When a doctor, nurse or therapist is well trained and adequately prepared to recognize lymphatic disorders, the diagnosis of lymphedema is usually a straightforward affair. A correct diagnosis will generally proceed from a thorough discussion and physical examination of the patient with attention to such features as: predisposing features for lymphedema (surgery, trauma, infection, radiation therapy); onset and duration of swelling; symmetry and distribution; skin changes; presence or absence of Stemmer's sign (the inability to “tent” the skin between the toes in a lymphedematous foot); “squaring-off” of the toes, also typical of lymphedema in the lower extremity; and absence of findings to suggest a readily apparent alternative cause for swelling of the involved limb(s). Nevertheless, looks sometimes can be deceiving. An astute clinician always should be prepared for the challenging cases when another diagnosis can masquerade in the form of lymphedema. Sometimes, an ancillary diagnostic test, for example, an imaging study of the lymphatic system (a lymphoscintigram) or MRI, can help to confirm or dispel suspicions about lymphedema.

When the pieces don't all fit, or when the lymphoscintigram is negative or inconclusive, here are some other common conditions to be considered.

**CHRONIC VENOUS INSUFFICIENCY AND POST-PHLEBITIC SYNDROME.** This is a very common condition and the one that is perhaps most readily confused with lymphedema of the legs. It is estimated that perhaps 5% or more of the adult population may be affected by this problem. Women are more typically afflicted than men. Perhaps this reflects the effects of the female hormone, as well as the mechanical effects of child-bearing. In this condition, it is either obstruction of the deep veins or incompetence of the venous valves that promotes fluid accumulation in the tissues. The term post-phlebitic syndrome is used when the condition arises after an episode thrombophlebitis, in which inflammation and blood clotting in the deep veins can lead to chronic structural damage to the venous system.

In addition to edema, patients with chronic venous insufficiency are very likely to manifest additional symptoms. Most characteristically, these might include aching in the lower legs when they are exposed to effects of gravity (sitting or standing). Patients often describe either dull pain or a bursting discomfort. Pain usually is relieved when the legs are elevated. Later on, when the skin becomes affected, there also may be complaints of chronic itching, particularly over the regions of the leg where the communicating veins from the deep system are plentiful (i.e., the inner aspect of the leg and ankle).

Physical findings in chronic venous insufficiency are often quite characteristic. Pain or palpation is very common. In addition to pitting edema, there is often discoloration caused by multiple pinpoint deposits of blood-derived pigment (called hemosiderin) in the skin. The increased pigment is found in areas of prior inflammation and the legs and feet may appear dusky when they are allowed to hang down from a sitting position. Although post-phlebitic is distinct from varicose veins, patients often develop secondary varicosities in the skin. When the condition is present for some time, patients may become predisposed to ulceration and infection of the skin in areas where there are prominent, insufficient communicating veins.

Conservative treatment of chronic venous insufficiency is often quite successful. As with lymphedema, compression reduces the degree of edema and also reduces discomfort and speeds healing of skin ulceration. However, in this condition, lesser degrees of compression are necessary than in lymphedema and the ancillary treatment techniques for lymphedema will be less helpful. In severe or resistant cases, there are surgical interventions to ligate or interrupt the faulty venous structures. This kind of surgery will help to alleviate some of the manifestations of the disease and reduce the likelihood of additional skin ulceration. On the other hand, post-phlebitic syndrome and venous insufficiency, if improperly managed, can predispose to secondary changes of lymphedema, as well.

**MYXEDEMA.** The thyroid gland is responsible for the elaboration of a hormone that has profound effects on the body's normal metabolism. In any acquired disorder of thyroid function, myxedema can occur. This special form of edema arises when abnormal deposits of mucinous substances accumulate in the skin as a result of thyroid disease. When the thyroid is overactive, this process occurs in a very localized manner in the regions overlying the shin bone (tibia); in underactive states, the myxedema is more generalized.

In myxedema, hyaluronic acid-rich protein is deposited within the dermis of the skin. These deposits draw additional fluid into the skin and the resulting edema disrupts the structural integrity, reducing the elasticity of the skin.

Clinically, the patient with myxedema will experience skin swelling with particularly prominent involvement around the eyelids, the hands, the lower legs and the feet. On examination, the changes in skin consistency resemble those of advanced lymphedema to a great degree. However, concomitant findings may lead to the diagnosis of hypothyroidism. These include roughening of the skin over the palms, soles, elbows and knees; brittle, uneven nails; dull, thinning hair; yellow-orange discoloration of the skin; and reduced sweat production.

Fortunately, once suspected, these conditions can be readily diagnosed by a simple examination of the blood, where abnormal concentrations of circulating thyroid hormone will confirm the presence of either under- or over-activity of the thyroid gland. Treatment is also straightforward and will lead to prompt reversal of the myxedema once hormonal balance is restored.
restored.

**LIPEDEMA.** This condition often poses perplexing difficulty in the differential diagnosis of lymphedema. It is a condition that affects women almost exclusively. It almost certainly has a hormonal basis, since it arises in men only when they have concomitant disturbances in hormone balance that accentuate feminine body attributes.

Like lymphedema, lipedema is a chronic condition accompanied by swelling. In the case of lipedema, however, the swelling of the bodily tissues is caused primarily by the abnormal accumulation of fatty substances in the subcutaneous regions. This fatty accumulation typically is distributed between the pelvic bone and the ankle, with sparing of the feet. Although understanding of the mechanisms of this disease is still very incomplete, it is clear that there is an overproduction of fat-containing cells (adipocytes) in the subcutaneous tissues and that there are characteristic structural alterations in small vascular structures within the skin. In fact, it has been hypothesized that there are regional abnormalities of the circulation that cause the initial accumulation of fat in the affected regions.

In lipedema, it is the characteristic distribution of the swelling and thickening, with typical foot sparing that points toward the correct diagnosis. Most often, the medical history will disclose that the condition began within one to two years following the onset of puberty. In addition to the near lifelong history of heavy LEGS and THIGHS and HIPS, affected patients often will complain of painful swelling and a marked propensity to bruising that is based upon heightened fragility of capillaries within the adipose tissue.

On examination, the symmetrical deposits that end above the ankles are quite characteristic. Initially, the skin surface is even, with nodularity that is palpable beneath the skin. Later, there is orange discoloration and an uneven surface to the skin, which ultimate becomes superficially deformed by the growing deposits of fatty tissue beneath.

There are several characteristics that serve to distinguish lipedema from lymphedema. Lipedema tends to be more symmetric than the typical case of lymphedema and, whereas the latter is painless, lipedema patients often complain of pain that can be reduplicated by palpation on physical examination. Lipedema predisposes to bruising and subcutaneous bleeding, which is absent in lymphedema, while the risk of infection, so typical of lymphedema, is absent in lipedema. The absence of a Stemmer's sign and the sparing of the foot are additional clues that diminish the likelihood of lymphedema.

Unfortunately, there is no highly effective therapy for this condition. Uncomplicated lipedema does not respond to complex decongestive therapy and medications are not effective. However, the use of Class II-III compressive stockings and bandaging appears to provide some therapeutic benefit. When there is concomitant, generalized obesity, a weight reduction program should be recommended also.

**MALIGNANT LYMPHEDEMA.** It must be stressed that, at least in the United States, the leading cause of lymphedema of both upper and lower extremities is malignancy and its resultant treatments. Consequently, it cannot be overemphasized that, in the differential diagnosis of lymphedema, or in the worsening of a pre-existing edema, recurrence of cancer must always be considered. Lymphedema appearance or worsening can occur because of spread of tumor cells through the lymphatics, leading to obstruction of lymph flow. Extrinsic obstruction of the lymphatics by tumor can also occur. Clearly, any of these conditions would mandate prompt diagnosis and treatment. Fortunately, there are some distinguishing features of malignant lymphedema that aid in its recognition, and help to distinguish it from the much more common, benign versions of lymphedema. In conditions caused directly by tumor spread to the lymph nodes or compression of the normal lymphatics by the contiguous tumor, there is a tendency for rapid development and relentless progression, particularly involving the legs, abdomen and trunk. In addition, pain may be a feature, where it is generally absent in benign lymphedema. Finally, while benign lymphedema most often begins in the hand or foot and progresses up the limb with time, the malignant form tends to begin more centrally. Often, the tissue is quite firm from the outset, without the soft consistency that is so characteristic of early stages of benign lymphedema. Any of these warning signs should prompt early diagnostic re-evaluation.

It is important to acknowledge that any of the conditions discussed here can, with time, entail the development of a secondary form of lymphedema as a consequence of the primary pathologic process. Therefore, the straightforward distinctions between lymphedema and venous insufficiency, myxedema, lipedema, and malignancy can readily become blurred and render the differential diagnosis more difficult. At times, a complete therapeutic approach to the patient will require attention to multiple components of the condition that lead to edema formation. It is not always lymphedema, but when it's not lymphedema, the astute diagnostician will find the answer.

**SUGGESTED READING**


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