Casual Friday Series

Functional Blood Chemistry Series EBV and the Importance of Drainage Pathways

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Etiology of Chronic Disease: A Discussion on Epstein-Barr Virus

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Abstract

Epstein-Barr Virus (EBV) is a common human herpes virus and is one of the most common and prolific viral infections in humans. Over 95% of adults carry this virus, and most children are infected as well. Chronic disease is the clinical manifestation of primary infection with Epstein Barr virus. Infection with EBV is often asymptomatic. But once the virus inserts itself into immune B cells, it reprograms them, effectively evading programmed cell death and escaping recognition and destruction by cytotoxic T cells. EBV can manifest in a range of pathologies including various cancers, Infectious Mononucleosis (IM), autoimmune disorders, chronic fatigue syndrome, thyroid disease, meiners disease, type 1 diabetes, Lyme disease, and numerous other conditions.

What are the popular "channels" saying?

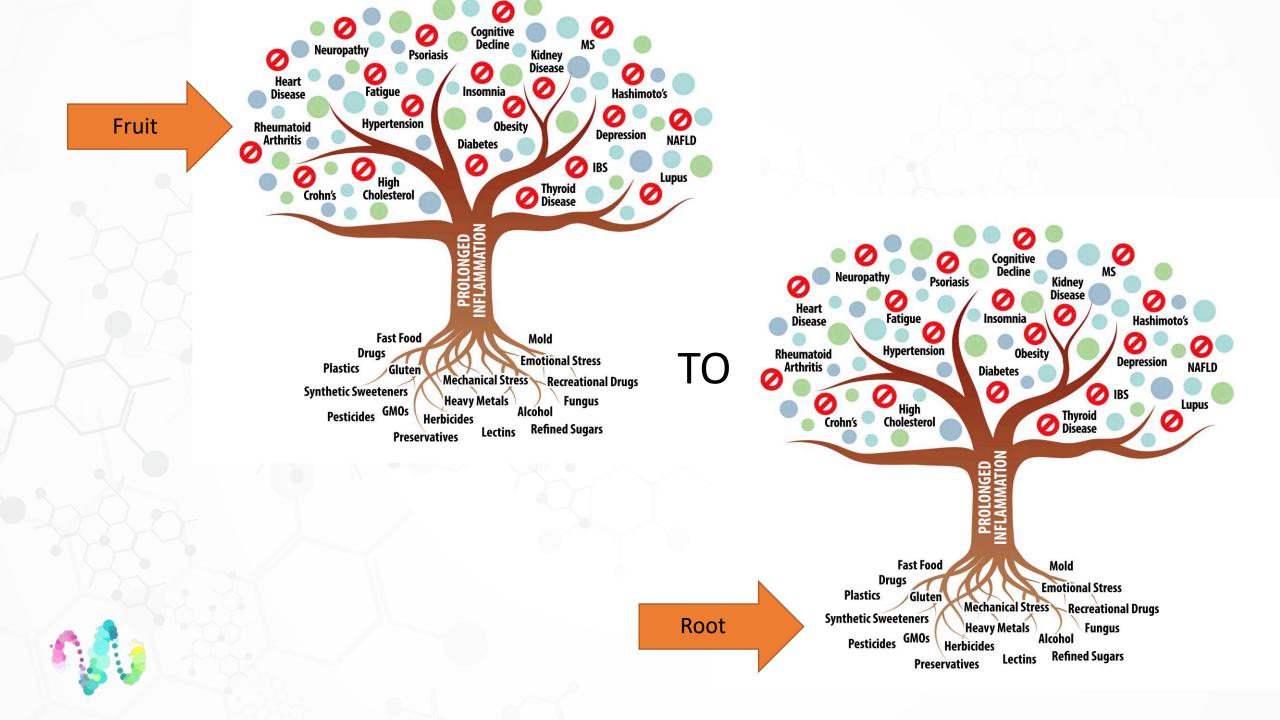


Cleveland Clinic on EBV

- •Epstein-Barr virus (EBV) is a very common viral infection that spreads through saliva and body fluids.
- •Most cases of EBV don't cause symptoms. Other cases, especially in adolescents and young adults, can lead to infectious mononucleosis.
- •Once you get EBV, the infection stays within your body for your entire life in a dormant state where it's inactive or sleeping.
- •You can reactivate the virus and experience symptoms again, regardless of when you first acquired the virus.
- •Certain events can trigger EBV to wake up (reactivate) and make it contagious to others, potentially causing symptoms in the host. Events that trigger EBV reactivation include:
 - Stress.
 - Weak immune system.
 - Menopause or hormone changes.
- •The virus attaches to white blood cells (lymphocyte B cells) in your body. White blood cells help fight infection. When the virus attaches to your white blood cells, your cells are unable to fight the infection properly and you experience symptoms
 - Sore throat and throat inflammation (swelling).
 - Fatigue or feeling extremely tired.
 - Fever.

CDC on EBV

- •EBV is found all over the world. Most people get infected with EBV at some point in their lives
- •Many people become infected with EBV in childhood. EBV infections in children usually do not cause symptoms, or the symptoms are not distinguishable from other mild, brief childhood illnesses.
- •People who get symptoms from EBV infection, usually teenagers or adults, get better in two to four weeks.
- •However, some people may feel fatigued for several weeks or even months.
- •After you get an EBV infection, the virus becomes latent (inactive) in your body. In some cases, the virus may reactivate. This does not always cause symptoms, but people with weakened immune systems are more likely to develop symptoms if EBV reactivates.
- •Symptoms of EBV infection can include
 - •fatigue
 - •fever
 - inflamed throat
 - •swollen lymph nodes in the neck
 - enlarged spleen
 - swollen liver
 - ·rash



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PMID: <u>27833448</u>

A possible link between the Epstein-Barr virus infection and autoimmune thyroid disorders

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The Epstein-Barr virus (EBV), also known as human herpesvirus 4, is a member of the Herpesviridae virus family. EBV infection can cause infectious mononucleosis (IM) in the lytic phase of EBV's life cycle. Past EBV infection is associated with lymphomas, and may also result in certain allergic and autoimmune diseases. Although potential mechanisms of autoimmune diseases have not been clearly elucidated, both genetic and environmental factors, such as infectious agents, are considered to be responsible for their development. In addition, EBV modifies the host immune response. The worldwide prevalence of autoimmune diseases shows how common this pathogen is. Normally, the virus stays in the body and remains dormant throughout life. However, this is not always the case, and a serious EBV-related illness may develop later in life. This explains the chronic course of autoimmune diseases that is often accompanied by exacerbations of symptoms. Based on the present studies, EBV infection can cause autoimmune diseases, such as systemic lupus erythematosus (SLE), multiple sclerosis (MS), rheumatoid arthritis (RA), Sjögren's syndrome, and autoimmune hepatitis. The EBV has also been reported in patients with autoimmune thyroid disorders. Although EBV is not the only agent responsible for the development of autoimmune thyroid diseases, it can be considered a contributory factor.

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PMID: <u>34572593</u>

Stress-Induced Epstein-Barr Virus Reactivation

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Marshall Williams, Academic Editor

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Abstract

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Epstein-Barr virus (EBV) is typically found in a latent, asymptomatic state in immunocompetent individuals. Perturbations of the host immune system can stimulate viral reactivation. Furthermore, there are a myriad of EBV-associated illnesses including various cancers, post-transplant lymphoproliferative disease, and autoimmune conditions. A thorough understanding of this virus, and the interplay between stress and the immune system, is essential to establish effective treatment. This review will provide a summary of the interaction between both psychological and cellular stressors resulting in EBV reactivation. It will examine mechanisms by which EBV establishes and maintains latency and will conclude with a brief overview of treatments targeting EBV.

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Chronic Active Epstein–Barr Virus Disease

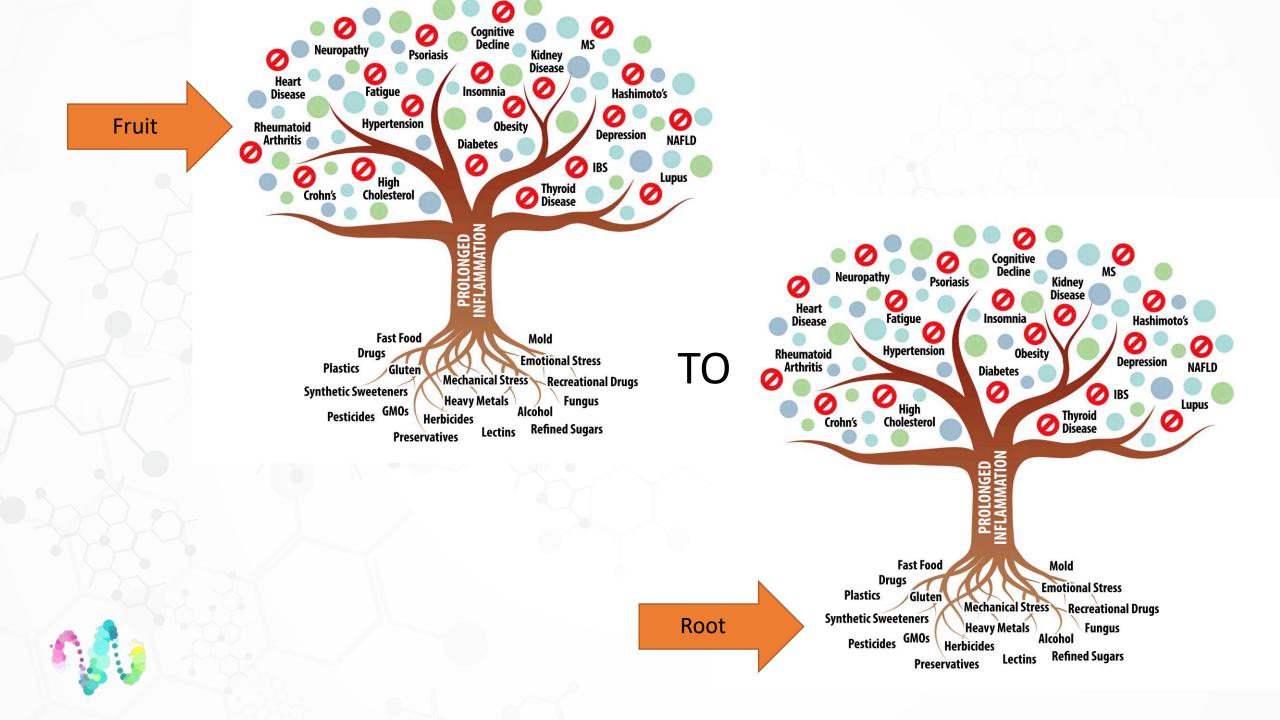
Hiroshi Kimura¹ and Jeffrey I. Cohen^{2,*}

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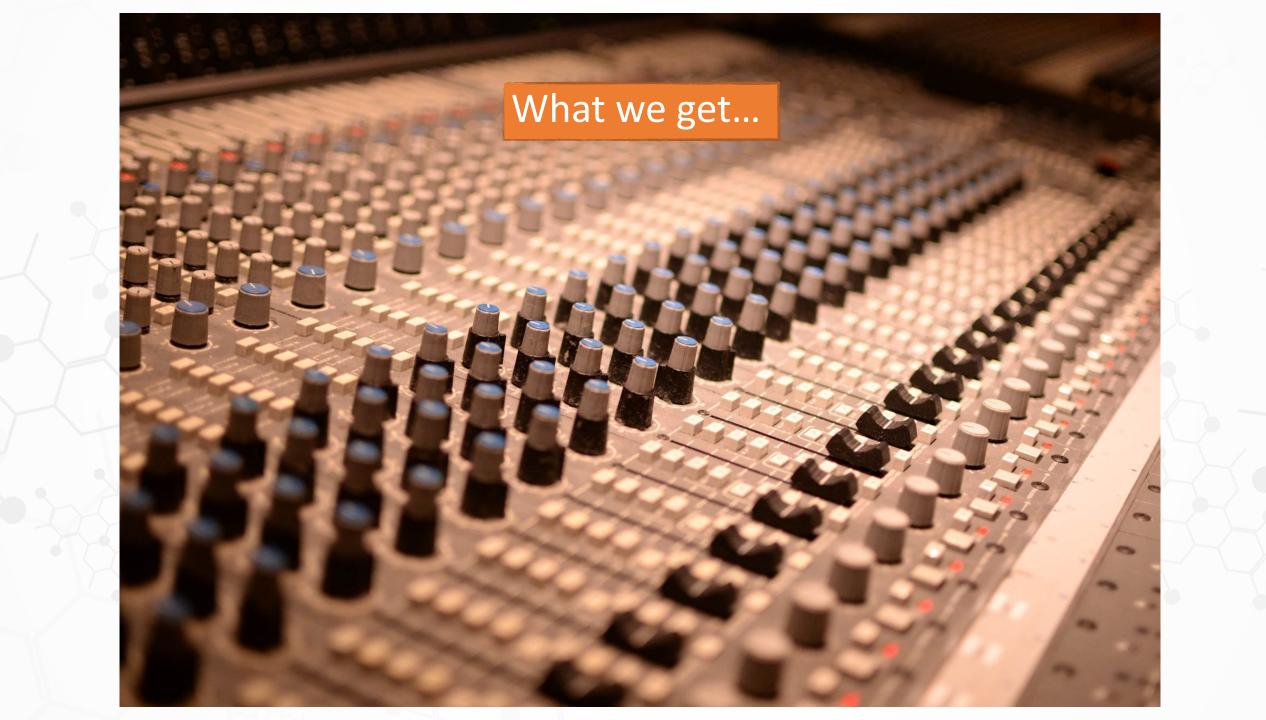
Abstract

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Chronic active Epstein–Barr virus (CAEBV) disease is a rare disorder in which persons are unable to control infection with the virus. The disease is progressive with markedly elevated levels of EBV DNA in the blood and infiltration of organs by EBV-positive lymphocytes. Patients often present with fever, lymphadenopathy, splenomegaly, EBV hepatitis, or pancytopenia. Over time, these patients develop progressive immunodeficiency and if not treated, succumb to opportunistic infections, hemophagocytosis, multiorgan failure, or EBV-positive lymphomas. Patients with CAEBV in the United States most often present with disease involving B or T cells, while in Asia, the disease usually involves T or NK cells. The only proven effective treatment for the disease is hematopoietic stem cell transplantation. Current studies to find a cause of this disease focus on immune defects and genetic abnormalities associated with the disease.

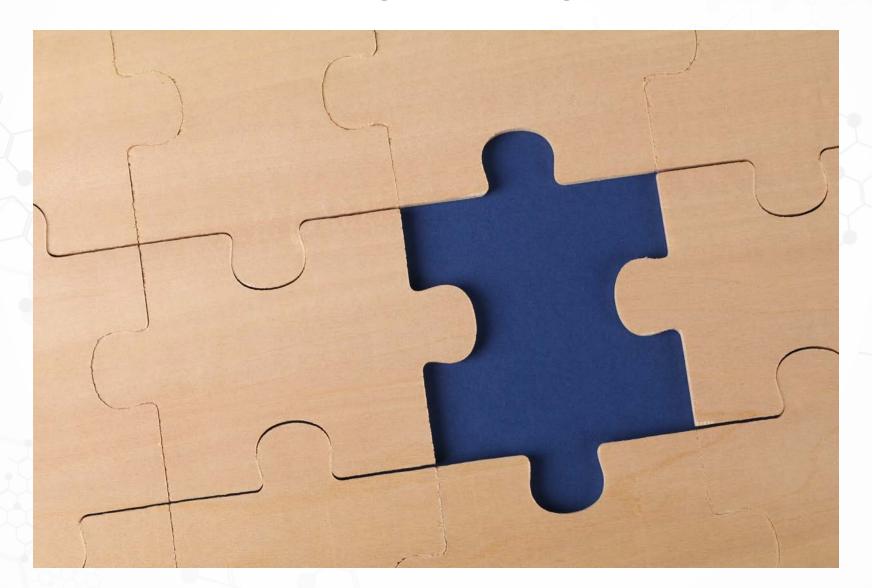




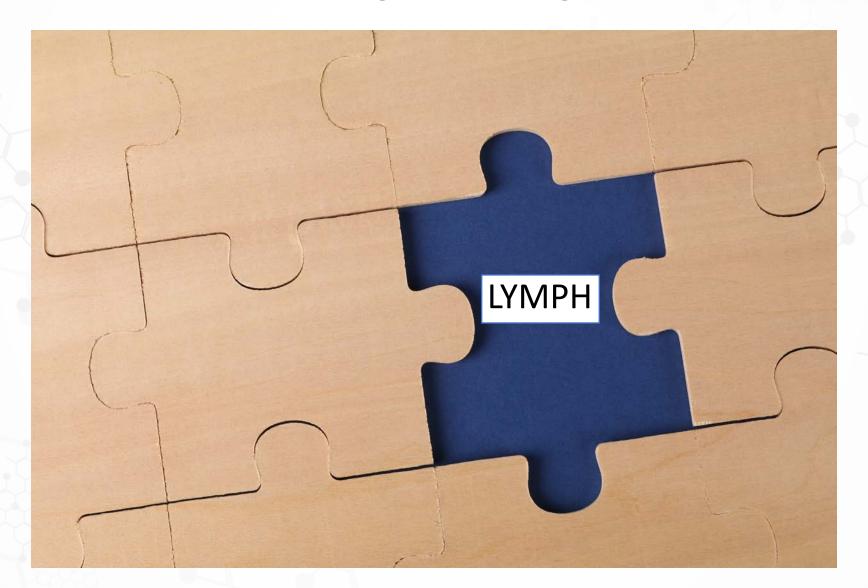




But is there a Missing or Forgotten Piece?

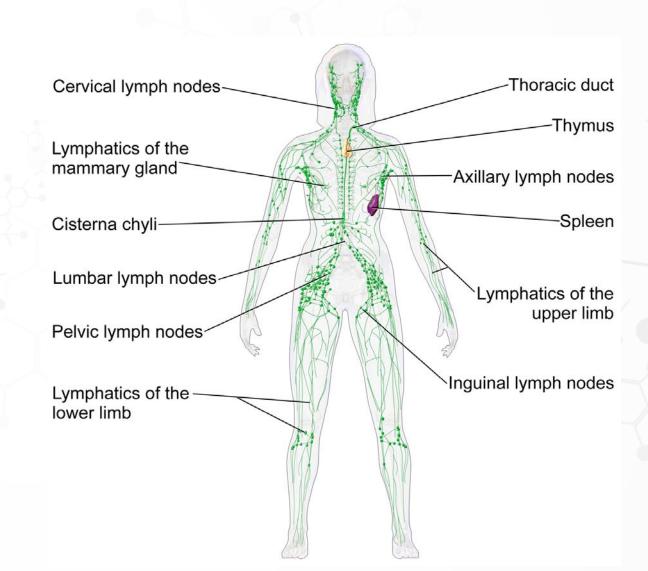


But is there a Missing or Forgotten Piece?



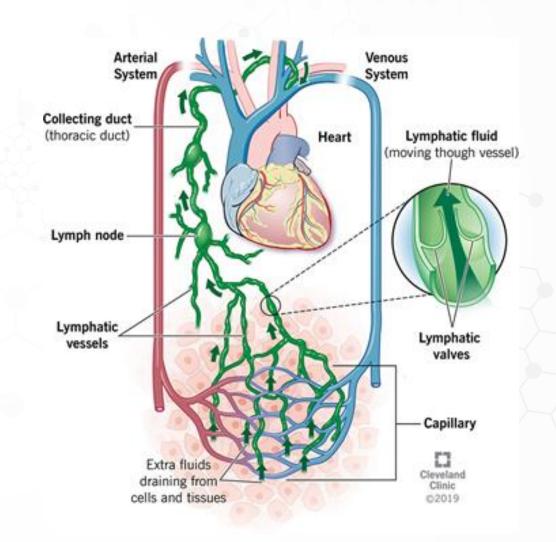
The Lymphatic System

- Lymph Vessels
- Lymph Nodes
- Spleen*
- Bone Marrow
- Tonsils*
- Thymus



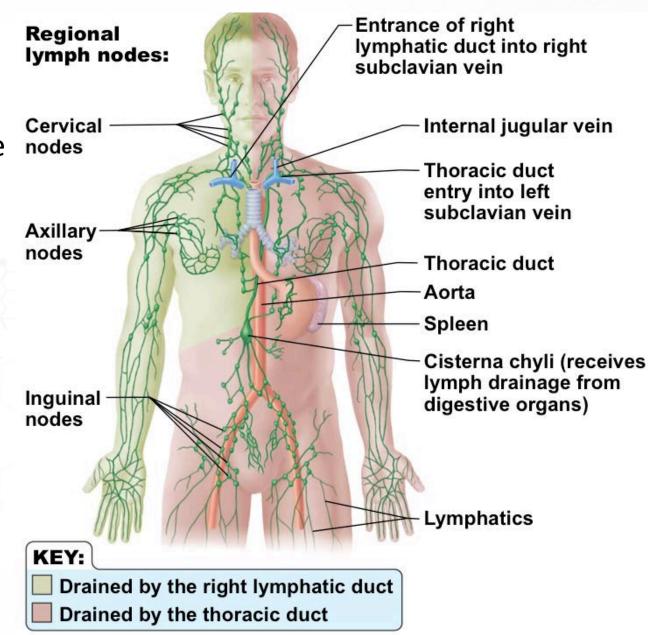
Mirror of the Vascular System

- Vasculature for Oxygen and Blood... Lymph for waste and toxins
- 70% is just under the skin
- No pump and a one way street
- Lymph fluid flows up the body to the clavicles where it is returned the blood supply



Lymph Nodes

- Reminder that most are located in the head, gut, and joints.
- Their job is to Filter through the waste, remove toxins, and destroy anything that is a threat.
- Will produce Neuts or Lymphs based on what is passing through.
- If a node is swollen or hard it is going to prevent flow
- Main "drain" is near the clavicle called the termini.



Important Features of Lymphatics for EBV

- Removal of Excess Body Fluid and Waste Products
- Production of Immune Cells to Help Fight Infection
- Absorption of Fatty Acids from Digestion.
- We have between 600-1000 Lymph Nodes in our body
 - About 30% in the Head and Neck
 - 50% are located in the Gut
 - Most of the remainder are in our Joints

PMCID: PMC4397130

NIHMSID: NIHMS651175

PMID: 25534659

Lymphatic System: An Active Pathway for Immune Protection

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Lymphatic vessels are well known to participate in the immune response by providing the structural and functional support for the delivery of antigens and antigen presenting cells to draining lymph nodes. Recent advances have improved our understanding of how the lymphatic system works and how it participates to the development of immune responses. New findings suggest that the lymphatic system may control the ultimate immune response through a number of ways which include guiding antigen/dendritic cells (DC) entry into initial lymphatics at the periphery; promoting antigen/DC trafficking through afferent lymphatic vessels by actively facilitating lymph and cell movement; enabling antigen presentation in lymph nodes via a network of lymphatic endothelial cells and lymph node stroma cell and finally by direct lymphocytes exit from lymph nodes. The same mechanisms are likely also important to maintain peripheral tolerance. In this review we will discuss how the morphology and gene expression profile of the lymphatic endothelial cells in lymphatic vessels and lymph nodes provides a highly efficient pathway to initiate immune responses. The fundamental understanding of how lymphatic system participates in immune regulation will guide the research on lymphatic function in various diseases.

Symptoms Associated with a Congested Lymphatic System

- Depression
- Digestive Issues
- Dry, Itchy skin
- Enlarged Lymph Nodes
 - Fluid retention
 - Food Sensitivities
 - -Get sick easily

- Allergies
- Bloating
- Brain Fog
- Breast swelling
- -Chronic fatigue
- Cold hands and feet
 - Constipation

- Headaches
- Muscle or Joint pain
- Parasite Infections
 - -Sinus Infections
- Stiffness in the am
 - Weight gain

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PMID: <u>30936872</u>

Regulation of Immune Function by the Lymphatic System in Lymphedema

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The lymphatic vasculature has traditionally been thought to play a passive role in the regulation of immune responses by transporting antigen presenting cells and soluble antigens to regional lymph nodes. However, more recent studies have shown that lymphatic endothelial cells regulate immune responses more directly by modulating entry of immune cells into lymphatic capillaries, presenting antigens on major histocompatibility complex proteins, and modulating antigen presenting cells. Secondary lymphedema is a disease that develops when the lymphatic system is injured during surgical treatment of cancers or is damaged by infections. We have used mouse models of lymphedema in order to understand the effects of chronic lymphatic injury on immune responses and have shown that lymphedema results in a mixed T helper cell and T regulatory cell (Treg) inflammatory response. Prolonged T helper 2 biased immune responses in lymphedema regulate the pathology of this disease by promoting tissue fibrosis, inhibiting formation of collateral lymphatics, decreasing lymphatic vessel pumping capacity, and increasing lymphatic leakiness. Treg infiltration following lymphatic injury results from proliferation of natural Tregs and suppresses innate and adaptive immune responses. These studies have broad clinical relevance since understanding how lymphatic injury in lymphedema can modulate immune responses may provide a template with which we can study more subtle forms of lymphatic injury that may occur in physiologic conditions such as aging, obesity, metabolic tumors, and in the tumor microenvironment.

What causes Stagnant Lymph?

- Sitting/Lack of Movement/Sedentary Lifestyle
- Tight clothing (bras, socks, yoga wear, tight jeans/pants)
- Conventional Dairy Consumption
- Injury or Surgery
- Improper Breathing

How do we get Lymph Moving?

- MOVEMENT =)
- Manual Lymphatic Massage
- Proper Nutrition
- Diaphragmatic Breathing
- Vibration or Rebounding
- Proper Sleep
- Herbs and Supplements



