Side Effects

Changes to Your Face and Body (Lipodystrophy & Wasting)

Changes in body fat became a signature struggle among the HIV population during the early years of the modern era of antiretroviral (ARV) treatment, which began in 1996 with the introduction of the first of the triple combination drug cocktails. Lipodystrophy, which refers to an abnormal distribution of fat in the body, soon replaced wasting and Kaposi sarcoma (KS) lesions as the most prominent physical manifestation of HIV. It was a cruel irony that some of the very drugs that helped return so many HIV-positive people to robust health during that time wound up making many look sick, at least in the eyes of the uninformed.

Lipodystrophy and wasting syndrome can be disfiguring and emotionally devastating conditions, fortunately both are less common in people living with HIV today thanks to advances in ARV treatment. Click below for more on the causes of and treatments available for these conditions:

- Lipodystrophy
- Facial lipoatrophy
- Wasting syndrome

What is lipodystrophy?
Lipodystrophy is an umbrella term that refers to both:

Lipohypertrophy: abnormal accumulation of fat in certain parts of the body
Lipoatrophy: abnormal loss of fat in certain parts of the body

As new and improved ARVs have come out, replacing the drugs infamous for causing lipodystrophy, the side effect has become much less common. But because these changes in fat distribution are more or less permanent, they typically persist in those who have already developed them. Also, because HIV itself can apparently cause these changes, even people who have never taken those older ARVs may still develop fat abnormalities. The good news is that many HIV-positive people these days never experience lipodystrophy.

The most common forms of lipohypertrophy are:
Accumulation of fat around the organs, known as visceral fat or visceral adipose tissue, which causes a firm, enlarged abdomen. An excess of this kind of fat can raise the risk of a heart attack and diabetes.

• Breast enlargement (gynecomastia), which can occur in both men and women
• A fat pad on the upper back and neck area (known as the “buffalo hump”)
• Enlargement of the neck
• Round lumps of fat under the skin (lipomas).

Severe, abnormal accumulation of fat can cause physical discomfort, such as back pain from the burden of excess breast fat, and can sometimes impair breathing, range of motion or other bodily functions.

Most commonly, lipoatrophy occurs in the:

• Face, particularly the cheeks, “smile lines” (nasolabio folds), temples and eye sockets
• Arms
• Legs
• Buttocks, which can make sitting uncomfortable and make finding pants that fit a challenge, especially if this effect is coupled with an increase in belly fat
• Soles of the feet (less common)

Such loss of fat can make veins look very prominent, especially in the limbs.

Women are more likely to experience fat build-up in their breasts and bellies. Men are more likely to lose fat in the legs, arms, buttocks and face.

HIV-positive individuals who experience lipodystrophy, especially facial lipoatrophy, tend to have trouble with their body image and are more likely to become depressed and socially isolated, and to suffer from low self-esteem. Such psychological effects may also lead individuals to become less adherent to their medications. It’s very important for your health that you keep taking your HIV treatment and, if you and your health care provider decide you should switch meds, only to do so under the supervision of your physician.

Lipodystrophy is also associated with what are called metabolic abnormalities, including:
An abnormal amount of fats in the blood (dyslipidemia), including triglycerides and cholesterol. High cholesterol can raise the risk of heart attack or stroke. Increased triglycerides can raise the risk of damage to the pancreas.

- Insulin resistance and a high level of sugars in the blood (hyperglycemia), which can lead to diabetes.
- Increased lactic acid in the blood. This can lead to a rare, dangerous condition known as lactic acidosis. Symptoms include fatigue, loss of appetite, nausea and vomiting, stomach pain, and weight loss. Signs of life-threatening lactic acidosis can include elevated heart rate, rapid breathing, jaundice (yellow skin and the whites of the eyes), and muscle weakness. Contact a medical professional immediately if you suspect you may be experiencing this condition.

As for weight loss or wasting syndrome, modern ARV treatment has greatly reduced the risk of these conditions. However, a small proportion of people with HIV still do experience them.

It’s very important that you mention to your clinician if you are experiencing any unexpected changes in the distribution of your body fat or in your weight. During your medical checkups, you should also get regular lab tests to check for all the metabolic changes mentioned above.

What causes lipodystrophy?
The causes of lipodystrophy are not very well understood, unfortunately. Research suggests that there are many contributing factors, including:

- The see-saw effect as HIV depletes the immune system and antiretroviral (ARV) treatment leads to its resurgence
- ARVs themselves
- Abnormal shifts in the body’s metabolism of fatty acids
- Hormonal changes
- Genetics
- Diet and obesity.
- Damage, caused both by HIV and some ARVs, to the mitochondria of cells. A component of all cells, mitochondria are responsible for regulating energy.

HIV-positive people most at risk for lipodystrophy include:
• Whites
• Older people
• People who have been living with HIV for longer
• Those who start HIV treatment with lower CD4 cell counts
• Those who start HIV treatment with higher viral loads
• Individuals who take the following older ARVs, which are specifically known to cause lipoatrophy, or fat loss (and which are rarely used today):
  ◦ Retrovir (AZT, or zidovudine)
  ◦ Retrovir is a component of Combivir (zidovudine/lamivudine) and Trizivir (abacavir/zidovudine/lamivudine)
  ◦ Zerit (d4T, or stavudine)
  ◦ Videx (ddl, or didanosine)
• Obese individuals, and those who experience significant shifts in weight

According to the European Medicines Agency (EMA), there is no clear evidence that any medications to treat HIV cause fat accumulation, or lipohypertrophy. HIV-positive people who have never taken ARVs do sometimes experience abnormal changes in fat distribution. The EMA has narrowed its general warning of ARVs causing lactic acidosis to include only Retrovir, Zerit and Videx.

What is the treatment for lipodystrophy?
When it comes to tackling both the physical and metabolic changes (such as high fats or sugars in the blood) associated with lipodystrophy, you should first have a comprehensive discussion with your doctor. You should discuss your HIV medication history, as well as your personal and family medical history, particularly any incidence of high lipid counts, diabetes or insulin resistance, and heart disease.

Equally important is how you feel about the changes in your body—how they are affecting your self-esteem, your relationships, and your ability to do your work and the things you enjoy. Part of the treatment may be a referral to some form of psychological counseling to help you deal with living with the condition on an emotional level.

Since it’s pretty rare these days for people to take any of the older ARVs that are implicated in causing lipoatrophy, switching HIV medications is unlikely to affect that condition. Even when people were taking those ARVs, going off of them only meant the potential for modest and slow return of limb fat.
The changes in fat distribution resulting from both lipoatrophy and lipodystrophy are generally permanent.

However, there are options for reconstruction through plastic surgery, and some other treatment options for fat gain in particular. There are also lifestyle changes you can make to improve your appearance and your overall health.

Eating a healthy diet and exercising regularly may help you build up lean muscle mass and reduce unwanted fat build-up. Strength training, such as through weight-lifting, can also help improve your overall ratio of muscle to fat. Engaging in regular cardiovascular exercise may help reduce the accumulation of belly fat, and can likely do so without affecting lipoatrophy (fat loss). Regular exercise can also help regulate cholesterol, triglycerides and sugar in the blood. It’s best to avoid rapid weight loss, because you’ll risk losing vital lean body mass.

Consider consulting with a registered dietician to devise the best nutritional strategy to help you combat changes associated with lipodystrophy, as well as any unwanted shifts in the fats and sugars circulating in your body. It’s a good idea to eat less saturated fat (not all fat, just saturated fat—an important distinction), limit your sugar intake, and cut back on alcohol. Eating less saturated fat may help lower your cholesterol too.

Other Treatments For Fat Gain:

- **Egrifta** (tesamorelin) is a synthetic growth hormone-releasing factor analogue. In 2010, the U.S. Food and Drug Administration (FDA) approved the drug to treat excess abdominal fat in people with HIV experiencing lipodystrophy. On average, the daily injectable drug reduces belly fat by about 18 percent over a one-year period. Some who take the drug have a better response than others. Once individuals stop taking the drug, any lost belly fat will rapidly return. Side effects include joint pain, redness and rash at the injection site, stomach pain, swelling and muscle pain. Additionally, Egrifta may cause blood sugar to rise.

- **Serostim** (somatropin) is a daily injectable human growth hormone. It was approved by the FDA in 1996 to treat HIV-related wasting, and may reduce visceral fat around the organs (belly fat), although it is not FDA approved for the latter purpose. The most common side effects include muscle or bone pain and swelling in the hands and feet. Some people taking Serostim develop carpal tunnel syndrome, a painful condition in the hands and fingers.

- **Liposuction** is an option for the fat pad on the upper back/neck (buffalo hump), although the fat often returns. Liposuction is not a possibility for reducing belly fat, because that fat is around
the organs, as opposed to directly under the skin (subcutaneous). It is too dangerous to try to suck out fat from so deep in the abdomen.

- Breast reduction surgery can reduce fat accumulation in the breast, both for men and women. However, the fat often returns.
- Treat increased lipids by switching HIV meds. Some ARVs are believed to have less of an effect on cholesterol and triglycerides than others. Statins are common drugs are used to control cholesterol levels. They also lower triglycerides.
- Treat high blood sugar, insulin resistance and diabetes with medications that can treat these health conditions. Or consider switching HIV meds. A change in your ARV regimen may improve your glucose levels.
- Myalept (metreleptin) is an injectable, synthetic version of the hormone leptin that was approved to treat the complications of a deficiency of the hormone among people with lipodystrophy. In a clinical trial, those taking the drug showed improved measures in their blood sugar and triglycerides. Side effects include headache, low blood sugar, weight loss and belly pain. The drug can also increase the risk of lymphoma.
- Metformin has shown moderate success treating belly fat accumulation among HIV-positive people with insulin resistance. However, it may cause lipoatrophy symptoms to progress. Those with chronic liver or kidney disease need to use caution when taking the drug.
- Psychological counseling may help you cope with how the physical changes of lipodystrophy are affecting your everyday life, your emotions, your relationships, and so on.

What is facial lipoatrophy?
Facial lipoatrophy, also known as facial wasting, occurs when individuals lose volume in the fat that normally pads the face. Typically, fat is lost from the cheeks, the smile lines (nasolabial folds), and the temples. Lipoatrophy can also affect the eye sockets. This can give the face a skeletal, sunken, or hollow look, often with deep smile-line furrows.

Dealing with facial lipoatrophy can be particularly difficult for HIV-positive individuals. The condition can lead to depression, anxiety and social isolation, as well as to poor adherence to HIV treatment. Not only do many find the physical changes unattractive, but they feel that HIV is, in effect, written on their faces. This can ultimately accentuate the effects of HIV stigma. Other people who recognize the condition on the face of someone experiencing lipoatrophy may know
that it is a sign of HIV, while others may think that it indicates some sort of illness.

What causes facial lipoatrophy?
The causes of lipodystrophy, including lipoatrophy (abnormal fat loss) and lipo hypertrophy (abnormal fat gain) are not very well understood. However, what is known is that three older antiretrovirals (rarely used today) are associated with fat loss in the face, including:

- Retrovir (AZT, or zidovudine)
- Retrovir is a component of Combivir (zidovudine/lamivudine) and Trizivir
  (abacavir/zidovudine/lamivudine).
- Zerit (d4T, or stavudine)
- Videx (ddI, or didanosine)

An estimated 40 to 50 percent of people who were treated with these antiretrovirals experienced some form of lipodystrophy as a result. Since these drugs have been replaced by newer, less toxic medications, new cases of facial lipoatrophy have become far less common among people living with HIV.

What is the treatment for facial lipoatrophy?

Facial reconstruction
An array of fillers are used to restore volume lost to HIV-related facial lipoatrophy. 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. Also ask if the clinician uses a needle or what is called a cannula to perform the injections, as the latter implement is safer. Costs may vary a great deal, depending on the practitioner and the place where you live.

Sculptra (poly-L-lactic acid)

- Approved by the U.S. Food and Drug Administration (FDA) to treat HIV-related facial lipoatrophy in 2004.
- Cost: about $700 to $800 per vial. Mild facial lipoatrophy requires about four cumulative vials, moderate about eight to 10 vials, and severe perhaps 12 or more.
- For information about the Sculptra patient access program, call 866-310-7551.
- Typically applied in stages: three to four sessions, scheduled every month or so.
- Effects build up over a few months, last for about two to three years.
- Perhaps one in five people who receive Sculptra will develop nodules, which are bumps under
the skin that typically fade over the course of months. Other side effects include pain during injection, bruising, swelling and tenderness.

Radiesse: (calcium hydroxylapatite)

- FDA approved in 2006 to treat HIV-related facial lipoatrophy.
- Cost: about $600 to $700 per syringe. Mild facial lipoatrophy requires about four syringes, moderate about six to eight syringes, and severe 10 or more.
- Effects are immediate, and then fade over the course of about a year.
- For information about the Radiesse patient access program, call 866-862-1211.
- May be used with Sculptra, so the Radiesse provides an immediate effect that fades as the Sculptra builds up over time.
- Side effects include pain during injection, bruising, swelling, tenderness and bumps under the skin that disappear in time (the risk of bumps is apparently much lower than with Sculptra).

Restylane, Perlane, Hylaform, Juvéderm, Juvéderm Voluma (hyaluronic acid)

- These are gel fillers.
- Cost: about $800 vial, with mild lipoatrophy requiring two vials and higher levels of fat loss requiring four or more.
- Effects are immediate and last about six to 12 months.
- Voluma is more expensive, at about $1,000 a vial, but tends to last longer.
- Side effects include bruising, redness, swelling, pain, tenderness and itching.

Bellafill (formerly ArteFill)

- Semi-permanent
- A combination of bovine collagen and a permanent acrylic-based filler known as polymethyl methacrylate, or PMMA.
- Injected in a series of treatments over perhaps a year. Following each treatment, the collagen portion will gradually dissipate, while the base of permanent filler will remain.
- Cost: about $800 to $1,000 per syringe. Moderate to severe facial lipoatrophy may require 35 or
more syringes total. The upside of the high cost is the lasting effect of the treatment.

- Side effects include lumps at the injection site, redness, swelling, pain, tenderness and itching.

Fat transfer

- Transferring your own subcutaneous fat from one part of your body to another through a surgical procedure.

- A higher upfront cost than with temporary synthetic injectable fillers. But it may cost less money in the long run because of its relative permanence; a single treatment may do the trick.

- It can be hard to find fat to harvest in those who have experienced a great deal of lipoatrophy.

- Compared with Sculptra treatments in particular, fat transfers have a much lower rate of adverse reactions, outside of possible dissatisfaction with the results on account of overcorrection or asymmetry.

Collagen

- Collagen fillers are a thing of the past, except as a component of Bellafill.

- Liquid Silicone

- Health care providers have largely turned away from liquid silicone, a permanent filler. It can drift, leading to jowls, and cause hard bumps known as granulomas. It cannot be removed.

What is wasting syndrome?

HIV-related wasting is a consequence of an abnormal metabolism, in which the body’s ability to process carbohydrates, proteins and fats and ultimately to produce energy and build tissue has been altered. This can lead to:

- Unintended weight loss of more than 10 percent of total body weight that occurs with diarrhea or chronic weakness and fever for at least 30 days and that is not as a result of a non-HIV condition. This weight can be hard to gain back.

- Lowered physical endurance

- Loss of lean body mass, including muscle

- People experiencing such weight loss may have little or no appetite.
Wasting syndrome was a major health problem among people with HIV during the first 15 years of the AIDS epidemic, when there were no adequate treatments for the virus. Even though wasting syndrome is now much less common thanks to modern antiretroviral (ARV) treatment for HIV, it still occurs in a small proportion of people living with the virus. Even those with higher CD4 counts and lower viral loads may experience HIV-associated wasting. Significant weight loss can be a major detriment to an individual’s quality of life.

What causes wasting syndrome?
Scientists don’t have the firmest grasp on what causes wasting. It appears to have many overlapping causes. Possible contributing factors include:

- Proinflammatory cytokines—this is a natural immune response that HIV prompts, even when it is fully suppressed by ARVs
- Low hormone levels, such as testosterone levels
- The body’s resistance to growth hormone
- A rise in how many calories the body burns at rest, known as resting energy expenditure (REE)
- Infections
- Recreational drug use
- Depression and isolation
- Loss of appetite
- Reduced food intake as a result of nausea (a common side effect of HIV medications), depression, fatigue, altered taste perception, social isolation or inability to purchase adequate food
- Difficulty swallowing, possibly because of symptoms from oral and esophageal conditions such as candidiasis and aphthous ulcers
- Diarrhea, which is a common side effect of HIV medications. Also, HIV causes immediate and largely permanent damage to the gut shortly after infection, raising the overall risk of diarrhea among those living with the virus.

What is the treatment for wasting syndrome?
There are various steps you can take, in terms of lifestyle changes, treating HIV, and taking medications, to tackle the condition.

Diet
Eating the right kind of foods is key for coping with wasting syndrome. You may want to increase the number of calories and amount of fat you consume, while also consuming plenty of protein to help prevent the loss of muscle mass. Strongly consider consulting with a registered dietician, one who has experience working with individuals with HIV-related wasting, so they can help devise nutritional strategies for you. However, just upping your calories without tackling other potential causes of weight loss may not be enough to turn the tide and help you gain weight.

Antiretroviral treatment
Antiretroviral treatment prevents the onset of AIDS, which is a major risk factor for wasting syndrome. A major study recently confirmed that it is better for the overall health of people with HIV to begin treatment soon after diagnosis, rather than waiting for the CD4 cell count to drop.

Exercise
Undergoing a strength-building routine by lifting weights can help you build muscle mass, provided you also eat enough. Note that if you engage in aerobic exercise without eating enough of the proper nutrients, you could lose even more weight.

Treat low testosterone
Among men with low testosterone, testosterone replacement therapy, injectable or administered through the skin through a patch, cream or gel, can lead to significant weight gain, including lean body mass gain. Such treatment may increase the risk of heart disease.

Nutritional Supplements
High-calorie liquid supplements include Ensure, Sustacal, Jevity, and Replete. To meet individual dietary needs, some are free of wheat, dairy (lactose), or other components that can be difficult to digest.

Serostim (somatropin)
The human growth hormone Serostim is approved by the Food and Drug Administration for the treatment of HIV-related weight loss. Serostim has been shown to increase muscle and help the body convert fat into energy. The drug is usually taken once a day using a hypodermic needle or a needle-free pump-like gadget that pushes the drug directly through the skin. It has been shown to lead to weight increase, including lean body mass, while reducing fat mass. The most common side effects include muscle or bone pain and swelling in the hands and feet. Some people taking Serostim develop carpal tunnel syndrome, a painful condition in the forearms or wrists. The drug is highly expensive and insurance coverage can be hard to secure.

Appetite Stimulants:

Megace (megestrol acetate)

- Approved by U.S. Food and Drug Administration (FDA) to treat HIV-associated anorexia (loss of appetite)
• An appetite stimulant that is a synthetic form of the hormone progesterone
• Mostly leads to weight gain in the form of fat
• Side effects include upset stomach, gas, vaginal bleeding, mild skin rash, weakness, insomnia, decreased interest in sex, erectile dysfunction, difficulty having an orgasm.

Marionol (dronabinol)
• FDA-approved to treat HIV-associated anorexia
• A synthetic form of an active ingredient in marijuana
• Studies have shown the drug increases appetite, although the drug is not consistently associated with weight gain.
• Side effects include mood changes, dizziness, difficulty concentrating, feeling high, weakness or lack of coordination, anxiety, confusion, stomach pain, nausea, vomiting diarrhea, warmth or tingly feeling, insomnia.

Marijuana
• Medicinal pot is now legal in some states.
• Research suggests smoking pot stimulates the appetite and can lead primarily to fat gain.
• Side effects include increased heart rate, bloodshot eyes, dizziness, impaired concentration and memory, slower reaction time, addiction, increased risk of heart attack or stroke, and breathing problems.

Treat gastrointestinal disorders
Finding ways to combat diarrhea, such as through the use of antidiarrheals, can improve the absorption of food and combat wasting. Other gastrointestinal disorders may also contribute to wasting. For example, infections in the gut can have a serious effect on the way nutrients in food are absorbed into the blood. A clinician may want to take a stool sample to test for such infections and then devise a treatment to counteract them. Drugs to control nausea and vomiting (antiemetics), possible side effects of ARVs, can also improve food intake.

Switch HIV medications
If certain antiretrovirals could be causing side effects, such as nausea or diarrhea, that may be interfering with food intake or absorption, switching to a different HIV treatment regimen may help you put on weight.
Psychotherapy
Depression and social isolation can diminish your appetite. Seeing a counselor or taking antidepressant medications may help improve your overall mood and sociability, and along with them, your interest in food.

Recombinant human growth hormone
Recombinant human growth hormone has been shown to lead to significant weight gain, including lean body mass, among people with HIV-associated wasting. Side effects include joint and muscle pain, puffiness and diarrhea. Adjusting the dose can help with side effects.

Treat opportunistic infections (OIs) and conditions that affect swallowing
Opportunistic infections, common among those with compromised immune systems, can interfere with swallowing and reduce overall food intake. Such infections include candidal, herpes or cytomegalovirus (CMV) esophagitis (inflammation of the esophagus). Aphthous ulcers can also interfere with swallowing. Additionally, treatments for conditions such as Mycobacterium avium complex (MAC), tuberculosis (TB), and Kaposi sarcoma (KS) are often associated with increased weight.

Thalidomide
Research has shown that the drug thalidomide leads to increases of about 4 percent in body weight among people experiencing HIV-associated weight loss. Studies have also shown it can reverse oral aphthous ulcers, which can make swallowing difficult and reduce food intake, as well as reduce the number of bowel movements per day among those experiencing chronic diarrhea. In both cases, this shift can lead to weight gain. Side effects include sleepiness/drowsiness, peripheral neuropathy, hypersensitivity (the immune system reacts in exaggerated way, such as with allergies or autoimmune disorders) and neutropenia (low levels of a particular kind of white blood cell that fights infections, particular bacterial and fungal infections). Thalidomide was once widely used as a sedative as well as a treatment for morning sickness, and led to terrible birth defects in the late 1950s and early 1960s. Consequently, it can be difficult to access, and those who do use it must take considerable precautions not to become pregnant.

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