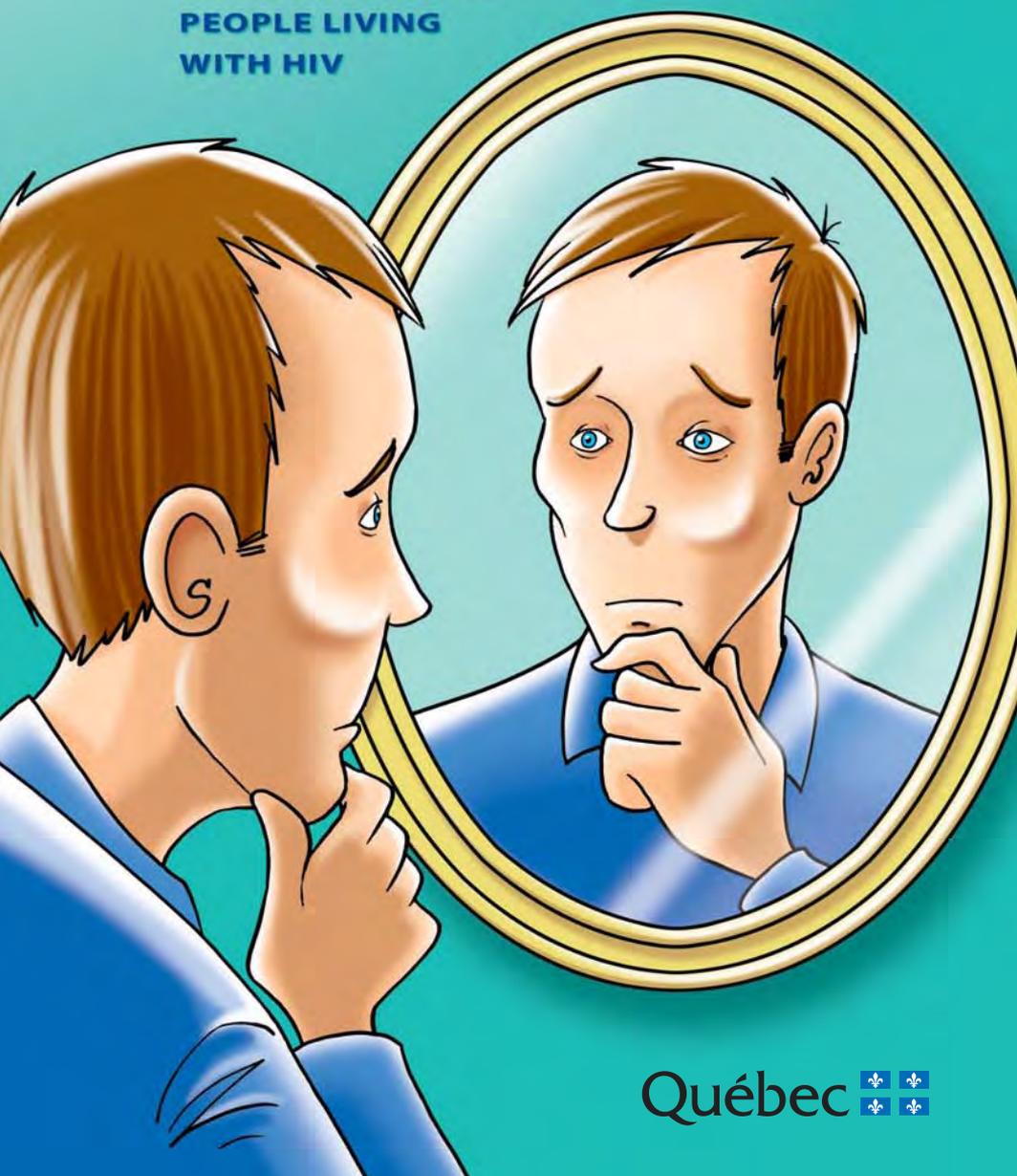


Lipodystrophy

INFORMATION FOR
PEOPLE LIVING
WITH HIV



This document is intended for people living with HIV. It was revised in January 2004 by members of the Comité consultatif pour la prise en charge clinique des personnes vivant avec le VIH-SIDA in collaboration with COCQ-SIDA and CPAVIH. A document with more detailed information has been produced in conjunction with this brochure and is intended for health professionals¹.

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¹ *Le syndrome de lipodystrophie chez les personnes infectées par le HIV, Guide pour les professionnels de la santé du Québec.* Ministère de la Santé et des Services sociaux du Québec.

Are you c©NCerned about lipodystrophy?

Some people living with HIV may have noticed they have lost or gained weight in various parts of their bodies. These types of body fat changes, called “lipodystrophy”, are linked to anti-HIV treatments.

This document describes the body changes that have been associated with anti-HIV therapy. It presents the symptoms of lipodystrophy and its known causes, as well as required medical follow-up and existing treatments. This information can help you play an active role to ensure that you receive the best possible follow-up and treatment.

Until recently, there were long delays before the first symptoms of lipodystrophy were identified in someone receiving anti-HIV therapy. Now that more is known about this condition, doctors and people living with HIV are more sensitive to the first symptoms.



What are the **SYMPTOMS**?

THE SYMPTOMS OF LIPODYSTROPHY CAN BE DIVIDED INTO FOUR MAIN GROUPS.

Fat loss (also called lipoatrophy)

- **in the face:** can make a person look thinner or like he or she has hollow cheeks and temples;
- **in the legs and arms:** can make veins look more prominent;
- **in the buttocks:** can make sitting uncomfortable.

Fat gain (also called lipoaccumulation)

- **in the stomach and breasts in men and women:** the main effect of fat accumulating in the stomach is increased waist size, which can change someone's physical appearance. In serious cases, internal organs are compressed, making normal functions like breathing and eating more difficult;
- **in the neck:** the term "buffalo hump" is given to the accumulation of fat across the back of the shoulders. It is not always related to complications of anti-HIV therapy and may be caused by something else. In some cases, fat also accumulates under the chin;
- **under the skin:** small fatty lumps called lipomas sometimes develop. Lipomas usually cause no symptoms but can occasionally be painful.

Fat loss and accumulation (also called mixed syndrome)

- Some people can both lose and gain fat at the same time in different parts of the body.

symptoms?

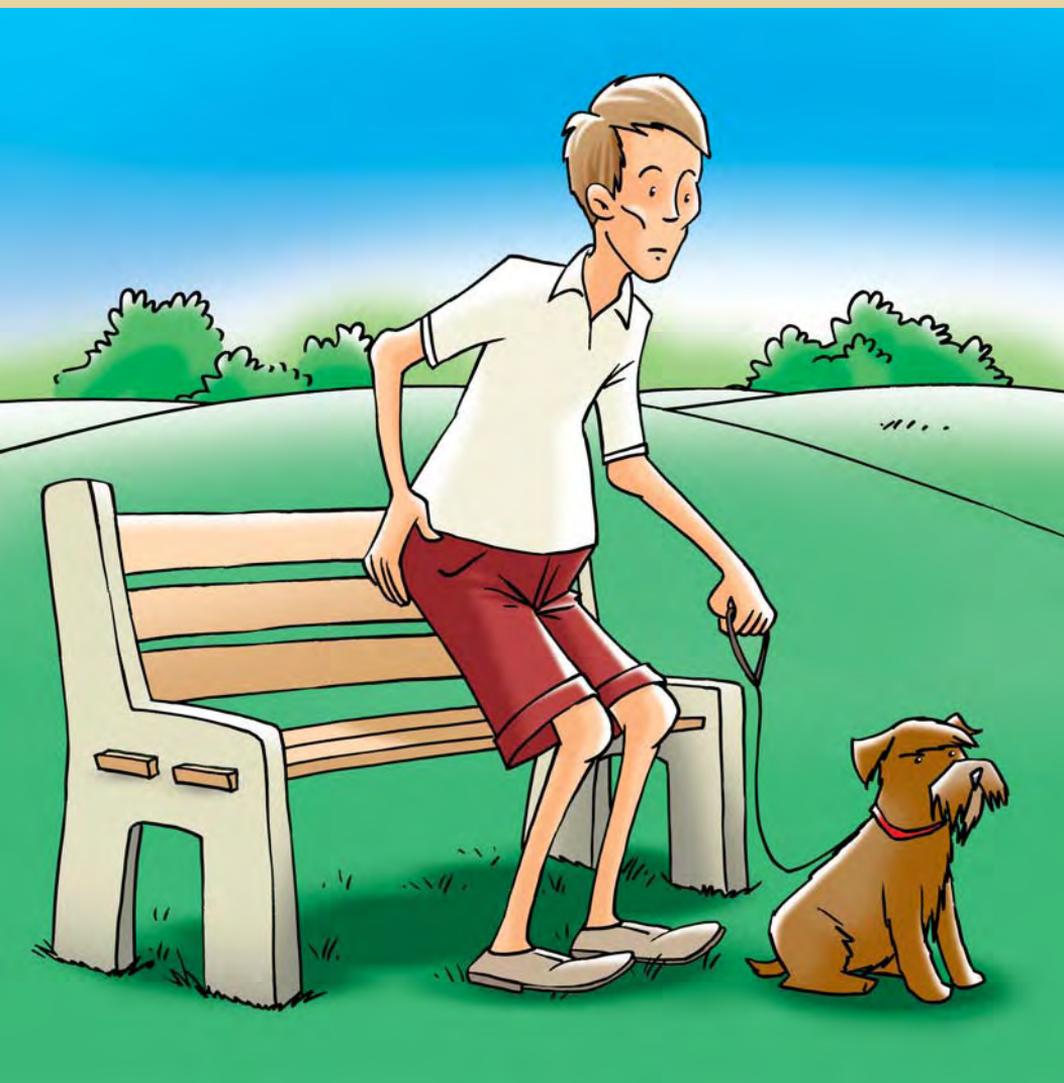
Abnormal blood tests

Some people also have abnormal blood tests (called metabolic changes) that can include:

- increases in blood fat levels (triglycerides and cholesterol);
- increases in blood sugar levels, which can predispose to diabetes or, less frequently, lead to overt diabetes;
- increases in lactic acid in the blood which, in rare cases, lead to a serious or even potentially deadly condition called lactic acidosis.

According to recent studies, fat loss is the most common characteristic of lipodystrophy syndrome. An accumulation of fat can sometimes be difficult to tell apart from obesity, a problem affecting a large part of the population. However, in cases of lipodystrophy, fat in the stomach accumulates around internal organs and not under the skin, as is often the case for ordinary obesity. Some people also have abnormal test results for blood fat levels (triglycerides and cholesterol) or blood sugars (diabetes).

People living with HIV are very concerned with fat gain and loss since these changes can significantly alter their physical appearance and quality of life. Someone with visible signs of lipodystrophy could be identified as having HIV, which could possibly lead to discrimination. Lipodystrophy can also harm one's social or love life, provoke anxiety or cause depression. It can sometimes cause problems at work or make it difficult to get a new job. Do not hesitate to discuss this issue with your doctor, pharmacist, another health professional or someone working with a community group so you can learn how to better cope with lipodystrophy. Talking to someone about this problem can be helpful.



What caUSES lipodystrophy?

Of all the possible side effects of anti-HIV therapy, lipodystrophy is the most complex to sort out, since different studies have come to varied conclusions. Current research has suggested several causes, such as the effects of medications or the immune system's response to effective treatment.

The most significant factor associated with lipodystrophy is HIV treatment, although other factors also play a role. It has been noted that lipodystrophy affects HIV-positive individuals receiving treatment much more frequently.

Four classes of medications are used to treat HIV infection:

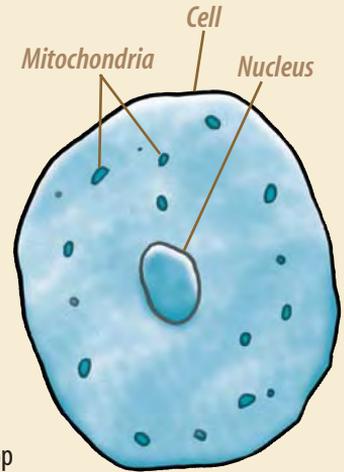
- nucleoside or nucleotide reverse transcriptase inhibitors (NRTI);
- non-nucleoside reverse transcriptase inhibitors (NNRTI);
- protease inhibitors (PI);
- fusion inhibitors (FI).

Table 1 presents these classes of medications.

Fat loss is especially associated with use of nucleoside reverse transcriptase inhibitors (NRTI), while fat accumulation is related to protease inhibitors (PI). It is believed that fat loss is mostly provoked by nucleoside inhibitors, which cause mitochondrial toxicity (damage to the energy-producing mechanism in cells).

Several factors could be associated with lipodystrophy including HIV infection, medications, time of onset on HIV treatment, stage of the disease, age, sex or race. There does not seem to be only one cause. Thus, it has been observed that lipodystrophy occurs more frequently in:

- people aged 40 or over;
- people who have been taking medications for a long time;
- people whose CD4 cell count was lower (under 200) before treatment;
- people who have higher levels of triglycerides in their blood;
- people who are taking a combination of protease inhibitors and nucleoside inhibitors;
- people who are taking stavudine (d4T); several studies have shown that taking stavudine (d4T) causes lipoatrophy to develop more quickly or more often than taking the other nucleoside inhibitors, but these results have been contradicted by other studies.



Lipodystrophy has been diagnosed in men, women and children from different ethnic backgrounds. Fat gain is seen more often in women. Fat loss affects white men more than black men.

TABLE 1

NRTI	NNRTI	PI	FI
AZT (Retrovir™)	Nevirapine (Viramune™)	Saquinavir HGC (Invirase™)	T 20 (Fuzeon™)
3TC (3TC™)	Delavirdine (Rescriptor™)	Saquinavir SGC (Fortovase™)	
ddI (Videx™ or Videx ECT™)	Efavirenz (Sustiva™)	Ritonavir (Norvir™)	
ddC (Hivid™)		Indinavir (Crixivan™)	
d4T (Zerit™)		Nelfinavir (Viracept™)	
Abacavir (Ziagen™)		Amprenavir (Agenerase™)	
AZT + 3TC (Combivir™)		Lopinavir (Kaletra™)	
AZT + 3TC + Abacavir (Trizivir™)		Atazanavir (Reyataz™)	
Tenofovir (Viread™)			



How **COMMON** is lipodystrophy?

It is sometimes difficult to diagnose lipodystrophy accurately. Various studies have shown that frequency of lipodystrophy varies. It is estimated that about 50% of people taking anti-HIV medications will develop lipodystrophy during the first three years of treatment. It is impossible to predict who will be affected before treatment begins.

Monitoring body shape changes

You are undoubtedly more sensitive to physical changes in your body than your doctor or your family and friends. A person living with HIV is often the first to notice changes in his or her body. There are several ways of measuring and monitoring body shape changes.

The most simple ways of recognizing the symptoms of lipodystrophy are:

- to look for fat loss in the face, for example by comparing recent photographs with older ones. Ideally, the photographs should have been taken from the same distance and in the same type of light;
- to watch for new appearances of bulging veins on the arms or thighs;
- to pay attention to changes in your weight;
- to measure the circumference of your waist at the navel while standing. Record any changes. Clothes that are now tight around the waist or neck, or too loose around the buttocks also indicate changes.

Researchers also use other methods to monitor lipodystrophy. Sometimes these methods are costly and researchers are still not sure which results should be considered normal and which ones indicate lipodystrophy. For this reason, these tests are not part of the medical care provided, and some are only available for research purposes. These tests are:

- measuring fat under the skin using skin-fold callipers, which gives an idea of the amount of fat sitting under the skin;
- bio-impedance analysis (BIA), which measures the body's total fat and lean (muscle) content, using very low intensity electric current. However, this test does not provide information on fat distribution in the limbs and abdomen and it does not accurately measure changes due to lipodystrophy;
- DEXA scan, an x-ray test that evaluates the amount of fat in various parts of the body;
- SCAN, or magnetic resonance (MRI).

Since the usefulness of these tests has not been confirmed, at this time we are relying only on physical examination and symptoms to diagnose lipodystrophy.

How is lipodystrophy treated?

Currently, no treatment for lipodystrophy is both accessible or proven effective. Several studies are underway and some are showing encouraging results. There are arguments both for and against every possible treatment. Consequently, it is important to get information and talk to your doctor before deciding on a treatment.

SHOULD HIV TREATMENTS BE DELAYED?

ARGUMENTS FOR

If HIV treatments are delayed, the total duration of the treatment is reduced and, therefore, the risk of developing lipodystrophy decreases.

ARGUMENTS AGAINST

Waiting too long can result in too sharp a drop (under 200) in CD4 cell count. If the immune system is too weak, the risk of developing lipodystrophy increases and treatment efficacy can be diminished.

RECOMMENDATION

In general, it is recommended to start treatments when CD4 count is between 200 and 350.



STOPPING TREATMENT

ARGUMENTS FOR

Before the year 2000, patients started HIV treatment earlier in the course of the disease. However, studies have shown that some people can safely stop treatment if they had started it when their CD4 cell count was over 350. In a few cases, the symptoms of lipodystrophy declined but only several months after stopping treatment.

ARGUMENTS AGAINST

Stopping treatment can cause symptoms of the disease to reappear and CD4 cell count to fall. In some cases, the virus may become resistant to the medications administered if treatment is stopped. Stopping treatment for a short period (less than six months) has no visible effect on lipodystrophy.

RECOMMENDATION

If you started to take medications when your CD4 cell count was over 350 and it has always remained stable, talk to your doctor about the advantages and inconveniences of stopping treatment. With certain combination of drugs, you should be aware that some of the triple therapy medications must be stopped before others. Stopping treatment is not usually recommended if you started taking medications when your CD4 cell count was below 350 or if you have symptoms of AIDS.

CHANGING MEDICATIONS

ARGUMENTS FOR

A few studies that looked at switching from d4T (stavudine) or AZT (zidovudine) to abacavir have demonstrated improvements in some cases of lipoatrophy. An increase in limb fat could be detected with tests but was visible in only a minority of patients. For most patients, the effects of changing treatments seem to become only apparent after several years. In most of the cases, treatment efficacy does not diminish when one medication is replaced with an equivalent one.

ARGUMENTS AGAINST

Replacing a protease inhibitor (PI) with another type of treatment has not proven to be effective against lipodystrophy. Most studies have focused on the effects of switching d4T for abacavir but noticeable long-term effects have not been definitely proven. Changing medications can result in new side effects or allergies. In some cases, a new treatment can even turn out to be less effective than the previous one.

RECOMMENDATION

If you develop lipodystrophy or if you are concerned with this issue, talk to your doctor about the advantages of continuing or changing your current treatment. Some medications, such as d4T and protease inhibitors, could cause more lipodystrophy. The decision on whether or not to use these medications depends on a number of factors, including the resistance of your virus to medications and the other side effects of alternate medications.



Other possible interventions include:

Treatment or intervention	Arguments for	
Diet and exercise	Studies have shown that diet and exercise have had a positive effect on reducing body fat build-up.	
Growth hormone	Several small studies have demonstrated that recombinant human growth hormone (rHGH) has the potential to reduce fat accumulation in the abdomen, back and neck.	
Medications for diabetes and lipid problems (cholesterol and triglycerides)	Some studies have evaluated the possible role of these medications in increasing subcutaneous fat.	
Cosmetic treatments	Liposuction	Liposuction has proven effective in removing buffalo humps.
	Fat injection for facial lipoatrophy	Studies show that subcutaneous fat can be taken from the body and injected into the cheeks.
	Injection of polylactic acid (New-Fill) for facial lipoatrophy	Injections of New-Fill every two weeks for a few weeks have shown rapid and promising results. New-Fill does not replace fat but generates new collagen growth (essentially by making the skin grow thicker) up to a maximum of one centimetre. This process continues for months after the injections have finished. It seems that the effects of this treatment last at least two years. Long-term results are awaited with much interest.
	Surgical removal of lipoma	This type of surgery is especially useful in case of pain caused by lipomas.

Arguments against	Comments
<p>A diet that is too strict or too much exercise can aggravate fat loss, if this is your main problem.</p>	<p>Exercise and a balanced diet improve health and decrease fat build-up. It is recommended to consult a nutritionist, if this service is available.</p>
<p>These benefits were observed over the short term, but fat accumulation reappeared after treatment was stopped. This treatment is expensive. It has been approved for use in Canada, but is not reimbursed by provincial programmes. Growth hormones can increase insulin resistance and cause diabetes.</p>	<p>The use of recombinant human growth hormone is still mostly experimental due to its cost and side effects.</p>
<p>Results are preliminary and not very encouraging.</p>	<p>These medications are not indicated for people who do not have diabetes or lipid problems.</p>
<p>In some cases, the hump reappeared after the intervention. This treatment cannot be used to remove fat inside the abdomen.</p>	<p>This treatment can be used to remove buffalo humps but is not readily available. Few doctors are familiar with this technique.</p>
<p>Most patients do not have enough subcutaneous fat to extract, and the long-term effectiveness of this treatment is not known.</p>	<p>This technique is not readily available.</p>
<p>New-Fill is not available in Canada since Health Canada has not approved it yet. Some people obtain it elsewhere but it is very expensive: \$700 per set of injections, with a minimum of three or four sets of injections required. The long-term (over two years) effectiveness and safety of this product are not known.</p>	<p>This treatment has not yet been approved for use in Canada, but access to New-Fill will improve quality of life over the short term for a number of HIV-positive individuals who have facial lipoatrophy.</p>
<p>Surgery can leave scars.</p>	<p>Lipoma that cause persistent discomfort can be removed surgically.</p>

In conclusion

Lipodystrophy is a significant and common manifestation in people living with HIV infection. There is no known effective treatment for lipodystrophy. Much research is being done on lipodystrophy and in the future, new knowledge will emerge to help prevent and treat this condition. By remaining vigilant, you can keep your doctor better informed of your situation and take an active role in monitoring your condition. We should not forget that, despite this undesirable effect of antiviral therapies, the benefits of anti-HIV treatments are much greater than their inconveniences.

For more information, contact CPAVIH's Info-Traitements service at (514) 521-8720 or 1 800 927-2844 toll free outside the Montréal area, or at info.traitement@cpavih.qc.ca

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