Lipedema Medical Therapy

Karen L. Herbst, PhD, MD
Associate Professor, University of Arizona
Director, TREAT Program
Disclosures

• Funded by the Lipedema Foundation
• Tactile System’s Speaker’s Bureau
Lipedema is hypertrophic subcutaneous adipose tissue (SAT) disorder
Supporting Evidence: Fat Cell Disturbance in Lipedema

- Hypertrophy (enlarged) and hyperplasia of fat cells
  J Cutan Pathol 2009;3:3
- Gynoid SAT inhibits lymph flow and increases capillary leak
  Metabolism 2003;52:805-9
- Lower resting energy expenditure in women with lipedema
  Ann Intern Med 1951;34:1243-50
Supporting Evidence Change in Tissue Structure

- Hypermobility common in women with lipedema
  Archives of Medicine, 2015 Vol. 7 No. 4:10

- Low tissue resistance; increased tissue capacitance
  Lymphology, 1988, 21:152-160

- Capillary leak and swollen arterial cushions
  Journal des Maladies Vasculaires, 1986; 11-303-309
• A - Hyper-permeable capillary with 5 adjacent adipocytes and transudate that diffuses into the capillary space
• B – Thickened capillary basement membrane
• C – Dilation of post-capillary venule

Histology Lipedema: Capillary Leak and Venule Dilation

Journal des Maladies Vasculaires (Paris), 1986; 11-303-309
Fig 3.—Normal lymphangiogram.

Fig 4.—Abnormal lymphangiogram shows multiple, small, “leaking” lymph vessels, which occurred in two patients.
1. Reduce inflammation
2. Break up proteins in the interstitium that hold water
3. Improve the lymphatic pump
4. Reduce excess leakage from capillaries, veins, lymphatic vessels
5. Reduce pain
6. Reduce fibrosis
7. Normalize fat cell size – make them healthier
8. Reduce hyperplasia
# Treatment for People with Lipedema

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Who</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Food</td>
<td>Everyone</td>
<td>If man made it, don’t eat it</td>
</tr>
<tr>
<td>Movement</td>
<td>Everyone</td>
<td>H₂O; WBV; yoga, Pilates, Nordic walking</td>
</tr>
<tr>
<td>MLD</td>
<td>Everyone with heavy tissue</td>
<td>Treatment and info on response</td>
</tr>
<tr>
<td>Wrapping</td>
<td>Anyone with lymphedema</td>
<td>Stop if no response or pain</td>
</tr>
<tr>
<td>Compression</td>
<td>Everyone with heavy tissue or venous disease</td>
<td>8-15 mm Hg; 20-30 mm Hg; arms, legs, abdomen</td>
</tr>
<tr>
<td>Sequential Pneumatic</td>
<td>If + response to MLD; + pain; + fibrosis</td>
<td>E0652 (Flexitouch; LymphaPress; Basic pumps with abdominal piece)</td>
</tr>
<tr>
<td>Compression Pumps</td>
<td>People with generally healthy limb around the vein</td>
<td>Take care not to overwhelm nearby veins</td>
</tr>
</tbody>
</table>

www.acpcongress.org
Lipedema Compression Challenges

• Compression is important for treatment of venous and lymphatic disease in lipedema
• Patients may not tolerate and may not need heavy bandaging
• Uncomfortable with heavy, dense elastic stockings.
• May need to use lower level of compression than for a lymphedema limb of similar size (Class I-II)
• Therapists creatively use padding under compression bandages in certain areas such as the ankle cuff to avoid tourniquet effect
• Consider yearly Venous Duplex US in women with lipedema
• Venous reflux should be treated; the risk for a lipedema limb is worsening of the veins near the damaged vein
• Some women have had worsening lipedema after vein treatments or developed lymphedema
• Deep tissue treatments may improve lipedema tissue and reduce risk after vein treatments – includes wrappiong
Selenium (Sodium Selenite) – a Mineral

- Inhibits inflammatory matrix metalloproteinase (MMP)-2
- Decreased edema in two placebo controlled trials for post-mastectomy and head and neck radiation-induced lymphedema.
- Increased efficacy of PT for lymphedema; reduced erysipelas infections.
- ↓O₂ radical production by ↑glutathione peroxidase/thioredoxin reductase.
- ↓glycoprotein adhesion molecules for immune cells in a dose-dependent manner; may unclog lymphatic capillaries.
- ↑efficacy of cytotoxic T-lymphocytes; stimulates macrophage degradation of excess tissue proteins.
- Does not improve diabetes Endocrine. 2014;47:758-63
Selenium Dosage

• 500-600 mcg daily to reduce lymphedema
• 3 Brazil nuts unshelled / 6 nuts shelled, per day supplies ~600 mcg

The US National Research Council defines the individual maximum safe dietary intake for selenium as 600 mcg daily; no adverse effect level as 800 mcg daily.
Monitor selenium levels by a simple blood test to ensure levels do not become high.
Pycnogenol

- Derived from pine tree bark: **Pinus pinaster**.
- Standardized to 70 ± 5% procyanidins: catechin, epicatechin, caffeic acid
- **Attaches to collagen in the vessel basement membranes improving vessel strength**
- Inhibits histamine production; decreases permeability
- A number of studies have shown improved endothelial function
- Women with lipedema can lose skin elasticity; Pycnogenol improves skin elasticity.

Skin Pharmacol Physiol. 2012;25:86-92
Doses of Pycnogenol

• ADHD: 1 mg/kg of body weight/day
• Asthma: 1 mg/lb/day
• Cholesterol/dyslipidemia: 120-150 mg/day
• Chronic venous insufficiency: 150-360 mg/day
• Diabetes: 50-200 mg/day
• Dysmenorrhea: 30-60 mg/day
• Melasma: 75 mg/day

• Muscle cramps: 200 mg/day
• Osteoarthritis: 100-150 mg/day
• Perimenopause: 200 mg/day
• Platelet function: 25-200 mg/day
• Retinopathy: 20-160 mg/day
• Endometriosis: 60 mg/day
• Erectile dysfunction: 120 mg/day
• Hypertension: 100-200 mg/day
Diosmin: Decreases edema by increasing lymphatic contractility and drainage

Rutosides: Improve lymph flow

Amphetamines: phentermine, dextroamphetamine, amphetamine and amphetamine salts (Adderall)

Butcher’s broom: Improves lymph flow
Diosmin

AKA: Phlebodia 600, Daflon 500, Oraescin, Vasculera

- Manages venous tone by increasing smooth muscle contractibility
- Lymphatic vessels have smooth muscle too!
- Inflammatory cells generate high levels of tissue destructive reactive oxygen species (ROS)
- Scavenger of ROS, which may help to protect endothelial cells from damage associated with inflammation and acute oxidative stress

Angiology. 1994 Jun;45(6 Pt 2):524-30
Biochem Pharmacol. 1993 Apr 6;45(7):1531-5
Lymphatic pumping

- Adrenergic receptors (α1-, α2- and β-AR) are on lymphatic vessels
- Norepinephrine increased the efficiency of lymphatic pumping
  

- Low intra-arterial doses of adrenaline increased lymph flow even with marked arterial vasoconstriction
  
  Micheli and Glasser, 1975

- Lymphatics in lymphedema had a slightly greater contractile response to adrenaline and serotonin
  
Norepinephrine and electrical field stimulation frequency-response curves in the same lymphatic vessel.
Dextroamphetamine Side Effects

Common Side Effects

• Increased alertness
• Apprehension
• Increased concentration
• Decreased sense of fatigue
• Mood swings
• Increased initiative
• Insomnia or wakefulness
• Self-confidence
• Sociability

Less common side effects

• Anxiety
• Change in libido
• Grandiosity
• Irritability
• Repetitive or obsessive behaviors
• Restlessness
Statin Medications

• Lowers cholesterol.

• Reduces inflammation and leakage from small vessels (microcirculation)
  Br J Anaesth. 2010;104:183-90

• Reduces microvascular inflammation during endotoxemia
  Naunyn Schmiedebergs Arch Pharmacol. 2015;388:557-64

• Simvastatin prevented microvascular permeability.

• Side effects: myalgia
L-Arginine – reduces leaky vessels

- Doses range from 1-30 grams daily in divided doses
- A common dosage is 2-3 grams three times a day

Take 12-15 grams daily as a powder or get a long-acting arginine supplement

Modified from: Cardiovasc Res. 2015 Jul 1;107(1):89-97
Avoid NSAIDs

• NSAIDs cause fluid retention and edema through effects on the kidney.
• Weight gain 2-5 lbs, typically within the 1st week of therapy (edema/sodium retention).
• In rare serious cases, increased sodium reabsorption can result in marked edema, weight gain, and exacerbations of heart failure.
• NSAIDs can reduce benefits of diuretic therapy; moderate increases in blood pressure are sometimes observed.
• Diabetes mellitus, renal disease, circulatory compromise, and advanced age may predispose people to NSAID-related sodium retention and edema.
Ketoprofen: NSAID

- Ameliorates experimental lymphatic vascular insufficiency in mice. 
  *PLoS One 2009;4[12]*
- May ameliorate lymphedema in people.
- Dosed as 50-75mg three times a day; or 200mg ER daily.
- I usually only recommend ketoprofen if the patient is already taking an NSAID regularly; they must have pain.
- Monitor for effectiveness = ↑urination and ↓swelling.
- Take with a PPI and a B100 complex.
Meds and Supplements that Reduce Fibrosis

1. Losartan reduces TGFβ and fibrosis
   PNAS USA. 2011;108:2909–14

2. Relaxin reorganized the collagen matrix (Skelaxin/metaxalone)

3. Superoxide dismutase even applied topically reduces post-irradiation induced breast cancer fibrosis - Consider eating The Charentais French Melon

4. Metformin and resveratrol effectively inhibited HIF-1α activation-induced fibrosis and inflammation in adipose tissue
Loosen Extracellular Clumped Protein

- Interstitial (extracellular) proteins not picked up by lymphatic vessels form clumps, resisting removal
- Diuretics such as Lasix (furosemide) amplify protein clumping
- Mucolytics break up protein clumps
  - N-acetyl-cysteine (NAC) 500 mg twice a day
  - Guaifenesen ER 600 mg twice a day

Sexual Dimorphism in Glucose and Lipid Metabolism during Fasting, Hypoglycemia, and Exercise
Eat to starve lymphedema and lipedema with foods that fight these conditions

www.amazon.com

Barnesandnoble.com
Quadrivas Treatments

Each treatment:
• 90 - 120 minutes
• Whole body
• 2 or 3 times per week

Lipedema:
• Stage 1 & 2  24 - 40 treatments
• Stage 3/4  30 - 60 treatments

Slimming:  10 - 24 treatments

Bodyweight >120 kg - multidisciplinary approach

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Slide Courtesy Alyna Eekma
Summary

• There are no large randomized controlled trials of medications or supplements for people with lipedema
• Treatment of lipedema relies on improvement in symptoms
• Supplements and medications work well in some but not others – data is needed to personalize treatment
• **Favorite supplements and medications**: dextroamphetamine, diosmin, guaifenesin and NAC, seed extracts (horse chestnut seed extract gel; Brazil nuts)
• Research is needed to understand the physiology and genetics of lipedema and design treatments based on the genes and physiology
TREAT Program

• Funded by the Lipedema Foundation
• Goals: Develop educational materials: patients, medical students, residents, fellows, primary care and specialist physicians
• Multiple collaborators to understand the physiology of lipedema and Dercum’s disease

http://treat.medicine.arizona.edu/
Thank you!