3. Body Weight and Body Shape Changes

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Figuring out the cause

The causes of body changes in HIV are not fully understood. In some cases, body changes may result from some combination of drug side effects, changes in the body that occur when antiretroviral therapy leads to a stronger immune system and the effects of HIV disease itself, especially how HIV affects the ways in which the body stores and uses blood fats. In other cases, these body changes are the same type seen in HIV-negative people and are the result of an unhealthy diet, lack of exercise and aging.

Along with the gradual slowing of metabolism that is common as we grow older, weight gain can happen in people with HIV in the same way and for the same reasons as it does in people who do not have HIV. People with HIV, like everyone else, can simply gain weight as a result of eating too much of the wrong foods, not exercising or both. However, there are several factors related to HIV disease that can lead to the weight and body changes that are part of the lipodystrophy syndrome.

Some people with HIV will lose weight. Planned weight loss can be the result of exercise and diet. Unintentional weight loss has many possible causes and can be HIV-related or not. Common causes include:

- depression, which can cause you to lose interest in eating
- hyperthyroidism, a condition caused by an overactive thyroid that causes you to burn calories quickly
- problems with your mouth, teeth or throat that make eating painful
- using street drugs
- infections, including those caused by parasites
- cancer.

The most extreme form of weight loss is HIV-associated wasting. Although this is seen much more rarely than in the past due to improvements in HIV diagnosis and treatment, it does occur, especially in those who are diagnosed late. HIV-associated wasting is a complex problem that requires a multi-step approach, including antiretroviral therapy; appetite stimulation, if needed, and appropriate diet supplementation to boost calories and provide nutrients; hormone replacement therapy, particularly testosterone, as appropriate; glutamine supplementation; treatments for anything that affects food intake and absorption, such as nausea or problems of the mouth; treatments for any infections; and in advanced cases, human growth hormone therapy.
Lipodystrophy syndrome

**Lipodystrophy syndrome** is the term used to describe a range of symptoms that include changes in body shape and metabolism. Lipodystrophy-associated body changes can involve fat loss and/or fat gain in specific parts of the body.

**Lipoatrophy** is the loss of fat in the face, arms, buttocks and legs. This fat loss can cause veins to protrude in the arms and legs and create sunken cheeks, along with loss of fat elsewhere in the face.

**Lipohypertrophy** is the accumulation of fat that results in enlarged breasts, an enlarged belly, as well as fat on the base of the neck and shoulders known as a “buffalo hump.” Some people also develop lipomas, which are round, moveable lumps of fat under the skin. These are sometimes called fatty tumours but they are not cancerous.

Some studies report that lipodystrophy may be different in men and women. Women may be more likely to see fat gain in their stomachs and breasts. Men may be more likely to see fat loss, particularly in their face, arms, buttocks and legs. However, many men and women have both fat loss and fat gain. Researchers are not sure why this difference exists. It may be related to hormones or to how fat is burned differently in the male and female body.

Although some people consider fat changes to be a “cosmetic” issue, they can cause considerable discomfort when:

- the buffalo hump leads to difficulty sleeping, headaches and neck pain and makes it harder to turn your neck or shoulders, which can affect side vision and makes driving difficult
- the abdominal fat causes breathing, digestive and back problems
- the facial fat loss and body changes cause emotional distress, isolation and non-adherence to medications.

Additionally, inside the body, other changes, such as problems managing blood sugar levels and increased cholesterol and other fatty substances in the blood, are taking place.

**Antiretroviral drugs**

Several classes of antiretroviral drugs have been associated with fat accumulation. Protease inhibitors (PIs) may alter the function of certain enzymes needed for maintaining healthy, functional fat cells and healthy levels of blood fats. The result is fat accumulation. The older PIs may be more likely to cause fat accumulation, whereas at least two of the newer PIs, atazanavir (Reyataz) and darunavir (Prezista), have not been associated with fat accumulation in studies to date.

Nucleoside analogues (nukes) can cause fat accumulation in some people, possibly because they contribute to insulin resistance, which is associated with an increase in gut fat. Non-nucleoside reverse transcriptase inhibitors (non-nukes) and integrase inhibitors have much less commonly been associated with fat accumulation.

**Fat loss** has most commonly been associated with two of the oldest nukes, d4T (Zerit) and AZT (Retrovir, and in Combivir and Trizivir). Researchers believe these drugs damage mitochondria, which are your cells’ energy factories. This damage can cause fat cells to lose their ability to function normally and can distort their shape. In some cases, the cells can die. If enough fat cells are affected by this mitochondrial damage, it can cause wasting of fat tissue in the face and other parts of the body.
Nukes that have *not* been linked to fat loss include:

- 3TC (lamivudine, and in Combivir, Trizivir and Kivexa)
- FTC (emtricitabine, in Truvada, Atripla, Complera and Stribild)
- tenofovir (Viread, and in Atripla, Truvada, Complera and Stribild)
- abacavir (Ziagen, and in Trizivir and Kivexa)

Whether ddI (Videx EC), which is rarely used in Canada today, causes fat loss is not clear.

Fat loss has also been associated with the non-nuke efavirenz (Sustiva, and in Atripla) though it is not known how efavirenz causes this fat loss.

**Reversing changes** in fat distribution associated with lipodystrophy is difficult. The best option is to choose drugs that have a lower chance of causing fat changes. Also, monitoring closely for changes — some people regularly take pictures of their face or body and then compare them for changes — means any issue that arises can be caught early before significant damage has occurred.

For people who have developed lipoatrophy, clinical trials have found that discontinuing the older nukes and substituting either tenofovir or abacavir can help. Fat loss will usually stop after the problematic drugs are stopped, and in some people fat loss may actually reverse somewhat. Restoration of fat is usually only partial and generally occurs very slowly, with visible changes taking six months to several years. People who have the best results with fat restoration after switching drugs have generally been those who had not been on the problematic drugs very long and had not experienced serious fat loss.

**Supplements**

Because of the link between lipoatrophy and mitochondrial damage, some people seek to prevent or reverse mitochondrial damage by taking a combination of:

- a potent multivitamin that includes the whole B complex of vitamins and a broad spectrum of antioxidants (vitamin C, carotenoids, selenium and others)
- acetyl-L-carnitine (500 mg, three times daily with meals).

A separate supplement of N-acetyl-cysteine (NAC; 600 mg, three times daily with meals) can be added to boost glutathione levels, since glutathione is an antioxidant that can be deficient in HIV disease. Talk to your doctor or pharmacist about any supplements you plan to take so they can help you make the right choice based on your other health conditions and treatments.

**Anabolic steroids, exercise and growth hormone stimulators**

The use of *anabolic steroids* combined with exercise can help boost “lean tissue,” including muscle size, but this combination does not significantly improve fat loss or accumulation. In studies of people using the steroids oxymetholone or nandrolone, muscle size increased but there were no reductions in accumulated fat, and there were worrisome decreases in HDL cholesterol (the healthy kind of cholesterol). In those using oxymetholone, there were also increases in liver enzymes, indicating possible toxicity to the liver. Neither oxymetholone nor nandrolone is available by prescription in Canada.

**Exercise** alone has generally been shown to have either a small benefit or no benefit in terms of losing the fat associated with lipodystrophy. But exercise does have many other benefits, including boosting cardiovascular fitness, mental well-being and self-esteem.

The synthetic growth hormone-releasing medication called **tesamorelin** (Egrifta) is available in Canada. It is approved for the treatment of HIV-associated fat accumulation. Clinical trials showed that Egrifta reduced visceral gut fat, but also that it would have to be used long-term; when the drug was stopped, gut fat returned. The drug is expensive and used only by people with private drug insurance coverage. The cost of this drug is not subsidized by provincial/territorial drug formularies.

**Surgeries, facial fillers and related therapies**
Liposuction can remove fat in some areas of the body. It has been used successfully with buffalo humps and lipomas. Standard surgery can be done for breast reduction, although the fat sometimes returns over time. Neither liposuction nor other surgical techniques can be used in the belly because of the high risk of bleeding.

To help fill out sunken cheeks and restore a fuller appearance to the face, a variety of facial fillers and other therapies have been used. Results have varied. In fact, some have serious drawbacks and possible complications, so it is important to choose carefully. These surgeries can be costly; talk to you doctor to find out if there is any coverage for these surgeries in your region.

Two non-permanent facial fillers available in Canada are poly-L-lactic acid (Sculptra) and calcium hydroxylapatite (Radiesse). Both require multiple injections into the areas of the face with fat loss. These fillers stimulate the production of collagen around the areas where it is injected. The collagen grows for several months after the injections, helping to fill the face out.

The change in facial appearance usually lasts for around one year to 18 months, after which another treatment is required to maintain the results. Although some people have thought of its lack of permanence as a disadvantage, it can actually be an advantage. If excess collagen develops in a given area, it will gradually fade over time. If your own fat cells begin to recover, you will not end up with too much bulk under the skin. It is important to choose a plastic surgeon or dermatologist very experienced in the use of these fillers.

There are two other non-permanent fillers sometimes used for facial wasting. Hyaluronic acid is a substance that is a normal component of connective tissue. Synthetic forms of hyaluronic acid (such as Juvederm or Restylane) are injected into the face. The length of time the results last varies. Collagen has long been used as a treatment for facial wrinkles.

Results vary widely among individuals using these fillers for facial wasting, and are not generally long-lasting. The skill of the doctor injecting these substances is important for the best results. There have been no studies of these products in HIV-associated facial wasting, but there are anecdotal reports of improvements lasting up to six months.

A number of permanent fillers are available to treat facial wasting, including polyalkylimide, polymethylmethacrylate, implants and silicone oil.

Polyalkylimide (Bio-Alcamid) is a synthetic product approved in Canada for the treatment of facial wasting. It requires multiple injections into the face. There have been reports of very serious problems with this product, including infections that develop in the area where the substance was injected, sometimes well after the initial procedure. This product has also been reported to migrate from the site where it was originally injected. Bio-Alcamid can also result in lumps and bumps in the face. Although removal is possible, it is painful and expensive and becomes increasingly difficult the longer the product has been in the face. Due to greater awareness of the many problems associated with Bio-Alcamid, many plastic surgery societies no longer recommend the use of this product.

Polymethylmethacrylate (PMMA; Artefill, Precise, Metacrill) is a synthetic compound used in cosmetic surgery as a permanent facial filler. All of these products contain small particles of PMMA. Multiple injections of PMMA into the skin are normally done but alternative techniques have been used in other countries.

Expanded polytetrafluoroethylene (ePTFE) implants (SoftForm, Gore-Tex) and hard silicone implants are solid implants used for large sunken areas in the face. These implants can be problematic in people with serious facial fat loss because the edges of the implants may be visible. Some doctors recommend these implants be used in combination with a product that boosts collagen production. The idea is that over time, with enough collagen production, the solid implant might be less visible. There is a risk of post-operative complications, including infection and scarring. The cost for implants can be very expensive.

Silicone oil has been used to treat HIV-associated lipoatrophy but the use of injected liquid silicone remains controversial. Case reports and one study have shown positive results for reversal of HIV-associated facial lipoatrophy, but there is concern about the potential for side effects, including long-term inflammation, migration of the product and inflammatory reactions called granulomas. Once injected, liquid silicone cannot be removed. The cost is variable, depending on the amount of silicone oil needed and the fee for injections, but can be very high. Silicone oil implants are not widely used in Canada and their long-term safety in HIV-positive people is not clear.
Finally, an **autologous fat transplant** involves taking fat from another part of the body and injecting it into the face. Since people with lipoatrophy may have lost a lot of subcutaneous fat, it can be difficult to find enough fat for use in the face. Nonetheless, this process can be effective in restoring facial appearance when done by a skilled plastic surgeon. Only one or two treatments are required initially, but later treatments are required to maintain the benefits. Results last for as short as three months in some people and as long as a year or more in others.
Disclaimer

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

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