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(205) DIFFERENTIAL DIAGNOSIS: LIPEDEMA vs LYMPHEDEMA vs VENOUS DISEASE



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Objective

- At end of this session 95% of learners will report in post activity evaluation increased confidence in their ability to diagnose & manage lipedema, lymphedema and venous disease.



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DISCLOSURE OF FINANCIAL RELATIONSHIPS

I do not have any relevant relationships to disclose



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WHAT DISEASE IS OFTEN CONFUSED WITH CELLULITE?



- Lipedema?
- Lymphedema?
- Venous Disease?



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LIPEDEMA



- 1 in 9 women affected in US; global prevalence ranges 10%-15%
- Mostly women, following autosomal dominant inheritance, & onset correlates with estrogen peaks in life (puberty, pregnancy)
- Family members with history of inability to lose weight in lower body
- Misdiagnosed as bilateral primary lymphedema or morbid obesity



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Diagnosis

- Primarily diagnosed through physical examination
- Bilateral, symmetrical, disproportionate fatty tissue hypertrophy on legs occasionally arms (feet & hand spared (cuff phenomenon)
- If untreated, Lipedema tends to progress....



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Lipedema Characteristics

- Swelling bilateral & symmetrical, feet-sparing
- Tender to palpation
- Bruising common
- Hard nodules in tissues
- Nonpitting edema
- Stemmer sign-Negative



*positive Stemmer sign (2ndary lymphedema)-skin fold between 2nd & 3rd toe thickened & cannot be lifted



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Treatment Options




- Compression Therapy:** medical-grade compression garments (stockings, sleeves) reduce fluid buildup & pain
- Manual Lymphatic Drainage (MLD):** gentle massage to stimulate lymph fluid flow to minimize swelling
- Physical Activity:** Low-impact exercises- cycling, swimming, Pilates, walking to lose weight, improve circulation
- Diet:** Anti-inflammatory, low-carb, or keto diets for weight management, lipedema resistant to traditional dieting
- Pneumatic Compression:** Home devices to aid with lymphatic drainage
- Skin Care:** Maintaining skin health i.e., moisture barriers to counteract dryness, scaliness




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Treatment based on Stage




Lipedema Stages

- > **Stage 1:** Nodules small; treat with compression, diet, exercise
- > **Stage 2:** Larger nodules, skin texture changes; higher mmHg compression & potential lymphatic massage
- > **Stage 3:** Significant fatty tissue distortion; requires complex, layered compression & frequently surgical intervention
- > **Stage 4:** Lipo-lymphedema: advanced with lymphatic blockage & fat accumulation; Comprehensive Decongestive Therapy (CDT)- manual lymphatic drainage, compression garments, skin care, exercise




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Surgical Treatment of Lipedema




- Liposuction** maybe alternative to compression therapy when compression therapy not helpful. Not enough research if liposuction as effective as compression therapy for newly diagnosed patients
- Liposuction (Reductive Surgery)** uses techniques like Water-assisted (WAL) or Power-assisted (PAL) to remove abnormal fat while sparing lymphatic vessels. May improve mobility, decrease pain
- Excision/Manual Extraction** for advanced stages to remove large, fibrotic, or nodular tissue




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Medications





- No specific FDA approved medications** for Lipedema
- Weight Management Medications:** GLP-1 agonists may decrease obesity-related inflammation, reduce overall limb volume, improve mobility; may not reverse fibrous tissue but lack research studies showing benefit
- Diosmin/Hesperidin:** Prescription bioflavonoid reduces inflammation. Doses of 450-1350 mg daily for 1-6 months. Caution-interactions- Carbamazepine, Fexofenadine, Diclofenac
- Selenium 400 mcg/daily** due to possible deficiency seen with lipedema, lipo-lymphedema (Pfister, 2020)



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Definition, Prevalence of lymphedema

- ❑ Lymphedema develops when lymphatic drainage disrupted with progressive accumulation of protein-rich interstitial fluid, chronic inflammation with fibrosis
- ❑ Estimated 250 million worldwide but underreported; dependent on age, gender, etiology
- ❑ Primary lymphedema rare, affecting about 1 in 100,000 cases in USA
- ❑ Secondary lymphedema- 8 to 10 million affected individuals in USA





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Types of lymphedema



- ❑ **Primary Lymphedema** (less common)- congenital lymphedema with abnormalities of lymphatics often due to genetic mutation
- ❑ **Secondary Lymphedema** (more common; acquired)
 - Etiology of lymphedema- Surgery to remove cancer &/or lymph nodes
 - Radiation damages lymph nodes; scarring impairs lymphatic flow
 - Infections from parasites (filariasis), rare in USA, leading cause in tropical & subtropical regions of globe
 - Vascular conditions- CVI, vasculitis, DVT, reconstruction/harvesting veins
 - Obesity/BMI > 40/trauma (orthopedic/burns)




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Pathophysiology of Lymphedema

- Chronic, progressive disease characterized by:
 - inflammation
 - increased adipose deposition
 - tissue fibrosis with lymphatic system's transport capacity insufficient despite normal capillary filtration with fluid stagnation & progressive edema



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Symptoms of lymphedema

- Pain, discomfort
- Fatigued, heavy/tightness of limbs
- Reduced joint range, gait changes, impaired ADLs
- Recurring infections (Cellulitis)
- Often involves feet-“Sausage Toes” –toes appear large; sausage-like



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Physical Exam

- ❑ Stemmer sign + (skin fold between 2nd & 3rd toes thickened & cannot be lifted)
- ❑ Edema pitting early stages; nonpitting as fibrosis advances
- ❑ Skin changes-hyperkeratosis (rough dry patches), papillomatosis (wart like papules), pitted skin texture resembling orange rind (peau d'orange)



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What are the lymphedema skin changes?



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Phlebolymphe~~ma~~

- ✓ Combination of CVI & lymphatic failure
- ✓ Damage to venous & lymphatic systems with limb edema. Interdependence leads to overloading causing both systems to fail
- ✓ Diagnosis based on signs/symptoms of venous & lymphatic malfunction
- ✓ Symptoms- itching, pain, changes in skin color, loss of suppleness, fibrosis, varicose veins





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Fluid Volume Assessment



- Circumferential measurements
every 10 cm for legs, start at ankle (medial malleolus) move proximally
Measurements of ≥ 2 cm difference between limbs significant
- Perometry (infrared light)
3D scan of limb's circumference & volume, identify subclinical changes in fluid volume
- Bioelectrical impedance spectroscopy (BIS)
non-invasive, measures body fluid for early lymphedema detection, differentiates extracellular (ECF) & intracellular (ICF) fluid. Changes in current strength indicate presence of fluid in tissue

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Diagnostics for Lymphedema

- Duplex ultrasonography- rule out DVT
- Lymphoscintigraphy-gold standard, uses radiotracers to evaluate anatomy & function of lymphatic system
- Indocyanine green (ICG) lymphography-fluorescent to map lymphatic vessels, Very sensitive in identifying early-stage lymphedema compared to lymphoscintigraphy
- Magnetic resonance lymphangiography (MRL)- Visualizes deep lymphatic channels & soft tissue changes


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Staging System



- **Stage 0 (Latent):** Compromised lymphatic transport; no visible swelling
- **Stage 1:** Reversible swelling subsides with elevation; pitting may occur
- **Stage 2:** Persistent swelling does not subside with elevation; pitting present
- **Stage 3 (Elephantiasis):** Severe fibrosis, adiposity, trophic skin changes; no pitting

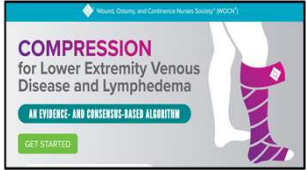
❖ The Diagnosis and Treatment of Peripheral Lymphedema: 2023 Consensus Document of The International Society of Lymphology. *Lymphology*. 2023;56(4):133-151.



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Management of Lymphedema

Compression for Lower Extremity Venous Disease and Lymphedema algorithm (<https://vlu.wocn.org/#home>) to identify appropriate level and type of compression



COMPRESSION
for Lower Extremity Venous Disease and Lymphedema

AN EVIDENCE- AND CONSENSUS-BASED ALGORITHM

GET STARTED

Wound Care

Compression for Lower Extremity Venous Disease and Lymphedema (CLEVDAL)


Update of the VLU Algorithm

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ABSTRACT

The Wound, Ostomy, and Continence Nurses Society (WOCN) Society changed its focus with updating the revised *Wound, Ostomy, and Continence Nursing Practice Guideline: Compression for Lower Extremity Venous Disease and Lymphedema (CLEVDAL)*. As part of this process, the task force was charged to develop consensus-based recommendations for clinical practice related to CLEVDAL. The consensus was reached by a multidisciplinary working group made up of experts in the field of venous disease and lymphedema. The WOCN Society sponsored a panel of experts to develop consensus statements to assist users for those with lower extremity venous disease and lymphedema. These consensus statements represent a consensus of expert opinion and do not represent a clinical practice guideline. The consensus statements are available at <https://vlu.wocn.org/#home>. The task force members are: Ratliff CR, Yates S, McNichol L, Gray M.


Ratliff CR, Yates S, McNichol L, Gray M. Compression for lower extremity venous disease and lymphedema (CLEVDAL): update of the VLU algorithm. *JWOCN*. 2022 Jul 1;49(4):331-46.



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Treatment of Lymphedema

- ❑ **Complete decongestive therapy (CDT)**- gold standard, combines manual lymphatic drainage (MLD), compression, exercise, skin care
 - Phase I (Reduction Phase) intensive, daily or 4–5 days/week, bandaging to reduce swelling & soften fibrotic tissue, lasts 2–12 weeks
 - Phase II (Maintenance Phase): Focus compression garments, self-massage, & exercises
- ❑ **Manual lymphatic drainage (MLD)**- massage promotes drainage by guiding fluid out of affected area for recirculation. Certified Lymphedema Therapists teach individuals to perform self MLD. Pneumatic compression devices also provide effective MLD for home maintenance
- ❑ **Compression**-low-stretch bandages/foam wraps during reduction phase, transition to fitted garments (sleeves/stockings) for maintenance



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Treatment

- Meticulous skin care (e.g., frequent skin cleansing, using low pH lotions, & emollients)
- Exercises of lower extremities (calf pumping exercises) part of daily activities (walking, using stairs) promotes external limb compression
- Patient selection, choice, physical ability, & cost when assessing mobility & compliance (including use of alternative compression devices)
- Highest compression level tolerated most beneficial
- Lymphedema Treatment Act (LTA)
<https://lymphedemaadvocacygroup.org/wp-content/uploads/2024/10/Provider-Handout.pdf>



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Medications



- Diuretics not beneficial due to volume depletion. Diuretics remove water from cells but not protein. Lymphedema high protein edema. Diuretic stopped; concentrated proteins pull more water back into interstitial spaces which increases edema.
- Topical emollients & keratolytics- ammonium lactate, urea, salicylic acid may improve hardened or thickened skin
- Micronized Purified Flavonoid Fraction (MPFF)- improves symptoms with single dose of 1000 mg daily or 500 mg twice daily
- Selenium 400 mcg/daily due to deficiency seen with lymphedema (Pfister, 2020)



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Surgeries

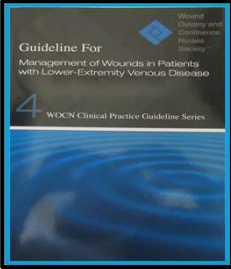


- Debulking procedures remove tissue & excess skin in folds on limb. Done selectively & require continued compression garments to maintain limb volume reductions
- Vascularized Lymph Node Transplant removes lymph nodes from 1 area of body to replace lymph nodes; removed or damaged from another region




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Lower Extremity Venous Disease (LEVD)



<https://wocn.digitellinc.com/p/a/lower-extremity-wounds-due-to-venous-disease-arterial-disease-or-diabetes-mellitus-and-or-neuropathic-disease-clinical-resource-guide-14008>




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Compression for Lower Extremity Venous Disease and Lymphedema algorithm (<https://vlu.wocn.org/#home>) to Identify appropriate level and type of compression






Ratiff CR, Yates S, McMillan L, Gray M. Compression for lower extremity venous disease and lymphedema (CLEVDAL): update of the VLU algorithm. JWOCN. 2022 Jul 1;49(4):331-46.




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Prevalence & Incidence of Lower Extremity Venous Disease (LEVD)



- ❖ Same as Chronic Venous Insufficiency (CVI) or Chronic Venous Disease (CVD)
- ❖ Progressive disorder of venous system from mild edema to venous leg ulcers
- ❖ Estimated 7 million worldwide have LEVD with 2 million progressing to ulcers
- ❖ Venous ulcers are the most common lower extremity ulcers making up 80-90% of all leg ulcers



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Risk Factors

- Family history
- Pregnancy-multiple, close together
- Advanced age (55 or older)
- Female
- Cardiovascular disease
- Hypertension
- High BMI/ Obesity
- Injection drug use
- Varicose veins
- Oral contraceptive use
- Tobacco use
- History of DVT or thrombophlebitis
- History of leg injury
- Prolonged standing or sitting
- Sedentary lifestyle



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Symptoms, Physical Examination

- Legs-aching pain, tightness/heaviness, dry itchy skin, fatigue, swelling worse with dependency but improves with elevation
- Physical findings- telangiectasias ("spider veins" < 1mm diameter), reticular veins (1-3mm diameter)-bluish color, bulging, varicose veins-superficial large, twisting, dilated, may be painful
- Hemosiderosis-reddish brown pigmentation in ankle region(RBCs breakdown & iron from hemoglobin released into tissue causing hemosiderin staining)
- Atrophie blanche-smooth ivory white atrophic skin with or without dilated capillaries, confused with scar tissue
- Lipodermatosclerosis-legs with induration, fibrosis, hyperpigmentation, "inverted champagne bottle"



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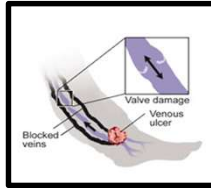
What are these LEVD skin changes?



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Pathophysiology of LEVD

- ❑ Venous hypertension- elevated venous pressures in calf lead to valve incompetence and/or obstruction
- ❑ Chronic long term venous insufficiency may result in secondary lymphedema



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Triggering Event

- 74% of VLU's have triggering event- injury/trauma, cellulitis, contact allergic dermatitis; rapid onset of leg edema; dry skin/itching; insect bite
- Diagnosed on clinical findings- increasing soft pitting edema with chronicity skin becomes fibrotic, hardened
- Location- legs & feet; toes atypical, unilateral/bilateral



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Venous Eczema/Dermatitis (Chronic)

- ❑ Chronic itching, thickening, crusting, scaly i.e., signs of LEVD
- ❑ Unilateral or bilateral
- ❑ Labs-WBCs normal, Blood culture negative. Skin swabs may show Staphylococcus aureus



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Cellulitis (Acute)

- Fever, warm to touch, erythema, swelling, bullae, serous drainage, painful
- Unilateral
- Labs-WBCs, ESR, C-reactive protein maybe elevated but normal values do not rule out cellulitis. Blood culture usually negative.



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VLU Wound Assessment

- Onset, duration, location, dimensions,
- Located superior to medial malleolus but anywhere on lower leg including back of leg/posterior calf
- Wound bed shallow, moist, ruddy red, or loose adherent yellow slough
- Wound edges-irregular; epibole (rolled edges)
- Periwound macerated, crusty, scaly with hemosiderin staining
- Exudate moderate to heavy with odor
- Bleeding may be present



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CEAP Classification of LEVD

- C**linical signs: skin changes
- E**tiological factors: congenital, primary, 2ndary
- A**natomical distribution: superficial, deep, or perforators, alone or in combination
- P**athophysiologic Dysfunction: reflux, obstruction, alone or in combination



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The CEAP (Clinical-Etiology-Anatomy-Pathophysiology) classification is an internationally accepted standard for describing patients with chronic venous disorders

CEAP Classification System and Reporting Standard Revision 2020

C (Clinical Manifestations), **E** (Etiology), **A** (Anatomic Distribution), **P** (Pathophysiology)

C0	No visible or palpable signs of venous disease
C1	Telangiectasias or reticular veins
C2	Varicose veins
C2r	Recurrent varicose veins
C3	Edema
C4	Changes in skin and subcutaneous tissue secondary to chronic venous disease
C4a	Pigmentation or eczema
C4b	Lipodermatosclerosis or atrophie blanche
C4c	Corona phlebectatica
C5	Healed
C6	Active venous ulcer
C6r	Recurrent active venous ulcer

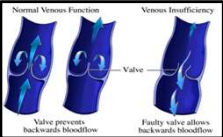

Lurie et al. J Vasc Surg Venous Lymphat Disord, May 2020
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Diagnosis



- **Venous duplex ultrasound**- assess deep & superficial veins for valvular incompetence & reflux in superficial veins.
- **Venous reflux**- retrograde flow > 0.5 seconds in superficial veins (greater saphenous vein (inner leg) & smaller saphenous vein (back of leg) of > 0.5 seconds & > 1 second in deep veins (femoral & popliteal) diagnostic for venous reflux.

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Measures to Improve Venous Return

- 30-40 mmHg compression if ABI is \geq than 0.80
- Highest level of compression patients can tolerate
- Consider intermittent pneumatic compression for immobile patients, intolerant of stockings or bandaging systems
- Do not rely on antiembolism stockings/hose** which provide low pressure (\leq 20 mm Hg) & are not designed for therapeutic compression to prevent or treat LEVD
- Wear life-long compression to reduce recurrence





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Types of Compression



- Compression Stockings**- graduated pressure; tight ankle & decreases up leg
- Short-stretch bandages (Inelastic)**- high pressure during activity & low pressure at rest
- Long-stretch bandages (Elastic)**- constant, high pressure even at rest
- Intermittent Pneumatic Compression (IPC) Devices**-used for VLUs/ lymphedema to pump fluid out of extremities
- Compression Wraps/Touch Fastener Wrap**- adjustable wraps easier to apply
- Multilayer Bandage Systems**- 2 to 4 layers with padding & compression




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Mixed venous/arterial disease

- Use reduced compression (23–30 mmHg) with LEVD, wounds, & edema if ABI is < 0.80 and ≥ 0.50
- Do not apply compression if ABI <0.50

ABI	Perfusion Status
>1.3	Distended or noncompressible vessels
>1.0	Normal
0.91-0.99	Borderline PAD
<0.9	LEAD
<0.6-0.8	Borderline ischemia
<0.5	Severe ischemia
<0.4	Critical ischemia, limb threatened



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Management of LEVD

- Elevate legs above heart level: 30 minutes, 4 times per day; increase exercise (e.g., walking, calf muscle exercise, toe lifts, ankle flexion)
- Avoid constricting garments, crossing legs, prolonged standing, high-heeled shoes
- Stop tobacco use; manage weight; healthy nutrition


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Procedures




- Superficial reflux- foam sclerotherapy, endovenous thermal ablation, or stripping
- Perforator reflux- sclerotherapy, endovenous thermal ablation, subfascial endoscopic perforator surgery (SEPS)
- Deep vein reflux-valve reconstruction or valve transplant
- Bioprosthetic venous valve device for femoral vein implantation

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Medications





- Pentoxifylline (400 mg 3x daily)- Improves blood flow by reducing blood viscosity, costly, GI side effects
- Micronized Purified Flavonoid Fraction (MPFF)- 500 mg twice daily) increases venous tone, reduces edema, enhances lymphatic drainage; GI side effects
- Horse Chestnut Seed Extract (HCSE 300 mg daily)-decrease in leg pain, edema, pruritic. Not recommended with Pentoxifylline, Acetylsalicylic Acid, Warfarin Sodium



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Morbidities for Lipedema, Lymphedema, LEVD

- Reduced health-related quality of life with lowered self-esteem, depression, diminished activities of daily living
- Recurrent infections (cellulitis)
- Musculoskeletal conditions (e.g., limited range of motion, weakness, pain)
- Neurologic disturbances (e.g., sensation changes)
- Altered clothing-barrel, wide leg

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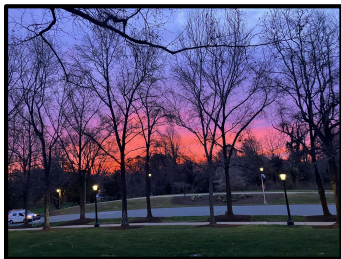
Summary

- ❑ **Lipedema**- fat deposition, affects women, bilateral swelling of legs, skin feels rubbery, irregular, bruises easily. Edema nonpitting or hard if longstanding
- ❑ **Lymphedema**- lymphatic flow damage, primary (hereditary) or secondary (infection, trauma, surgery). Involves entire leg, often bilateral with soft, pliable skin, + Stemmer's sign, protein-rich edema fluid
- ❑ **LEVD**-venous hypertension of legs & feet, usually bilateral with skin thickening, pigmentation, venous skin changes with soft, pitting edema, skin hardens



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Questions ????



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- The Lipedema Surgical Solutions- <https://lipedema.net/lipedema-resources-and-community-support/>
- Fat Disorders Resource Society - <https://www.fatdisorders.org/>
- National Lymphedema Network- <https://lymphnet.org/search/custom.asp?id=7347>
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- Lymphatic Research and Education Network- <https://lymphaticnetwork.org/>
- Lymphoedema Support Network- <https://www.lymphoedema.org/>
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