What Do These Diseases Have in Common?
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- Lymphedema
- Lymphatic vascular malformations
- Visceral lymphatic diseases
- Gastrointestinal infections and *Clostridium difficile* colitis
- Peritonitis
- Cancer and metastasis
- Chronic infections and inflammation
- Organ transplantation
- Autoimmune diseases (inflammatory bowel disease, arthritis)
- Neuro-immune disorders
- Metabolic syndrome
- Burn and hemorrhagic shock
- Obesity, lipedema, and fat disorders
- Diabetes mellitus
- Integumentary impairment

**Lymphatic dysfunction, inflammation, and altered immunity**

### Relationship of AVL Systems
- Circulatory system: 3 components
  - Closed blood circulatory system
    - Arteries
    - Veins
  - Half-open lymphatic system
- Veins and lymphatics: Similar embryologic origin and anatomy
- When pathologic changes occur in venous system, microangiopathic changes of both the vascular and lymphatic networks

### Anatomy
- Connected to every organ and system of the body except the central nervous system
- Lymphatic structures are found everywhere except
  - Cornea
  - Striated muscles
  - Bone marrow
  - Joint cartilage
  - Hair, nails, teeth
  - Alveoli of lungs

### Lymphatic System Functions
- Circulation of interstitial space fluid
- Defense: Removes and destroys toxic substances
- Safety valve for fluid overload - helps control edema
- Digestive aid: Transports lipids from intestine to blood stream
- Homeostasis of extracellular environment
**Lymphoid Organs**

- Part of lymphatic system
- Called lymphoid organs because home to lymphocytes
- Sites where cells of immune system originate and develop
- Include:
  - Spleen
  - Thymus
  - Tonsils
  - Peyer's patches
  - Bone marrow
  - Lymph nodes
  - MALT-Mucosa Associated Lymphoid Tissue

**Lymph Node**

- Small oval structures that filter lymph, catching debris or cells
- Responsible for purifying and draining lymph fluid

**The Lymphatic System: The Body’s Drainage System**

- Lymphatic capillaries $\rightarrow$ precollectors $\rightarrow$ collectors $\rightarrow$ lymph nodes

**Immune Function of Lymphatic System**

- Production, maintenance, and distribution of:
  - Macrophages
  - B- and T-lymphocytes
  - Plasma cells
  - Reticular cells

**Lymphokinetic Motion & Pressure Gradient**

- Lymph collects in angions (between two valves)
- Smooth muscle and respiratory pumps force lymph forward
- Aided by function of the one-way semilunar valves
- Ultimately lymph fluid empties into venous system

**Lymphangiomotoricity (flow of the lymph)**

- Lymph collects into interstitial fluid
- Interstitial fluid flows into lymphatic capillaries
- Lymphatic capillaries converge into lymphatic vessels (collectors)
- Collectors form lymphatic nodes
- Lymphatic nodes: filter, purify, and drain lymph fluid

**Lymphocytes attacking a cancer cell**
Lymphatic Load
- Plasma and plasma proteins escape from small blood vessels
- Lymphatic reabsorbs/transport substances not absorbed by venous system (Starling’s Law/Equilibrium)
- Lymphatic load includes:
  - Dead cells
  - Bacteria
  - Endotoxins
  - Enzymes (MMPs: matrix metalloproteinases) WOUND MILIEU/CHRONIC WOUND FLUID COMPONENTS

What Is Lymphedema?
- Chronic condition; swelling in one or more limbs
- May include corresponding quadrant of trunk
- Swelling may affect other areas (eg, head/neck, breast, genitalia)
- Not curable at this time
- Manageable appropriately if treated early
- Ignored or inappropriately treated (eg, diuretics), progresses; becomes difficult to manage

Incidence and Prevalence
- In the United States (numbers likely under-reported)
  - Primary lymphedema: 2 million
  - Secondary lymphedema: 2.5 to 3 million
  - ~1% of the population
- In the world
  - Post-filarial (parasitic) lymphedema: 90-120 million
  - Leading cause of lymphedema in the world
  - More than a billion people at risk

Incidence and Prevalence (cont)
- Worldwide
  - Chronic venous insufficiency (CVI) edema affects 300 million
  - Phlebolymphedema numbers likely under-reported in the CVI population
  - Medscape 2015: "2%-5% of all Americans have some changes associated with CVI; 6-16 million with 2° lymphedema from CVI"
  - ESVS 2015: "CVI (C3-C6) affects about 5% of the population—16 million with 2° lymphedema from CVI"
  - Post-mastectomy lymphedema affects ~20 million
  - Primary lymphedema and post-traumatic edema cases ~40 million
  - Considering all causes, 1 of every 40 people in the world may be affected by lymphedema

Lymphedema Definition
- Chronic, incurable condition characterized by an abnormal accumulation of interstitial proteins causing edema as a result of an anatomic alteration in the lymphatic system
- Ultimately failure of lymphatic drainage
Cancer and Lymphedema Statistics

- ~30% of patients who undergo mastectomy with lymph node resection due to breast cancer develop secondary lymphedema of the upper extremity.
- Lower extremity lymphedema (and/or genital lymphedema) after radical lymph node dissections secondary to prostate cancer ~ >70%.
- Lymphedema may present immediately or years after treatment. Most occur within first 18 months.


Lymphedema

- Etiology: obstruction of lymphatic channels & impairment in return of lymph to venous channels.
- Lymphatic transport capacity decreases.
- Result: increased accumulation of high protein fluid.

Lymphatic Filariasis

- Most common cause of lymphedema worldwide.
- Identified by World Health Organization as a leading cause of permanent and long-term disability in world.
- Endemic in more than 80 countries-tropics and sub-tropics.
- Affects 120 million people in 83 countries.
- Caused by threadlike, parasitic filarial worm that live almost exclusively in humans.
- Worms transmitted by mosquitoes.
- Toxic waste produced by worms results in inflammation and obliteration of lymphatic system.


Stage 0 Lymphedema

- Sub-clinical stage, pre-stage, latency stage
- Transport capacity of lymphatic system reduced but still able to cope with normal amount of lymphatic load.
- Often not clinically detectable.
- Patient may have subjective symptoms.
- Sensations of heaviness and tightness.
- Patients at risk of lymphedema progression.

https://www.bestveintreatment.com/vein-disease-symptoms/lymphedema/
Stage 1 Lymphedema
- Reversible stage
- Edema reduced with elevation
- Pitting edema that begins distally (at the hand/foot)
- Negative or borderline Stemmer’s sign
- No palpable fibrosis or secondary tissue changes

Stage 2 Lymphedema
- Spontaneously irreversible
- Clinically persistent edema not reduced by elevation
- Positive Stemmer’s sign
- Pronounced fibrosis
- Connective tissue proliferation (fibrosis) due to long-standing accumulation of protein-rich fluid
- Frequent infections ✲ cellulitis
- Can become life-long stage

Stage 3 (Lymphatic Elephantiasis)
- Massive enlargement and distortion of limb caused by breakdown of skin’s elastic components
- Pronounced skin alterations
- Lymphostatic fibrosis
- Papillomas
- Cysts
- Fistulas
- Deep skin folds
- Hyperkeratosis
- Infections
- Cellulitis
- Fungal infections (skin, nails)

Classifications of Edema
- High-protein and low-protein
- Chronic venous insufficiency edema: Low-protein, mostly water
- Lymphedema: High-protein edema
- Lymphatic system responsible for picking up and transporting proteins (large molecules) back into venous system
- When proteins not picked up by lymphatic capillaries (due to some problem with the lymphatic system), they are left behind in interstitial tissues
- Proteins cause fibrosis of tissues
- Proteins hydrophilic: Attract more water to the interstitial tissues, making the swelling or lymphedema worse

Pathophysiology of Phlebolymphedema
- Chronic venous insufficiency
- Waterload exceeds lymphatic transport capacity
- Lymphatic damage leads to fibrofissures

Venous Insufficiency & Lymphedema
AKA Phlebolymphedema
- Lymphedema underlying pathology contributing to formation of venous ulcers
- High filtration pressure/increase fluid in tissues
- Low protein edema
**Lymphedema-Associated Infections**

- Dry/scaly lymphedema skin loses acid mantle, which protects skin from bacteria/pathogens.
- Deep skin folds support growth of bacteria.
- Prolonged presence of protein-rich edema and accumulated waste creates breeding ground for infection.
  - **Cellulitis**: Acute infection of skin and deeper soft tissues.
  - **Lymphangitis**: Local infection of lymph vessels.
  - **Erysipelas**: Acute dermal infection caused by streptococcus bacteria associated with cellulitis; affects skin and tissues immediately under skin; may include lymphatic vessels and nodes.

**Assessing for Lymphedema**

- **Stemmer’s Sign**: Lymphoscintigraphy
  - Lymphoscintigraphy: Nuclear medicine study used for imaging lymph vessels and lymph nodes.

**Lymphoscintigraphy**


**Indocyanine Green (ICG) Near-Infrared Fluorescence (NIRF) Lymphatic Imaging**

- Healthy System
- Damaged System

**Treating Lymphedema**
Complete Decongestive Therapy (CDT)

- Main treatment
  - Also called combined, complex, or comprehensive decongestive therapy
  - Considered 'gold standard' of care
  - Safe and effective

- Effects
  1. Decrease swelling
  2. Increase lymph drainage from the congested areas
  3. Reduce skin fibrosis and improve skin condition
  4. Enhance patient's functional status
  5. Relieve discomfort and improve quality of life
  6. Reduce risk of cellulitis and Stewart-Treves-syndrome, a rare form of angiosarcoma

Complete Decongestive Therapy (CDT) (cont)

- Manual lymph drainage (MLD)
  - Highly specialized techniques requiring extensive training
- High-level compression therapy (40-60 mmHg)
  - Multi-layer manual wraps
  - Pneumatic compression pumps controversial

- Lymphatic decongestive exercises
  - Stimulate intact lymphatics
  - Increase lymph transport rate

- Skin and nail care
  - Infection control
  - Maintain supple skin to prevent breaks in skin

- Kinesio taping

- Education in self-management, elastic compression garments

Manual Lymphatic Drainage

Compression Therapy for Lymphedema

- Bandaging
  - Short-stretch compression wraps
    - Generate low resting pressures
    - Generate high working pressures
  - Working Pressure
    - Pressure exerted when muscles inside compressive bandage attempts to expand as a result of active contraction
    - Active muscle contraction increases the pressure in the tissue
    - The more rigid the bandage material, the more working pressure will develop in response to an active muscle contraction
  - Long-stretch compression wraps for sedentary and non-ambulating patients

Compression Bandaging

- Inelastic (rigid) (short-stretch) bandages

Compression Therapy

- Compression pumps controversial
- Sequentially-inflating multi-chambered sleeves considered more effective than single-chambered sleeves
- Compression garments once limb to optimal size
Types of Compression Pumps for Lymphedema

• Kinesio taping - supports overall lymphedema treatment
• Structurally lifts skin, opening up superficial lymphatic pathways of affected area
• Can provide a directional pull that guides the lymphatic fluid in the desired direction of drainage

Elastic Therapeutic Tape for Lymphedema

Compression Garments

Lymphedema: It Is Manageable!

Lipedema

• Congenital disorder of lipid metabolism
• Chronic disease caused by extensive deposits of subcutaneous fatty tissue
• Usually bilateral and symmetric
• Associated with hormonal disorders
• Occurs almost exclusively in women
  • Men rare - hormonal therapy, cirrhosis of the liver
• Typically manifests during puberty
• Etiology unknown

Phase 1 - Intensive Clinic Program

• 5 times/week in clinic
• 2 to 4 weeks duration
• Bandages worn 23/24 hours per day, 7 days a week
• 45 minutes of manual lymph drainage massage
• MLD immediately followed by reapplication of bandages
• Education is ongoing and includes exercise, edema prevention, skin and wound care, long-term self-management, self-bandaging
• Patients with severe lymphedema may need to return yearly (for a few years) for a brief intensive repeat of Phase 1
Phase 2 - Self Management

- Continuation of self-bandaging in the evening or wearing of night device such as the Reid sleeve or the Legacy
- Compression garments are worn during the day
- Regular exercises are performed with compression bandages or garments on
- Regular self massage (to areas patient can reach)
- Skin care and prevention guidelines followed meticulously
- Self measuring to monitor limb size