judgment of your doctor is crucial.

Changing medications due to side effects

If your antiretroviral medications are successfully keeping your viral load suppressed but you can't tolerate the side effects, the first thing to do is to find out if what you're experiencing is a side effect of the medications or a symptom of another infection or condition. Start by discussing with your doctor whatever you're experiencing.

Many side effects can be managed. Your doctor will likely have suggestions. You may also want to talk to your pharmacist, nurse or other healthcare professional who is knowledgeable

I became resistant to almost everything [in 2003]... We were waiting for a new drug called T-20. At one point my doctor pulled me off everything because the T-20 has to be taken in combination with other drugs, and if I'd stayed on all the drugs I would have become resistant to them all and the T-20 would have been useless.

—Joe

Two weeks into taking meds for the first time, I became so nauseous it was horrible. I ended up developing resistance to my drugs because I couldn't keep them down. I finally saw a specialist who switched me to a different cocktail that I tolerated really well. My advice? Don't compromise your quality of life. I needlessly suffered because I didn't feel I could be honest with my doctor about the problems I was having. I thought I was going to disappoint her. Looking back, all I did was prevent myself from getting the best treatment.

—Marlo

about HIV treatment. Next, read CATIE's *Practical Guide to HIV Drug Side Effects*, available at www.catie.ca or by calling 1-800-263-1638. It contains practical remedies for the most common side effects. By combining the best available drugs with the remedies that can help eliminate side effects, you may be able to benefit from your current combination of drugs while eliminating the problems it is causing.

If you still find the side effects unbearable despite all these coping strategies, then it's time to talk to your doctor about changing your combination. Together, you should be able to figure out which of your drugs is responsible for the side effect, and then pick an alternative that's likely to be more tolerable and still be effective. Many antiretrovirals are known to commonly cause certain side effects—this can make it fairly easy to spot the offending drug. However, a little more puzzle-solving with your doctor may be needed if the side effect is an unusual one.

Note that there are a few drugs that you should never go back to if you have stopped taking them because of their side effects. Abacavir (Ziagen, also found in Kivexa and Trizivir) and nevirapine (Viramune) are the prime examples: If you have had a "hypersensitivity" reaction to abacavir or nevirapine, you should never start taking it again. The reaction you experienced the first time can recur, much worse the second time around, and it could even be fatal. Make sure to get all of the most up-to-date safety information about any drug you are taking.

What Next?

**We wrap this guide up with a look into the future—
that is, as far as we can see it.**

- ⦿ While the prospect of living nearly normal lifespans with HIV is more realistic than ever, many people with HIV are also living with long-term side effects from ART and from the virus itself. **Living with HIV and ART Over the Long Haul** talks about some of these long-term hopes and concerns for people who are on treatment.
- ⦿ Finally, we take a quick peek into the crystal ball in **The Future of HIV Drug Treatment**, to make some educated guesses as to where we may be in the not-too-far-off future.

Living with HIV and ART Over the Long Haul

In a Capsule

- Many people are doing so well on antiretroviral drugs that many experts predict they may be able to live nearly as long as HIV-negative people.
- However, as people with HIV live longer, other health problems are becoming more common, including cardiovascular (heart) disease, diabetes, kidney disease, cancer and thinning bones.
- Being HIV-positive, taking ART and growing older may all increase a person's risk of these problems.
- It's important to carefully monitor your health and take whatever steps are possible to minimize potential problems.

When HIV treatment was first introduced, nobody really knew how well or for how long it would work. Now, with the advances that have been made, it seems that treatment is more successful than we might have dared to hope at first. Many experts are predicting that HIV drug treatment may allow people with HIV to live out nearly normal lifespans. While that remains to be seen, and some people might be more skeptical than optimistic, we do know that people with HIV are living longer than ever before.

Of course, that means dealing with the consequences of growing older, as well as dealing with the long-term effects of treatment and of the underlying HIV infection. The relationship between aging, HIV and drug treatment is the subject of much research, and it is not always clear which is most responsible for some health problems. However, we do know that as people with HIV age, they are more at risk for cardiovascular disease, kidney disease, thinning bones and certain types of cancers.

Some people with HIV develop **lipodystrophy**—the visible loss of body fat (called *lipoatrophy*) or buildup of body fat (called *lipohypertrophy*). Lipoatrophy includes the loss of fat in the face, arms, legs and buttocks, causing a gaunt and veiny look. Lipohypertrophy involves the buildup of fat in the breasts, belly or base of the neck. This can sometimes occur together with fat loss in other areas. Many people are very concerned about developing “lipo” because it is so visible. Although many people think of lipo as purely a side effect of treatment, it is probably due to a combination of treatment toxicity and long-term HIV infection. Experts do not have a complete understanding of what causes lipodystrophy or how to treat it. However, experts have identified d4T, and to a lesser extent AZT, as two drugs likely to cause lipoatrophy. Because of this, other drugs from the same class (called nukes) are often used instead.

Cardiovascular disease (CVD) includes diseases of the heart and blood vessels, including *coronary heart disease*, *heart attacks* and *strokes*. Among people with HIV—as for anyone else—smoking is the number one factor that increases the risk of CVD. CVD also becomes more of a risk for everyone as they age, although there are many other risk factors. One risk factor—high levels of cholesterol in the blood, especially LDL

cholesterol—has received particular attention in HIV care because many antiretroviral drugs (including several of the protease inhibitors) can raise cholesterol levels. Other risk factors for CVD include being overweight, a family history of CVD, diabetes, alcohol use, physical inactivity, high blood pressure and a high-fat diet. HIV-positive people should limit their risk factors for CVD as much as possible. While this may include choosing antiretroviral drugs that don't raise cholesterol levels, it can also mean eating healthily, getting moderate amounts of exercise and watching your alcohol intake. For smokers, quitting smoking is the single most effective means of lowering risk. There are also drug treatments that can lower cholesterol levels if heart-healthy changes to lifestyle are not enough.

Because some people on HIV treatment have abnormally **high levels of blood sugar** (or blood glucose), your regular lab tests will likely include a test to measure your blood sugar. The same “healthy living” measures that help keep your heart healthy can also help to keep blood sugar under control. If there are concerns about your blood glucose levels, you may have to take special care with the food you eat. In more extreme cases, glucose-controlling medications may be needed.

Thinning of the bones is another problem that is often seen in people as they age, especially in women after menopause. As bones slowly lose minerals—mainly calcium—they become less dense and more porous and sponge-like. When bone loss occurs too quickly, it can lead to *osteopenia* and, in more severe cases, *osteoporosis*. The bones become fragile and more prone to breaking. Osteoporosis is common among people with long-term HIV infection—men as well as women. The process of bone loss is painless and may go undetected until a person breaks a bone.

Bone scans can detect whether bone loss is taking place. Find out from your doctor whether it is possible to get a bone density scan in your area. If you get a scan now, it will allow you and your doctor to track any changes that may occur in the future. Ideally, you'll get this “baseline” scan when you first test HIV-positive and then have follow-up scans at regular intervals thereafter.

Vitamin D₃ is important for bone health and a lack of it can lead to bone loss. Studies have found a deficiency of vitamin D₃ to be very common among people with HIV, and many experts recommend taking vitamin D₃ supplements regularly. Talk to your doctor to find out more.

For nine years, my motto was:
'If it ain't broke, don't fix it.'
That's why, despite worsening lipodystrophy, I clung to the drug regimen that was keeping me alive. Though my viral load was still below detection, my doctor was urging me to make a change. She wanted me to replace d4T [with another drug] because of increasing evidence that d4T was responsible for my sunken cheeks and stick-like arms and legs.

—Maggie

The Future of HIV Drug Treatment

In a Capsule

- Treatment choices are constantly expanding as new antiretroviral drugs are developed.
- Other forms of treatment, such as immune boosters and therapeutic vaccines, are also being investigated.

When I tested positive in the '80s, there wasn't much hope. There was no medication available. It was a death sentence. You had maybe a few years. I wish I had known then that researchers were working on medications that would mean that you could one day lead a somewhat normal and productive life.

—Christian

Nobody can predict the future. However, new antiretroviral drugs are constantly being developed—some that belong to existing classes of drugs and some that belong to entirely new ones. As this guide is being written, a new class of drugs called *integrase inhibitors* is already available both for people who are starting treatment for the first time and for those who are “treatment experienced,” and studies are looking at drugs from other classes as first-time options as well. The more options, the more alternatives to switch to down the road. Having entirely new classes to work with makes it much easier for people whose HIV is resistant to multiple drugs to build effective combinations.

Caution is needed with any new drug: Drug toxicities do not always show up right away and may only become apparent after people have been on medications for some time. There may be longer-term problems with integrase inhibitors and other newer meds that we will only become aware of in the future. This tends to divide people with HIV and their doctors into more conservative and more adventurous camps. Some prefer to stay with more “tried and true” drugs, despite the drugs’ known shortcomings. Others are more willing to try out newer options that appear to be safe and effective in the short term, despite not knowing the possible long-term risks.

In addition to antiretroviral drugs, other forms of treatment are being studied as well:

- Immune boosters—Immune boosters do not interfere directly with the HIV virus. Rather, they are intended to increase the number of CD4 and other immune cells, or otherwise boost the body’s immune function.
- Therapeutic vaccine—Although most vaccines are designed to protect people from infection in the first place, HIV-positive people may also one day benefit from a type of vaccine called a therapeutic vaccine, meant to improve the immune system’s ability to fight HIV.

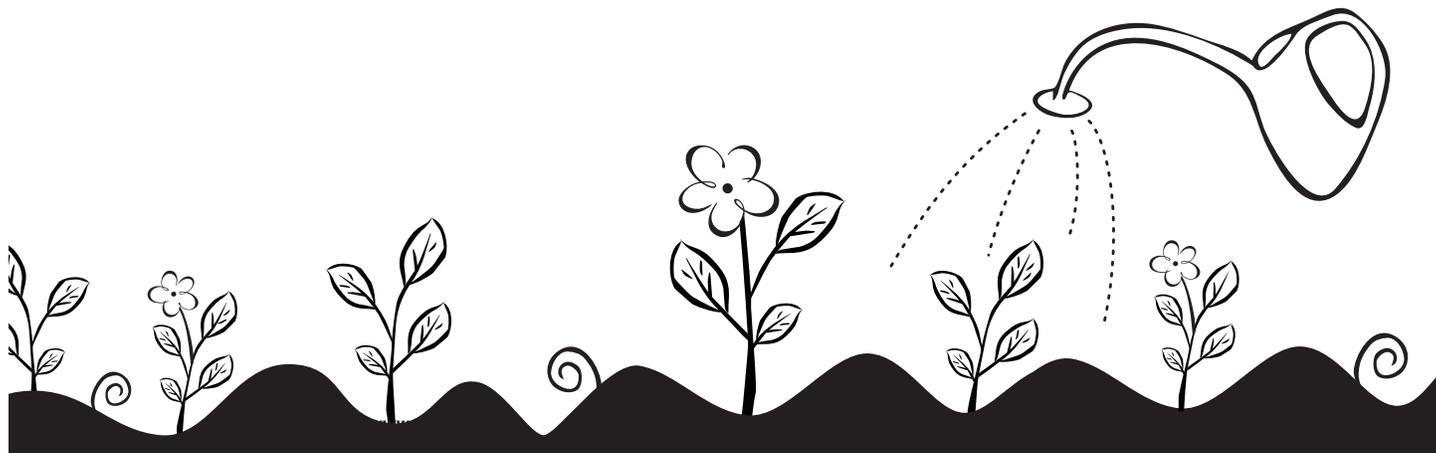
So far, the results of studies of immune boosters and therapeutic vaccines have been disappointing. Some people hope that, one day, these sorts of treatments might delay the need for antiretroviral drugs, by keeping the immune system strong for a longer period of time. Most experts do not believe they will ever replace antiretroviral drugs. Only time and further study will tell whether this turns out to be the case.

The End . . . But Not Really

HIV treatment information changes regularly. By the time you read this, there may be new information that could affect your treatment choices. In this guide, we have tried to focus less on particular antiretroviral drugs and more on ways to go about making decisions, which should stay reasonably constant over time.

When you're looking for information about current treatment options, always reach for the very latest information—via treatment newsletters (CATIE publishes *TreatmentUpdate* and *CATIE News*), websites (check us out at www.catie.ca), your local AIDS service organization and, of course, your doctor and other healthcare providers. You can also call CATIE's information support line at 1-800-263-1638 to speak with one of CATIE's knowledgeable educators. They can answer your questions about the prevention and treatment of HIV and hepatitis C.

With that, we hope you'll make the best possible treatment decisions. We wish you good luck and long-lasting good health.



Resources

Managing Your Health—a guide for people living with HIV

CATIE-News—Bite-sized HIV/AIDS news bulletins

Treatment Update—treatment digest on cutting-edge developments in HIV/AIDS research and treatment

HIV and aging—a booklet covering some of the issues facing older adults living with HIV

The Positive Side—health and wellness magazine with articles such as:

- “Growing Old Gracefully” (HIV and aging)
- “Have a Heart” (HIV and the heart)
- “A Mind of Her Own” (HIV and the brain)
- “Good to the Bone” (nutrition for bone health)

Look in the e-zine index for more (www.positiveside.ca).

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

Notes

Appendices: Antiretroviral Drugs, Drug Combinations and Drug Resistance

These appendices contain more detailed information about currently available antiretroviral drugs and building treatment combinations. There are five appendices:

- ◎ **Appendix A:** an outline of the HIV life cycle that shows how the different classes of antiretroviral drugs fight the virus at different points in the cycle
- ◎ **Appendix B:** a list of the currently available classes of antiretroviral drugs and the drugs approved within each class
- ◎ **Appendix C:** an introduction to building an HIV drug combination
- ◎ **Appendix D:** an overview of first-time combinations
- ◎ **Appendix E:** an explanation of how HIV can become resistant to antiretroviral drugs and the tests used to detect drug resistance

Stay up to date!

The information in these appendices can change. New drugs are continually being approved, and recommendations for treatment combinations change as new information becomes available. Always make sure to seek out the most recent, most reliable information on HIV treatments.

Appendix A: The Viral Life Cycle and Antiretroviral Drugs

HIV cannot multiply by itself. Instead, it must get inside a cell to make copies of itself. When HIV infects a cell, it takes over the “machinery” of a cell and uses it to make new copies of itself (this is called **viral replication**). The newly created viruses leave the infected cell and go on to infect other cells. Experts estimate that up to 10 billion copies of HIV may be made every day in a person who is not on treatment.

Understanding how HIV replicates (the **viral life cycle**) allows us to understand how antiretroviral drugs work. The following illustrations show the distinct steps of the viral life cycle and the class of drugs that interferes with each step. (Appendix B lists all of the currently available drugs, by class.)

HIV is made up of two strands of genetic material called RNA. Along with the RNA, HIV contains three key **enzymes**:

- reverse transcriptase
- integrase
- protease

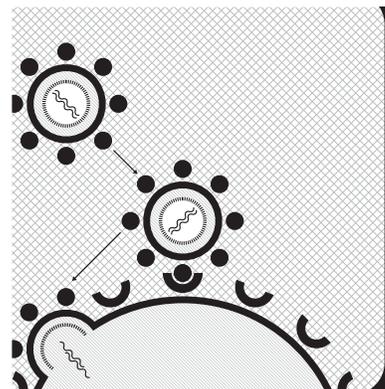
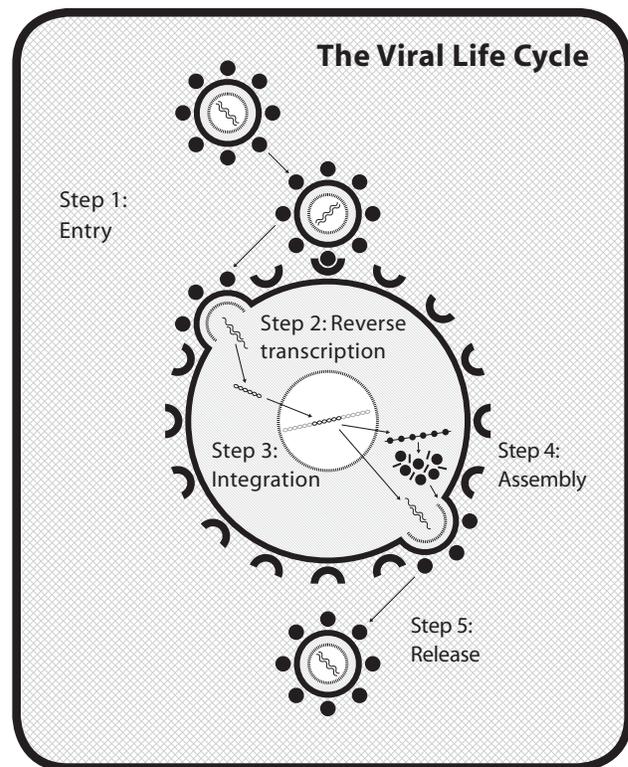
These enzymes are proteins that help the virus make copies of itself.

Step 1: Entry—HIV enters a cell

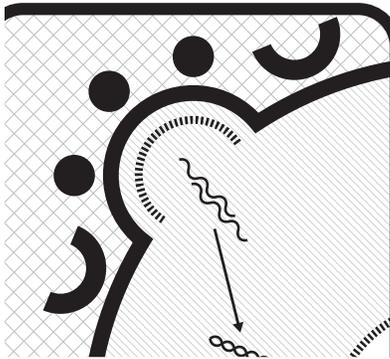
The outer surface of the virus is covered with proteins. Human cells also have proteins on their outer surface, called *receptors*. These receptors come in millions of different shapes. The HIV virus has proteins on its surface that fit perfectly into the receptors on the surface of certain cells, including CD4 cells, like a key in a lock. Once HIV attaches to these receptors, the virus can fuse with the cell. Then the contents of the virus are inserted into the cell.

Before HIV can infect a cell, it has to bind to not just one, but two receptors on the surface of the CD4 cell. One of these is called the *CD4 receptor*. The second is called a *co-receptor*. There are several different co-receptors, including two called CCR5 and CXCR4.

Many drugs are being developed to stop HIV from getting inside a cell. Drugs that stop HIV from joining to the CD4 receptor and fusing with the cell surface are called **fusion inhibitors**.



Drugs that block HIV from using a cell's co-receptors are called **receptor blockers** or **co-receptor antagonists**. They can have more specific names, based on the receptor they block. For example, **CCR5 inhibitors** interfere with the interaction between HIV and the CCR5 co-receptor on CD4 cells.



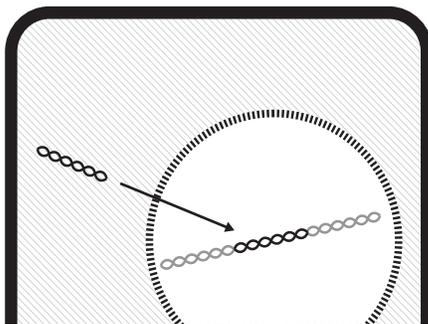
Step 2: Reverse transcription—HIV takes control of the cell

Once inside the cell, HIV takes control of the cell. One of the HIV enzymes, the *reverse transcriptase* (RT) enzyme, converts the genetic material of the virus (called RNA) into another kind of genetic material called DNA. Now the genetic material of the virus matches the genetic material of the “host” cell.

A class of drugs called **reverse transcriptase inhibitors** slow down or stop the action of the RT enzyme. These drugs come in two subtypes:

- nucleoside analogue reverse transcriptase inhibitors (NRTIs), commonly called nukes
- non-nucleoside analogue reverse transcriptase inhibitors (NNRTIs), commonly called non-nukes

Nukes were the first drugs approved for the treatment of HIV. Used in pairs, nukes continue to be a major part (the so-called “backbone”) of most drug combinations. To make up an effective drug combination, the two-nuke “backbone” is paired with a drug (or sometimes more than one drug) from another class. This is usually a non-nuke or a protease inhibitor, but may also be an integrase inhibitor.



Step 3: Integration—HIV becomes part of the infected cell

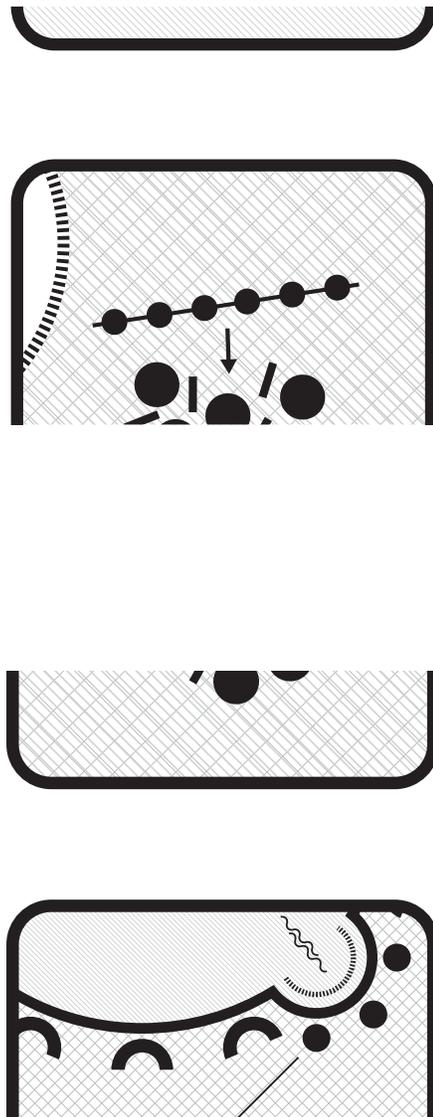
At this point, a second viral enzyme called *integrase* inserts the newly converted viral DNA into the cell's own DNA. With the viral DNA integrated into the DNA of the cell, the virus has become part of the cell. This process has been compared to putting a bug in a computer software program. Drugs that stop, or inhibit, HIV from integrating into human cells are called **integrase inhibitors**.

Steps 4 and 5: Assembly and release—HIV tricks the infected cell into making copies of itself

An HIV-infected cell can remain inactive for a long time. If the infected CD4 cell becomes activated, it will start making and releasing new virus. When a new copy of HIV is produced, it starts out as a single long chain of viral protein. The *protease* enzyme then works like scissors to snip these protein chains into smaller pieces. These newly cut pieces are then assembled into new virus particles, which “bud” from the host cell and go on to infect other cells.

Protease inhibitors (PIs) are drugs that interfere with the action of HIV’s protease enzyme. They prevent protease from cutting the long chains of new viral protein. When PIs are used, new viruses can still be formed, but they are defective and cannot infect new cells.

Researchers are working to develop new and different classes of drugs that interfere with the final steps of the viral life cycle, including the final assembly of the virus particles and budding from the cell.



Appendix B: Antiretroviral Drugs Available in Canada

Fusion inhibitor		
Common name	Brand name	Manufacturer
T-20, enfuvirtide	Fuzeon	Roche

Co-receptor inhibitor		
Common name	Brand name	Manufacturer
maraviroc	Celsentri	ViiV Healthcare (formerly Pfizer)

Nukes (nucleoside and nucleotide analogues, or NRTIs)		
Common names	Brand name	Manufacturer
abacavir, ABC	Ziagen	ViiV Healthcare (formerly GlaxoSmithKline)
AZT, zidovudine	Retrovir	ViiV Healthcare (formerly GlaxoSmithKline)
d4T, stavudine	Zerit	Bristol-Myers Squibb
ddl, didanosine	Videx EC (enteric-coated)	Bristol-Myers Squibb
FTC, emtricitabine	FTC is only available in Canada co-formulated with tenofovir, as Truvada.	Gilead Sciences
tenofovir*	Viread	Gilead Sciences
3TC, lamivudine	3TC	ViiV Healthcare (formerly GlaxoSmithKline-Shire BioChem)

Non-nukes (NNRTIs)		
Common name	Brand name	Manufacturer
delavirdine	Rescriptor	ViiV Healthcare (formerly Pfizer)
efavirenz	Sustiva	Bristol-Myers Squibb
etravirine	Intelence	Tibotec
nevirapine	Viramune	Boehringer Ingelheim

*Strictly speaking, tenofovir (Viread) is not a nucleoside analogue but a very similar molecule called a nucleotide analogue. This is largely a fine technical distinction; in practice, most HIV-positive people and their doctors refer to tenofovir as a nucleoside.

Integrase inhibitor

Common name	Brand name	Manufacturer
raltegravir	Isentress	Merck

Protease inhibitors

Common name	Brand name	Manufacturer
atazanavir	Reyataz	Bristol-Myers Squibb
darunavir	Prezista	Tibotec
fosamprenavir	Telzir	ViiV Healthcare (formerly GlaxoSmithKline)
indinavir	Crixivan	Merck
lopinavir-ritonavir	Kaletra	Abbott Laboratories
nelfinavir	Viracept	ViiV Healthcare (formerly Pfizer)
ritonavir	Norvir	Abbott Laboratories
saquinavir	Invirase	Hoffmann-La Roche
tipranavir	Aptivus	Boehringer Ingelheim

Co-formulations

Co-formulations take two or more different drugs and combine them into a single pill, reducing the number of pills that need to be taken.

Brand Name	Consists of	Manufacturer
Atripla	efavirenz + FTC + tenofovir	Bristol Myers-Squibb/Gilead Sciences
Combivir	AZT + 3TC	ViiV Healthcare (formerly GlaxoSmithKline)
Kaletra	lopinavir + ritonavir	Abbott Laboratories
Kivexa	3TC + abacavir	ViiV Healthcare (formerly GlaxoSmithKline)
Trizivir	AZT + 3TC + abacavir	ViiV Healthcare (formerly GlaxoSmithKline)
Truvada	FTC + tenofovir	Gilead Sciences

Appendix C: Building a Treatment Combination

In this section we will provide some background on how treatment combinations are built. We will also look at the characteristics of the different classes of antiretroviral drugs. Our goal is to provide you with enough information so that you can play an active role in choosing a combination with your doctor.

As mentioned, treatment combinations are usually composed of three antiretroviral drugs from two different classes. Generally, two of the drugs are nukes (also called nucleoside analogues or NRTIs). These two drugs form the “backbone” of the combination, which is completed by a third drug from a different class.

For HIV-positive people **choosing their first combination**, the group of possible combinations is fairly well defined. See “First combinations” on page 51 for an overview of recommended first combinations. Then check out Appendix D to learn why you might choose one combination over another.

For people who have already been on treatment and are **changing their drug combination**, choosing the best combination is a more individualized matter. Sometimes—especially early on, when fewer medications have been tried—the most appropriate combinations may be similar to those for first-time treatment.

For more **treatment-experienced people with more drug resistance** (see Appendix E), combination choices will depend on which drugs are most likely to be effective. Later combinations may need to contain more drugs; the goal is to have the equivalent of three “active” antiretroviral drugs. This often involves three drugs, but sometimes it involves combining several drugs that are only partially effective with the hope that together they will suppress the virus.

The “backbone”: two nukes ...

The base or “backbone” of a drug combination is two nukes. Nukes have a long clinical history—AZT was the first antiretroviral drug to be brought to market, in 1987. The nukes currently available are effective and well tolerated by most people.

There are currently seven nukes approved in Canada. Newer nukes and 3TC are usually preferred because they have fewer side effects. Tenofovir, FTC, abacavir and 3TC are all commonly used. Older nukes, such as d4T and ddI, are seldom used, as they have been linked to side effects, such as lipodystrophy and peripheral neuropathy. Our knowledge of the side effects and toxicities of each of the drugs is constantly evolving, so it is best to talk to your doctor for the latest information.

Because two different nukes are usually taken at the same time, drug manufacturers have produced several co-formulations, where two or more drugs are put into a single pill. Common nuke co-formulations are Truvada (tenofovir and FTC), Kivexa (abacavir and 3TC) and Combivir (AZT and 3TC). Trizivir is one pill that contains three nukes: AZT, 3TC and abacavir (even though Trizivir contains three medications, it is not a preferred combination). One advantage of having several co-formulations is that when it comes time to switch medications, it might be possible to switch to a different co-formulation and thereby continue taking few pills.

Some people have an allergic reaction (or *hypersensitivity reaction*) to abacavir. A simple blood test, done before starting any medications, can tell whether you are one of the people at risk of having this reaction: if so, you should choose a different nuke.

... plus one more drug

When choosing this third drug, consider the known drug interactions, potential side effects and pill-taking schedule of each possibility. Although drugs within each class often share some common characteristics, they can also be significantly different. As with the nukes, there are also recommended drugs within the other classes.

If you are switching to a new anti-HIV drug, you and your doctor will decide whether to switch to a drug of the same class or to a drug from a different class. This decision will be guided by the resistance profile of your virus and the side effects of the individual drug.

Non-nukes

Non-nukes are a class of antiretroviral medications known for their ability to quickly and effectively reduce a person's viral load when taken as part of a drug combination. However, resistance to a non-nuke sometimes develops more easily than to drugs from other classes, and HIV that is resistant to one non-nuke is often resistant to nearly all members of this class. (Etravirine, the newest non-nuke, may still work in people who are resistant to the other non-nukes.)

There are currently four non-nukes approved in Canada:

- Efavirenz (Sustiva, also a component of Atripla) is the most commonly used non-nuke and is a preferred option for first combinations, except for women who are pregnant or planning to become pregnant because it poses a risk to the fetus.
- Nevirapine (Viramune) is an alternative non-nuke but should not be started in people with higher CD4 counts (more than 250 cells in women or more than 400 cells in men) because of a high risk of liver toxicity.
- Delavirdine (Rescriptor) is rarely used because it is not as powerful as newer drugs and needs to be taken three times daily.
- Etravirine (Intelence), the newest non-nuke, is currently used in people infected with strains of HIV that are resistant to efavirenz and nevirapine.

Protease inhibitors (PIs)

PI-based combinations tend to involve more pills than combinations that contain non-nukes, and many have to be taken with food. Many PIs can also cause metabolic problems, such as high levels of cholesterol. Some are associated with an increased risk of cardiovascular disease, and a few are associated with increased blood sugar levels. One advantage of PIs is that if HIV develops resistance to one PI, other PIs can remain effective, providing future treatment options.

A small dose of ritonavir (Norvir) is almost always added to PIs. This dose may be co-formulated in one pill or you may need to take ritonavir in addition to the PI. Adding ritonavir to PI regimens (which is called "boosting") has the following advantages:

- Ritonavir boosts the levels of the other PIs in the blood, resulting in more powerful anti-HIV activity.
- This allows a person to take a smaller dose of the PI, which usually means fewer pills.
- Ritonavir also prolongs the time that the PI remains in the blood, so that the PIs can be taken less frequently. Most PIs are taken once or twice a day.

However, PIs boosted with ritonavir are prone to many possible drug interactions.

Integrase inhibitor

Raltegravir (Isentress) is the only integrase inhibitor currently approved. It was originally studied in HIV-positive people who had previously taken non-nukes and PIs, and it was very effective in that group. More recently, raltegravir has been approved for use as a first-line option and has shown good results so far. It appears to be very effective at inhibiting HIV, with mostly minor side effects.

Other classes

Currently, non-nukes, PIs and integrase inhibitors are the only classes recommended as the “third drug” in a first-time combination. Drugs in other classes are currently reserved for people who have already been on one or more standard HIV drug combinations.

The only *fusion inhibitor* currently available is enfuvirtide (T-20, Fuzeon), which has powerful anti-HIV activity but has to be taken twice a day by injection. Although this is obviously far from desirable, T-20 is still an important option for people who are resistant to many different antiretrovirals.

CCR5 inhibitors (a kind of co-receptor inhibitor) are yet another newer class of drugs. Like the fusion inhibitors and integrase inhibitors, CCR5 inhibitors have been studied mostly in people who have previously tried other treatment combinations. These drugs have generally proven to be quite effective, but only against a strain of HIV called *R5-tropic*. CCR5 inhibitors are not of any use in fighting X4-tropic virus, the other major strain of HIV, which tends to develop in people who have been infected longer. A simple screening test is able to determine whether you have the R5-tropic strain; if so, CCR5 inhibitors are a viable option. Maraviroc (Celsentri) is the first, and currently only, CCR5 inhibitor approved for use.

Appendix D: First Combinations

Table 1 below outlines possible drug combinations for people starting HIV drug treatment for the first time. The combinations listed here are those recommended by many major treatment guidelines at the time this guide was published.

Table 2 lists a few of the advantages and disadvantages of the drugs in Table 1. You can use the information in these tables as a starting point for discussing treatment options with your doctor. When looking at the options, remember that these are only guidelines and that another combination, perhaps not listed here, may be the right one for you.

The cost of some of these drugs may not be covered by provincial or territorial prescription drug plans. Your doctor and pharmacist can give you more information.

Table 1: Possible antiretroviral drug combinations for people starting treatment

2 nukes	+ a 3rd drug	such as
Truvada (tenofovir + FTC) OR Kivexa (abacavir + 3TC)	a non-nuke	efavirenz (Sustiva)
	OR	
	a boosted PI	atazanavir (Reyataz), darunavir (Prezista), fosamprenavir (Telzir) or saquinavir (Invirase), boosted by ritonavir (Norvir)
		OR
		lopinavir-ritonavir (Kaletra)
	OR	
an integrase inhibitor	raltegravir (Isentress)	

Table 2: Potential advantages and disadvantages of some antiretroviral drug combinations

Two nukes (nucleoside reverse transcriptase inhibitors or NRTIs) combined in one pill ...		
Drug	Potential advantages	Potential disadvantages
Kivexa (abacavir + 3TC)	<ul style="list-style-type: none"> Has been used for many years and both drugs penetrate well into the brain. 	<ul style="list-style-type: none"> Abacavir can cause a hypersensitivity reaction in some people (a blood test can be done before you start taking the medication to see if you're at risk). There have been recent questions about whether abacavir is associated with an increased risk of heart attacks, particularly among people who are already at increased risk (for example, older people, smokers or people with high blood pressure).
Truvada (tenofovir + FTC)	<ul style="list-style-type: none"> Also available in combination with efavirenz (Sustiva) as Atripla, which is one pill taken once a day. 	<ul style="list-style-type: none"> There are concerns about the possible effect on kidney function and about weakening of the bones when tenofovir is used for many years.
Other nukes	<p>Other nukes include the individual components of Kivexa and Truvada (for example, abacavir (Ziagen), lamivudine (3TC) and tenofovir (Viread)). Others include AZT (zidovudine, Retrovir), ddI (didanosine, Videx EC) and d4T (stavudine, Zerit). These are chosen mainly for people who have viruses with resistance to some of the primary drugs and need specific drugs based on testing of their virus. In Canada, FTC (emtricitabine) is only available co-formulated with tenofovir, as Truvada.</p>	
... plus one non-nuke (non-nucleoside reverse transcriptase inhibitor or NNRTI) ...		
Efavirenz (Sustiva)	<ul style="list-style-type: none"> Available in combination with tenofovir and FTC as Atripla, which is one pill taken once a day. 	<ul style="list-style-type: none"> May cause vivid dreams and other sleep or mental disturbances. May increase cholesterol levels, but studies have not found any increased risk of heart disease. Women who are or might become pregnant should not take efavirenz.
Other non-nukes	<ul style="list-style-type: none"> Nevirapine (Viramune) is a "first-generation" non-nuke that cannot be started in men whose CD4 count is higher than 400 cells or in women whose CD4 count is higher than 250 cells. It penetrates well into the brain and may increase levels of good cholesterol and reduce triglycerides. However, it may cause an allergic reaction (rarely fatal) for which there is no test to determine risk in advance. Etravirine (Intelence) is a "second-generation" non-nuke that is usually only taken by people who are resistant to efavirenz or nevirapine. 	

... OR a protease inhibitor ...		
Atazanavir (Reyataz)	<ul style="list-style-type: none"> Doesn't cause an increase in cholesterol (if used without ritonavir). 	<ul style="list-style-type: none"> May cause jaundice (yellow eyes or skin), which is either mild or reversible (goes away if the medication is stopped). NEVER stop taking a medication before discussing it with your doctor, as you will need a replacement drug. Atazanavir is almost always boosted by ritonavir if it is taken with tenofovir (also a component of Truvada).
Darunavir (Prezista)	<ul style="list-style-type: none"> Effective in many people with resistance to older PIs, especially when combined with other effective drugs. 	<ul style="list-style-type: none"> May (rarely) cause liver toxicity; should not be used by people with severe liver damage. Because it remains effective even when other PIs fail, darunavir is often saved for second or later treatment combinations.
Lopinavir-ritonavir (Kaletra)	<ul style="list-style-type: none"> Preferred treatment for pregnant women. 	<ul style="list-style-type: none"> Can increase levels of cholesterol, triglycerides (another type of fat) and sugar in the bloodstream.
Boosting with ritonavir (Norvir)	<ul style="list-style-type: none"> Increases drug levels of other PIs and keeps the medication in the bloodstream longer. 	<ul style="list-style-type: none"> Greater likelihood of side effects. An extra pill to take. Ritonavir may cause mild diarrhea and a small increase in cholesterol. Ritonavir can interact with many medications.
Other PIs	<p>Most other PIs (including nelfinavir (Viracept), saquinavir (Invirase), indinavir (Crixivan), fosamprenavir (Telzir) and tipranavir (Aptivus)) will cause some increase in cholesterol and sometimes liver enzymes. Most are used for individuals who cannot, for some reason, use Kaletra, (boosted) atazanavir or darunavir.</p>	
...OR an integrase inhibitor		
Raltegravir (Isentress)	<ul style="list-style-type: none"> Many people experience fewer short-term side effects with raltegravir than with other antiretrovirals. 	<ul style="list-style-type: none"> Because raltegravir is a relatively new drug, its long-term effects are unknown.

Appendix E: Drug Resistance and Resistance Testing

This appendix looks at how HIV can develop resistance to antiretroviral drugs and how labs test for drug resistance.

At the base of drug resistance is the fact that HIV is a little sloppy about making copies of itself. The new copies often contain changes, called *mutations*. These small changes in the genetic material of the virus result in changes to the way the virus is put together. Some mutations may allow the virus to replicate even when antiretroviral drugs are being used. This ability to replicate in the presence of antiretroviral drugs is called **drug resistance**.

If the HIV in your body becomes resistant to one or more drugs, those drugs won't work anymore. If you keep taking those medications, they won't stop HIV from replicating and infecting cells in your body. Your viral load will increase and the damage to your body and immune system will increase. This situation is called *treatment failure*. To get HIV back under control, you and your doctor will likely switch your drug combination, but because you can't re-use a drug the virus is resistant to, you will have fewer options to choose from. (See page 68 for a discussion of treatment failure.)

Resistance to one drug can cause **cross-resistance** to other drugs in the same class, even if you haven't taken those other drugs before. (For instance, most non-nukes are highly cross-resistant: if you are resistant to nevirapine, you'll probably also be resistant to efavirenz, and vice versa.)

It is possible to become infected with a strain of HIV that is already resistant to certain drugs. Drug resistance can also happen when you end up with a small amount of drug in the body but not enough to fully suppress the virus. This can happen as a result of missing doses or not taking your antiretroviral drugs regularly. If you're taking enough of a drug consistently, resistance is highly unlikely. It's that middle ground—when you're taking a drug, but not enough of it—that can lead to resistance. That's why it's so important to take your meds regularly and on schedule; this is called *adherence*. (See page 61 for tips and tricks to sticking to your medication schedule.)

It is possible to do a blood test to check whether your HIV is resistant to any drugs. These tests may be useful in two situations:

- Before you start treatment—drug-resistant HIV can be transmitted from one person to another, so it's possible to have resistance to one or more anti-HIV drugs even if you have never taken any yourself.
- If your treatment has failed—as shown by your viral load coming back up after becoming undetectable or by never becoming undetectable in the first place.

In either case, it makes sense to check whether you have virus that is resistant to any anti-HIV drugs and, if so, which ones. In Canada, *genotypic tests* are routinely used to identify drug resistance. Genotypic tests identify specific mutations in the virus that can lead to resistance to a particular drug.

There is another type of test called a *phenotypic test*, which measures the amount of drug needed to de-activate a sample of virus: the more drug that is needed, the more resistant the virus is. Phenotypic tests are not commonly used because they are considerably more difficult to run and few labs offer them. Phenotypic tests also take a lot longer to do than genotypic tests and are significantly more costly. There is no evidence to suggest that either type of test provides better results.

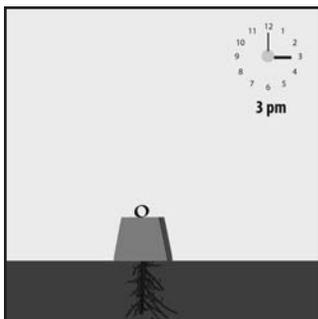
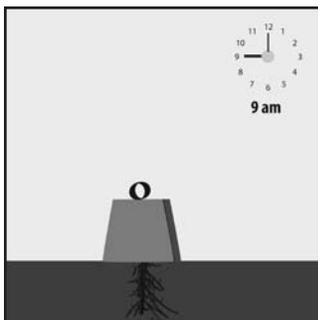
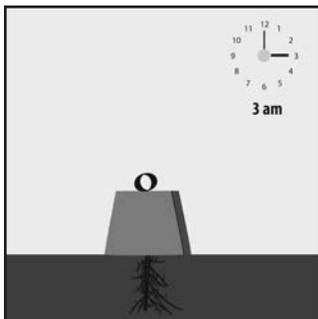
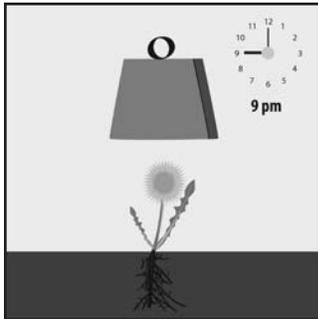
Both the genotypic and phenotypic tests have limitations. If you only have a small amount of virus that is resistant to a drug, the test may not detect it. As a result, the tests will be able to accurately tell you which drugs will *not* work for you, but they will not be able to say with certainty which drugs *will* work.

Resistance test results are complex and are best interpreted by an HIV doctor with a good deal of experience working with viral resistance. In the right hands, and combined with a knowledge of which antiretroviral drugs you've already taken, resistance testing can be an extremely useful tool for figuring out which drugs will work best for you.

For more information, see "Resistance Assistance" in the Fall/Winter 2005 issue of *The Positive Side* (www.positiveside.ca).

How HIV drug resistance develops: a visual story

Part One: HIV is a weed; treatment stops the weed from growing
HIV is like a weed with deep roots. In these pictures, antiretroviral therapy is represented by a heavy block that crushes the weed and keeps it from growing. However, the block doesn't eliminate the roots of the weed. Similarly, antiretroviral therapy keeps HIV from reproducing, but it does not eliminate the virus that lies hidden in cells inside your body.



Here's an example:

Imagine you had to take your antiretroviral medications once every day, let's say at 9 pm.

Starting antiretroviral treatment keeps HIV from multiplying inside your body, just like covering this weed with a large block keeps it from growing.

The amount of antiretroviral medications in your body is highest shortly after you've taken a dose—shown here by a large block. Over the next 24 hours, the amount of antiretroviral drugs in the body gradually decreases. In our analogy, the block gets smaller over the course of the night (3 am) and following day (9 am and 3 pm).

However, as long as the block remains large enough, the weed can't grow back. Your dosing schedule is designed so that even between doses, there is still enough drug in your body to keep HIV under control.

The next night, at 9 pm, you take your next dose and the block over the weed grows back to full size—the same as it was in the first picture on this page. As long as you keep taking your antiretroviral drugs on time, the weed can't grow back.

Taking your medications cannot get rid of the roots of the weed—HIV will stay hidden inside your cells. However, as long as you keep taking your medications on time, your drug combination can keep HIV undetectable day after day, year after year.

Part Two: Missing doses allows the weed to grow

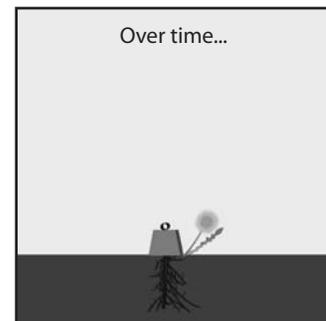
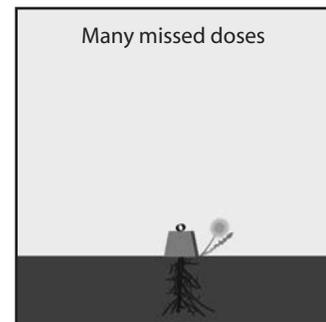
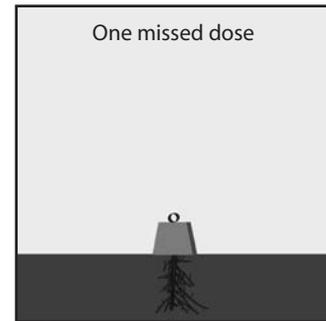
Antiretroviral therapy keeps the weed (HIV) from growing but does not kill its roots. Missing doses of your drugs gives the “weed” a chance to start growing again.

While you should try to not miss a dose of your medication, missing just one dose is probably not enough to stop your treatment from working. When you miss a dose, the block shrinks more than it should and gives the weed a bit of room to grow. But missing just one dose doesn't give the weed much time to grow. Taking your next dose should squash any tiny bit that had a chance to grow.

However, if you miss too many doses, the block will get so small that the weed is able to grow back; that is, the virus will start making copies of itself again.

The more doses you miss, the more often the weed roots are exposed and the greater the chance the weed will grow back. Or, for your treatment, the more chances HIV has to start making copies of itself.

After enough missed doses, the weed will learn how to grow *around* the block. If that happens, it will keep growing even if the block becomes full size again. In terms of your HIV treatment, the virus will become resistant to the drugs you're taking. Your viral load will stay detectable even if you go back to taking every dose of your medication. To get the virus under control again, you will have to carefully choose another combination.



Other CATIE Publications

Managing Your Health, 2009 edition

A comprehensive guide for living with HIV, including social, legal, health-related and practical issues

CATIE Fact Sheets

Concise overviews of conditions, symptoms, medications, side effects, complementary therapies, vitamins, supplements and other treatment issues

The Positive Side

Holistic health and wellness magazine for people with HIV

TreatmentUpdate

CATIE's flagship treatment digest on cutting-edge developments in HIV/AIDS research and treatment

HIV & AIDS Basic Facts

A brochure that offers the basics on HIV transmission, testing and treatment

You Can Have a Healthy Pregnancy if You Are HIV Positive

An easy-to-read booklet for women with HIV who are pregnant or considering becoming pregnant

HIV and Aging

A booklet that highlights some of the issues adults 50+ living with HIV might face and how they can stay healthy—physically, mentally, emotionally and sexually

A Practical Guide to
HIV Drug Treatment

for People Living with HIV

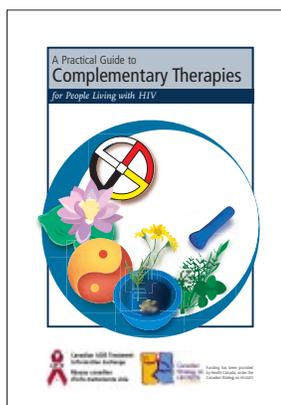
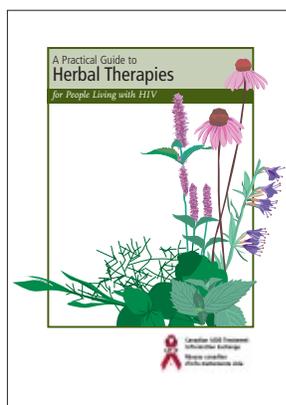
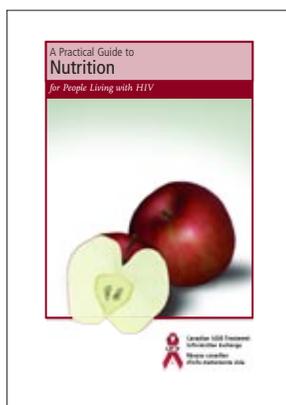
This guide is one of a series of practical guides for people living with HIV. The other titles in the series are:

A Practical Guide to HIV Drug Side Effects

A Practical Guide to Nutrition

A Practical Guide to Complementary Therapies

A Practical Guide to Herbal Therapies



Read the guides online or download a copy from www.catie.ca. You can also order a free print copy through the CATIE Ordering Centre at www.catie.ca or 1-800-263-1638.

Production of this guide has been made possible through financial contributions from the Public Health Agency of Canada, Bristol-Myers Squibb Canada and ViiV Healthcare in partnership with Shire Canada.



555 Richmond St. W.
Suite 505
Toronto ON M5V 3B1
1-800-263-1638
web: www.catie.ca
em: info@catie.ca

CATIE Ordering Centre Catalogue Number ATI-40217
(aussi disponible en français, ATI-40218)