THE PATHOPHYSIOLOGY OF LYMPHEDEMA

Online-only content for “Post–Breast Cancer Lymphedema: Part 1,” by Mei R. Fu, PhD, RN, ACNS-BC, Sheila H. Ridner, PhD, RN, ACNP, and Jane Armer, PhD, RN, FAAN in the American Journal of Nursing, July 2009, p. 48-54.

The lymphatic system, a component of the circulatory and immune systems, has been described as “a one-way drainage route,” eliminating excess interstitial fluid and particulate matter from tissue through the lymph, lymph vessels, and lymph nodes.

Lymph (also called lymph fluid), which is clear and colorless, consists of interstitial fluid, white blood cells, proteins, and other particulate matter; the exact composition varies somewhat, depending on where it forms. Some plasma crosses the arterial wall of capillaries and enters the interstitial space,
becoming interstitial fluid and picking up waste products from surrounding cells. About 90% of this fluid then reenters the circulatory system through the venous wall of capillaries; about 10% enters the lymphatic system instead, via small, efferent lymph vessels that have unidirectional valves (see Figure 1A).

Therefore, the exchange of fluids and particulate matter between blood and lymph occurs at the interface of the capillary, the interstitial space, and the lymph vessel (see Figure 1B).

From these smaller vessels, lymph flows to the lymph nodes. Lymph nodes are small oval or bean-shaped structures arranged in groups or chains along lymph vessels throughout the body (see Figure 2). Lymph node groups are named for the body area they drain; for example, axillary lymph nodes drain the area of the axilla. Most people have between 500 and 1,500 nodes that vary greatly in size throughout the body; in healthy adults, a node's longitudinal diameter can range from 2 mm (about the size of a sesame seed) to 30 mm (about the size of a grape).

Lymph nodes serve as filters, removing potentially harmful substances such as dead or cancerous cells, bacteria, and viruses from lymph; they also produce lymphocytes.

From the nodes, lymph flows into two large lymph-collecting vessels—the lymphatic duct and the thoracic duct—which route lymph back into circulation through the right and left subclavian veins, respectively. About 75% of the body's lymph passes through the thoracic duct, which drains lymph from the entire left side of the body as well as the lower right abdomen and right leg. The remaining 25% passes through the lymphatic duct, which drains lymph from the right side of the head and neck, the right arm, and the right side of the thorax (see Figure 3).

Three mechanisms influence the movement of lymph through the lymphatic system. As lymph vessel segments become full, they contract, pushing the lymph through the downstream valves into the next segments. Contractile filaments in lymph vessel endothelial cells also help push the lymph along, as do compressions of the vessels by external forces (such as contractions of surrounding muscle, extremity movement, and arterial pulsations). Damage to any lymphatic structures can cause lymph to accumulate in the affected area. Normal physiologic variations from one person to another, such as in the number or size of lymph nodes, make it difficult to quantify an individual's risk of lymphedema.

Post-breast cancer lymphedema is caused by trauma to the lymphatic system, specifically that caused by breast surgery, the removal of axillary lymph nodes, radiotherapy, or a combination of these. Women who have undergone these treatments are at increased risk for developing lymphedema in the treated breast, arm, or thoracic area. (Although men who survive breast cancer are also likely to be at risk, there has been little research on lymphedema in that population. Similarly, women who don't have breast cancer but undergo cosmetic breast surgery (such as breast enhancement or reduction) and women who have prophylactic...
Radiation indirectly impairs the lymphatic system by causing fibrosis of tissues surrounding the lymph vessels. Radiation can also cause fibrosis in soft tissue or muscles that are used to help propel lymph through the lymphatic system. One study found that it caused changes in basal lymph circulation and lymph flow in the affected area. While lymph vessels are relatively insensitive to radiotherapy, lymph nodes are highly sensitive to conventional doses. They respond first with lymphocyte depletion as the nodes lose the ability to produce these cells, followed by fatty replacement of existing lymphocytes and then by fibrosis. Over time the damage affects the nodes’ ability to filter and transport lymph and alters immune system function.

Whether chemotherapy contributes to the development of lymphedema, and if so to what degree, remains unclear. Research in this area has yielded conflicting results.

Certain patient-related factors can increase one’s risk of developing lymphedema. Several studies indicate that among women who have survived breast cancer, obesity (a body mass index of 30 kg/m² or higher) makes lymphedema more likely. Mastectomies are probably at risk for lymphedema, but research is needed to establish that.)

Surgery for breast cancer, which can involve dissection of lymph vessels, biopsy or removal of lymph nodes, and damaging soft tissue, immediately disrupts the lymphatic system. In general, the more radical the surgery, the higher the risk of lymphedema, but even more conservative treatment carries some risk. Although axillary lymph node dissection (the removal of 10 to 30 axillary lymph nodes) is more disruptive, sentinel lymph node biopsy (SLNB) has also been associated with a risk of lymphedema. Lymph nodes do not regenerate. Postsurgically, the formation of scar tissue surrounding the lymph vessels can create blockages, as can fibrosis associated with the buildup of interstitial proteins. Such disruptions and blockages reduce the ability of the lymphatic system to transport and filter lymph; the system becomes functionally overloaded and cannot process its normal volume. As a result, abnormal amounts of lymph accumulate in the affected area, causing edema.

Radiotherapy also damages the lymphatic system. Although breast-conserving surgery (such as lumpectomy) and SLNB have replaced more radical surgical treatment in many cases—lessening the degree of surgical trauma and thereby perhaps lowering the risk of lymphedema—radiotherapy to the breast, the axilla, or both remains standard. Radiation indirectly impairs the lymphatic system by causing fibrosis of tissues surrounding the lymph vessels. Radiation can also cause fibrosis in soft tissue or muscles that are used to help propel lymph through the lymphatic system. One study found that it caused changes in basal lymph circulation and lymph flow in the affected area. And while lymph vessels are relatively insensitive to radiotherapy, lymph nodes are highly sensitive to conventional doses. They respond first with lymphocyte depletion as the nodes lose the ability to produce these cells, followed by fatty replacement of existing lymphocytes and then by fibrosis. Over time the damage affects the nodes’ ability to filter and transport lymph and alters immune system function.

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factors include prolonged heat exposure, infection, and injury to the affected area. Survivors are often advised against heavy lifting and other activities involving upper-body exertion as a precaution, although it’s unclear whether such activities in themselves increase risk. One study found that a higher level of hand use on the job made lymphedema more likely. And there is some evidence that air travel can trigger or worsen lymphedema, although a recent review stated that “larger prospective studies are required to clarify the degree of risk imposed by flight.” Comorbid conditions such as orthopedic problems, diabetes, and hypertension have also been noted in breast cancer survivors with lymphedema.

REFERENCES