9
Lipedema

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9.1 Definition, Signs and Symptoms

Lipedema is a disease of unknown etiology which predominately affects women. According to an epidemiological study performed by the authors in 2001, lipedema is present in 11% of the female population. Lipedema often manifests itself at menarche, or menopause, or during pregnancy. Although rarely found in men, such cases of lipedema are accompanied by a significant imbalance of male sex hormones and/or a disturbance to liver function. In the authors’ experience, there is also a higher incidence of lipedema after cranial trauma and after surgery for pituitary adenomas.

Lipedema can be described as a bilateral, symmetrical, flabby swelling of the legs that arises from deposition of adipose tissue starting at the hips and ending at the ankles, like riding breeches. There are two different forms: a column-shaped, cylindrical form (Fig. 9.1) and a lobal form (Fig. 9.2). Both can be either a descending or ascending kind. The former begins centrally in the area of the hips and thighs, while the latter starts in the lower leg. In the early stages of the illness, the skin is smooth. Later, the typical signs of “cellulitis” develop (see Section 9.7, Fig. 9.3).

In late stages – especially in elderly, untreated patients – subcutaneous nodules are palpable, as a result of sclerosis of the subcutaneous connective tissue. In severe cases, immobility can result from elephantiasic swelling of the legs. The color of the skin is normal, unless lipedema is accompanied by erythrocyanosis crurum pullofarum. Sometimes there are also hemispherical fat pads medially at the level of the knee joints. Occasionally lipedema of the legs is accompanied by lipedema of the arms. In such cases, the swelling ends at the level of the wrizt.

Occasionally lipedema can also affect the upper extremities. In these cases, swelling spreads from the shoulder to the wrist.

Some authors use the term “lipodystrophy” instead of lipedema. This term should not be used because:
1. Allen and Hines, who gave the first description of the above syndrome, coined the term “lipedema” and
2. some authors use the terms lipodystrophy and lipatrophy synonymously. Lipatrophy, however, is a disease clearly distinct from lipedema. This may lead to some confusion.

Additional signs and symptoms include:
- On a normal day for patients who lead an orthostatic, ambulatory lifestyle, i.e., on a day not spent lying in bed, edematous fluid often accumulates in the lipedematous limb. This happens in the second half of the day, and particularly on warm days. Then in the evening, pitting appears over the shin bone and ankles. In the lipedematous region there is tenderness to pressure. Pressure that is not painful to a healthy person or to a person with lymphedema can elicit a strong pain reaction in a person with lipedema.
- A minor trauma that would leave no trace in normal tissue can cause a “blue spot” in the lipedematous region. The blue spot is a hematoma in the subcutaneous adipose tissue.
- Lipedema often causes great emotional distress: patients feel ugly and misshapen, which strongly impairs their quality of life. In their first description of lipedema, Allen and Hines reported that these women avoid swimming in public and wear long skirts to

Fig. 9.4 Early stage of column-shaped lipedema [M150]
hide their obese legs. Depression in patients with lipedema often leads to additional problems and complications (see Section 9.3).

9.2 Pathophysiology and Pathology

Three fat layers can be distinguished in the subcutaneous tissue of adults (for details see Chapter 1). Like the adipose lobules, they are separated by septa of connective tissue. From the upper layer, protrusions of adipose tissue — so-called “papillae adiposae” — reach the dermis. Every single fat cell has its own blood supply via a blood capillary and is innervated by an adrenergic nerve fiber. It is assumed that adipose tissue has sensory innervation, as well. Lymph capillaries can be found within the fibrous septa, but not between the fat cells themselves. The few reticular fibers between the fat cells serve as guide rails for a long, prelymphatic drainage system.

Microangiopathy in the area of the adipose tissue is what initially sets in motion the changes underlying lipedema. The microangiopathy results in increased permeability to proteins and increased fragility of the blood capillaries.

As a consequence of the increased permeability, protein-rich fluid accumulates in the area around the cells. The increased fragility explains the typical blue spots.

Tenderness of the adipose tissue can lead to neurogenic inflammation, which further aggravates the microangiopathy. Ryan is of the opinion that the tenderness is due to an impairment of the autonomous nervous system. In his view, this impairment may lead to a misinterpretation of proteopathic sensory inputs — like sensation of pressure, temperature or posture — as is known, for example, in Sudeck-Leriche syndrome.

Pericellular fluid accumulation is synonymous with dilation of the prelymphatic drainage system. This has the result that interstitial fluid flows only very slowly towards the initial lymph vessels.

The lymph capillaries of the skin show pathological alterations. In studies using fluorescent microlymphangiography, Bollinger et al. found aneurysm-like structures and conspicuously narrow segments. The perme-
ability of the lymph capillary wall was elevated. These are findings specific to lipedema.

Widening of the prelymphatic channels, as well as functional and morphological abnormalities of the lymph capillaries, suggest impairment of lymph formation.

In addition, a disturbance to lymphangion motor activity has been observed. Early findings using oil-contrast lymphangiography showed wavy corkscrew-like suprafascial lymph collectors. In cases of elephantiasic swelling, immobility further impairs lymph formation and lymphangiomotoric activity.

Isotope lymphography has shown accelerated aging of the lymph pump.

In lipedema the elasticity of the skin is strongly reduced, i.e., its compliance is increased. This has the following severe consequences:

- The skin loses its role as an abutment for the venous leg pump. In healthy people, pressure in the veins of the dorsum of the foot is 100 mmHg while in a standing position; during walking, it drops to about 30 mmHg. This mechanism does not work properly in lipedema patients. The resulting passive hyperemia leads to high net ultrafiltration (see Chapter 11). Because of the increased compliance of the skin, a much higher volume of interstitial fluid is needed in order to raise the interstitial pressure. One consequence is that lymph formation is impaired even more; another is that one of the passive defense mechanisms against edema barely functions anymore.

- Another important aggravating factor is the fact that the veno-arteriolar reflex is absent (Strößenreuther). In healthy people, this reflex causes vasoconstriction under orthostatic conditions. The resulting reduction in the perfused capillary area reduces the net ultrafiltration volume in the legs. Thus this reflex is an important defense mechanism against edema that is absent in lipedema.

- In adipose tissue there are hardly any macrophages that can eliminate cellular plasma proteins outside the lymph vessels. For this reason, fibrosis develops in between the adipose cells fairly quickly; collagen fibers appear.

In lipedema, the reason why edema with pitted skin often develops in the second half of the day during warm weather is that the warmth leads to active hyperemia, which increases the lymphatic water load.

If an edema associated with water retention joins with a lipedema, the insufficiency of the lymph vascular system exists. This is because the safety valve function of the normal (sufficient) lymph vascular system hinders the formation of edema.

In lipedema, the lymphatic water and protein load is increased. Lymph formation and lymphangion motor activity are disturbed. Thus, the safety valve function of the local lymphatic system fails.

### 9.3 Complications and Combinations with Other Diseases

Lipedema complications may be caused by the patients themselves or they may be iatrogenic (Table 9.1).

Complications caused by the patients themselves are secondary to emotional depression caused by the lipedema. Anorexia nervosa can develop after repeated failed attempts to achieve slimmer legs by fasting or intensive jogging. Anorexia nervosa causes severe metabolic disturbances, is sometimes accompanied by generalized edema, and can even result in death.
9.3 Complications and Combinations with Other Diseases

Table 9.1  Complications of Lipedema

- Anorexia nervosa
- Bulimia
- Diuretics/laxatives
- Liposuction
- Sclerotherapy of varicose veins
- Varicectomy without an absolute indication
- Gastric banding, gastric bypass
- Lipo-lymphedema
- Lipedema + cyclic idiopathic edema syndrome
- Lipedema + arthropis
- Lipedema + chronic venous insufficiency

Bulimia, an excessive feeling of hunger – also referred to as an “eating-vomiting addiction” – can also develop. A complication of bulimia is obesity (Fig. 9.4). It is known that obesity often leads to diabetes, high arterial blood pressure, congestive heart disease with hypoxia, varicose veins, and chronic insufficiency of leg veins (see Chapter 11). Other complications of obesity are osteoarthritis in the back and legs, elevated uric acid levels in the blood, and – often in combination with mycoses – overflowing abdominal skin folds and intertrigo (a superficial dermatitis) under the breasts. Local lymphedema can develop in heavy hanging skin folds on the lower abdomen. In the lobar forms, such changes and complications also develop between the skin flaps and on their drooping edges.

Among the iatrogenic complications, the most notable is Pseudo-Bartter-syndrome, which is caused by regular use of diuretics. The Bartter syndrome that is also known as “juxtaglomular cell hyperplasia” is accompanied by hyperaldosteronism and hypokalemia (“pseudo” means a false, misleading similarity to another condition or illness).

Surgical removal of adipose tissue, lipectomy, can cause lymphedema as a complication, because lymph vessels are always removed along with the fat. It is particularly dangerous if fat pads medial to the knee joints are excised – as previously explained, the ventromedial lymph vascular bundle is located in this region. Lymphedema is a much more serious disease than lipedema. People do not die of lipedema, but lymphedema can lead to angiosarcoma.

Incidently, lipectomy is not a minor procedure. The operation can even result in death, as a consequence of a fat embolism.

In the discussion of iatrogenic lymphedema in Section 5.2.2, liposuction was mentioned as one of the causes. The fact that lymph vessels are inevitably damaged in liposuction is demonstrated in a study by Baumeister (cited in Strößenreuther “Lipödem und Cel lulitis,” 2001):
The corresponding tissue regions were carefully dissected and examined for detectible injury to the lymphatic pathways from a macroscopic perspective. Prior to the suctioning, the lymphatic pathways had been dyed blue for this purpose, by peripheral injection of Patent Blue. Findings were distinguished at three different levels, thus allowing for classification into three degrees of damage.

Absence of macroscopically visible damage to the lymph vessels was labeled "0" degree damage. Minor discharges of blue dye in the immediate vicinity of the lymphatic pathways, i.e., a distance of less than 2 mm, were designated 1st degree damage.

Large discharges of dye extending into the broader surroundings of the lymph vessels, or the appearance of blue dye in the collection canister of the suction device, were classified as 2nd degree damage.

The results indicated a significant difference between the two directions of suction:

<table>
<thead>
<tr>
<th>Damage to Lymph Collectors (in %)</th>
<th>0° degree</th>
<th>1° degree</th>
<th>2° degree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parallel to axis of leg</td>
<td>78</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>Crosswise to axis of leg</td>
<td>7</td>
<td>43</td>
<td>50</td>
</tr>
</tbody>
</table>

The data show that significant differences did indeed exist between the two directions of suction, but the "parallel" type of liposuction also caused lymph vessel damage.

A proposit liposuction — also known grandiosely as "liposculpture" — we quote from the articles, "Liposuction — No Problem?" penned in 2003 and 2004 by the plastic surgeons Lenhardt et al.1,2:

"Liposuction is considered a safe and effective procedure for removing esthetically displeasing subcutaneous pads of fat like ‘saddle bag thighs’ ... In the Federal Republic of Germany the surgery is performed by doctors from differing fields of specialization on an increasingly more frequent basis, not the least because of its lucrative earnings potential (Fig. 9.5). According to information provided by the Association of German Plastic Surgeons, 150,000 to 200,000 liposuctions are performed in Germany every year, with this trend on the rise ..."

In the years 1998–2002, Lenhardt et al. sent questionnaires to intensive care units and institutes of pathology and forensic medicine in Germany, Austria and Switzerland, to members of the Association of German Plastic and Cosmetic Surgeons, to health insurance companies, and government prosecutors. A total of 3383 questionnaires were sent and 1150 replies (34%) were received. Seventy cases of severe complications were reported. The most common complication was necrotizing fasciitis. Other complications reported were skin necroses, perforations of hollow organs (gall bladder, small intestine), secondary hemorrhages, pulmonary edema caused by hyperhydration, embolisms, sepsis, septic shock, cardiovascular arrest, shock/epilepsy from hypohydration. There were 19 deaths. In two cases, the cause of death was gangrene (Fig. 9.6).

It should be noted that 2233 of the institutions and offices contacted failed to reply. If one assumes that unreported incidents occurred at the same frequency as reported incidents, the number of severe complications would be at least 206, including more than 62 deaths!

The authors emphasized that patients who opt for elective cosmetic surgery must be informed about the results that can be expected and about potential complications; this information should be detailed and frank, and should be thoroughly documented.

We have printed the lines regarding counseling of patients in boldface type. This is, after all, the critical issue — and one that has specifically been neglected in publications by top professionals who have not encountered any complications themselves, and who are enthusiastic about the successful results they have achieved. For example, the complications noted here were not described in a 2005 article by Meier-Vollrath3 et al. in the Deutsches Ärzteblatt. Only lymphedema was mentioned, and it was asserted that this complication is no longer observed “when new techniques are used.” Not every physician is a top specialist in liposuction, however. Government social welfare agencies do not pay for it, patients pay out of their own pockets, and there is a very real danger that inexperienced doctors will give liposuction a try (every German doctor gets this medical jour-

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9.5 Diagnosis and Differential Diagnosis

According to Yoho et al. (2005), "The risks associated with liposuction ... compare favorably with those from most general surgical procedures."

We strongly warn against obliterating varicose veins on lipedematous legs, and also against performing surgery on varicose veins if there is no absolute indication for it. The patient’s condition will deteriorate in most cases.

The spontaneous complications listed in Table 9.1 can appear alone or in various combinations. The most important complication is lipo-lipedema. Its origin is explained by the pathophysiology described. According to statistics compiled by the authors of this chapter, untreated lipedema turns into this combination form after 17 years. Lipo-lipedema can be associated with all the described complications of lipedema (there is also a combination form called “lympho-lipedema.” This form occurs when a case of lipedema later develops lipedema).

9.4 Prognosis

Regarding mortality, the prognosis of uncomplicated lipedema is good; however, regarding healing, the prognosis is poor unless adequate treatment is provided. If patients receive appropriate treatment before they reach the age of 35, the likelihood of recovery is high. Otherwise, the pathological process continues: liposclerosis develops and, as previously noted, 17 years after onset of lipedema, on average, the combination form, lipo-lymphedema develops. The prognosis for the combination forms lipo-lymphedema and lympho-lipedema is the same as for lymphedema. If the lipedema is accompanied by a complication, the prognosis depends on the prognosis of the complication.

9.5 Diagnosis and Differential Diagnosis

It is quite possible to diagnose lipedema and to differentiate it from lymphedema and lipo-lymphedema (or lympho-lipedema) on the basis of a thorough medical history and clinical examination (see Table 9.2). In practice, however, there are problems, as demonstrated by the fact that lipedema is often confused with lymphedema. Out of 100 patients who were referred to our clinic with a diagnosis of "lymphedema," 17 actually had lipedema, and 38 had lipo-lymphedema.

Imaging procedures are not necessary. Direct lymphography with oily contrast media is contraindicated. Indirect lymphography findings are of great scientific interest: in lipedema, the prelymphatic channels show up as giant pools (Partsch). The aqueous contrast medium injected epidermally moves along the "papillae adipose" from the dermis into the edematically dilated system of prelymphatic channels located between the adipocytes. There are images that are unlike any other disease presentation. Lymphoscintigraphy (radioisotope scanning) cannot be used for establishing a diagnosis. Some authors report normal findings, others report abnormal findings in a few cases, while still others report pathological findings in over 50% of cases.

Functional lymphoscintigraphy is unnecessary for differentiating lipedema from lipo-lymphedema.

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Table 9.2  Differential Diagnosis: Lipedema/Lymphedema/Lipolymphedema/Lympholipedema

<table>
<thead>
<tr>
<th></th>
<th>Lipedema</th>
<th>Lymphedema</th>
<th>Lipolymphedema</th>
<th>Lympholipedema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence</td>
<td>no</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Frequency</td>
<td>no</td>
<td>rare</td>
<td>frequent</td>
<td>positive</td>
</tr>
<tr>
<td>Affected</td>
<td>negative</td>
<td>normal</td>
<td>positive deep-</td>
<td>positive</td>
</tr>
<tr>
<td>Lymphangiopathy</td>
<td>no</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Deepened</td>
<td>no</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
</tbody>
</table>

According to Weissleder et al., non-pathologic lymphoscintigraphy results rule out a disturbance to the lymph vessels "with a high degree of probability." However, a negative Stemmer sign rules this out with certainty! The opinion of these authors that lymphoscintigraphy is indicated for "demonstrating or ruling out lymphogenous damage in lipedema" is sensible if the patient still wants liposuction after thorough counseling, because lymphangiopathy accompanying lipedema is "regarded as a contraindication for this type of treatment." In this connection it must be stressed that, as mentioned, lipedema is always accompanied by lymphangiopathy.

Constitutional fat pads on the hips must be differentiated from lipedema.

9.6 Therapy

First, it must be stressed that lipedema, which can lead to serious, sometimes life-threatening complications, is not a "subjective problem." It is not a matter of "fat legs in a healthy woman" or a "constitutional variation," as is sometimes claimed. Lipedema is a disease that requires treatment.

In lipedema, too, treatment must be preceded by diagnosis and differential diagnosis. A thorough, comprehensive examination is always necessary. For example, the treatment of choice, complete decongestive therapy (CDT) would be initially contraindicated in the case of an older woman with congestive heart failure, who is generally obese in addition to having lipedema.

CDT could only be begun after successful treatment of the heart failure. If blood pressure is elevated, it must be normalized before physical therapy is begun. In the combination form, lipedema-plus-obesity, it is essential that CDT be accompanied by a professionally supervised weight reduction program; otherwise the CDT will not have any notable success.

Diseases of the musculoskeletal system need to be alleviated as much as possible so that the venous leg pump will work more efficiently.

Since obesity often accompanies lipedema and since this complication worsens the lipedema, hastening the transition to the combination form, lipedema-plus-obesity, doctors should prescribe preventive measures that include a calorie-conscious, low-fat, low-carbohydrate diet and exercise.

If there is a hormone disorder, this should be corrected with appropriate medicine; the lipedema, however, will not be affected by such treatment.

Regarding Phase I, the decongestion phase, CDT should be performed without compression bandages for the first few days, because of the tenderness to pressure. After a few days, compression bandages can cautiously and gradually be applied. Even in cases where the edema does not leave pits, Phase I often results in conspicuous reduction of the legs' volume. The transition from Phase I to Phase II, the maintenance and optimization phase, must be seamless. In this second phase, wearing of compression hose is an absolute requirement.

As explained in detail in Chapter 5, compression treatment is an integral part of CDT. Some doctors who have no experience in treating lipedema with CDT claim that nothing can be expected from compression treatment in this case, because fat cannot be compressed. Even Ryan expressed this opinion in 2001: "Because of the pressure dispersement by adipose tissue, hosiery and bandaging is compromised and relatively ineffective."
Table 9.3: Effects of CDT in Lipedema

<table>
<thead>
<tr>
<th>Pathological alteration</th>
<th>Mode of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin elasticity ↓</td>
<td>Skin elasticity ↑</td>
</tr>
<tr>
<td>edema protective mechanism ↓</td>
<td>edema protective mechanism ↑</td>
</tr>
<tr>
<td>Lack of veno-arteriolar reflex →</td>
<td>Veno-arteriolar reflex re-established →</td>
</tr>
<tr>
<td>lymphatic fluid load ↑</td>
<td>lymphatic fluid load ↓</td>
</tr>
<tr>
<td>Prelymphatic drainage towards septa ↓</td>
<td>Prelymphatic drainage towards septa ↑</td>
</tr>
<tr>
<td>Transport capacity of lymph vessels ↓</td>
<td>Transport capacity of lymph vessels ↑</td>
</tr>
<tr>
<td>Calf muscle pump ↓</td>
<td>Calf muscle pump ↑ (speculative)</td>
</tr>
</tbody>
</table>

Using duplex sonography, it can be seen that adipose tissue is in fact compressible.

The combination of compression treatment and movement therapy (which is also a part of CDT) has multiple effects: a number of pathological-physiological disturbances are reduced or eliminated (Table 9.3). In particular, we point out that accumulated pericellular fluid is shifted from the area of the adipose tissue into the connective tissue of the septa, and is thus provided with access to the initial lymph vessels situated in this location. Water cannot be compressed, but pressure makes it move away, as happens in an injection, for example!

In this context, the following sentences of Ryan are very instructive:

"The movements of the body are designed to make use of the normal structure of the skin: they stretch and tense the collagen and elastic fibers. As a result, mechanical signals are converted into biochemical signals on a cellular level... If the skin is diseased, then compression garments or bandages are what make it possible for the tissues to feel the movements of the body, and for muscle contractions to have an effect in the skin region."

It should also be noted that adipose tissue does not tolerate pressure. Abdominal fat disappears in the area of a tight belt that is constantly worn, and the pressure of a violin also causes a decrease in local fat ("violin player's neck"). Phase 2 measures can gradually be phased out. Of course, this does not apply to lipo-lymphedema or lympho-lipedema. Unfortunately, patient compliance is worse in lipedema than in lymphedema, not only in regard to consistent use of compression tights (which must be worn in summer, as well!), but also in regard to maintenance of normal body weight. A psychiatrist must be brought in as part of the treatment team in cases of severe emotional depression, anorexia nervosa, or bulimia (Fig. 9.7).

We strongly emphasize that in lipedema, localized deposits of fat do not respond either to exercise or to weight loss programs. Even a fasting program at a "fat farm" will be unsuccessful.

Performance of vertical banded gastroplasty (gastric banding) with the goal of reducing the stomach is a very controversial procedure even for treatment of extreme obesity. Use of this procedure in lipedema is malpractice! The same is true of gastric bypass operations. Attempts to treat lipedema with diuretics are also misguided (also see Chapter 12).

The typical signs of "cellulite" are present in most lipedema patients.

The textbook of dermatology by Braun-Falco et al describes "cellulite" as follows:

"The term is used by non-professionals in particular. It refers to a change in the subcutaneous adipose tissue of younger women, particularly in the thighs and buttocks. It changes the appearance of the skin to resemble the "peau d'orange" appearance. There were no histological findings indicating inflammatory processes like panniculitis (inflammation of the subcutaneous adipose tissue) or vasculitis. At most, there is only minor lymph congestion and edematization of dermal connective tissue, accompanied by proliferation of subcutaneous adipose tissue. The findings were given the designation..."

In their article on "Surgical treatment of morbid obesity, assisted by an adjustable band around the stomach" Berg et al (see References) describe a complication referred to as "slippage" that occurred in 2.8% of their cases (there are other complications as well): "Slippage is a complication that requires urgent emergency intervention."
"adipositas oedematosa." This is a constitutional, gender-specific, localized type of obesity that grows worse with overeating and increasing age; it is not a disease. Medical treatment is not possible. Measures recommended as helpful include prompt weight reduction and exercise involving the legs, such as jogging, bicycling, and massage."

Ryan and Curri found a close correlation between "cellulite," lipedema, cyclic mastopathy (premenstrual, painful swelling of the breasts, found in 40% of the...
microangiopathy (microaneurysm) of the blood capillaries

pericellular high-protein edema

infiltration by white blood cells

pericellular fibrosis (collagen) fibrin deposits surrounding the blood capillaries

sclerosis of the septa and pericellular micronodules

Fig. 9.9 Lipodermatosclerosis. [M 150]

women) and lipodermatosclerosis due to chronic venous insufficiency (see Chapter 11). In all these diseases, microangiopathy is an early histological finding. As a consequence, pericellular protein-rich edema of the adipose tissue occurs, leading to edematous panniculopathy. If the process continues, white blood cells infiltrate the edematous regions, collagen synthesis is increased, and finally fibrosis and sclerosis result. During physical examination, the latter present as visible and palpable subcutaneous nodes and nodules (Fig. 9.8 and 9.9).

In cyclic mastopathy, axillary lymph nodes are enlarged and tender during premenstrual swelling.

Ryan and Curri suggest using the term "panniculopathy oedematosclerotica" instead of the imprecise term "cellulite."

9.8 References


