What is lipodystrophy

Lipodystrophies are a group of rare diseases involving the unexpected loss of body fat from various places of the body. They are frequently associated with conditions like high blood sugar, diabetes, high triglycerides in the blood, and an abnormal amount of fat in the liver. The fat loss can vary from very small areas on one part of the body to almost no fat in the entire body. Lipodystrophy can be inherited (genetic) or caused by other illnesses or drugs (acquired).

***Genetic lipodystrophies*:** These are caused by gene changes and can be seen either soon after birth or later in life depending on type of gene change. Congenital generalized lipodystrophy and familial partial lipodystrophy are the two main types of inherited lipodystrophy; other types are extremely rare.

***Acquired lipodystrophies*:** These usually occur during childhood, adolescence or adulthood and can be seen in some autoimmune disorders, or due to unknown reasons (this is called "idiopathic") or caused by medications such as medications to treat HIV. Common types of acquired lipodystrophy include acquired generalized lipodystrophy (Lawrence syndrome) and acquired partial lipodystrophy (Barraquer-Simons syndrome).

Criteria for Diagnosis of Lipodystrophy

Diagnosis of lipodystrophy is based on a detailed medical history and a thorough clinical exam to evaluate body fat loss. Tools used to help measure the loss of body fat including skin fold measurements, dual-energy X-ray absorptiometry (DEXA), and whole-body MRI. A variety of other tests including genetic testing, leptin levels and a full metabolic panel can be helpful for the patient and family members who may be at risk for genetic lipodystrophies. In patients with acquired lipodystrophy, there are special lab tests that can be ordered, including serum complement levels and autoantibodies. These tests help can help with the diagnosis of four major types of lipodystrophies:

Congenital generalized lipodystrophy (CGL) is also known as Berardinelli-Seip syndrome. Individuals have little to no body fat and have a muscular appearance soon after birth. It is often associated with metabolic abnormalities such as insulin resistance, hypertriglyceridemia, and diabetes mellitus.

Acquired generalized lipodystrophy (AGL) is a condition where individuals have a progressive loss of subcutaneous fat (the fat just under the skin), typically during childhood or adolescence but can occur in adulthood. Some individuals may experience a skin condition called panniculitis or rheumatological conditions before losing fat. It is often associated with metabolic abnormalities such as insulin resistance, hypertriglyceridemia, and diabetes mellitus.

Familial partial lipodystrophy (FPL), is characterized by the selective loss of subcutaneous fat from certain parts of the body depending on subtype, such as the extremities and buttocks, while fat accumulation may occur in other areas such as the face, neck and abdomen. It often

becomes apparent during puberty or early adulthood. Individuals often have a family history of this condition and develop metabolic complications similar to those seen in other forms of lipodystrophy.

Acquired partial lipodystrophy, also known as Barraquer-Simons syndrome, is a condition where individuals experience the progressive loss of subcutaneous fat from certain parts of the body, such as loss of fat from the face, neck, shoulders, arms, forearms, chest, while fat accumulation may occur in other areas such as the hips and legs.

What Does a Diagnosis of Lipodystrophy Mean?

Once the diagnosis of lipodystrophy is made, clinicians should find out if the lipodystrophy is generalized, partial, or localized. In generalized forms, total or near-total loss of fat underneath the skin can be observed over the entire body. In partial forms, fat loss affects large areas, particularly the arms, and legs, but fatty tissue may build up in areas such as the abdomen, face, and neck. Localized forms of lipodystrophy are limited to small body areas. Some forms of lipodystrophy are progressive and patients with lipodystrophy can develop health problems related to lipodystrophy as they age. Some examples include diabetes mellitus requiring very high insulin doses, very high levels of triglycerides (extreme hypertriglyceridemia), abnormal fat storage in the liver, heart problems, and other organs and potentially life- threatening inflammation of the pancreas (acute pancreatitis). Management requires continuous coordinated efforts of a team of specialists including lipid specialists, cardiologists, endocrinologists, gastroenterologists, registered dietitian nutritionists, and occasionally nephrologists and rheumatologists.

Lifestyle Recommendations for Individuals with Lipodystrophy

One size does not fit all for lipodystrophy. Patients should work closely with their medical team to determine what works best for their unique type of lipodystrophy. In general, simple sugars should be avoided and high-fiber complex carbohydrates are preferred. If triglycerides are very elevated, it is important to follow very low fat (<20 grams) diet. Individual needs differ, and seeing a registered dietitian nutritionist with experience in this area can be very helpful.

Treatment Options

Treatment options vary depending on the type of lipodystrophy and individual health complications.

Metreleptin

Metreleptin is an injected medication that acts like a naturally occurring substance called leptin. Leptin is a protein that helps to regulate fat stores in the body and also how the brain perceives satiety the feeling of being full after eating). It is used by patients with lipodystrophy who may not be producing fat tissue appropriately. This medication should be diluted in sterile water and injected into a fatty area of the skin such as the abdomen once daily around the same time each day. The specific dose of the medication depends on the weight of the child and should be decided by the Healthcare Team. It can be taken with or without eating. In most cases, Metreleptin treatment is only appropriate for patients with low leptin levels. There can be risks with this medication, including changes in blood sugar and

the development of binding antibodies, there have also been a reports of cancer in individuals with acquired lipodystrophies; however, it can still play a crucial role in patients' management of this condition in collaboration with the patient's healthcare.

Fish Oils

Fish oils are medications that are widely available over the counter, meaning without a prescription, or with a prescription from a member of your healthcare team. Fish oils are contain two omega-3 fatty acids, known as EPA and DHA, that help to lower triglycerides, Fish oils that are available without a prescription contain differing amounts of EPA and DHA and may not work well. Prescription omega-3 fish oil should be used for treating hypertriglyceridemia in children. Prescription fish oils are gel-like capsules that contain liquid omega-3 fish oil and can be given once or twice daily, depending on the prescribed dose. They should be taken with a meal and should not be broken or crushed before swallowing. These medications are usually well tolerated but can lead to some upset stomach and fishy-smelling burping. Very rare side effects include variable heart rates or increased risk of bleeding. Fish oil medications should not be used in patients with a seafood allergy, and a child's healthcare team should be consulted if there is a concern for increased bleeding, such as dark stools or easy bruising.

Fibrates

Fibrates are a class of medication that reduces triglycerides by reducing the creation of triglycerides and the breakdown triglycerides in the body. Examples of these medications include fenofibrate or gemfibrozil. Fenofibrate is the most used medication in this class and can be given at variable doses, mostly once daily, with or without food, in a capsule or tablet formulation. These medications may cause a risk of muscle aches when used with statin medications. Monitor for these muscle aches when the cause is not known and discuss with the healthcare team if this occurs. Patients with a history of gallbladder issues or kidney disease may need to avoid these medications; however, for individuals without these conditions, they are typically well tolerated.

For all of these medications, it is important to talk to your healthcare team prior to starting any new medications or supplements to ensure that they are safe to take with prescribed medications. Following the start of new medications, dose adjustments, or discontinuation of certain cholesterol-lowering medications, your healthcare team will request repeat laboratory tests to check the impact of the medication on cholesterol levels, which can serve as a marker for risk of heart disease. Additional monitoring tests, such as liver tests, may be needed on a less frequent basis. As always, if you have any concerns with medications, please discuss them with members of your Healthcare Team.

Patient Journeys

Coming Soon!

Finding a Specialist in Your Area

It can be challenging to find a physician that specializes in lipodystrophy. Your primary care clinician may know the lipid specialists in your area. On the website for your health care system, review clinicians in cardiology and endocrinology and look for key interests like "lipid clinic", "cholesterol", or "triglycerides", or search those terms under medical conditions the system treats.

Lipodystrophies are rare disorders. So, many people with lipodystrophy do not know anyone else who has this problem. Patient groups like Lipodystrophy United can connect patients with lipodystrophy with other people with the same disorder.

Clinical Trials

1. Study to Evaluate the Safety and Efficacy of Daily Subcutaneous Metreleptin Treatment in Subjects With PL (METRE-PL). ClinicalTrials.gov ID NCT05164341
2. Compassionate Use of Metreleptin in Previously Treated People With Generalized Lipodystrophy. ClinicalTrials.gov ID NCT02262832