

DISORDERS OF THE LYMPHATIC SYSTEM

ANATOMY

The lymphatic system is composed of **lymphatic capillaries** that collect interstitial fluid, **transporting vessels**, and **lymph nodes**. Lymphatic capillaries are the site of interstitial fluid absorption throughout the body. These empty into the transporting vessels that traverse the extremities and body cavities to eventually empty into the venous system via the thoracic ducts. Lymph nodes periodically interrupt these transporting vessels. In the lymph nodes the lymph is filtered, and these structures serve a primary immunologic function.

A number of tissues have no lymphatic drainage, including the **epidermis**; the **central nervous system**; the **layers of the eye**; and **skeletal muscle**, **cartilage**, and **tendon** in the extremities.

PHYSIOLOGY

The circulation of lymph is a complex and incompletely understood process. All the tissues of the body are bathed in interstitial fluid, and when an excess amount of this fluid accumulates, it is referred to as edema. Edema may result from excessive production of interstitial fluid or from inadequate removal. Excess production of interstitial fluid occurs when

- permeability of the capillary membrane increases, such as during local inflammation
- hydrostatic pressure is not counterbalanced by colloid osmotic pressure as might occur from hypoproteinemia.
- If the pressure on the venous side of the capillary is high, as in acute obstruction from venous thrombosis, less fluid is reabsorbed, and the volume of interstitial fluid increases and is observed as edema. Similarly,
- if the transport of interstitial fluid by the lymph system is inadequate, excess interstitial fluid accumulates.

Excessive accumulation of interstitial fluid because of lack of lymphatic transport is termed **lymphedema**. Normally between 2 and 4 liters of interstitial fluid is filtered each day and must be returned to the vascular system by the lymphatic system.

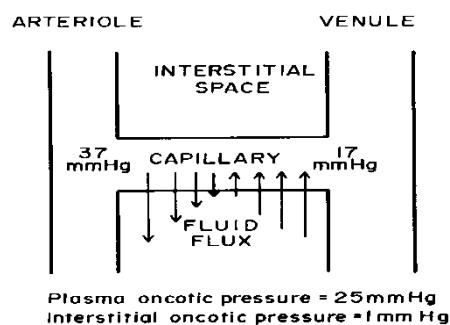


Figure 1. Fluid flux across the capillary is dependent on the net hydrostatic and oncotic pressure gradient. This is positive near the arteriolar end leading to outflow of fluid and negative near the venular end, where most of the fluid returns to the capillary lumen.

Net efflux normally exceeds net influx, and this extra fluid returns to the circulation by way of the lymphatics. Normal lymph flow is 2 to 4 liters per day. The rate of flow is greatly influenced by a number of local and systemic factors, including protein concentration in plasma and interstitial fluid, local arterial and venous pressure relationships, and capillary pore size and integrity.

Lymphatic transport may become deficient when lymphatic vessels are absent, hypoplastic, or obstructed. This impairment of lymphatic flow may be **congenital**, as in lymphatic dysplasias, or **acquired** when lymphatics become obstructed as a result of disease or surgical extirpation.

CLINICAL EVALUATION OF THE SWOLLEN EXTREMITY

Extremity swelling may be due to a

- **systemic disorders that cause extremity edema** include
 1. right-sided heart failure
 2. constrictive pericarditis
 3. renal diseases
 4. liver cirrhosis

5. hypoproteinemia
 - acute or chronic obstruction in the venous system
 - abnormality of the lymphatic system.
 - **acquired or congenital arteriovenous fistula**
 - occasionally, **allergic disorders**.

The **clinical appearance of lymphedema** is *variable* and depends on the severity and duration of the syndrome.

⊗ **Initially**, protein-rich fluid accumulates in the affected tissues. Typically, this **swelling is soft and pits easily** with pressure. This early edema is **often responsive to elevation and may decrease or disappear entirely** with elevation of the limb. This type of swelling **typically involves the distal aspect of the extremity** and characteristically involves the **dorsum of the foot and toes**, which may help distinguish it from edema due to venous obstruction.

⊗ **Over a period of years**, the edema becomes **woody in texture** because the presence of the protein-rich fluid incites an **inflammatory fibrosis**, and **pitting becomes less prominent**. Limb elevation and compression with elastic garments then are much less successful at reducing the extremity volume. The **skin becomes thickened, hypertrophic, and hyperkeratotic**. The eczema and ulceration seen in venous disease are not characteristic of swelling due to lymphedema. Approximately half of patients with lymphedema experience **recurrent spontaneous attacks of bacterial cellulitis**. These episodes are characterized by increased swelling due to local inflammation, pain, and high fever. This increased susceptibility to bacterial infection is believed to be related to loss of local immune defenses because of diminished lymphatic function.

Classification of Lymphedema

PRIMARY LYMPHEDEMA

are relatively common, occurring at a rate of 1 in 10,000, and are classified by age at the onset of symptoms.

- **Lymphedema congenita** is a **severe** form of lymphedema that is **usually apparent at birth** or becomes so during early infancy. This condition most often involves the lower extremity, and **the right side is affected more** commonly than the left. However, in 25% of cases the condition is bilateral. In a few cases there is a familial history, termed **Milroy's disease**. Many of these patients, however, have associated lymphatic abnormalities, including ◆involvement of the external genitalia, ◆intestinal lymphangiectasia with protein-losing enteropathy, ◆cystic hygroma in the neck, and ◆pulmonary lymphangiectasia.
- **Lymphedema praecox** is the **most common** form of primary lymphedema, accounting for more than 80% of the cases. In this form of the disease, swelling begins about the time of **puberty**. There is a **3:1 female predominance**. Why swelling does not begin until adolescence is unclear. One hypothesis suggests that the lymphatic transport is marginally adequate at birth but decompensates with the increased demands associated with growth at the time of puberty. This disease usually involves the lower extremities only.
- **Lymphedema tarda** refers to **lymphedema that does not appear until the third or fourth decade**. Approximately half of these are associated with an inciting event, such as infection and injury.

SECONDARY LYMPHEDEMA

Secondary lymphedema due to acquired lymphatic obstruction is commonly seen in surgical patients.

The causes of acquired lymphatic obstruction are

- ◆infiltration of regional nodes by tumor
- ◆surgical excision of regional nodes in treatment for malignancy
- ◆fibrosis after infectious or inflammatory processes or radiation.

The most common tumors infiltrating lymph nodes causing lymphatic obstruction are carcinoma of the prostate in men and lymphoma in women.

In Western countries, perhaps the most common cause of secondary lymphedema occurs in the arm after surgical excision of lymph nodes for carcinoma of the breast followed by axillary and chest wall radiation therapy.

In tropical countries, **infestation by filaria** is the most frequent cause of secondary lymphedema.

Radiographic Evaluation

The classic method of radiographic evaluation of the swollen extremity includes

✕ **lymphangiography**. The **absence of a cannulatable lymphatic vessel after subcutaneous injection of dye is considered evidence of lymphatic hypoplasia or aplasia**.

✂ **Lymphoscintigraphy** This technique is relatively noninvasive, and serial examinations can be obtained without significant risks or patient discomfort. Excellent sensitivity and specificity have been reported using this technique.

✂ **Magnetic resonance imaging** One advantage of magnetic resonance imaging is that it demonstrates lymph trunks, lymph nodes, and soft tissues proximal to sites of lymphatic obstruction .

Analysis of Tissue Fluid

Characteristically, lymphedema fluid has a protein content of more than 1.5 g/dL, in contrast to that of edema fluid from venous hypertension, which usually is less. The ratio of albumin to globulin also is higher in lymphedema fluid than in plasma, which is helpful in the presence of an inflammatory exudate in which the protein content is high but the albumin-to-globulin ratio is normal.

TREATMENT OF LYMPHEDEMA

Nonoperative Therapy

Most patients with lymphedema can be managed with a program of

- **meticulous skin hygiene**
- **elastic support garments (compression garments)**
- **extremity elevation**
- **special massage techniques**
- **avoidance of local injury.**
- If cellulitis occurs, it should be treated promptly with effective antibiotics and bed rest with elevation of the involved extremity.
- the use of **benzopyrones** to reduce the formation of high-protein edema.

Surgical Therapy

Three surgical strategies have been used to treat severe disabling cases of lymphedema.

✂ Excision of the hypertrophic fibrotic subcutaneous tissues known as the **Charles operation** Or, relatively thick skin flaps can be mobilized in a staged fashion with excision of the underlying subcutaneous tissue, known as the **Kondoleon procedure**.

✂ **A second surgical strategy** involves the pedicle transfer of lymphatic-bearing tissue into the affected limb with the intention of creating spontaneous connections to the dysfunctional lymphatic channels in the swollen limb.

✂ **The third surgical approach** involves the **microvascular bypass** of obstructed lymphatic segments.

LYMPHATIC TUMORS AND MALFORMATIONS

Lymphangiomas. Lymphangiomas are congenital malformations of lymphatic vessels. More than half of these lesions are present at birth, and 90% are present by the end of the second year of life. The lesions usually grow slowly but may infiltrate the local tissues, although **malignant degeneration is rare**.

Three types of lymphangiomas have been described:

- (1) **lymphangioma simplex**, consisting of small capillary-sized lymphatic channels
- (2) **cavernous lymphangioma**, formed from dilated lymphatic channels, often with a fibrous capsule
- (3) **cystic hygroma**, a lymphatic malformation consisting of an endothelial-lined cyst, usually found in the neck or axilla. Because they form a disfiguring mass, many of **these lesions are treated by surgical excision with preservation of surrounding vital structures. Radiation therapy is ineffective**, as are attempts at injection of sclerosing solution.

Chylous Syndromes. Chyle is formed in the lacteals of the small intestine by absorption of the products of fat digestion. Chyle is normally transported to the cisterna chyli and then to the thoracic duct. Chyle may be found outside of the normal channels if there is an acquired or congenital obstruction of the thoracic duct or incompetence of the lymphatic valves. **Fistulization may occur into** the •peritoneal, •pleural, or •pericardial cavities.

Chylous ascites and chylothorax may respond to a ***medium-chain triglyceride diet**. Occasionally, ***direct suture closure of a chylous fistula** is indicated if conservative measures fail.

Lymphangiosarcoma. Lymphangiosarcoma is a **rare** lesion that may develop in a lymphedematous extremity regardless of the cause of the lymphedema. Malignant degeneration is more frequent in cases of secondary lymphedema. The lesion appears as **purple-red nodules in the skin**; it is an aggressive, rapidly fatal lesion.