



Lymphedema: An Overview

Here's a close look at this unappreciated circulatory system.

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What Is Lymphedema?

Lymphedema affects approximately 300 million people worldwide. Although parasitic filariasis is the most common cause affecting approximately 100 million people,¹ phlebolymphedema or secondary lymphedema due to long-standing chronic venous insufficiency (CVI) is the most common type seen in the United States.² Lymphedema occurs because of lymphatic system dysfunction that affects the body's ability to remove excess fluid from the extremities, or other organs. In addition, the lymphatic system is an immunological defense system that triggers the production of lymphocytes (natural killer cells, T cells, and B cells). The millions of channels of the system collect infecting micro-organisms and antigenic substances that find their way into the interstitium and transport them to the lymph nodes, where they are eliminated from the system or antibodies are produced that rapidly neutralize the offending agents.

Immunodeficiencies ensue when the lymphatic system is impaired, and lymphedema is present, allowing for infections and increased risk of malignancies and/or metastases.

Phlebolymphedema is a secondary lymphedema that develops in patients with chronic venous insufficiency (CVI). There are a number of factors that contribute to an increase in the incidence of lower extremity edema in the population. These include: increased survival of heart failure patients, numerous medications associated with edema, and the increased incidence of obesity. "With the aging of the baby boomers and

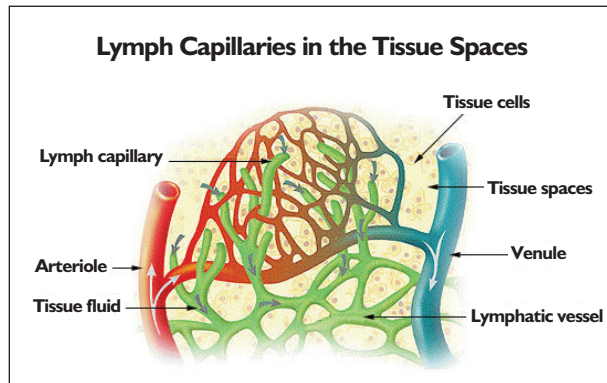


Figure 1: Lymph capillaries. Source: Wiki Commons

the lack of education of caregivers in proper treatment of lymphedema, the incidence will almost certainly increase in upcoming decades.²²

connection between the organs—also serve as a great reservoir of fluid and molecular substances that must be continually drained from the spaces. There is a vast system of delicate open-ended lymphatic capillaries and pre-collectors that passively receive these fluids (Figure 1). They actively move them from the periphery through lymphatic capillaries to the lymph nodes and larger lymphatic veins to a series of places along the venous system where the fluids re-enter the circulation, the largest of which is the thoracic duct (Figure 2). Fluid

Lymphedema occurs because of lymphatic system dysfunction that affects the body's ability to remove excess fluid from the extremities, or other organs.

Anatomy

The lymphatic system is made up of three primary components—the lymph fluid it transports, the transportation network, and the lymphatic organs. The system is an open-ended circulatory system that completes the closed system we are most familiar with. The closed system consists of the heart, arteries, arterioles, capillaries, venules, and veins. If this were all we had to transport nutrients and gather waste from the tissues, we would quickly die because the system is porous and fluid continually leaks out into the interstitial spaces. The myriad nooks and crannies in the connective tissues—the structural

movement is facilitated by a series of one-way valves and delicate muscles known as lymphangions.

The lymph nodes act as a filtration system to remove foreign materials and invading organisms from the blood and expose them to the immune cells, which mount an attack on the unwanted invaders. The nodes are part of an adaptive immune system where the B and T lymphocytes and other white blood cells recognize and engulf or produce antibodies to the substances. Aberrant cells such as cancer cells are also identified and engulfed, whereas toxins are passed on to the liver and kidneys that complete the

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removal process. Additional components of the system are the lymphatic organs (the spleen and the thymus), responsible for regulation of the blood components, and additional immune response and manufacture of T lymphocytes (Figure 3).

Pathophysiology of Lymphedema

When the normal lymphatic flow is disrupted, protein-rich fluid accumulates in the tissues, triggering a chronic inflammatory reaction that manifests itself in swelling of what the *NY Times* reported as the newest undiscovered organ, the interstitium.¹ White blood cells are attracted to the area by the presence of extracellular proteins, and release cytokines, calling other inflammatory cells to the area. The macrophages ingest foreign materials and microbes and use lysosomes containing free radicals, peroxide, and hypochlorous acid to denature proteins and oxidize cell membranes of invading organisms. The macrophages also release cytokines and activate fibroblasts, which are stimulated to produce collagen scar tissue, resulting in fibrosclerosis of

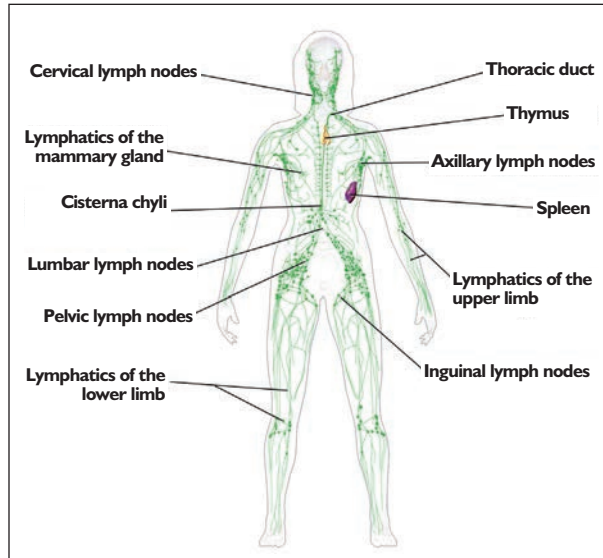


Figure 2: Lymph system. Source: Wiki Commons

the dermis and subcutaneous tissues. On a cellular level, this skin change interferes with antigen processing, stagnates immune cells, and in some regions impairs Langerhans cells and keratinocytes, resulting in a thickening of the tissues and a loss of skin barrier function.

Types of Lymphedema

Primary lymphedema can be described as a hereditary or congenital disorder, affecting females more than males, associated with impaired lymphatic vessel development and resulting in lymphedema. Primary lymphedema can be divided into three forms depending upon age of onset: congenital lymphedema (at birth), lymphedema praecox (1-35), and lymphedema tarda (35+).⁴ Some of the conditions associated with congenital lymphedema include: Meige disease, Milroy's disease, Aagaens syndrome, and Turner syndrome.

Secondary lymphedema is caused by an acquired impairment of the lymphatic system due to several causes: cancer and its treatment, infection, inflammatory disorders, obesity, long standing venous insufficiency (phlebolymphedema) and other chronic forms of lymphatic overload.^{2,5-7}

Causes of Secondary Lymphedema

Cancer-associated lymphedema arises as a result of obstructed or infiltrated lymphatic channels or nodes, lymphadenectomy, regional lymph node irradiation, or the adverse effects of some medications.^{5,8} The most common cancer associated with lymphedema is breast cancer secondary to lymphadenectomy of the axillary nodes.⁹⁻¹⁰ The manifestations of lymphedema usually appear within one to five years of the surgery.¹¹ Cancers associated with lymphedema include sarcoma, lower extremity melanoma, cervical, Hodgkin's lymphoma, and prostate.⁹ The addition of radiation to lymphadenectomy exponentially increases the risk of lymphedema compared to lymphadenectomy alone. In breast cancer treatment, lymphadenectomy and adjuvant radiation have an approximately 24% increased rate of lymphedema compared to lymphadenectomy alone.¹²

Parasitic infections such as lymphatic filariasis, and skin infections such as cellulitis and erysipelas can lead to the development of lower extremity lymphedema. *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori* are parasitic roundworms endemic to Africa, Southeast Asia and Eastern South America that enter the body in a larval stage when the host is bitten by a carrier mosquito. The adult nematodes mature in the lymphatic channels and lymph nodes, producing a devastating lymphatic elephantiasis in the affected limb. It is usually acquired in tropical and subtropical territories during one's childhood but can be asymptomatic in those younger than five years old.¹³

In the United States, elephantiasis from parasites is very rare but repetitive cellulitis from multiple insect bites from an infestation of mosquitoes or fleas may in rare cases produce an inflammatory secondary lymphedema similar in appearance to elephantiasis. In pa-

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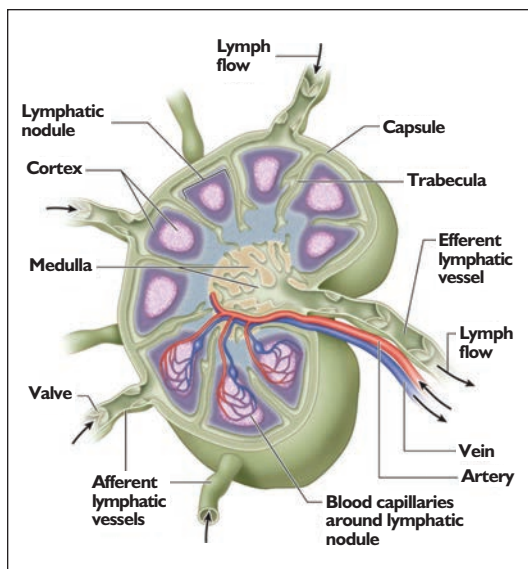


Figure 3: Lymph node. Source: www.anatomynote.com Used with permission, 2018



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tients with chronic lymphedema or in the later stages of venous insufficiency, there is an increased risk for recurrent cellulitis and erysipelas infections. Cellulitis is a common complication in those who have undergone inguinal lymphadenectomy and have developed subsequent lower extremity lymphedema. Cellulitis can also be a risk factor for the onset and progression of lymphedema in patients with chronic venous insufficiency.

Simple uncomplicated lymphedema is due to a mechanical failure of the lymphatic system that results in a low flow state. Pathological processes have reduced the ability of the lymphatic system to move fluid efficiently from the extremities to the thoracic duct. The system can no longer manage the normal lymphatic load, resulting in a backup or overload of the interstitium. When the ambient pressure in the interstitial tissues is increased, movement of fluid into the fragile lymphatic collectors decreases and serious swelling can ensue. An example of this is a patient with phlebolymphe-
 ma due to chronic venous insufficiency who develops an infection from an ulcer or traumatic wound of the lower extremity.

The inflammatory response to the infection initially results in the production of a vasodilatory transudate followed by a protein-rich exudate that overwhelms the system, producing a pathohistological state of chronic inflammation, with infiltration by mononuclear cells, stimulation of angiogenesis, and proliferation of connective tissue with fibrosis and fibrosclerosis of the skin.¹⁴ This alone is reason for patients with edema to practice diligent skin care to prevent epidermal disruption and secondary infection. The more infections, the more immune deficiency, and the more significant the changes in skin morphology.

Whether the entire limb is involved or just a small area of a more transient nature, lymphedematous regions are highly prone to infections because of a local immune deficiency caused by many factors. Immune cells passing through regions affected by fluid stagnation become sluggish and find it hard to migrate through the thick web of scar tissue produced by overstimulated fibroblasts. Lymph nodes in the area likewise become overwhelmed with protein-rich edema interfering with antigen and microbe processing. Skin function is impaired, resulting in a loss of normal barrier function provided by the intricate web of lymphatic collectors just below the skin and the Langerhans cells and keratinocytes.

In addition, areas of congestion have impaired processing of malignant or abnormal cells and are more prone to malignancy. This is referred to as lymphostatic immunopathy and produces a region with low resis-



Figure 4: Lymphostatic Dermopathy

tance to infection and inflammation, and an increased risk of carcinogenesis. Prolonged lymphostasis leads to a state of chronic localized inflammation. Another term, lymphostatic dermopathy, refers to the changes in the skin that result in a failure of the skin as an immune organ (Figure 4).¹⁵

Signs and Symptoms

Lymphedema is assessed using several staging systems, the most popular of which is the International Society of Lymphology (ISL). ISL staging uses two criteria to diagnose and classify lymphedema. There is a softness scale and one noting changes after elevation. The first evaluates the degree (mild, moderate, severe) of fibrotic soft tissue change and the second the presence of volume change with elevation. Stage 0 is a sub-clinical or latent condition where swelling is not evident despite impaired lymphatic transport. Stage 0 may exist for months or years before lymphedema occurs. Stage I lymphedema or reversible edema is character-

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ized by the accumulation of fluid during standing and ambulation that subsides with limb elevation. Pitting edema with no evidence of dermal fibrosis may be present. Stage II does not resolve with elevation alone.

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As limb fibrosis progresses, pitting disappears. Stage III lymphedema is characterized by lymphostatic elephantiasis. Pitting is absent, and the skin has noticeable skin changes that include fatty deposition, acanthosis, and warty overgrowths.¹⁶

Visible skin changes and signs are also the basis for the classification of chronic venous insufficiency using the CEAP classification (Clinical, Etiologic, Anatomic Pathologic) developed by the American Venous Forum.¹⁷ Although the entire classification is a bit complicated, the clinical portion is quite useful when evaluating the skin lesions associated with developing venous insufficiency and phlebolymphe-
dema:

C0: no visible or palpable signs of venous disease.

C1: telangiectasies or reticular veins.

C2: varicose veins.

C3: edema.



Figure 5: Lichenification Secondary to Phlebolymphe-
dema

C4a: pigmentation and eczema.

C4b: lipodermatosclerosis and atrophie blanche.

C5: healed venous ulcer.

C6: active venous ulcer.

The remaining elements of the classification are: an S or A delineation used for whether the skin lesions are symptomatic or asymptomatic; etiology includes Ec congenital, Ep primary, or Es secondary; the anatomical portion, s,p,d localizes pathology to superficial, perforators, or deep veins; and the pathological portion includes Pr reflux, Po obstruction, Pr,o reflux and obstruction, and Pn no venous pathophysiology identifiable.

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Skin Changes

Phlebolymphe-
dema develops slowly and worsens over time. The swelling is not typically painful with the severity of involvement marked by skin changes in thickness, texture, and shape. This skin change occurs secondary to the chronic inflammatory response to the protein-rich interstitium and an overgrown stratum corneum. The fibrotic proliferation causes hyperkeratosis, papillomatosis, and lichenification. Hyperkeratosis presents as a scaly brown/gray patch of over-proliferated keratin. Papillomatosis is lumpy, bumpy skin or fibrotic wart-like projections of the skin. Lichenification presents as thick, leathery patches of skin that occur in response to excessive itching or rubbing, resembling alligator skin or tree bark (Figure 5).

The epidermis can be xerot-



Figure 6: Lichenification with Warty Projections and Lymphorrhea

ic or macerated depending on the presence of open lesions. When the epidermis is xerotic, there is a decreased resistance to infectious organisms. When the epidermis is

macerated or broken by small areas of skin, breakdown referred to as dermal disruption or venous dermatitis, lymphorrhea or weeping of lymphatic fluid through skin, can occur (Figure 6).

While lymphorrhea is common, skin ulcers are not commonly associated with primary lymphedema but are much more common when lymphedema is secondary to chronic venous insufficiency (phlebolymphe-
dema). Unlike fluid edema, lymphedema affects the digits and the resultant brawny fibrotic edema makes it difficult to pinch or tent the skin over the dorsum of the proximal phalanx of the digits of the foot, a clinical sign known as the Stemmer's sign. Those with a positive Stemmer's sign have edematous legs with square shaped toes, deep creases and folds, fibrotic tissue, and a lack of limb contours (Figure 7).

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Diagnosis

When evaluating a patient for lymphedema, there are several components of history that should be obtained: age of onset, areas of involvement, associated symptoms and their progression, past medical history such as cancer and genetic abnormalities, surgical history, travel history, and family history. Associated symptoms would include swelling, pain, and tightness. Unilateral lower extremity swelling can be seen in patients who have undergone inguinal lymphadenectomy. The swelling may initially present in just a portion of the distal limb. As the swelling progresses, there may be a decrease in range of motion and activities of daily living.

During the physical exam, you should always evaluate the arterial vascular system to be sure there is no inflow problem complicating outflow. Pitting is variable and may be present in early stages of lymphedema and is generally absent in advanced disease. It should be noted at this point that lymphatic edemas always affect both the leg and the foot. When you see an enlarged leg that appears to be lymphedema but spares the foot, which appears normal, you are dealing with lipedema. Lipedema and Lymphedema may sound alike but are very different. They both cause non-pitting edema in the lower extremity, occur bilaterally and sym-



Figure 7: Positive Stemmers Sign

metrically, and affect women primarily.

Lipedema is an X-linked or autosomal dominant condition characterized by progressive leg edema secondary to fatty deposition. Lipedema is painful, can be complicated by orthostatic edema and bruising, and generally does not improve with leg elevation.²⁷ Brawny or fibrotic edema is a classic sign of advanced lymphedema.^{1,10}

Diagnostic Imaging

The imaging modality of choice is the duplex ultrasound which can help indicate the underlying

etiology of edema, lymphatic compression, tissue variations, and even the presence of parasites. Duplex US scans also help confirm the existence of chronic venous insufficiency and DVT. Computed tomography and magnetic resonance imaging allow one to visualize the accumulation of lymphatic fluid in soft tissue and can be used to detect venous disease of the lower extremity and is considered to be highly sensitive and specific (Figure 8).¹⁸

Lymph vessels and nodes can be further evaluated via: lymphangiography, isotopic lymphoscintigraphy, and indocyanine-Green (ICG) lymphography. Lymphangiography allows for visualization of the content of the lymphatic system using a radiocontrast agent. Isotopic lymphoscintigraphy involves radio-labeled proteins to detect lymph flow, lymph nodes, and lymph reflux. This test is performed during a period of time lasting from 30 minutes to 2 hours,

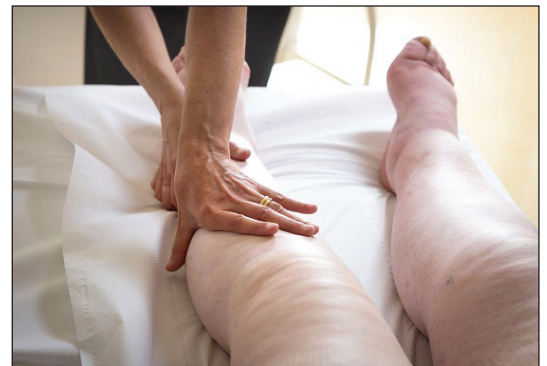


Figure 9: Manual Lymphatic Massage. Source: Alpha Health Services, Toronto, ON. Used with permission, 2018

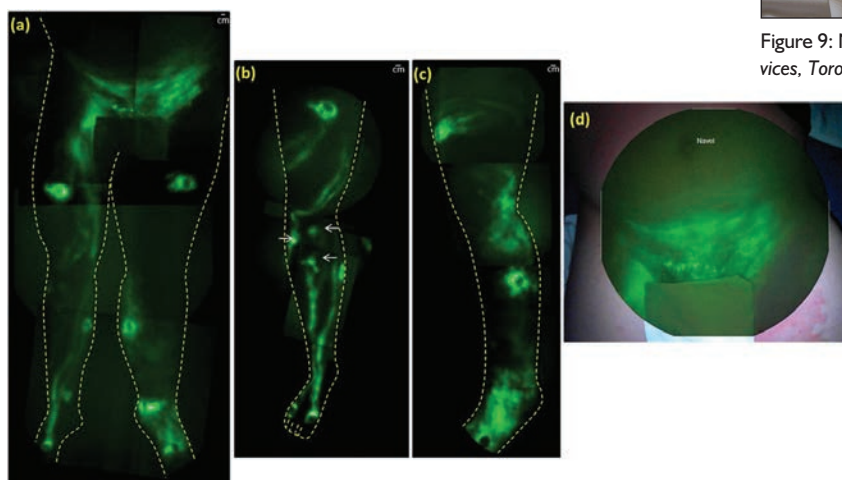


Figure 8: NIRFLI montage of right (unaffected) and left (affected) limbs. Source: Eva M Sevick, PhD, In Burrows, P. E., Gonzalez-Garay, M. L., Rasmussen, J. C., Aldrich, M. B., Guillod, R., Maus, E. A., ... & Sevick-Muraca, E. M. (2013). Lymphatic abnormalities are associated with RASA1 gene mutations in mouse and man. *Proceedings of the National Academy of Sciences*, 110(21), 8621-8626. Used with permission, 2018

and before and after stress activity. Isotopic lymphoscintigraphy is a test that is used to evaluate congenital lymphedema. Near-Infrared Fluorescence Lymphatic Imaging (NIRFLI) is a technique using an indocyanine green (ICG) dye and near-infrared red fluorescence to visualize lymphatic vessel anatomy, functional capacity, and dermal reflux. ICG lymphography can be used to see abnormalities prior to the presence of significant swelling (Figure 8). Near-Infrared Fluorescence Lymphatic Imaging (NIRFLI).^{1,19-20}

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Lymphangiography

Simple assessment of approximate limb volume can be obtained by serial measurements of the lower extremity limb circumference bilaterally. According to the American Physical Therapists Association, you should take limb circumference measurements at the metatarsal-phalangeal joints, 2 cm superior to the medial malleolus, 10 cm below the inferior pole of the patella, and 10 cm above the superior pole of the

ciated with an abnormal psychological component.

Several systemic conditions, if chronic, are associated with bilateral pitting edema that may lead to lymphedema. These include: hepatic insufficiency, renal failure, cardiac decompensation (CHF), and thyroid disorders.

Conservative Treatment

Lymphedema is an “orphan” disease with no one medical specialty taking up the cause.²⁸ Most patients are treated by specially trained physi-

Anasarca is general massive swelling of the whole body due to abnormal fluid retention in major sickness and infection

patella.²¹ Actual limb volume can be measured by determining water displacement, optoelectronic volumetry, and by using a truncated cone calculation. Water displacement has been the gold standard to measure limb volume but is considered to be too inconvenient to be used often today. When using water displacement, a limb volume difference of at least 200mL between opposing limbs indicates lymphedema.²²⁻²³ Perometry uses infrared beams to scan the limb and calculate its volume. Perometry is more reliable than the water displacement.²⁴⁻²⁵ To use the truncated cone formula, the lower extremity limb is measured at 4 cm intervals starting from the ankle and an estimated volume is calculated.²⁶

Differential Diagnosis

Anasarca is general massive swelling of the whole body due to abnormal fluid retention in major sickness and infection. Anasarca is most commonly seen with heart failure and pericardial diseases, or systemic allergic reactions.

Factitious lymphedema is a condition that is self-induced by applications of tourniquets, tight clothing, self-inflicted wounds that result in cellulitis, or maintenance of the limb in a prolonged immobile dependent state. This condition is usually asso-

ciated with an abnormal psychological component. Several systemic conditions, if chronic, are associated with bilateral pitting edema that may lead to lymphedema. These include: hepatic insufficiency, renal failure, cardiac decompensation (CHF), and thyroid disorders. Most patients are treated by specially trained physical therapists who have received certification in manual lymph drainage (MLD), which is part of a total approach referred to as complete decongestive therapy (CDT). The ultimate goals are to reduce build-up and edema in lymphatic tissues, reduce limb size, and get the patient on a maintenance program that controls what is a life-long problem. Physicians who understand the disease and are well trained in the medical and physical management of it are sorely needed.¹⁶⁻²⁹

The primary treatment approach is CDT, which includes compression wraps, garments, and pneumatic pumps to maintain the gains achieved in therapy. Complete decongestive therapy is performed by a physical therapist or lymphedema therapist and requires many hours of training in the techniques of exercise and MLD (Figure 10). Manual Lymph Drainage).¹⁶⁻²⁹

Exercise improves venous return, lymphatic drainage, range of motion, relieves tightness, and improves strength of ligaments, tendons, and bones. It is recommended that patients with lymphedema not participate in any sports due to the risk of trauma to the skin and the inability of the limb to recover from activity-induced swelling.³⁰ Exercise

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can be used to control body weight if done in conjunction with a diet of restricted calories and avoidance of excessive salt and water.

Manual Lymphatic Drainage Uses

Manual lymphatic drainage uses gentle skin massage with specific strokes and light pressure to promote the movement of lymph from areas of stagnation to areas of normal flow (Figure 9). Facilitated by modern imaging studies, MLD can reduce limb volume significantly. Treatment gains are maintained by the application of short stretch wraps that prevent rebound edema between treatments.

Compression wraps are more effective in treating venous insufficiency and phlebolymphedema. Standard compression systems can be applied to those with an ABI of at least 0.8 but reduced compression can be applied to those with an ABI between 0.5–0.8 with careful supervision and frequent dressing changes.

There are three types of wraps for lower extremity edema: non-stretch, short-stretch, and long stretch. They all facilitate the foot-calf muscle pump during ambulation. Non-stretch compression is dependent on the foot-calf muscle pump during ambulation and does not provide any resting pressure, making it essentially a retention wrap when sedentary. Short stretch wraps also utilize the calf muscle pump during ambulation but recoil slightly to provide some resting pressure and to accommodate the limb as edema decreases.

Long stretch wraps work with both the mobile and immobile patient but can be risky for those with PAD. The compression can be applied via single or multilayer wraps, with multilayer wraps demonstrating a slight edge in effectiveness. The Cochrane review of 48 RCTs reporting 59 comparisons (4,321 participants in total) concluded that: some compression is better than none; single component compression bandage systems are less effective than multi-component compression; two and three layer systems containing an elastic bandage healed more ulcers at one year than one without

an elastic component; and five RCTs suggested significantly faster healing with four layers than with short stretch bandages.³¹

On the other hand, in a comparison of elastic and inelastic dressings, Mosti, et al. found that inelastic ban-

proximally with decreasing pressures as it approaches the knee or groin. Each segment fills and holds pressure, and then the garment deflates, and the cycle begins again. The peristaltic waveform mimics the peristaltic action of the intestines. Distal segments

contract just like the sequential devices but as the pressure progresses proximally, the distal segments release, producing a massaging effect to the limb.

The key to effective devices are the numbers of segments and the versatility of the system to dial in specific pressures for individual segments based on need and areas of pain. More recently, devices have been engineered to better address lymphedema. These devices operate at a lower pressure and mimic the gentle massaging strokes of CDT. Indications for pneumatic compression include: venous disease,

chronic or transient edema, stasis and/or VLUs, phlebolymphedema, lymphedema, and arterial disease complicated by edema.

Conventional treatment for lymphedema does not recommend using pneumatic compression because it was felt that pumping does not remove plasma proteins or exudate from edematous areas but only removes free fluid or transudate. Recent studies have shown that protein removal by the lymphatic system is facilitated by using the segmental compression pumps. There can be higher levels of protein seen initially with pump use because of the amount of water processed using the pump. This is a temporary condition and with continued use of the pump, the protein levels also decrease and return to more normal levels.³⁴

Surgical Treatment

Surgical procedures have a common goal of bypassing the occluded lymphatic channels and/or nodes. These surgical options tend to be more effective in those with secondary lymphedema than primary lymphedema. Direct methods such as lympho-lymphatic or lympho-venous bypass anastomoses are constructed

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Figure 10: Intermittent Pneumatic Compression Pumps.

Source: Acute Wound Care—Wound Care Supplies & Compression Devices, Bonita Springs, FL. Used with permission, 2018

dages had an overall massaging effect and increased ejection fraction and ejection volume more than elastic bandages and were better tolerated by patients.³² Hofman, et al. found that bandage systems that deliver high working pressures and lower resting pressures (short stretch and non-stretch) have a better therapeutic effect even in mixed venous arterial disease.³³

Intermittent Pneumatic Compression Pumps

Intermittent pneumatic compression therapy is externally applied compression delivered to the extremity(ies), and possibly torso, by means of segmented pressurized sleeves (garments) (Figure 10). The devices use prescribed air pressures and pre-determined timing sequences in order to mobilize free fluid in an edematous limb.

The various waveforms or sequential patterns are used to encourage proximal migration of free transudate and exudate into the lymphatic and venous systems to facilitate a reduction of limb edema and improve small vessel blood flow. Two common waveforms are sequential and peristaltic. Sequential compression begins with higher pressure compression in the distal segments and proceeds



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between normal distal lymph nodes or channels and proximal lymph nodes or channels or to a vein to prevent lymphatic reflux. Lympho-venous bypass anastomosis is more common. If lympho-venous bypass is not possible, lympho-venous-lymphatic anastomosis is done.³⁴⁻³⁷

Free lymph node transplantation is an indirect method but has not been established as an effective procedure.³⁸⁻³⁹ Debulking procedures allow for the removal of edematous tissues but may cause rebound edema and or expanding fibrosis due to the scarring associated from the procedure.⁴⁰ Liposuction removes excess fat in areas of lymphedema, reducing limb size but does not address the underlying lymphatic obstruction and in many cases may actually make the problem worse.⁴¹

to decrease limb volume in lymphedema patients and the occurrence of infections in cancer patients.⁴²

Autologous lymphocyte injection immunotherapy has been shown to decrease excess protein levels in interstitial tissues. In patients with primary lymphedema, gene therapy is currently being explored. In a clinical study using model rats with breast cancer, lymph vessel neogenesis occurred via the release of hepatocyte growth factor, while at the same time maintaining motor ability of lymph vessels.⁴²

Physicians are only now becoming aware of the importance of the lymphatic system to limb health and homeostasis. The relationship of lymphatic function to wound healing and recovery after surgery or injury cannot be overstated. More education programs are picking up the banner for increased basic education for

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Autologous lymphocyte injection immunotherapy has been shown to decrease excess protein levels in interstitial tissues.

Medical Treatment

Prescription medication is available to decrease edematous extremities. Diuretics are not indicated for the treatment of lymphedema except for short periods of time in cases where the edema is due to hypertension or heart disease as they stimulate water excretion as urine. Because diuretics remove the free transudate from the limb and leave a concentrated protein rich exudate behind, a rebound edema increase may be noted. Benzopyrones, such as coumarin and flavonoids, promote edematous fluid resorption but can have the adverse effect of hepatopathy. Anti-microbials, including Ivermectin and Diethylcarbamazine citrate, are indicated if there is an underlying infection causing inflammation in the limbs and based on elevated hematological inflammatory markers and classic signs of infection. Sodium selenium therapy can be used as a non-toxic anti-inflammatory therapy and has been shown

health professionals and improved healthcare coverage for a highly under-funded and under-served public health problem. There is a dire need for more lymphedema therapists, and there is a great need for podiatric physicians educated in lymphatic function and treatment to address the problems of wound and skin care, mobility issues, and shoe fit problems. With many healthcare markets shrinking, this is one area where podiatric involvement has significant upside potential. **PM**

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