# A new paradigm for diagnosis and treatment of edemas

## The endothelial glycocalyx layer

### Advancements in the link between swelling and the lymphatic system

By Heather Hettrick and Robyn Bjork

## Introduction

Although edema can result from a variety of conditions, medications or other contributing factors, it is now understood that all edema is lymphedema through a spectrum of lymphatic insufficiency[1].This article will highlight the latest evidence supporting this paradigm shift by looking at the new understanding of hemodynamics at the Endothelial Glycocalyx Layer, and the associated links between the lymphatic and integumentary systems. Further, it will explain how this information is relevant to clinical practice to help you differentially diagnose and manage lower extremity edema.

## New lymphedema paradigm

One of the most significant recent changes regarding lymphedema is a more refined explanation of fluid hemodynamics impacting our historical understanding of Starling's Law. Previously, it was thought that 90% of fluid moving from the blood to the interstitium was reabsorbed back into the venous end of the capillary, yet the lymphatic system was only responsible for managing 10% of the fluid load. The new paradigm of the Endothelial Glycocalyx Layer (EGL) as the gatekeeper of fluid filtration from blood capillaries explains how there is only diminishing net fluid filtration across the blood capillary bed and no reabsorption at the venous end; 100% of all interstitial fluid is reabsorbed by the lymphatic capillaries alone during homeostasis[2-3].

Acting as a complex molecular sieve, the EGL precisely regulates fluid and protein movement through the capillary wall into the tissues[4-6]. Conversely, the EGL also prevents movement of proteins and fluid back into the venous side of the capillaries, even when interstitial hydrostatic pressure is increased, or tissue oncotic pressures remains higher within the blood capillaries. Thus, all fluid and proteins exiting the blood capillaries must be removed from the interstitium by the lymphatic capillaries alone. This has led to the new understanding that all edemas are on a lymphedema continuum and represent relative lymphatic insufficiency or failure[1,7]. The system is either temporarily overwhelmed (transient lymphedema/dynamic insufficiency) or the system is abnormally developed, damaged or permanently impaired leading to the disease of chronic lymphedema (mechanical lymphatic failure).

## Lymphedema pathophysiology

The lymphatic system is analogous to the body's sewer or recycling system. It is responsible for maintaining fluid homeostasis by managing interstitial fluid and mobilizing waste products (proteins, senescent cells, macromolecules, etc.). The lymphatic system is also tasked with the absorption and transportation of lipids and fatty acids to the circulatory system, and transporting antigens, antigen-presenting cells and other immune cells to the lymph nodes where adaptive immunity is stimulated. Collectively, all components within the fluid transported by the lymphatic system are called the "lymphatic load"[9].

Pathophysiologically, chronic lymphatic dysfunction or failure presents unique changes affecting the integumentary system. When the lymphatic load is not readily reabsorbed by the lymphatic system from the interstitial tissues, a pathohistological state of chronic inflammation results. Free radicals trapped in the tissues denature proteins and oxidize cell membranes attracting monocytes to the area that differentiate into macrophages. These macrophages take in proteins through pinocytosis, which activates the macrophages to release cytokines. This, in turn, activates fibroblasts, which are stimulated to produce excess collagen[8,9]. Excess collagen formation causes connective tissue proliferation and fibrosis resulting in the thickened, fibrotic skin and wart-like projections (papillomatosis and verrucous) commonly seen with chronic lymphedema[10]. Additionally, other fibroblasts differentiate into adipocytes[9]. If treatment is not implemented, the chronic inflammatory process persists and the clinical presentation eventually can result in enlargement of the body part, thickened and fibrotic dermal and subcutaneous tissues, and other significant integumentary changes[11].

**Heather Hettrick PT, PhD, CWS, CLT-LANA, CLWT, CORE** is a Professor in the Physical Therapy Program at Nova Southeastern University in Florida. As a physical therapist, her expertise resides in integumentary dysfunction where she holds four board certifications/credentials. She is faculty and Director of Wound Education at the International Lymphedema & Wound Training Institute.

**Robyn Bjork, MPT, CWS, CLT-LANA, CLWT** is Founder and President of the International Lymphedema & Wound Training Institute. She is a Physical Therapist who holds multiple board certifications in wound and edema/lymphedema management. Bjork is a featured speaker at national & international conferences and is dedicated to the advancement of Lymphatic & Integumentary Rehabilitation.