

Current evidence on lipoedema development and management.

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Background

- Little research in lipoedema
- But improving
- Lot of "received wisdom"
- Some of these "facts" are now being reconsidered
- Therefore, there are a lot of uncertainties / unknowns

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Background

- This will not be a comprehensive review of all the current research evidence
- Will consider important areas of uncertainty encountered in clinics
- Important issues for patients
- Some remarks are based on experience in our clinics and shared discussions with other centres
- "Health warning"
- It is important to be able to share these uncertainties with patients and be ready to change our practice when new evidence appears

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Diagnosis of lipoedema

- Often not clear cut
- No diagnostic test
- Various criteria
- Classical lipoedema
- Lipoedema or lymphoedema
- Lipoedema and obesity
- What is lipolymphoedema?

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Classical lipoedema

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Lipoedema or lymphoedema?

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Lymphoedema : definition

- tissue swelling due to a failure of lymphatic drainage

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However.....

- Pure lymphoedema is probably very rare and other factors eg changes in venous function co-exist in most people with chronic swelling / "lymphoedema"

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"Chronic oedema":

- a term which covers this more complex picture and includes pure lymphoedema
- oedema of limbs / mid-line structures.
- > 3 months duration

(Moffatt et al Q J Med 93: 731-8 (2003))

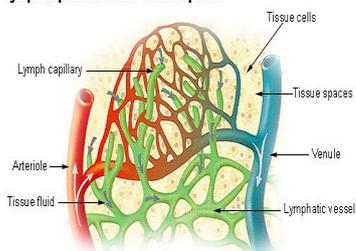
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Chronic oedema includes:

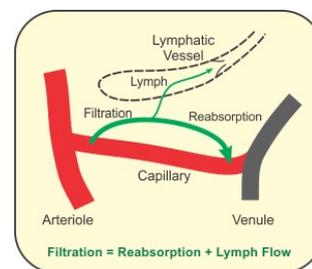
- lymphoedema (primary & secondary)
- oedema due to venous disease
- oedema associated with immobility
- oedema associated with obesity
- often multifactorial which may include medications

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Lymph Capillaries in the Tissue Spaces

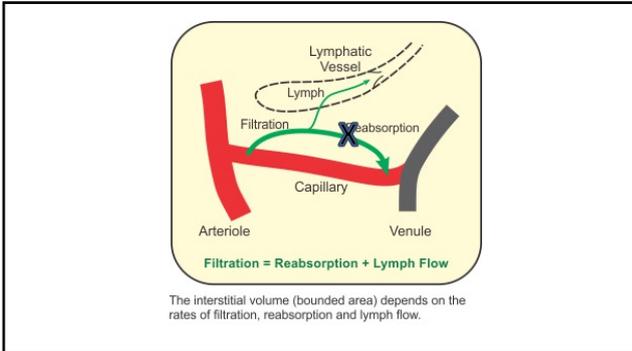


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The interstitial volume (bounded area) depends on the rates of filtration, reabsorption and lymph flow.

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New physiology

- In steady state in most capillaries, there is no reabsorption into the venous end of the capillary
- The lymphatic is the main route for flow of fluid (and macro molecules) out of the interstitial space
- All oedema has a lymphatic component

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Nevertheless.....

- Some people prefer the term “lymphoedema” and use it to mean the same as “chronic oedema”
- Some use chronic oedema/lymphoedema

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Differences between lipoedema and lymphoedema

- A variety of tables comparing the 2 have been published
- E.g Milken Institute

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Table 1: Differential diagnosis of oedema vs lymphoedema vs obesity vs Chronic

	Lipoedema	Lymphoedema (Primary and Secondary)	Obesity	Phleboedema, Chronic Venous Insufficiency
Distribution	Symmetrical fat deposition and swelling in legs and/or arms, but not the face or hands	Fat deposition and swelling in affected limbs, including hands or feet	Widespread fat deposition, with the potential for swelling due to cellulite	No fat, but swelling and itchy areas over oedema with a brownish discoloration of lower legs
Sex	Almost all female	Males and females	Males and females	Males and females
Onset	During hormonal shifts (puberty, pregnancy, menopause) and periods of weight gain	Primary: Congenital, due to presence of genetic mutations secondary: Due to damage to the lymphatic system	Age independent	During pregnancy or onset of menopause, such as obesity, diabetes, or hypertension
Pain	Yes, in affected tissues	Discomfort and itching can occur over time	Yes, chronic pain associated with cellulite	Yes, in affected areas
Impact of Caloric Restriction and Exercise on fat	Limited	None	Weight-loss strategies can be effective	Not applicable
Risk of Cellulite	No	Increased	Increased	Increased risk in areas affected by oedema. Itchy and discoloured areas with oedema can look like cellulite
Reversibility	Potential	Primary lymphoedema can be reversed	Potential	Potential

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Effects of high BMI

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Is it lipoedema + obesity or obesity or obesity related lymphoedema/chronic oedema?

- Differential weight loss?
- Pain / tenderness / fibromyalgia?
- Oedema? Stemmer sign? Swollen feet?
- Skin changes of lymphoedema?
- Easy bruising?
- Family history? etc

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Lipo-lymphoedema

an increasingly controversial term

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Does lipolymphoedema exist?

- Lipoedema with superimposed fluid oedema = lipolymphoedema (Stage 4) (ie represents a progression)
- Mild lipoedema without weight gain – swelling around ankles – gravitational effect on fat deposits? Local oedema? Feet unaffected.
- More extensive oedema seems to be mainly related to other conditions e.g added weight gain. Feet affected.
- Weight gain seems to be the major factor which can lead to the progression of lipoedema.
- Lipo-lymphoedema is not a helpful term

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Exceptions / unusual patterns!

- A small number of women with both lipoedema and primary lymphoedema ?

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Summary

- Significant fluid oedema is uncommon in mild lipoedema without an added weight problem
- More extensive fluid oedema (lymphoedema) usually associated with weight gain in those with lipoedema.

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Weight and lipoedema

- Does lipoedema cause obesity?
- Does weight management improve lipoedema?
- Does weight management prevent progression of lipoedema?

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Case examples of relationship between leg volume and weight

- Weight loss by diet / exercise
- Weight loss by bariatric surgery

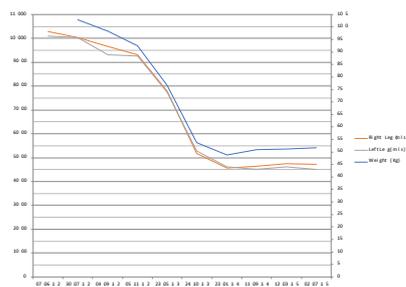
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1) Weight loss and volume loss after bariatric surgery

- Approx 50% weight loss
- Approx 50% volume loss

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Graph demonstrates relationship between weight loss and limb volume over time.



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Fat thickness on US scan

- Right leg
- Mid-thigh anteriorly - 31mm to 5mm
- Anterior upper pretibial - 27mm to 5mm
- Medial upper calf - 38mm to 16mm
- Lateral ankle - 19mm to 6mm

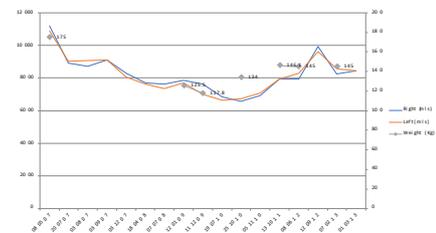
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2) Weight loss and volume loss after bariatric surgery

- Approx 30% weight loss (175kg to 125kg)
- Approx 30% volume loss (10.5l to 7.5l)

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Weight change and limb volumes



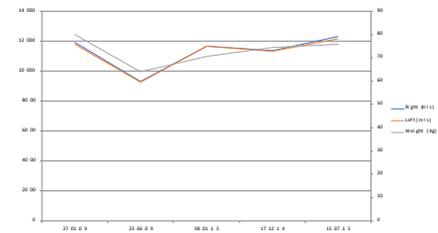
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3) Weight loss with diet and exercise

- Long standing lipoedema
- Variations in weight
- Different diets
- Sustained period of diet and exercise (gym) over 6 years
- Weight loss from approx. 160kg to approx. 63.5kg.

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Weight and limb volume changes



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Weight loss and volume loss

- 2009 figures only
- Weight loss - Approx 20% (80kg to 65kg)
- Volume loss - Approx 20% (12l to 9.2l)

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Weight management

- Importance of this
- Isabel Forner-Cordero's work on factors which lead to the progression of lipoedema:
 - % volume change in legs
 - lipoedema stable in 2/3 cases; progression 1/3
 - weight gain was the most important factor.
 - weight change and % volume change related (ISL 2019; n=69; median follow-up 3.8yr)

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Importance of these results

- For many young women a major fear is the relentless progression of the condition
- It seems that this may be preventable by careful weight management (avoidance of weight gain) with healthy diet and exercise

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Weight management in those with an added weight problem

- Importance of slow steady weight loss e.g. by diet / exercise or if severe problem weight loss surgery
- Rapid weight loss is difficult to sustain and yoyo-ing weight seems to lead to progression
- Impression: that during rapid weight loss, the loss seems to be mainly from the upper body and less from the legs; with weight gain, weight seems to go on the legs as well as elsewhere -> progression
- Does weight loss work for everyone with lipoedema and a weight problem?

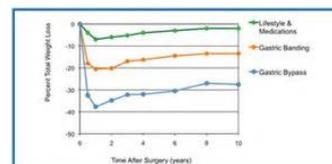
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Bariatric surgery

- Adjustable gastric bands
- Gastric bypass
- Gastric sleeve
- Produce sustained weight loss in obesity

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Results of bariatric surgery



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Bariatric surgery

- Not a quick fix
- Long term effects (e.g. need for supplementation of vitamins etc) / complications)
- Needs careful informed consideration / tiered weight management programme - multidisciplinary assessment and advice
- Successful approach for certain individuals

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Compression

- Does compression have a role in treating lipoedema / reducing risk of progression?
- Lack of evidence for this
- Isabel Forner Cordero's study – concordance with the use of compression did not seem to prevent progression

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Compression

- Some controversy over role in lipoedema
- Our experience:
 - Use if oedema present, especially in those with an added weight problem
 - Use to improve discomfort / pain – sports compression

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Manual Lymphatic Drainage (MLD)

- Anecdotal reports of benefit
- Lack of research evidence in lipoedema
- Limited research evidence of additional benefit to compression in lymphoedema (danger of extrapolation to lipoedema)
- Short duration of effect likely
- Isabel Forner Cordero's study suggested MLD did not affect progression
- Not routinely recommended in our clinic

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Genetics of lipoedema

- unknown
- ? genetic component
 - Family History in 15% (?)
 - autosomal dominant with sex limitation
- hormonal influence

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Investigation of clinical characteristics and genome associations in the 'UK Lipoedema' cohort

- a tightly phenotyped cohort of 200 lipoedema patients (from two UK specialist clinics).
- genome wide association study (GWAS) performed (n=130).
- revealed genetic loci associated with the lipoedema phenotype (supported by an independent cohort taken from the 100,000 Genomes Project).
- top single nucleotide polymorphisms (SNPs) included loci associated with **lipoma formation, biosynthesis of hormones and lipid hydroxylation**
- consistent with fat and hormone hypothesis but needs further detailed research to confirm

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- importance of confirmed diagnosis and strict phenotype inclusion criteria
- issue of added weight problem / different genes?

- Ref: Grigoriadis D et al (2022) Investigation of clinical characteristics and genome associations in the 'UK Lipoedema' cohort. PLoS ONE 17(10): e0274867. <https://doi.org/10.1371/journal.pone.0274867>

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Which drugs may affect lipoedema?

- The fat in lipoedema
- General weight
- Oedema causing drugs

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Drugs which may affect the fat in lipoedema?

- Oestrogens

Combined Oral Contraceptive Pill

Hormone Replacement Therapy

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Drugs which cause weight gain

Drug group	Examples
Anti-depressants, anti-anxiety, mood stabilizers	Selective serotonin reuptake inhibitors (SSRIs); Older anti-depressants e.g. Amitriptyline.
Antipsychotics	Risperidone
Diabetes medications	Insulin
Steroid hormones	Corticosteroids e.g. Prednisolone Anastrozole* Tamoxifen*
Anticonvulsants, anti-migraine, neuropathic pain	Pregabalin
Anti-hypertensives	Beta blockers e.g. atenolol
Antihistamines	Getirizine

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Drugs which cause oedema

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Drug group	Example drug	Frequency of peripheral oedema
Calcium channel blockers (Non-lipophilic dihydropyridines (DHP))	Amlodipine	up to 14.6%
Non-steroidal anti-inflammatory drugs	Ibuprofen	1-10%
Corticosteroids	Prednisolone	1-10%
Antidepressants	Trazodone	1-10%
	Mirtazapine	1-10%
Anticonvulsants	Pregabalin	up to 12%
Antidiabetics	Rosiglitazone	1-10%
Antipsychotics	Risperidone	1-10%
Antispasmodics	Baclofen	1-10%
Chemotherapy	Docetaxel	Lymphoedema - 1-10% Initial fluid retention - 60%
Anti-Parkinsonian	Pramipexole	1-10%
Analgesics	Morphine	1-10%
Hormone treatments	Tamoxifen	>10%
	Anastrozole	1-10%
Anticoagulants	Rivaroxaban	1-10%

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Conclusions

- Many uncertainties / unknowns in lipoedema
- Importance of discussing these with patients
- Consider changing practice when new evidence available

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THANK YOU!

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