Standing Tall

Understanding lipodystrophy among people living with HIV, including visceral fat and hard belly.

June 22, 2020 By Liz Highleyman

Lillibeth Gonzalez, 65, celebrated her 28th “HIVersary” in early June by dancing in her New York City apartment and chatting with her son and her friends via Zoom. Having survived addiction, domestic violence and the AIDS-related deaths of three siblings, she is doing well today, but living with HIV for 28 years has taken its toll.

“There are days I wake up feeling well, and there are days I wake up feeling like I’m 90 years old,” she says. “The good part is that from zero [CD4] T cells, I was able to come up to 1,030, due to the medications. I’m healthy enough to work and exercise. When I feel good, I do as much as I can.”

People living with HIV—nearly half are now 50 or older—are prone to a variety of health conditions as they age. Research has shown that HIV-positive people may experience problems such as cardiovascular disease and non-AIDS-related cancers as much as a decade earlier than their HIV-negative peers.

One of these problems is lipodystrophy, or abnormal body fat distribution. Although not limited to older people, the chances of developing lipo increase with age. These days, lipodystrophy is most often seen among long-term survivors who took older antiretroviral drugs with more side effects—and Gonzalez has taken plenty of them over the years.

Lipodystrophy is often accompanied by metabolic complications, such as diabetes, high cholesterol and hypertension, which raise the risk of cardiovascular disease and other health problems. What’s more, it can lead to emotional distress, reduced adherence to HIV treatment and poorer quality of life.

Gonzalez, who has worked as a community health educator at GMHC for 14 years, after starting out there as a client, struggles with a big belly due to lipo as well as persistent gastrointestinal problems, arthritis and brain fog. But she doesn’t let that get her down.

“I look at myself in the mirror, and I say, ‘Oh my God! I’m getting old!’ I feel like I look like the man in Despicable Me, with the big stomach and the skinny legs. I’ve come to just laugh about everything because I do not want to stress out. I’m happy to be 65 and alive. Aging is just something you have to deal with as it comes. My body reminds me every day that I’m getting old, but my mind is keeping me young.”

What Is Lipo?

Lipodystrophy is an umbrella term that covers both fat loss (known as lipoatrophy), especially in the face, limbs and buttocks, and fat accumulation (known as lipohypertrophy), especially in the belly and breasts. Lipodystrophy was once thought of as body fat redistribution, but it is now understood that these conditions are independent—rather than reflecting a shift of fat from one area to another—and have different causes.

“While an individual may experience both, they are almost certainly separate processes,” says Marshall Glesby, MD, PhD, a professor of medicine and health care policy and research at Weill Cornell Medical College in New York City.

A gaunt face with sunken cheeks was once a common sign of AIDS, attributable both to overall wasting and the side effects of certain early medications. Although these drugs are no longer widely used and are not recommended in the United States, the facial fat loss they caused may never be fully reversed.

The advent of protease inhibitors and modern combination antiretroviral therapy in the mid-1990s finally enabled people to maintain control of their HIV. But soon after the new drugs arrived, many people who took them started seeing unexpected new health problems, including unusual body shape changes.

People with HIV may experience weight loss as their immune function declines, followed by weight gain as they return to health after starting treatment. But HIV-related lipohypertrophy goes beyond that.

Some people with HIV experience a buildup of fat around the midsection that may have little connection with how much they eat or exercise. Both women and men may experience breast growth (known as gynecomastia when it occurs in men), or they may develop a fat pad on the upper back known as a “buffalo hump.” A combination of fat loss and gain can give the appearance of a potato on toothpicks.

Fortunately, lipodystrophy is not as common as it used to be. In particular, facial fat loss is seldom seen among people who promptly start treatment with modern antiretrovirals, before they develop serious immune deficiency.

“Lipoatrophy is generally something that we see in people who were treated with older drugs like stavudine and zidovudine. It is rarely seen in people who have never been on these older drugs but is also not a problem that typically goes away,” says Glesby. “Lipohypertrophy, in contrast, is something that still occurs and in many cases may be similar to the abdominal obesity and metabolic syndrome that is relatively common in the general population.”

In recent years, there’s been a growing recognition that weight gain—often as much as several pounds—is common among people starting treatment with modern meds. Black women living with HIV appear to be particularly susceptible. Although this can occur after starting any type of

antiretroviral drug, integrase inhibitors and the newer form of tenofovir (tenofovir alafenamide, a component of Descovy and other combination pills) are frequently implicated.

But general weight gain and normal obesity are not the same as lipohypertrophy.

Fat buildup can occur in two different patterns, one of which is linked to more health risks than the other. Subcutaneous fat builds up beneath the skin, often around the abdomen, hips, buttocks and thighs. It is soft and squishy, hence the nickname “love handles.” People with mostly subcutaneous fat often have a pear-shaped body.

Visceral fat builds up inside the abdomen and surrounds the internal organs. This extra fat pushes up against the muscles of the abdominal wall, resulting in a taut, hard belly. People with mostly visceral fat typically have an apple-shaped body and a larger waistline in relation to the size of their hips. This type of fat can be harder to reduce with diet and exercise.

While obesity and lipo both lead to large abdomens, people with normal obesity usually have pinchable fat under the skin and rolls of soft fat on their belly. HIV-associated lipohypertrophy, in contrast, is distinguished by the kind of fat that causes a hard belly.

In some cases, fat buildup can be severe enough to cause pain, limit movement or interfere with sleep. A protruding hard belly is especially worrisome because of its link to other health problems, including heart disease. And along with its physical effects, lipodystrophy can also lead to emotional distress and loss of self-esteem. (Click here to read “The Stigma of Lipo.")

“This has changed my life in a terrible way,” Gonzalez says. “I used to model, so I was always a size 4 in clothing. But I saw my stomach growing and growing. The clothes that I liked didn’t fit me. I didn’t know how to shop for a size 10, 12 or even a 14. I got up to a size 14, but only because of my stomach. It’s the only thing that’s huge. My legs, hands and arms are slim.”

What Causes Lipo?

Four decades into the HIV/AIDS epidemic, experts still do not fully understand the causes of lipodystrophy or the best ways to manage it.

Older individuals are more likely to develop lipo. Men are more likely to experience fat loss, while women more commonly have fat buildup in the belly or breasts. People who have lived with HIV or used antiretrovirals longer, those who have a high viral load before starting treatment and those with low CD4 counts—especially if they ever had advanced immune suppression with very low CD4s—are also at greater risk.

In the case of lipoatrophy, the biggest culprits are first-generation nucleoside reverse transcriptase inhibitors, especially AZT (Retrovir or zidovudine) and d4T (Zerit or stavudine). These drugs are toxic to the mitochondria, the tiny energy-producing powerhouses in cells, and can damage fat cells known as adipocytes.

Fat buildup was initially blamed on early protease inhibitors—it was once dubbed “Crix belly” after

Crixivan (indinavir), one of the first drugs in this class—which can cause metabolic abnormalities that contribute to fat gain. But it soon became clear that this was not the whole story.

“We do not fully understand the causes of lipohypertrophy,” Glesby says. “Unlike lipoatrophy, there are not clear associations with use of specific antiretroviral drugs or classes of drugs. There are multiple hypotheses about the causes.”

HIV infection itself can lead to body fat changes. The virus can trigger chronic inflammation, raising the risk of health conditions including heart, liver and kidney disease. Inflammatory cytokines, or chemical messengers produced by immune cells, can alter metabolism in ways that promote fat buildup.

Fat doesn’t just take up space in the body. Rather, it is active tissue that produces cytokines and hormones of its own. Hormones made by fat tissue include estrogen, adiponectin (which regulates glucose and fat metabolism) and leptin (which controls appetite). Some of the cytokines released by fat cells can cause further inflammation, which, in a vicious cycle, can lead to more fat buildup.

HIV-related lipo often goes hand in hand with other metabolic abnormalities, such as insulin resistance, diabetes, high cholesterol and hypertension, collectively known as metabolic syndrome. It 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.

HIV can also affect hormones. For example, it has been linked to lower production of growth hormone by the pituitary gland in the brain or reduced responsiveness to it. This hormone helps build muscle and break down fat, and low levels can lead to excess belly fat.

Some experts think the seesaw effect of immune system damage caused by HIV, followed by immune reconstitution after starting treatment, also contributes to lipodystrophy—which helps explain why it occurs more often in those who have had low CD4 counts. Alterations in the gut microbiome related to HIV or antiretroviral drugs may also play a role, according to Glesby.

In addition, genetic traits, lifestyle factors such as diet and exercise and being overweight or having normal obesity can affect the likelihood of developing lipodystrophy. But for reasons that remain unclear, many people with HIV who appear to be at risk never develop lipo.

Managing Lipo

Suppressing HIV viral load, getting CD4 counts back into normal territory and adopting a healthy lifestyle are great for overall health, but they may not fully reverse body fat changes due to lipo. Lost facial fat, in particular, can be very difficult to restore, leaving a lasting legacy for long-term survivors.

People starting antiretrovirals for the first time or switching regimens should have their body weight and fat distribution monitored regularly, as it’s easier to address lipo early rather than

trying to reverse facial fat loss or belly fat buildup later.

The first step in managing lipodystrophy is a comprehensive checkup and discussion with your doctor. This can help determine which specific factors are contributing to your body fat changes and distinguish lipo from other conditions, including normal obesity. Your clinician will want to know about your HIV treatment history, diet, exercise, sleep, smoking, alcohol consumption and recreational drug use.

Your doctor will likely 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 bigger waistline relative to the size of the hips can be a sign of lipo. CT, MRI or DEXA imaging scans may help show how fat is distributed in the body.

Your clinician may run blood tests for metabolic or hormonal abnormalities. These include tests for blood sugar (glucose), lipids such as cholesterol and triglycerides, and certain hormones. An overactive thyroid can lead to weight loss, while a sluggish thyroid can cause weight gain. Cushing syndrome, caused by high levels of the stress hormone cortisol, can lead to body fat changes that look like lipo. These conditions can be treated with medications.

If you're taking older antiretrovirals that can cause lipoatrophy, you and your doctor may want to switch to newer medications with fewer side effects. This is often a good idea anyway, because modern meds are more convenient and may do a better job of controlling HIV. But while stopping problematic meds can halt further facial fat loss, it generally doesn't reverse existing lipoatrophy. And changing HIV regimens does not seem to have much effect on lipohypertrophy, according to Glesby.

Your provider will likely suggest lifestyle changes, such as improving your diet, getting more exercise, getting enough sleep and quitting smoking. 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. Stick with a diet and exercise program for at least six months to give it time to work.

"Dietary modifications and exercise are important as general health measures to reduce cardiovascular risk, and they may specifically have an impact on lipohypertrophy, though there is a shortage of good data on this," Glesby says. "Those with access to a registered dietitian could benefit from devising a tailored, balanced diet to reduce calories."

However, lifestyle changes alone are often not enough to alleviate lipodystrophy. If that's the case, adding medical treatments might help.

The medications Egrifta (tesamorelin) and Serostim (somatropin) may be helpful, especially if lipo is related to low growth hormone levels.

The Food and Drug Administration (FDA) approved Egrifta in 2010 to reduce excess belly fat in HIV-positive people with lipodystrophy. It's self-administered as an injection under the skin of the

belly, usually once daily. The newer formulation approved last year, Egrifta SV, is easier to prepare, does not require refrigeration and can be administered with a smaller needle.

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. Clinical studies showed that it reduced visceral hard belly fat by up to 18%, on average; some people have a better response than others. However, lost belly fat usually returns within a few months after stopping treatment. Recent research has shown that Egrifta can also reduce liver fat in HIV-positive people with non-alcoholic fatty liver disease, but it is not approved for this purpose.

“I took the shots for about six months, and it helped,” Gonzalez says. “This is a treatment that you must continue taking for the rest of your life, and I don’t know if I want to continue injecting my stomach for the rest of my life. My stomach was getting a little sore. So I changed my diet, and people are telling me that my stomach has gone down more. I exercise. And I might ask my doctor to prescribe Egrifta again.”

The older drug Serostim is a synthetic version of growth hormone approved by the FDA in 1996 to treat HIV-related wasting. Studies suggest it may also reduce visceral abdominal fat. Like Egrifta, it is administered as a daily injection.

Other medications may be used to manage the metabolic problems that often accompany lipodystrophy and reduce the risk of cardiovascular disease and other health problems. For example, Glucophage (metformin) may be prescribed to control blood sugar, and statins may be used to lower cholesterol levels. Some studies have found that Glucophage may help reduce visceral belly fat as well.

For some people, surgical approaches may be the answer. For those with lipoatrophy, 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) and Radiesse (calcium hydroxylapatite) are injectable synthetic fillers that stimulate the body to produce collagen to fill in the empty space. Both are approved by the FDA for treating facial lipoatrophy in people with HIV. The effects of Radiesse are apparent right away, while Sculptra builds up over a few months and lasts longer, typically around two to three years. While these fillers are broken down by the body over time, Bellafill (bovine collagen plus a synthetic filler) is semipermanent.

Liposuction, which uses a suction technique to remove fat tissue, may be an option for reducing excess breast fat or a buffalo hump. But 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.

However, the cost of medications, fillers and surgery for lipo can be a barrier, as many insurers

consider them to be cosmetic.

“My doctor recommended Egrifta injections, but Medicaid did not approve them. I had to wait till I was over 65, when Medicare kicked in,” Gonzalez says. “Medicaid hardly approves anything, and it’s so difficult to find a doctor who accepts Medicaid. That’s why people are falling out of care, and it gets me very angry. I wish I could do something about this health system.”

The manufacturers of Egrifta and Serostim offer patient assistance programs to help cover medication costs and insurance co-pays. Medicare covers Radiesse and Sculptra for people who experience depression due to HIV-related facial lipoatrophy. Some people have managed to obtain coverage for lipo procedures by having their doctor classify them as reconstructive.

Managing lipodystrophy can be challenging, and you and your doctor may have to try a variety of approaches—or a combination of them—before finding a solution.

Today, Gonzalez draws on her own experiences to help other people with HIV deal with the challenges of aging. “Helping others is what helps me,” she says.

“I’m on the long-term survivors page on Facebook. We discuss everything. I talk about my lipodystrophy and how I’ve managed it,” Gonzalez says. “I advise them to make sure they have a great rapport with their health care team. Look for what is best for you. You are the client.”

“What I can tell long-term survivors is that if we’ve come this far, we can continue living a healthy, happy life,” she continues. “What I offer them is to maintain a healthy mind, body and soul. It’s so important that you have a healthy spirit because your spirit is what’s going to lead you.”

Alicia Green assisted with reporting for this article.
