

Chapter 6

Physiology, Pathophysiology, and Lymphodynamics: General Overview

Stanley G. Rockson

The lymphatic system is a component of both the circulatory and the immune systems. The principal functions of this system include the prevention of edema and maintenance of interstitial fluid homeostasis, immune traffic (transportation of white blood cells and antigen-presenting cells to the lymphoid organs), and lipid absorption from the gastrointestinal tract.¹

Not surprisingly, this system requires a complex intersection of specific anatomy and physiological function to accomplish these goals. Lymphatics are found throughout the body, with the exception of the central nervous system, in which cerebrospinal fluid fulfills the normal role of lymph. Lymphatic vasculature and lymphoid tissue are prevalent in organs that come into direct contact with the external environment, such as the skin, gastrointestinal tract, and lungs.² This distribution likely reflects the protective role of the lymphatics against infectious agents and alien particles. Absorption of fat from the intestine occurs through the lymphatic system, which transports the lipids (chyle) to the liver. The lymphatic system also transports cellular debris, metabolic waste products, and excess fluid (edema safety factor) from local sites back to the systemic circulation.

In the extremities, the lymphatic system consists of a superficial (epifascial) system that collects lymph from the skin and subcutaneous tissue, and a deeper system that drains subfascial structures, such as muscle, bone, and deep blood vessels. The superficial and deep systems of the lower extremities merge within the pelvis, whereas those of the upper extremity merge in the axilla. The two drainage systems function in an interdependent fashion, such that the deep lymphatic system participates in lymph transport from the skin during lymphatic obstruction.³

Lymphatic capillaries are lined by a single layer of overlapping endothelial cells with a discontinuous basement membrane.⁴ These vascular structures, which lack

S.G. Rockson
Division of Cardiovascular Medicine, Stanford University
School of Medicine, Falk Cardiovascular Research Center,
Stanford, CA, USA

either pericytes or smooth muscle cell coverage, begin as blind-ended tubes that interface with the interstitium. Tissue fluid can enter these initial lymphatic vessels between discontinuous button-like cell junctions.⁵

Interendothelial openings may allow cells (macrophages, lymphocytes, erythrocytes) and cellular debris to directly enter lymphatics.^{6,7} Fluid transport into the initial lymphatics apparently occurs against a pressure gradient. It is believed that episodic increases in interstitial fluid pressure are created through tissue movement; this combines with suction forces generated through the contraction of the collecting lymphatics.⁸

The lymphatic capillary structures coalesce into progressively larger collecting lymphatic vessels and, ultimately, the cisterna chyli and thoracic duct. Lymph returns to the blood circulation through lymphaticovenous anastomoses. Since the lymphatics lack a central pump, lymph progresses through the concerted effects of respiratory motions, skeletal muscle contraction, and the autocontractility of the mural smooth muscle of the vasculature itself. In skeletal muscle, lymphatics are usually paired with arterioles, so that arterial pulsation can also contribute to the periodic expansion and compression of initial lymphatics to enhance fluid uptake.⁹

Lymph flow in the collectors depends predominantly on lymphatic contraction. The rate of lymph transport can be augmented substantially by humoral and physical factors that influence the rhythm and amplitude of spontaneous contractions. Lymph flow and lymphatic contractility increase in response to tissue edema, hydrostatic pressure (standing position), mechanical stimulation, and exercise.²

Failure of adequate lymph transport promotes lymphedema and likely contributes to the pathological presentation of a wide variety of lymphatic vascular diseases. Accordingly, a detailed understanding of lymphatic anatomy, physiology, and dynamics will certainly contribute to an informed response to diagnosis and therapeutic intervention. Similarly, a detailed understanding of normal lymphatic development should allow us to address pathological lymphatic conditions that lead to inflammation, autoimmunity, cancer, and other forms of human disease.¹

References

1. Oliver G. Lymphatic vasculature development. *Nat Rev Immunol*. 2004;4(1):35-45.
2. Szuba A, Shin WS, Strauss HW, Rockson S. The third circulation: radionuclide lymphoscintigraphy in the evaluation of lymphedema. *J Nucl Med*. 2003;44(1):43-57.
3. Brautigam P, Foldi E, Schaiper I, Krause T, Vanscheidt W, Moser E. Analysis of lymphatic drainage in various forms of leg edema using two compartment lymphoscintigraphy. *Lymphology*. 1998;31(2):43-55.
4. Cueni LN, Detmar M. The lymphatic system in health and disease. *Lymphat Res Biol*. 2008; 6(3-4):109-22.
5. Baluk P, Fuxe J, Hashizume H, et al. Functionally specialized junctions between endothelial cells of lymphatic vessels. *J Exp Med*. 2007;204(10):2349-62.
6. Ikomi F, Hanna GK, Schmid-Schonbein GW. Mechanism of colloidal particle uptake into the lymphatic system: basic study with percutaneous lymphography. *Radiology*. 1995;196(1):107-13.

7. Higuchi M, Fokin A, Masters TN, Robicsek F, Schmid-Schonbein GW. Transport of colloidal particles in lymphatics and vasculature after subcutaneous injection. *J Appl Physiol.* 1999; 86(4):1381-7.
8. Reddy NP, Patel K. A mathematical model of flow through the terminal lymphatics. *Med Eng Phys.* 1995;17(2):134-40.
9. Schmid-Schonbein GW. Microlymphatics and lymph flow. *Physiol Rev.* 1990;70(4):987-1028.