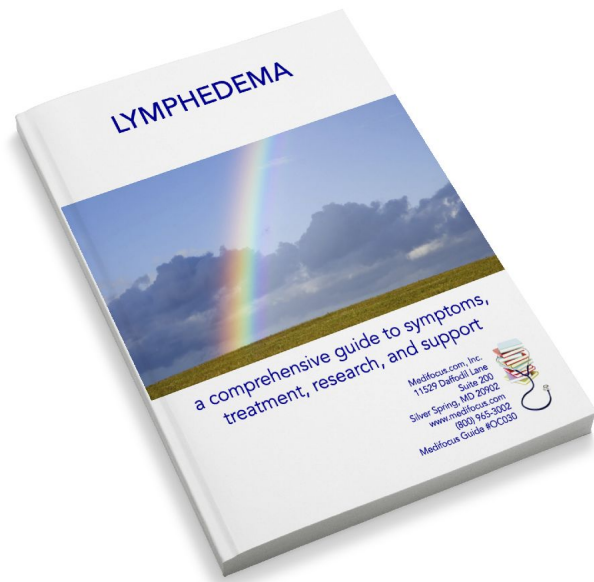


Preview of the Medifocus Guidebook on: Lymphedema

Updated June 21, 2017



This document is only a SHORT PREVIEW of the **Medifocus Guidebook on Lymphedema**. It is intended primarily to give you a general overview of the **format and structure** of the Guidebook as well as select pages from each major Guidebook section listed in the Table of Contents.

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1 - Background Information

Introduction

Chronic or life-threatening illnesses can have a devastating impact on both the patient and the family. In today's new world of medicine, many consumers have come to realize that they are the ones who are primarily responsible for their own health care as well as for the health care of their loved ones.

When facing a chronic or life-threatening illness, you need to become an educated consumer in order to make an informed health care decision. Essentially that means finding out everything about the illness - the treatment options, the doctors, and the hospitals - so that you can become an educated health care consumer and make the tough decisions. In the past, consumers would go to a library and read everything available about a particular illness or medical condition. In today's world, many turn to the Internet for their medical information needs.

The first sites visited are usually the well known health "portals" or disease organizations and support groups which contain a general overview of the condition for the layperson. That's a good start but soon all of the basic information is exhausted and the need for more advanced information still exists. What are the latest "cutting-edge" treatment options? What are the results of the most up-to-date clinical trials? Who are the most notable experts? Where are the top-ranked medical institutions and hospitals?

The best source for authoritative medical information in the United States is the National Library of Medicine's medical database called PubMed®, that indexes citations and abstracts (brief summaries) of over 7 million articles from more than 3,800 medical journals published worldwide. PubMed® was developed for medical professionals and is the primary source utilized by health care providers for keeping up with the latest advances in clinical medicine.

A typical PubMed® search for a specific disease or condition, however, usually retrieves hundreds or even thousands of "hits" of journal article citations. That's an avalanche of information that needs to be evaluated and transformed into truly useful knowledge. What are the most relevant journal articles? Which ones apply to your specific situation? Which articles are considered to be the most authoritative - the ones your physician would rely on in making clinical decisions? This is where *Medifocus.com* provides an effective solution.

Medifocus.com has developed an extensive library of *MediFocus Guidebooks* covering a wide spectrum of chronic and life threatening diseases. Each *MediFocus Guidebook* is a

high quality, up- to-date digest of "professional-level" medical information consisting of the most relevant citations and abstracts of journal articles published in authoritative, trustworthy medical journals. This information represents the latest advances known to modern medicine for the treatment and management of the condition, including published results from clinical trials. Each *Guidebook* also includes a valuable index of leading authors and medical institutions as well as a directory of disease organizations and support groups. *MediFocus Guidebooks* are reviewed, revised and updated every 4-months to ensure that you receive the latest and most up-to-date information about the specific condition.

About Your MediFocus Guidebook

Introduction

Your *MediFocus Guidebook* is a valuable resource that represents a comprehensive synthesis of the most up-to-date, advanced medical information published about the condition in well-respected, trustworthy medical journals. It is the same type of professional-level information used by physicians and other health-care professionals to keep abreast of the latest developments in biomedical research and clinical medicine. The *Guidebook* is intended for patients who have a need for more advanced, in-depth medical information than is generally available to consumers from a variety of other resources. The primary goal of a *MediFocus Guidebook* is to educate patients and their families about their treatment options so that they can make informed health-care decisions and become active participants in the medical decision making process.

The *Guidebook* production process involves a team of experienced medical research professionals with vast experience in researching the published medical literature. This team approach to the development and production of the *MediFocus Guidebooks* is designed to ensure the accuracy, completeness, and clinical relevance of the information. The *Guidebook* is intended to serve as a basis for a more meaningful discussion between patients and their health-care providers in a joint effort to seek the most appropriate course of treatment for the disease.

Guidebook Organization and Content

Section 1 - Background Information

This section provides detailed information about the organization and content of the *Guidebook* including tips and suggestions for conducting additional research about the condition.

Section 2 - The Intelligent Patient Overview

This section of your *MediFocus Guidebook* represents a detailed overview of the disease or condition specifically written from the patient's perspective. It is designed to satisfy the basic informational needs of consumers and their families who are confronted with the illness and are facing difficult choices. Important aspects which are addressed in "The Intelligent Patient" section include:

- The etiology or cause of the disease
- Signs and symptoms
- How the condition is diagnosed
- The current standard of care for the disease
- Treatment options

- New developments
- Important questions to ask your health care provider

Section 3 - Guide to the Medical Literature

This is a roadmap to important and up-to-date medical literature published about the condition from authoritative, trustworthy medical journals. This is the same information that is used by physicians and researchers to keep up with the latest developments and breakthroughs in clinical medicine and biomedical research. A broad spectrum of articles is included in each *MediFocus Guidebook* to provide information about standard treatments, treatment options, new clinical developments, and advances in research. To facilitate your review and analysis of this information, the articles are grouped by specific categories. A typical *MediFocus Guidebook* usually contains one or more of the following article groupings:

- *Review Articles*: Articles included in this category are broad in scope and are intended to provide the reader with a detailed overview of the condition including such important aspects as its cause, diagnosis, treatment, and new advances.
- *General Interest Articles*: These articles are broad in scope and contain supplementary information about the condition that may be of interest to select groups of patients.
- *Drug Therapy*: Articles that provide information about the effectiveness of specific drugs or other biological agents for the treatment of the condition.
- *Surgical Therapy*: Articles that provide information about specific surgical treatments for the condition.
- *Clinical Trials*: Articles in this category summarize studies which compare the safety and efficacy of a new, experimental treatment modality to currently available standard treatments for the condition. In many cases, clinical trials represent the latest advances in the field and may be considered as being on the "cutting edge" of medicine. Some of these experimental treatments may have already been incorporated into clinical practice.

The following information is provided for each of the articles referenced in this section of your *MediFocus Guidebook*:

- Article title
- Author Name(s)
- Institution where the study was done
- Journal reference (Volume, page numbers, year of publication)

- Link to Abstract (brief summary of the actual article)

Linking to Abstracts: Most of the medical journal articles referenced in this section of your *MediFocus Guidebook* include an abstract (brief summary of the actual article) that can be accessed online via the National Library of Medicine's PubMed® database. You can easily access the individual abstracts online via PubMed® from the "electronic" format of your *MediFocus Guidebook* by clicking on the corresponding URL address that is provided for each cited article. If you purchased a printed copy of a *MediFocus Guidebook*, you can still access the article abstracts online by entering the individual URL address for a particular article into your web browser.

Section 4 - Centers of Research

We've compiled a unique directory of doctors, researchers, medical centers, and research institutions with specialized research interest, and in many cases, clinical expertise in the management of the specific medical condition. The "Centers of Research" directory is a valuable resource for quickly identifying and locating leading medical authorities and medical institutions within the United States and other countries that are considered to be at the forefront in clinical research and treatment of the condition.

Inclusion of the names of specific doctors, researchers, hospitals, medical centers, or research institutions in this *Guidebook* does not imply endorsement by Medifocus.com, Inc. or any of its affiliates. Consumers are encouraged to conduct additional research to identify health-care professionals, hospitals, and medical institutions with expertise in providing specific medical advice, guidance, and treatment for this condition.

Section 5 - Tips on Finding and Choosing a Doctor

One of the most important decisions confronting patients who have been diagnosed with a serious medical condition is finding and choosing a qualified physician who will deliver high-level, quality medical care in accordance with currently accepted guidelines and standards of care. Finding the "best" doctor to manage your condition, however, can be a frustrating and time-consuming experience unless you know what you are looking for and how to go about finding it. This section of your *Guidebook* offers important tips for how to find physicians as well as suggestions for how to make informed choices about choosing a doctor who is right for you.

Section 6 - Directory of Organizations

This section of your *Guidebook* is a directory of select disease organizations and support groups that are in the business of helping patients and their families by providing access to information, resources, and services. Many of these organizations can answer your questions, enable you to network with other patients, and help you find a doctor in your geographical area who specializes in managing your condition.

2 - The Intelligent Patient Overview

LYMPHEDEMA

Introduction to Lymphedema

Lymphedema is a chronic, debilitating condition in which fluid called lymph, which circulates throughout the body through the lymphatic system, accumulates in body tissue and causes swelling. The limbs most commonly affected are arms and legs, although lymphedema can occur in the trunk, breast, neck, back, and shoulders. The extent of swelling in the affected limb ranges from mild (almost imperceptible swelling) to severe (massive, disfiguring swelling).

What is the Lymphatic System?

The human body contains two circulatory systems that work together to serve very critical functions:

- The *cardiovascular system* consists of the blood, blood vessels, and heart. Blood delivers oxygen, nutrients, hormones and antibodies to all parts of the body and carries away waste materials. The heart continuously pumps the blood through the cardiovascular system (arteries, veins, and capillaries) so that blood circulation continues without any interruption.
- The *lymphatic system* consists of a network of lymph nodes (dense tissue clusters that filter lymph fluid), and lymphatic vessels (valved structures that carry lymph fluid), that are found throughout the body, in tissue, and in organs (including bone marrow, spleen, thymus gland, tonsils, appendix). This complex network of interconnected vessels drains and filters fluid called "lymph" from tissue throughout the body and delivers it into the blood circulatory system via entry points into the subclavian vein (under the collarbone). The walls of lymph vessels are thinner than those of veins. Some are found close to the surface of the skin while others course through deeper fatty tissue. The lymph system also contains specialized cells called *lymphocytes* that help the body fight infection.

While each of these systems carry out life-sustaining functions separately, together they maintain *homeostasis*, the balance of fluids in the body necessary to sustain life.

There are several components of the lymphatic system, including:

- *Lymph* - a clear or straw-colored liquid consisting of water, large-molecule proteins, salts, and waste products (e.g., dead cells) collected from surrounding tissue.
- *Lymphatic capillaries* - very small vessels located under the skin which are the first points of collection for lymph.

- *Pre-collector vessels* - these vessels are larger in diameter than lymphatic capillaries and are located deeper in the tissue.
- *Collector vessels* - larger than pre-collector vessels, these are located quite deep in the tissue.
- *Lymph nodes* - dense clusters of tissue that filter lymph, lymph nodes are located primarily in the neck region, the armpits, and the groin.
- *Lymph ducts* - the largest diameter vessels of which there are two, the *thoracic duct* and the *right lymphatic duct*, that drain the lymph into the left and right subclavian veins (under the collarbone).

While the circulatory system is based on the constant pumping action of the heart, the lymphatic system depends on more subtle factors to achieve constant drainage, including:

- Pressure changes within the tissue which propel the lymph into draining vessels
- Smooth muscle within the walls of the larger lymphatic pre-collector and collector vessels that contracts and pushes the lymph forward
- Contractions of surrounding structures, such as arteries and muscles, which compress lymph vessels and propel fluid forward

Valves in the lymph vessels and contraction of muscles in surrounding tissue help move the fluid towards the larger collector vessels. Each section of collector vessels is called a *lymphangion* and fluid is propelled through each lymphangion until it reaches a lymph node.

Lymph nodes range in size from 1 mm up to 25 mm, or about the size of an almond. The outermost layer of the lymph node consists of densely packed lymphocytes (white blood cells) which activate the immune system, if needed. There are approximately 600 lymph nodes scattered throughout the trunk of the body, with some situated very deep in the tissue and others lying more superficially. Lymph nodes are located primarily in the neck region (cervical nodes), the armpits (axillary nodes), and groin area (inguinal nodes). Some stand individually while others are grouped into clusters.

The two primary roles of the lymphatic system are:

- **Homeostasis** - The lymphatic system plays an important role in maintaining fluid balance of the body (homeostasis) by filtering, collecting, and transporting excess lymph fluid that contains proteins, lymphocytes, salts, surplus fats, and other byproducts of cell metabolism, from the tissue into the circulatory system. The circulatory system then distributes or removes the excess liquid and waste components from the body.
- **Fighting infection** - The lymphatic system protects and defends the body from invasion by foreign microorganisms such as bacteria, fungi, and viruses. If these microorganisms invade the body, they eventually enter the lymphatic system which serves as a large "sieve" to trap, destroy, and eliminate the foreign invaders that can cause infections. Specialized white blood cells called *lymphocytes*, located within the chain of lymph nodes throughout the body, are responsible for mobilizing the immune system to defend and fight off infectious foreign microorganisms.

How Does the Lymphatic System Work?

The lymphatic system is a one-directional system wherein fluid is drained from tissue and delivered to the subclavian veins for transport to the *vena cava* (a major blood vessel that returns blood to the heart) and re-entry into the circulatory system. Valves found in the lymph vessels prevent the fluid from reversing direction. The process begins when fluid from the blood in *arterial capillaries* (the smallest vessels in the arterial system) seeps into the *interstitial spaces* (spaces between cells and tissue) throughout the body and provides the surrounding cells with nutrients. Changes in pressure in the surrounding tissue forces most of the fluid (80-90%) and cellular waste products to be reabsorbed into the *venous* capillaries and transported back towards the heart. The remaining 10-20% is forced into the *lymphatic* capillaries, where it is propelled by valves and vessel contractions through a series of increasingly larger-diameter vessels, through the lymph nodes, and ultimately into the large subclavian veins which carry all the blood back to the heart.

Thus, through a complex system of pressure created by *filtration* (removal of waste byproducts of cell metabolism) and reabsorption, the interstitial fluid levels in body tissue are kept at a steady level. The continual deposit of fluid into the tissue from the arterial capillaries is balanced by the continual flow of interstitial fluid back into venous and lymphatic capillaries, thereby preventing fluid buildup in the tissue. Interruption of this delicate balance leads to collection of fluid in the tissue and is called *lymphedema*.

What is Lymphedema?

The term *edema* refers to the accumulation of an excessive amount of fluid in cells, tissues, or organs, and is clinically characterized by swelling. A variety of conditions can produce edema, including chronic venous insufficiency, infection, and trauma. *Lymphedema* is a progressive condition that occurs when the lymphatic transport system falls below the capacity needed to handle the fluids that normally leak from the blood vessels into the lymph system. The obstruction of lymphatic vessels leads to an accumulation of fluid and subsequent swelling of subcutaneous tissue. Any disease process that interferes with or disrupts the normal mechanical process by which the lymphatic system collects, filters, and returns lymph fluid back into the circulatory system can result in excessive accumulation of lymph fluid in the area affected by the blockage. Since the arterial capillaries continue to function normally and deliver fluid to the tissue, the volume of fluid in the tissue increases significantly until the venous capillaries are no longer able to compensate for the defective lymph vessels. At the point where 80% or more of drainage has been reduced, symptoms of lymphedema become apparent.

While the various known causes of lymphedema will be addressed more fully below, the most common form of lymphedema develops very slowly over time and may take many months or years to manifest and cause an individual to seek medical treatment. The earlier the diagnosis of lymphedema is established and treatment initiated, the lower the risk of developing a large, distorted limb and multiple skin changes.

Although lymphedema can develop in any area where the normal flow of lymph fluid has been interrupted, it is most commonly seen in the extremities, and almost always takes place at the most superficial level of lymph vessels, namely directly under the skin (subcutaneous). Lymphedema

can develop in the head or neck region, upper and lower extremities, chest, back, breast, body cavities, pelvic region, and genitals.

The severity of lymphedema ranges from mild (little swelling) to severe (massive swelling), which can be associated with life-threatening complications. Initially, individuals may notice that one limb is slightly larger than the other. Approximately 50% of individuals with mild lymphedema report feelings of heaviness or fullness in the affected limb. As the swelling progresses, it may become difficult to fit clothing or jewelry onto the affected limb. Eventually, the size and weight of the edematous limb may cause fatigue and feelings of embarrassment, which may have a significant impact on the quality of life. Maximal girth of the affected limb is usually reached within the first year of onset of symptoms.

Lymphedema differs from *edema*. Edema is a secondary symptom of an underlying medical condition that is the result of too much fluid being released from the capillaries into the tissue, overwhelming the *capacity* of the lymphatic system. In lymphedema, however, it is the lymphatic system itself which is compromised. The arterial capillaries continue to function normally and continue to release their fluid in the interstitial spaces, but that fluid is not being drained away from the site because of a "faulty" lymphatic system. Although compensatory mechanisms may develop at early stages of faulty drainage, at some point, the increasing lymph load becomes too great it to be effective. This is why lymphedema may be latent for many years before the symptoms become evident.

If lymphedema is left untreated, serious complications ensue and may result in:

- Repeated infections, such as cellulitis (skin infection) and lymphangitis (inflammation of lymph vessels)
- Progressive trophic changes to the skin such as skin thickening or hyperkeratosis (scaly, warty growth)
- Progressive decline in quality of life and activities of daily living

Classification of Lymphedema

There are two types of lymphedema, *primary* and *secondary*.

Primary Lymphedema

Primary lymphedema is a rare congenital or inherited condition in which the lymph nodes or lymphatic vessels are either absent or abnormal. The vessels may be characterized by:

- *Hypoplasia* - the lymph collector vessels are so small that they are ineffective
- *Hyperplasia* - the lymph vessels are too large and are ineffective
- *Aplasia* - absence of lymph vessels

Primary lymphedema is usually apparent at birth or within the first two years of life and has been linked to several genetic chromosomal abnormalities. Swelling usually affects one lower leg; however, edema may also be present in multiple limbs, the genitalia, and the face.

There are three types of primary lymphedema:

- *Lymphedema praecox* - This is the most common form of primary lymphedema (up to 90% of cases). It affects women more than men by a ratio of about 10 to 1, and usually emerges during puberty. Most cases are unilateral (one-sided) and are limited to the foot or calf.
- *Congenital lymphedema* - This form accounts for up to 25% of cases of primary lymphedema. It affects females twice as often as males and is three times more likely to affect the legs than the arms. Most cases are bilateral (either both arms or both legs) and, while rare, it can also affect the face and genitalia.
- *Lymphedema tarda* also known as *Meige Disease* - This form of lymphedema becomes apparent only after the age of 35 and accounts for less than 10% of cases of primary lymphedema. Typically, patients have an overabundance of vessels which are very tortuous, with many oddly shaped bends and turns. Lymph valves are often absent or malfunctioning.

Secondary Lymphedema

Secondary lymphedema (called 'lymphedema' in the remainder of the Guidebook) is much more common than primary and is caused by a blockage or interruption of the lymphatic system, usually affecting lymph nodes of the groin (inguinal) or the armpit (axillary). There is almost always an identifiable cause for the inadequate functioning of the lymphatic system, such as surgery for cancer or radiotherapy. Other causes include:

- Vein stripping (a procedure to remove varicose veins)
- Peripheral vascular surgery
- Burns
- Insect bites
- Infection
- Inflammation
- Trauma

Secondary lymphedema of the arm is most likely to occur following radiotherapy or surgery for breast cancer, or axillary lymph node dissection (ALND), a procedure which involves the removal of several lymph nodes in the armpit area in order to determine the extent of spread of breast cancer. This is the most common cause of upper extremity lymphedema in the US. Lower limb lymphedema occurs in up to 47% of patients who have undergone pelvic or genital cancer surgery, especially if the procedure involves inguinal or pelvic lymph node dissection or radiation.

Secondary lymphedema can be further subdivided into acute and chronic subtypes.

Acute Lymphedema

According to the National Cancer Institute, there are four types of acute lymphedema, the first three of which are temporary, acute lymphedema:

- The first type of acute lymphedema occurs within a few days following the surgical removal of lymph nodes and is typically mild and temporary. This lymphedema usually resolves within a week or two if the limb is elevated and the muscles of the limb are periodically contracted.

- The second type of acute lymphedema is caused by inflammation of either the lymph vessels or veins. This form of lymphedema may occur six to eight weeks after surgery or radiation therapy. It usually resolves with limb elevation and anti-inflammatory medication.
- The third type of acute lymphedema is caused by a minor injury, such as a burn, or by an insect bite that causes an infection of the skin and lymphatic vessels. It usually resolves with elevation of the limb and antibiotics.
- The fourth type of acute lymphedema is the most common and occurs very gradually, sometimes not presenting with symptoms until many months or years after surgery or radiation therapy.

Temporary lymphedema may also follow conditions such as the temporary immobilization of a limb, or deep vein thrombosis, in which a blood clot causes blockage in a vein. Acute, temporary lymphedema typically lasts less than six months and is characterized by soft skin and *pitting*, meaning the skin remains indented when it is pressed. Pitting is a result of easy displacement of fluid in the tissue under external pressure.

Chronic Lymphedema

When acute lymphedema does not resolve and continues to progress, chronic lymphedema develops. This is the most difficult type of lymphedema to treat since the damaged lymphatic system is overwhelmed by the increased volume of fluid and does not respond as efficiently to treatment. It is often accompanied by other changes such as fibrotic, "non-pitting" skin. Chronic lymphedema may be caused by:

- Tumors that arise in the lymph nodes or spread to the nodes from another location
- Infection or injury to lymphatic vessels
- Radiation therapy
- Surgery
- Untreated or unsuccessful management of early stage acute lymphedema

Chronic lymphedema ranges from mild to severe, and is a lifelong, incurable condition that requires ongoing care and psychosocial support. Compliance with treatment and commitment to self-care are essential for a favorable outcome. Improvement can usually be achieved with non-operative treatment, although for patients who do not respond to conservative treatment, surgical options are available.

Risk Factors for Secondary Lymphedema

- Surgery for breast cancer (mastectomy or lumpectomy) together with lymph node dissection, and/or cancer radiation therapy to the region of the axillary nodes.
- Surgical removal of lymph nodes in the armpit, groin or pelvis, or head or neck area for pelvic area cancers, gynecologic cancers, prostate cancer, or melanoma. The risk of lymphedema increases with the number of lymph nodes removed.
- Radiation therapy for head and neck, axillary, or groin and pelvic area cancers.

- Cancer involving the lymph nodes (lymphomas).
- Tumors compressing lymph ducts, such as abdominal or pelvic tumors or tumor invasion of the lymph system.
- Infection or trauma causing a blockage of the lymphatic system.
- Repeated lymphangitis (inflammation of the lymph vessels).
- Chronic venous insufficiency (veins cannot pump enough blood back to the heart, causing slow blood circulation in the extremities).
- *Filariasis* - a group of tropical diseases that are transmitted to humans through parasitic roundworms and their larvae that burrow into the lymphatic vessels. The parasites can reach eight cm in length and usually nest in lymph nodes.

Lymphedema and Breast Cancer

Lymphedema is described by many women as one of the most feared after-effects of breast cancer and subsequent radiation. Lymphedema usually develops within three years of breast cancer diagnosis but the risk for its occurrence is lifelong. In the U.S., lymphedema of the arm following breast cancer treatment is the most common cause of lymphedema. Most cases of lymphedema following breast cancer are mild.

Why is breast cancer and its treatment so closely associated with lymphedema? There are three interconnecting lymphatic systems in each breast. Each lymphatic system drains primarily to nodes in the axilla (armpit), with a small portion draining to other sites. When a woman is diagnosed with breast cancer, it is necessary to determine if the tumor has spread into the axillary lymph nodes because the presence of cancer cells in that location is the strongest prognostic factor regarding survival. Metastatic spread to the lymph nodes occurs in up to 30% of patients. The extent of involvement of the lymph nodes in the spread of disease is crucial for determining the course of treatment, such as whether to undergo chemotherapy, surgery, or radiation therapy.

Until recently, one of the most common procedures for evaluating nearby lymph nodes for signs of metastatic spread of cancer cells has been *axillary lymph node dissection* (ALND) in which a pad of fat that sits along the bundle of blood vessels and nerves that pass through the armpit is removed. The lymph nodes are removed from the fat pad and examined by a pathologist to determine the presence of cancer cells. Side effects of ALND include pain, numbness, injury to the axillary vein, and lymphedema. Lymphedema is the most serious side effect and occurs in up to 56% of women who undergo ALND. The number of nodes removed increases the risk for developing lymphedema. ALND is no longer performed as frequently as before and is saved for specific circumstances, such as the presence of a palpable mass in the armpit that may raise suspicion of lymph node involvement in a woman with breast cancer.

A newer technique for mapping the involvement of lymph nodes in breast cancer is called *sentinel lymph node* (SLN) biopsy. The *sentinel lymph node* is the lymph node closest to the breast tumor that would filter cancer cells originating in the tumor, meaning that any spread of cancer cells beyond the tumor is most likely to pass through the sentinel lymph node. The sentinel lymph node is determined by injecting a blue dye and/or a radioactive tracer into the area around the tumor. As the dye passes through the breast, it follows the same route that cancer cells traveling away from the tumor would follow. The surgeon removes the first node that takes up the dye (sentinel node)

and it is examined by a pathologist. If cancer cells are detected, the surgeon may recommend the removal of additional lymph nodes and perhaps ALND. If no cancer cells are detected, the procedure is discontinued. Because fewer lymph nodes are removed with SLN compared to ALND, the risk of lymphedema is greatly reduced (up to 70%, according to some estimates). The reported incidence of lymphedema following sentinel lymph node biopsy is approximately 17%. It is important to note that SLN is not designed to replace ALND and is not appropriate for all women diagnosed with breast cancer.

There is an abundance of evidence that shows that the rate of complications is considerably lower for women undergoing ALND or SNL when the surgeon is highly trained, skilled, and experienced. This International Society of Lymphology (ISL) supports the recommendation to choose such a surgeon.

In addition to ALND and SLN biopsy, lymphedema may develop following surgery for breast cancer, such as mastectomy, and following radiation therapy for breast cancer. Because the surgery takes place in an area so close to the densely packed axillary lymph nodes, the risk of causing injury or the need to remove lymph nodes elevates the risk for developing lymphedema. Radiation therapy to the axillary are also elevates the risk due to the injury and cellular changes that occur as a result of the treatment.

Risk of Lymphedema and Breast Cancer Treatments

- Risk of lymphedema following standard ALND is approximately 50-56%. Risk of lymphedema increases with the number of lymph nodes removed during ALND.
- Risk is elevated if there is adjuvant radiotherapy to the regional lymph nodes, whether it follows breast-conservation therapy (lumpectomy) or mastectomy.
- Risk is much higher for women treated with radiotherapy following ALND (9-40%) than for women receiving radiotherapy without ALND.
- Risk is higher for radiotherapy following ALND than radiotherapy following SLN. Evidence indicates that the risk may be reduced by 70% following SLN biopsy.
- Risk of lymphedema increases each year after initial breast cancer treatment involving lymph node dissection.
- Women who have localized breast surgery (lumpectomy) with no axillary intervention (dissection or radiation) are not at risk for developing lymphedema.
- Tumor size
- Number of lymph nodes removed
- Obesity

Lower Limb Lymphedema

Lower limb lymphedema accounts for the majority of cases of lymphedema worldwide (80%). The most common cause of lower limb lymphedema worldwide is filariasis, a tropical, parasitic disease caused by an infestation of the lymphatic vessels by a threadlike worm called *filarial*. Filariasis occurs primarily in developing countries in the tropical and subtropical areas of Southeast Asia, South America, Africa, and the Pacific Islands.

In general, lower limb lymphedema occurs in both men and women and can be seen at any age. In

approximately 65% of cases, the lymphedema is unilateral and often involves genital lymphedema as well. The typical pattern of involvement is that lymphedema is initially seen in the distal part of the leg (the foot) and it extends proximally towards the trunk over time. Symptoms usually begin with painless swelling but there may be a sensation of heaviness or fullness in the leg, particularly in hot weather or at the end of the day. As with upper limb lymphedema, the swollen skin is soft and pits when pressed, but over time, the subcutaneous tissue becomes fibrotic, resulting in an absence of pitting when pressure is applied. The spread of the edema usually takes place in the first year, though enlargement of the limb can continue if treatment is delayed. The progression of symptoms is similar to upper limb lymphedema. For men, swelling may go up into the scrotum causing significant pain and discomfort.

Lower extremity lymphedema is most frequently associated with radiation and/or surgery for conditions such as:

- Prostate or testicular cancer
- Lung cancer
- Liver or abdominal cancer
- Lymphoma (cancer of the lymph cells)
- Gynecological cancers (ovarian, cervical, vulvar, uterine)
- Bladder cancer
- Melanoma

Lower limb lymphedema can also follow non-cancer related surgeries that take place in the groin or pelvic area.

Truncal, Chest, Breast, or Back Lymphedema

Lymphedema of the trunk, chest, breast, or back may occur with or without the presence of arm lymphedema. It is thought to be significantly underdiagnosed or misdiagnosed, especially when it occurs in the absence of arm lymphedema. This type of lymphedema is associated with treatments for breast cancer and lung cancer and can result from axillary lymph node biopsy, sentinel node lymph biopsy, and breast reconstruction procedures. The hallmark sign of truncal/chest/breast lymphedema is its persistence long after completion of the surgical procedure. Symptoms include:

- Intense pain, tenderness, and a sense of fullness or heat
- Swelling of the arm (may or may not be present)
- Swelling of the anterior chest wall over the affected breast, under the arm, over the collarbone or along scar lines
- Swelling of the back that appears like extra rolls of fat
- Discomfort with movement
- Visible indentation from bra strap on the affected side
- Fibrosis (skin thickening) on the breast or chest wall
- Asymmetry in the size of the breasts
- *Peau d'orange* appearance (bumpy, shiny, and thickened skin) on the affected breast

For more information about truncal/chest/breast/back lymphedema, please click on the following

link: <http://www.lymphnet.org/lymphedemaFAQs/questions/question0104.htm>

Complications of Lymphedema

If lymphedema remains untreated, swelling becomes more severe and the risk of complications rises significantly. Complications of untreated lymphedema include:

- Recurrent infections, especially *cellulitis* (skin infection) and/or *lymphangitis* (infection of the lymph vessels)
- Progressive damage to the lymphatic vessels
- Cosmetic and structural body changes
- Deep vein thrombosis
- Progressive trophic changes to the skin leading to *elephantiasis* (Stage III lymphedema); rare and usually associated with filariasis
- Pain due to pressure on nerves in the edematous area or to muscle involvement, such as loss of muscle tissue or scarring
- *Lymphangiosarcoma* - cancer of the lymph system

Cellulitis occurs in up to 50% of patients and is caused by a common pathogen called *beta-hemolytic streptococcus*. Individuals who experience infections are at a higher risk for future infections than those who have not had an infection. It is critical that treatment for any infection be initiated immediately since, if left untreated, localized infection can result in abscess, tissue degeneration, and/or sepsis (generalized infection), which are much more difficult to treat and can also become life-threatening. Signs of infection of the skin and subcutaneous tissue include:

- Redness
- Elevated skin temperature
- Pain
- Swelling
- Fever and chills

There is a 10% risk of developing lymphangiosarcoma following 10 years or more of chronic lymphedema. It is more commonly observed in post-mastectomy lymphedema (known as *Stewart-Trees Syndrome*) than following other types of surgery. Symptoms begin with a red/purple discoloration of the skin. This type of cancer is highly aggressive and carries a poor prognosis for survival.

Incidence of Lymphedema

The reported incidence of lymphedema varies widely and is therefore difficult to determine with certainty. It is estimated that over three million people in the U.S. suffer from lymphedema. Overall, lymphedema affects approximately 0.13% of the general U.S. population and that number rises to 0.5% for those over 65 years of age. The incidence of lymphedema is thought to be increasing because of rising survival rates from breast cancer and the delay of many years before lymphedema may develop in a subgroup of the surviving women.

The highest incidence of upper extremity lymphedema follows surgery for breast cancer, especially after post-surgical radiation therapy. It is estimated that up to 40% of women who undergo lymph node removal followed by radiation develop some degree of lymphedema, though the number may be much higher. The prevalence (number of cases present in a given population at a certain time) of lymphedema in women treated for breast cancer is thought to be approximately 25-30%.

In 2009, an article was published in the *Journal of Clinical Oncology* (Vol. 27(3):390-397) that summarized the statistics related to the incidence of breast cancer-related lymphedema in 631 women over a five-year period. The data indicated:

- 238 women (42%) were diagnosed with lymphedema at the end of the five-year study period.
- Of those women, 80% developed lymphedema within the first two years and 89% within three years.
- Among 433 women observed for three years, 23% reported mild lymphedema, 12% reported moderate to severe lymphedema, and 2% reported chronic moderate to severe lymphedema.

For more information, please click on the following link:

<http://www.ncbi.nlm.nih.gov/pubmed/19064976>

Lower extremity lymphedema accounts for the majority of cases (80%) of lymphedema worldwide. Some estimates report that up to 30% of women treated for gynecological cancers develop lower extremity lymphedema, while up to 47% of women undergoing treatment for vulvar cancer in particular are thought to develop lower extremity lymphedema. In general, it is estimated that there is a 47% incidence of lower limb lymphedema after pelvic or genital cancer surgeries involving the inguinal or pelvic lymph nodes.

A systematic review published by researchers at the M.D. Anderson Cancer Center in Texas regarding estimates of the incidence of cancer-related secondary lymphedema (not including breast cancer) concluded that the overall incidence was 15.5% and it varied by malignancy:

- Gynecologic - 20%
- Melanoma - 16% (upper extremity 5%; lower 28%)
- Genitourinary - 10%
- Sarcoma - 30%

Increased risk was noted for patients undergoing pelvic dissections (22%) and radiation therapy (31%). More information about this study can be seen at:

<http://www.ncbi.nlm.nih.gov/pubmed/20665892>

According to the World Health Organization (WHO), 1.1 billion people, or 20% of the world's population, live in areas where they are at high risk for developing filariasis (tropical and subtropical developing countries). The WHO estimates that 120 million people have filariasis and that approximately 30% of them show signs of lymphedema. Filariasis is the most common cause of lymphedema worldwide.

The **Intelligent Patient Overview** in the complete **Medifocus Guidebook on Lymphedema** also includes the following additional sections:

- **Diagnosis of Lymphedema**
- **Treatment Options for Lymphedema**
- **Complementary Medicine for Lymphedema**
- **Quality of Life Issues in Lymphedema**
- **New Developments in Lymphedema**
- **Questions to Ask Your Health Care Provider about Lymphedema**

To Order the Complete **Guidebook on Lymphedema** [Click Here](#)
Or Call 800-965-3002 (USA) or 301-649-9300 (Outside USA)

3 - Guide to the Medical Literature

Introduction

This section of your *MediFocus Guidebook* is a comprehensive bibliography of important recent medical literature published about the condition from authoritative, trustworthy medical journals. This is the same information that is used by physicians and researchers to keep up with the latest advances in clinical medicine and biomedical research. A broad spectrum of articles is included in each *MediFocus Guidebook* to provide information about standard treatments, treatment options, new developments, and advances in research.

To facilitate your review and analysis of this information, the articles in this *MediFocus Guidebook* are grouped in the following categories:

- Review Articles - 48 Articles
- General Interest Articles - 56 Articles
- Surgical Therapy Articles - 22 Articles
- Clinical Trials Articles - 32 Articles
- Complete Decongestive Therapy Articles - 3 Articles

The following information is provided for each of the articles referenced in this section of your *MediFocus Guidebook*:

- Title of the article
- Name of the authors
- Institution where the study was done
- Journal reference (Volume, page numbers, year of publication)
- Link to Abstract (brief summary of the actual article)

Linking to Abstracts: Most of the medical journal articles referenced in this section of your *MediFocus Guidebook* include an abstract (brief summary of the actual article) that can be accessed online via the National Library of Medicine's PubMed® database. You can easily access the individual abstracts online via PubMed® from the "electronic" format of your *MediFocus Guidebook* by clicking on the URI that is provided for each cited article. If you purchased a printed copy of the *MediFocus Guidebook*, you can still access the abstracts online by entering the individual URI for a particular abstract into your computer's web browser.

The **Guide to the Medical Literature** in the complete **Medifocus Guidebook on Lymphedema** includes the following sections:

- Review Articles - 48 Articles
- General Interest Articles - 56 Articles
- Surgical Therapy Articles - 22 Articles
- Clinical Trials Articles - 32 Articles
- Complete Decongestive Therapy Articles - 3 Articles

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4 - Centers of Research

This section of your *MediFocus Guidebook* is a unique directory of doctors, researchers, medical centers, and research institutions with specialized research interest, and in many cases, clinical expertise in the management of this specific medical condition. The *Centers of Research* directory is a valuable resource for quickly identifying and locating leading medical authorities and medical institutions within the United States and other countries that are considered to be at the forefront in clinical research and treatment of this disorder.

Use the *Centers of Research* directory to contact, consult, or network with leading experts in the field and to locate a hospital or medical center that can help you.

The following information is provided in the *Centers of Research* directory:

- **Geographic Location**

- United States: the information is divided by individual states listed in alphabetical order. Not all states may be included.
- Other Countries: information is presented for select countries worldwide listed in alphabetical order. Not all countries may be included.

- **Names of Authors**

- Select names of individual authors (doctors, researchers, or other health-care professionals) with specialized research interest, and in many cases, clinical expertise in the management of this specific medical condition, who have recently published articles in leading medical journals about the condition.
- E-mail addresses for individual authors, if listed on their specific publications, is also provided.

- **Institutional Affiliations**

- Next to each individual author's name is their **institutional affiliation** (hospital, medical center, or research institution) where the study was conducted as listed in their publication(s).
- In many cases, information about the specific **department** within the medical institution where the individual author was located at the time the study was conducted is also provided.

Centers of Research

United States

AZ - Arizona

Name of Author

Bernas M

Institutional Affiliation

Department of Surgery, University of Arizona, Tucson, AZ 85704, USA. michaelb@email.arizona.edu

CA - California

Name of Author

Chen SL

Institutional Affiliation

Division of Surgical Oncology, City of Hope National Medical Center, Duarte, California.

Dauphine C

UCLA Division of Plastic Surgery, Harbor-UCLA Medical Center, Torrance, CA, USA, DrJay@PlasticSurgery.LA.

Dominick SA

Moore UCSD Cancer Center, University of California, San Diego, La Jolla, CA, USA.

Granzow JW

UCLA Division of Plastic Surgery, Harbor-UCLA Medical Center, Torrance, CA, USA, DrJay@PlasticSurgery.LA.

Madlensky L

Moore UCSD Cancer Center, University of California, San Diego, La Jolla, CA, USA.

Merchant SJ

Division of Surgical Oncology, City of Hope National Medical Center, Duarte, California.

FL - Florida

Name of Author

Institutional Affiliation

The **Centers of Research** in the complete **Medifocus Guidebook on Lymphedema** includes the following sections:

- Centers of Research for relevant states in the United States
- Centers of Research listed for relevant countries outside the United States

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5 - Tips on Finding and Choosing a Doctor

Introduction

One of the most important decisions confronting patients who have been diagnosed with a serious medical condition is finding and choosing a qualified physician who will deliver a high level and quality of medical care in accordance with currently accepted guidelines and standards of care. Finding the "best" doctor to manage your condition, however, can be a frustrating and time-consuming experience unless you know what you are looking for and how to go about finding it.

The process of finding and choosing a physician to manage your specific illness or condition is, in some respects, analogous to the process of making a decision about whether or not to invest in a particular stock or mutual fund. After all, you wouldn't invest your hard earned money in a stock or mutual fund without first doing exhaustive research about the stock or fund's past performance, current financial status, and projected future earnings. More than likely you would spend a considerable amount of time and energy doing your own research and consulting with your stock broker before making an informed decision about investing. The same general principle applies to the process of finding and choosing a physician. Although the process requires a considerable investment in terms of both time and energy, the potential payoff can be well worth it--after all, what can be more important than your health and well-being?

This section of your Guidebook offers important tips for how to find physicians as well as suggestions for how to make informed choices about choosing a doctor who is right for you.

Tips for Finding Physicians

Finding a highly qualified, competent, and compassionate physician to manage your specific illness or condition takes a lot of hard work and energy but is an investment that is well-worth the effort. It is important to keep in mind that you are not looking for just any general physician but rather for a physician who has expertise in the treatment and management of your specific illness or condition. Here are some suggestions for where you can turn to identify and locate physicians who specialize in managing your disorder:

- **Your Doctor** - Your family physician (family medicine or internal medicine specialist) is a good starting point for finding a physician who specializes in your illness. Chances are that your doctor already knows several specialists in your geographic area who specialize in your illness and can recommend several names to you. Your doctor can also provide you with information about their qualifications, training, and hospital affiliations.

The **Tips on Finding and Choosing a Doctor** in the complete **Medifocus Guidebook on Lymphedema** includes additional information that will assist you in locating a highly qualified and competent physician to manage your specific illness.

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Or Call 800-965-3002 (USA) or 301-649-9300 (Outside USA)

6 - Directory of Organizations

American Cancer Society

1599 Clifton Road NE Atlanta, GA 30329

800.227.2345; 404.486.0100

www.cancer.org/docroot/MIT/content/MIT_7_2x_Lymphedema_and_Breast_Cancer.asp

American Lymphedema Framework Project

alfp@missouri.edu

www.alfp.org

Australasian Lymphology Association

POB 37 Mount Colah NSW 2079 Australia

admin@lymphology.asn.au

www.lymphology.asn.au

Australasian Lymphology Association

POB 37 Mt. Colah, NSW 2079

Jenny Collett

admin@lymphology.asn.au

www.lymphology.asn.au

BreastCancer.org

7 East Lancaster Avenue 3rd Floor Ardmore, PA 19003

www.breastcancer.org

Canadian Lymphedema Foundation

414 Cliffe Avenue SW; Calgary, AB; T2S 0Z4 CANADA

info@lymphovenous-canada.ca

lymphovenous-canada.ca

Canadian Lymphedema Framework

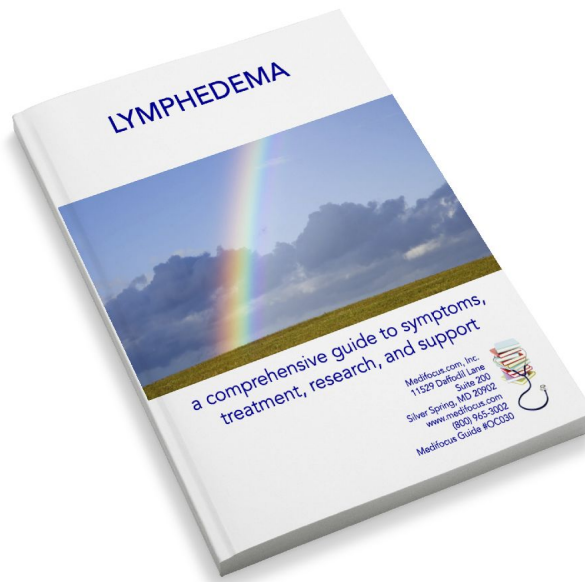
4161 Dundas Street West 1st Floor Toronto M8X 1Y2 CANADA

canadalymph@live.ca

www.canadalymph.org

The **Directory of Organizations** in the complete **Medifocus Guidebook on Lymphedema** includes a list of selected disease organizations and support groups that are helping people diagnosed with Lymphedema.

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This document is only a SHORT PREVIEW of the **Medifocus Guidebook on Lymphedema**. It is intended primarily to give you a general overview of the **format and structure** of the Guidebook as well as select pages from each major Guidebook section listed in the Table of Contents.

To purchase the **COMPLETE** Medifocus Guidebook on Lymphedema (153 pages; Updated June 21, 2017), please:

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 - 301-649-9300 (Outside the United States)
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