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# Letter to the Editor regarding Lipoedema – myths and facts, Part 1 and Part 5. European Best Practice of Lipoedema – Summary of the European Lipoedema Forum consensus. Phlebologie 2020; 49: 31–49

Lipedema is a disease of loose connective tissue (LCT)-not just fat. Constituents of LCT include cells and an extracellular matrix of collagen fibers around glycosaminoglycans (GAGs) bound to sodium and water.

A. **Edema:** The authors state "there is no evidence for the presence of edema in lipedema" [1]. Edema is defined as excess interstitial fluid (IF) [2] that is free, or bound in a GAG gel as in lipedema:

1. Overgrowth of blood vessels in lipedema tissue is not matched by increased lymphatic vessels [3], and capillaries are leaky [4] increasing IF.
2. The interstitium is enlarged in lipedema LCT [3, 5] with fibrosis and GAGs. [6, 7]
3. Extracellular fluid is higher in the legs of women with lipedema, controlled for BMI [8, 9]. In lipedema unlike lymphedema, GAG-bound IF doesn't flow to the hands and feet, sparing them.
4. GAGs bind sodium. Sodium content is higher in skin and LCT of women with lipedema [10].
5. Soft tissue inflammation increases interstitial sodium and GAG[11]. Inflammation [3, 5, 12] and excess sodium are present in lipedema LCT [10].
6. Lipedema tissue is highly compliant [13]. As IF increases, pressure does not increase accordingly, and excess IF and stasis occur. Many women with lipedema have hypermobility, a connective tissue disorder affecting tissue compliance [14, 15].
7. Edemas with non-pitting edema have increased GAGs including localized myxedema, venous disease and lymphedema [16].

B. **Manual therapy and compression:** The authors state "treatment of lipedema with manual lymphatic drainage (MLD) therapy is obsolete" [1]. US therapists use deep tissue manipulation during MLD to improve lipedema tissue structure and drain excess fluid. MLD normalizes lipolytic responsiveness of femoral fat tissue [17], improves microcirculation and capillary fragility [18], and reduces lipedema pain [19, 20]. Deep manipulation for lipedema [19] breaks down fibrotic fat, and reduces tissue volume, and fat by DEXA scan [21, 22]. We agree compression garments reduce inflammation; edema is part of inflammation.

C. **Lipohypertrophy:** The authors state, "lipohypertrophy is a painless disproportionate increase in adipose tissue" [1]. In a seminal paper, 40–50 % of women with lipedema had pain or tenderness in the legs [23]. Thus pain is not an absolute requirement for a lipedema diagnosis. A woman with painful lipedema who underwent therapy and has no pain, still has lipedema. Further research is needed to discern if/how lipohypertrophy differs from lipedema.

D. **Obesity, secondary lymphedema and bariatric surgery:** The authors state "women with lipedema develop lymphedema secondary to obesity" [1]. A biomarker, PF4, shows lymphedema and lipedema are distinct from obesity [24]. Lymphangioscintigraphy of women with lipedema ± obesity showed lymphatic system alterations [25], suggesting obesity is not a primary cause of lymphatic alterations or lymphedema in lipedema. Many severe obese women with lipedema do not develop lymphedema [26].

We recommend bariatric surgery for women with lipedema and obesity with metabolic complications [27–29]; long-term studies are needed to assess how lipedema progresses ± obesity.

E. **Psychology:** We agree women with lipedema experience appearance-related distress. We also agree depression and poor mobility adversely affect quality of life [30] and increase pain. We have no evidence to support the statement that: "psychological factors can contribute significantly to the development of lipoedema" [31].

F. **Liposuction:** We disagree that "Liposuction is not a treatment option in patients with a BMI > 35 kg/m$^2$ and central obesity (WHtR > 0.5)" [1]. Women can develop lipedema LCT on the abdomen [14]. Lipedema patients should be considered individually for liposuction.

In conclusion, we discuss evidence edema in lipedema exists bound to GAGs sharing features with other edemas but with a different clinical presentation than lymphedema secondary to obesity, will benefit from manual therapy and liposuction, and merits research to understand its role in lipedema etiology. The authors state treatment of obesity and lymphedema are "by no means enough to treat the complex disease of lipoedema adequately. Our greatest desire is to make this absolutely clear!" [1]. We agree.

## Conflict of interest

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