LIPEDEMA DIAGNOSIS, STAGING, AND PROGNOSIS

DIAGNOSTIC CRITERIA

Diagnosing lipedema involves a taking the medical history and performing a physical examination of the patient.[7] As the field lacks a diagnostic test, clinicians consider multiple criteria to determine whether an individual has lipedema. The following sections describe these criteria, as well as how lipedema is differentially diagnosed from lymphedema, obesity, Dercum's disease, and chronic venous insufficiency.

Allen & Hines diagnostic criteria

Lipedema was first described in 1940 by Allen and Hines. In 1949, Wold, Allen, and Hines published a seminal report that elaborated on the clinical presentation and proposed diagnostic criteria, based on 119 cases.[1,3] Because lipedema is commonly misdiagnosed as lymphedema (see box), the proposed diagnostic criteria were designed to distinguish between the two diseases. Still used today the criteria include:

1. Almost exclusive occurrence in women
2. A bilateral and symmetrical accumulation of adipose tissue (body fat) on the legs with minimal involvement of the feet, resulting in a bracelet effect or cuff at the ankle (Figure 1, A)
3. Minimal pitting edema and negative Stemmer's Test (Figure 1, B)
4. Pain and tenderness of affected tissue
5. Persistence of the tissue enlargement despite caloric restriction or stimulation of lymphatic flow through elevation of the extremities
6. Increased vascular fragility, and easy bruising

Lymphedema is a buildup of the fluid surrounding tissues, or interstitial fluid, in the muscle and skin leading to increased fat deposition. The disease can be hereditary (primary lymphedema) or arise from damage to the lymphatic system from different insults such as cancer, surgery, radiation therapy, trauma, or infection (secondary lymphedema).

It can occur in *both men and women* and presents as *unilateral or bilateral swelling*—most often in the arms or legs. Common presentations include *pitting edema* and *positive Stemmer's Test*; *swelling that responds to elevation changes*; a feeling of heaviness; restricted range or motion; discomfort; recurring infections; and hardening and thickening of the skin.

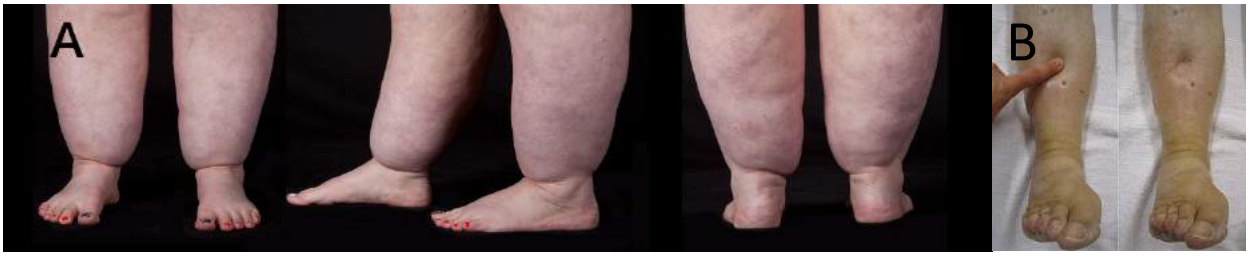

Figure 1: Visualization of Lipedema Diagnostic Criteria. (A) Front, side, and rear view of a lipedema patient's ankle cuffs. Wold *et al.* noted the presence of prominent inner ankle, or malleolar fat pads (rear). (B) Pitting edema is common in lymphedema, wherein application of pressure (left) leaves an indentation in the tissue (right). Images courtesy of the Fat Disorders Research Society (A) and Wikimedia Commons (B).

Clinical characteristics of lipedema

Treatment providers use the following criteria to facilitate a differential diagnosis of lipedema from other diseases.

Lipedema is characterized by **accumulation of fat on the limbs**, which can be **painful** and **feel nodular**. This fat build-up necessitates a differential diagnosis of lipedema from obesity and Dercum's disease. (Table 1)

- **Disproportional fat distribution** on the legs, without a similarly proportional buildup in the upper body/trunk region, is a key distinguishing characteristic of lipedema. This fat distribution is unlike that for obesity or Dercum's disease, in which fat accumulates at the trunk and throughout the body[4,20,21]. Because many lipedema patients are also obese, considerable debate exists regarding whether obesity begets lipedema or vice versa.[22]

- Unlike the smooth feel of obese fat, reports indicate that lipedema fat can present with **palpable nodules** – described as feeling like frozen peas in a bag or pearls – which can be more noticeably felt at later stages of the disease.[4,6] This nodularity is similar to the diffuse type of Dercum's disease.[6,24]

Dercum's disease, also known as adiposis dolorosa and Morbud Dercums, is a rare disease that often presents with general obesity and painful fat in affected areas.[21] Unlike the smooth feel of obesity fat, Dercum's disease fat can feel nodular when palpated, and form masses of fat tissue (lipomas or angiolipomas).

Dercum's disease is classified based on the areas of fat that experience pain: diffuse, widespread pain from in areas with fat tissue; nodular, intense pain in and around fat tissue with nodules or lipomas; and mixed.[6] The disease is more common in women than men, with the average of onset between the ages of 35-50, but has been reported to occur earlier.[22]

Table 1: Differential Diagnosis between Obesity, Dercum's Disease and Lipedema[4,6,20,23]

	Obesity	Dercum's Disease	Lipedema
Areas of excess fat accumulation	Trunk, throughout body	Trunk, throughout body	Arms and Legs
Tendency to bruise	Mild	Mild-Moderate	Moderate-Severe
Pain associated with fat	Mild	Severe	Moderate-Severe
Presence of nodular fat	No	Yes	Yes, especially at later stages
Comorbid with diabetes	Yes	Yes	No
Comorbid with hypertension	Yes	Yes	No

- Although the fat distribution between lipedema and Dercum's disease is different, the high prevalence of obesity in both populations increases the challenge of accurately diagnosing lipedema. The nodularity and pain associated with the fat lipedema and Dercum's disease further increases the complexity of differential diagnosis.

The **age of onset** for lipedema has been reported to occur primarily during puberty.[5] Furthermore, patients have reported development or exacerbation of lipedema during time periods surrounding pregnancy or menopause.[3,9,11]

Swelling or edema of affected regions worsens while standing upright (orthostasis) and during hot weather.[3,6] The presence of edema in lipedema contributes to a misdiagnosis of lymphedema.[4]

Vascular changes like **spider veins** and **telangiectasia** are present in lipedema-affected areas (Figure 2).[3,11] Because these vascular manifestations also occur in patients with chronic venous insufficiency (CVI), with advanced cases developing uni- or bilateral edema and swelling of the legs known as phlebedema, CVI is a differential diagnosis that requires consideration.[4,25]

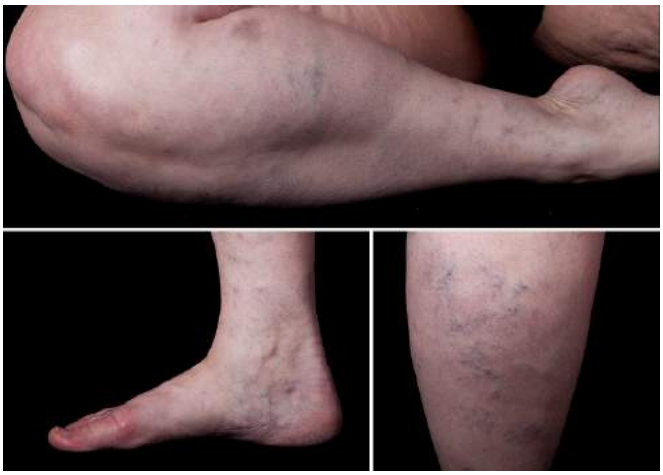

Figure 2: Spider Veins and Venous Manifestations on a Woman with Lipedema. (Top) Right leg, (Bottom left) right foot, and (Bottom right) left calf. Images courtesy of the Fat Disorders Research Society.

The **skin elasticity** is reduced in lipedema-affected areas, suggesting impaired connective tissue beneath the epidermis.[6,26] In some cases, the **skin** also feels cold to the touch but is not firm or hardened as in lymphedema.[6,27]

Lipedema is also considered to have a **heritability** component, because patient histories often refer to relatives with similar leg and body structure.[3] Pedigree studies from a single academic medical center suggest either an X-linked dominant inheritance, or autosomal dominant inheritance with sex limitation.[11] However, more studies are required to accurately determine the genetic architecture of lipedema.

Table 2: Differential Diagnosis of Lipedema vs Lymphedema vs Obesity vs CVI[6,25,28–31]				
	Lipedema	**Lymphedema (Primary and Secondary)**	**Obesity**	**Phlebedema, Chronic Venous Insufficiency**
Disease Presentation	Symmetrical fat deposition and swelling in legs and/or arms, but not the feet or hands	Fat deposition and swelling in affected limb, including hands or feet	Widespread fat deposition, with the potential for swelling due to comorbidities	No fat, but swelling and itchy areas near ankles with a brownish discoloration of lower legs
Sex	Almost all female	Males and females	Males and females	Males and females
Disease Onset	During hormonal shifts (puberty, pregnancy, menopause) and periods of weight gain	Primary: Congenital, due to presence of genetic mutations Secondary: Due to damage to the lymphatic system	Age independent	During pregnancy or onset of comorbidities such as obesity, diabetes, or hypertension
Presence of Pain	Yes, in affected tissues	Discomfort and aching can occur over time	Yes, chronic pain associated with comorbidities	Yes, in affected areas
Impact of Caloric Restriction and Exercise on Fat	Limited	None	Weight-loss strategies can be effective	Not applicable
Risk of Cellulitis	No	Increased	Increased	Increased risk in areas affected by edema. Itchy and discolored areas with eczema can look like cellulitis
Heritability	Potential	Primary lymphedema can be inherited	Potential	Potential

For further differential diagnosis tools, see:

- Differential Diagnosis: Approach to the Patient with Swollen Legs
- Fat Disorders Research Society Continuing Medical Education