HIV and Your Whole Health

Changes to Your Face and Body (Lipodystrophy and Weight Changes)

Although less common than it used to be, lipodystrophy, or abnormal fat distribution, remains a

concern for many people living with HIV. Lipodystrophy is an umbrella term that refers to two conditions:

- Lipoatrophy, or fat loss
- Lipohypertrophy, or fat accumulation.

In the early years of the AIDS epidemic, wasting syndrome, or unintended loss of both fat and muscle, was a prominent physical manifestation of HIV. After the first antiretroviral medications were developed, some people who used them developed facial lipoatrophy, characterized by sunken cheeks and deep smile lines. Today, this condition is seldom seen among people who start treatment with modern antiretrovirals, but it can be a telltale sign that someone is a long-term survivor.

Not long after the advent of protease inhibitors and modern combination antiretroviral therapy in the mid-1990s, people started seeing unexpected new health problems, including metabolic abnormalities and unusual fat gain. This fat accumulation was initially blamed on early protease inhibitors—it was once dubbed “Crix belly” after Crixivan (indinavir), one of the first drugs in this class—but it soon became clear that this was not the whole story.

More recently, there’s been a growing recognition that weight gain is common among people starting treatment with potent modern antiretrovirals. This phenomenon is still poorly understood, but this is an active area of HIV research.

Lipodystrophy and wasting syndrome can be physically disfiguring and emotionally devastating. Individuals who experience lipodystrophy, especially facial fat loss, may have a negative body image and may become depressed and socially isolated. Concern about lipodystrophy may lead some people to delay starting HIV treatment or to have poor adherence. However, it’s important for your health to stay on treatment and not stop or change medications without the advice of your doctor.

HIV-related fat loss or gain can be difficult to reverse, but lifestyle changes, reconstructive procedures and medications may help. Talk to your clinician if you are experiencing unexpected changes in weight or body fat distribution, and get regular lab tests to check for metabolic problems.

Click below for more information about the causes and management of these conditions:

- Lipohypertrophy (fat gain)
- Lipoatrophy (fat loss)
- Wasting syndrome
- Treatment-associated weight gain

What is lipohypertrophy?

Lipohypertrophy typically involves fat gain in the abdomen. Both women and men may also experience breast growth (known as gynecomastia when it occurs in men). Some people develop a fat pad on the upper back or back of the neck known as a “buffalo hump.” Lipomas, or round lumps of fat under the skin, are less common.

While lipohypertrophy and normal overweight or obesity can both lead to a large belly, the type of fat is different. People with normal obesity usually have soft, pinchable fat under the skin. HIV-related lipohypertrophy, in contrast, involves the buildup of fat deep within the abdomen surrounding the internal organs, known as excess visceral abdominal fat. This causes a firm or hard belly, and people with this type of fat generally have a larger waist circumference in relation to the size of their hips.

People with HIV-related lipohypertrophy often have other metabolic problems, including insulin resistance, high blood glucose, diabetes, abnormal levels of cholesterol and triglycerides in the blood (dyslipidemia), and high blood pressure (hypertension).

Excess visceral abdominal fat has been linked to health problems ranging from cardiovascular disease to dementia as well as to a higher risk of death. Visceral fat can sometimes accumulate inside the liver and other organs. Over time, fatty liver disease can lead to cirrhosis and liver cancer.

In some cases, fat buildup may be severe enough to cause discomfort, limit movement or interfere with sleep.

What causes lipohypertrophy?

Experts do not fully understand the causes of HIV-related fat gain, but several factors appear to contribute to the condition.

HIV and the drugs used to treat it can lead to body fat changes, which may be related to altered metabolism and hormone levels. Although lipohypertrophy was once blamed on protease inhibitors, it later became clear that it is not solely linked to the use of specific antiretroviral drugs or drug classes.

HIV can trigger chronic inflammation, and inflammatory cytokines (chemical messengers produced by immune cells) can affect metabolism in ways that promote fat gain. Hormones and cytokines produced by fat tissue can in turn cause further inflammation, which, in a vicious cycle, can lead to more fat buildup.

Older individuals are more likely to develop lipohypertrophy, as are those who start treatment with a lower CD4 count or higher viral load. Women are more likely than men to have fat buildup in the belly or breasts. Black women appear to be particularly susceptible to fat gain. Genetic factors and lifestyle factors, including diet and being overweight, appear to play a role. But many people with HIV who would seem to be at risk never develop lipohypertrophy.

How is lipohypertrophy managed?

The first step in managing HIV-related fat gain is to have a comprehensive conversation with your doctor. You should discuss your HIV treatment history, your personal and family medical history and any other conditions you may have that could lead to fat gain.

Your doctor may feel your belly to see whether it's hard or soft and measure your waist and hips to calculate your waist-to-hip ratio. Having a hard belly and a bigger waistline relative to the size of the hips can indicate excess visceral abdominal fat.

Your clinician may run laboratory tests to check for metabolic or hormonal abnormalities. These may include tests for blood sugar (glucose), insulin resistance, lipids such as cholesterol and triglycerides and certain hormones.

Lipohypertrophy can be difficult to manage. Switching to different antiretroviral medications generally does not help. Strategies for managing HIV-related fat gain include the following:

Diet and exercise. Eating a healthy diet and exercising regularly may reduce excess weight and improve metabolic problems associated with lipohypertrophy. Consider consulting a registered dietitian to devise a personalized nutritional strategy to help combat lipodystrophy and manage abnormal blood sugar and fat levels. But be aware that visceral fat buildup often does not respond to changes in diet and exercise alone.

Liposuction and surgery. This method, which uses a suction technique to remove fat tissue, may be an option for reducing excess breast fat or removing a buffalo hump. However, it is not a safe way to remove visceral fat deep within the abdomen. Breast reduction surgery is another option for those whose breasts have swelled enough to cause pain or limit movement.

Egrifta (tesamorelin). Egrifta is a growth hormone–releasing factor analogue, meaning it mimics a natural hormone produced in the brain that triggers the release of growth hormone. It was approved in 2010 to reduce excess visceral abdominal fat in HIV-positive adults with lipodystrophy; it is the only approved medication for this indication. Egrifta is self-administered as an injection under the skin of the belly, usually once daily. Clinical studies showed that it reduced visceral abdominal fat by up to 18%, on average. However, lost fat usually returns soon after stopping the treatment. A newer formulation of the drug, Egrifta SV, was approved in 2019.

Serostim (somatropin). This synthetic version of growth hormone was approved in 1996 to treat HIV-related wasting. It is not specifically approved for the treatment of lipohypertrophy, but some studies suggest it may help reduce visceral abdominal fat. It is also administered as a daily injection.

Medications for metabolic problems. Other medications may be used to manage the metabolic abnormalities that often accompany lipohypertrophy and to reduce the risk of cardiovascular disease and other health problems. Glucophage (metformin) may be prescribed to control blood sugar, while statins may be used to lower cholesterol levels. Some studies have shown that

Glucophage may help reduce visceral belly fat as well.

Equally important is how you feel about the changes in your body and how they are affecting your self-esteem, your relationships and your quality of life. Your doctor may refer you to some form of psychological counseling to help you deal with the condition on an emotional level.

What is lipoatrophy?

Lipoatrophy involves the loss of subcutaneous fat that lies under the skin. It usually affects the face, arms, legs and buttocks. Fat loss in the limbs may make veins look very prominent, while loss of fat in the buttocks can make sitting uncomfortable.

Facial fat loss can lead to hollow-looking cheeks, sunken temples and deep smile lines on the side of the mouth (nasolabio folds). In severe cases, this can give the face a skeletal look.

Dealing with facial lipoatrophy can be particularly difficult for HIV-positive individuals. Not only do many find the physical changes unattractive, but they may feel that HIV is, in effect, written on their faces. It can be a constant reminder of living with HIV, can worsen feelings of HIV stigma and can reveal to others that you have the virus, depriving you of control over when and to whom you disclose your status.

What causes lipoatrophy?
Today, facial lipoatrophy is most often seen among long-term survivors who used early antiretroviral medications. It is more common among men compared with women and among those who ever had a very low CD4 count.

Lipoatrophy is most strongly associated with having ever used first-generation nucleoside reverse transcriptase inhibitors, including AZT (zidovudine or Retrovir, also in the Combivir and Trizivir combination pills), ddI (didanosine or Videx) or d4T (stavudine or Zerit). These drugs are toxic to the mitochondria, the tiny energy-producing powerhouses in cells, and can damage fat cells known as adipocytes.

It is estimated that up to half of people who were treated with these antiretrovirals experienced some degree of lipoatrophy as a result. These drugs are no longer widely used and are not recommended in the United States, but the facial fat loss they caused may never be fully reversed.

How is lipoatrophy managed?

The first step in managing HIV-related fat loss is to have a conversation with your doctor. You should discuss your HIV treatment history, diet and any other conditions that could contribute to fat loss. The specific loss of subcutaneous fat can distinguish lipoatrophy from wasting syndrome, which involves an overall loss of both fat and muscle.

Lipoatrophy is difficult to manage. If you are still taking older antiretrovirals, you can switch to

newer medications with fewer side effects. (This is often a good idea anyway, because modern drugs are more convenient and may do a better job of controlling HIV.) But facial fat loss is generally considered irreversible even many years after stopping the offending drugs.

Adding fat or calories to the diet does not reverse lipoatrophy, and there are no medications to treat it. However, several options may help improve appearance in people with facial fat loss.

Facial fillers may be used to fill out sunken cheeks and smooth deep smile lines. In some cases, a fat graft can be transferred to the face from another part of the body.

Sculptra (poly-L-lactic acid) was approved to treat HIV-related facial lipoatrophy in 2004. It is typically applied in three or four sessions scheduled every month or so. The effects build up over a few months and last for about two to three years. Side effects may include pain during injection, bruising, swelling and hard nodules under the skin.

Radiesse (calcium hydroxylapatite) was approved for HIV-related facial lipoatrophy in 2006. Its effects are immediate and then fade over the course of about a year. Side effects are similar to those of Sculptra, but nodules are less common.

Bellafill (formerly ArteFill) is a combination of bovine collagen plus a permanent acrylic-based filler known as polymethyl methacrylate. It is injected in a series of sessions over perhaps a year. After each application, the collagen portion gradually dissipates while the permanent filler remains. Side effects may include pain, redness, swelling, itching and lumps at the injection site.

Hyaluronic acid fillers (brand names include Juvéderm, Perlane and Restylane) are approved as cosmetic facial fillers but not specifically for HIV-related lipoatrophy. Their effects are immediate, but they are the most temporary option, typically lasting around six to 12 months. Again, the side effects are similar.

When seeking out a clinician to perform such a procedure, ask about their training and experience with the technique, including how many similar patients they've treated. Costs vary a great deal, and fillers are often considered cosmetic and therefore not covered by most insurance. However, some people have been able to get these procedures covered by having their doctor classify them as reconstructive.

What is wasting syndrome?
Wasting syndrome was a major health problem among people with HIV during the first decade and a half of the AIDS epidemic, before the development of effective antiretroviral treatment.

Although much less common today, wasting syndrome is still seen in a small proportion of people living with the virus, and it may even occur in people with high CD4 counts and low viral load.

Wasting syndrome refers to unintended loss of more than 10% of total body weight that occurs with either diarrhea or chronic weakness and fever lasting at least 30 days that cannot be

explained by another non-HIV-related condition.

Unlike HIV-related lipoatrophy, which involves the loss of subcutaneous fat, wasting syndrome involves an overall loss of both fat and lean body mass, including muscle. As a result, people who experience wasting may experience fatigue and reduced physical endurance and have a poorer quality of life.

What causes wasting syndrome?

HIV-related wasting is a consequence of abnormal metabolism, in which the body's ability to process carbohydrates, proteins and fats and ultimately to produce energy and build tissue is altered. Scientists do not fully understand what causes wasting in people living with HIV. Possible contributing factors may include the following:

- Chronic inflammation, which can occur even while on effective antiretroviral treatment
- Damage to the gut lining, which occurs soon after HIV infection
- Low levels of hormones, such as testosterone, or resistance to growth hormone
- A rise in resting energy expenditure, or how many calories the body burns while at rest
- Opportunistic infections, cancers or other coexisting health conditions
- Reduced food intake as a result of appetite loss, nausea, fatigue, depression, social isolation or inability to afford adequate food
- Difficulty eating or swallowing, possibly due to oral or esophageal conditions, such as candidiasis or aphthous ulcers
- Persistent diarrhea—a common symptom of opportunistic infections and a side effect of certain HIV medications—which reduces absorption of nutrients.

How is wasting syndrome managed?

Severe wasting can be difficult to reverse, so it is best to address unintended and unwanted weight loss early. Talk to your doctor as soon as you start to experience unexplained weight loss.

There are various steps you can take to tackle the condition, including the following:

HIV treatment. Starting antiretroviral therapy and maintaining good adherence to treatment can mitigate weight loss caused by uncontrolled HIV, immune suppression and opportunistic illnesses. If one regimen causes side effects such as nausea or diarrhea, it may be possible to switch to better tolerated drugs.

Treatment for other health conditions. Various medications may be used to treat opportunistic

illnesses, gastrointestinal problems and other health conditions that can lead to reduced appetite, difficulty eating or poor absorption of nutrients. These include drugs to manage nausea and diarrhea.

Diet. A healthy diet is key for coping with wasting syndrome. Increasing the number of calories and the amount of fat in your diet can help, along with consuming plenty of protein to maintain muscle mass. Consider consulting a registered dietitian who has experience working with people with HIV-related wasting to devise nutritional strategies tailored to your needs.

Nutritional supplements. High-calorie liquid supplements, such as Ensure or Sustacal, can help you meet your dietary needs, especially if you're having trouble getting enough calories and nutrients from regular meals.

Exercise. A combination of regular cardiovascular exercise and strength training to build muscles is key. Experts recommend at least 30 minutes of moderate-intensity activity at least five times a week. However, if you exercise more without consuming enough calories and the proper nutrients, you could lose even more weight.

Testosterone therapy. Among men with low testosterone levels, testosterone replacement therapy can lead to substantial weight gain, including an increase in lean body mass gain. Testosterone may be administered via injection or patches, creams or gels applied to the skin. Side effects may include acne, changes in cholesterol levels and increased risk of cardiovascular disease.

Serostim (somatropin). This synthetic version of growth hormone was approved in 1996 to treat HIV-related wasting. It is self-administered as a daily injection. Studies have shown that Serostim leads to weight gain, increasing muscle mass even as it reduces fat. Side effects may include muscle or bone pain and swelling.

Marijuana. Medical cannabis is now legal in many states. Marijuana many be smoked or vaped, and its active compounds, including tetrahydrocannabinol (THC) and cannabidiol (CBD), may be consumed as oral extracts or in edibles, such as candies or baked goods. Marijuana has been shown to stimulate the appetite, but it may lead primarily to fat rather than muscle gain. Side effects may include mood changes, feeling high, dizziness, impaired concentration and memory, anxiety and drowsiness.

Marinol (dronabinol). This synthetic form of an active ingredient in marijuana is approved to treat HIV-associated anorexia (loss of appetite). Studies have shown that the drug increases appetite, although it is not consistently associated with weight gain. Side effects are similar to those of marijuana.

Megace (megestrol acetate). A synthetic form of the hormone progesterone, Megace is also approved to treat HIV-associated anorexia. It is administered as a daily oral solution. Studies have shown that it may lead to more fat gain than lean muscle mass. Side effects may include gastrointestinal symptoms, skin rash, insomnia, vaginal bleeding, decreased interest in sex and

erectile dysfunction.

Finally, depression and social isolation can diminish your desire to eat. A counselor or therapist may be able to help you manage depression, anxiety and other mental health concerns, which may increase your enjoyment of food and improve your overall quality of life.

What is treatment-associated weight gain?

In recent years, there has been a growing recognition that people starting modern antiretroviral treatment are prone to weight gain, sometimes as much as several pounds. Black women living with HIV appear to be particularly susceptible.

People with advanced immune suppression and opportunistic illnesses often gain weight as they return to health after starting antiretroviral therapy, but treatment-associated weight gain goes beyond this and can occur in people who have maintained a high CD4 count and were never severely ill.

Although weight gain can occur after starting any class of antiretroviral drug, it is commonly seen among those starting potent integrase inhibitors. Tenofovir alafenamide (TAF), the newer version of the drug in Descovy and other combination pills, appears more likely to lead to weight gain than the older tenofovir disoproxil fumarate (TDF) in Truvada and other coformulations.

Treatment-associated weight gain is still poorly understood—experts do not yet know what causes it or how best to manage it—but this is among the most active areas of HIV research.

Click here to learn more about weight gain among people living with HIV.

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