Point-counterpoint: Debating Lipedema

Response to "Therapy for Lipedema Incorporating New Clinical Guidelines."

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We read with interest the article by Guenter Klose in the Pathways Winter 2020/2021 edition of the magazine. While we agree with much of what Klose has written, we take issue with four concepts that we address here.

First, Klose states that there is no edema in lipedema. While some may think the presence of edema requires visible free fluid in the interstitial space of tissue on ultrasound and the presence of pitting edema on clinical exam, this ignores the second location where fluid accumulates: in the interstitial space bound to glycosaminoglycans (GAGs) and proteoglycans. The correct definition of edema was published by Drs. Mortimer and Levick as "increased fluid in the interstitial space".¹

The interstitial space is a vibrant and complex part of the extracellular matrix. Within the interstitial space are fibers including collagen and elastin, a multitude of proteins, and complex structures called proteoglycans that are protein backbones to which GAGs are bound. GAGs are branches of repeating disaccharides that have a strong negative charge allowing them to bind sodium and water within the interstitial space. A GAG called hyaluronan binds proteoglycans together. participates in the hydrodynamics of the interstitial space and serves many other functions including immunomodulation. When lymphedema begins, hyaluronan, as a marker of GAGs, increases in the interstitial space to bind up additional fluid.² If fluid continues to accumulate, hyaluronan stagnates in the interstitial space3 and fluid becomes visible by ultrasound as it overwhelms not only lymphatic vessel function but also the amount of proteoglycans the tissue can generate. Therefore, fluid in the interstitial space can be bound, free or both. In lipedema, or in early stages of lymphedema, prior to fluid becoming visible by ultrasound, fluid is primarily bound to GAGs/proteoglycans. For example, in Stage 0 lymphedema symptoms are present yet fluid is not visible by ultrasound and lymphatics appear normal by lymphangioscintigraphy, but dermal backflow of fluid (a sign of lymphedema) may be present on indocyanine green imaging.4 Would we say there is no lymphedema just because we cannot see fluid by ultrasound or feel it?

In support of edema in lipedema as bound fluid, as fat tissue increases in the body, so do proteoglycans in the interstitial space.⁵ Women with lipedema also have more extracellular fluid,

and more sodium in the skin and tissue than women without lipedema.^{6,7} Using the very powerful imaging modality, magnetic resonance lymphography, there is clearly free fluid present in lipedema tissue in later stages but also in individuals in earlier stages,⁸ which was clearly misstated by Erbacher and Bertsch.⁹ Lymphatic dysfunction has also been documented in early and late stages of lipedema¹⁰ and a new marker of lymphatic disease has been found for people with lipedema independent of the amount of fat tissue on the body.¹¹ Edema is present in lipedema tissue; we just need to incorporate into our educational curriculums the pathophysiology of the interstitial space that has been known for decades.¹²

Articles by Drs. Erbacher and Bertsch, including the Myths and Facts series, as well as Klose, seek to de-legitimize manual lymphatic drainage (MLD) as treatment for lipedema based on a flawed understanding of lipedema physiology and contravening clinical evidence. MLD can help reduce volume and pain in lipedema when it includes deeper tissue techniques that are different from the techniques recommended for lymphedema.

Secondly, the series of articles entitled Lipedema-Myths and Facts, Parts 1-5, by Bertsch and Erbacher cited by Klose are not a new paradigm for lipedema; instead, they begin to push lipedema back in time when it was viewed as "just obesity". According to Klose, "An additional challenge in diagnosing and treating lipedema is that patients often have comorbidities such as obesity and subsequent obesity-associated lymphedema. Because there is significant overlap between these conditions, clear differentiation may be impossible, even for very experienced professionals." The authors from the Foeldi Clinic in Germany primarily care for women with obesity and mistake women that have obesity for women that have lipedema.9 But not all women with lipedema are obese though the majority of women in the Foeldi Clinic may have obesity; the Foeldi Clinic population does not represent all women with lipedema.

The Myths and Facts authors state that women with lipedema can lose lipedema fat after bariatric surgery. However, part of the definition of lipedema is fat that resists loss by diet, exercise and bariatric surgery. The Foeldi Clinic authors support the concept of lipohypertrophy, an increase in fat tissue that looks like lipedema but has no pain or edema. Perhaps Drs. Bertsch and Erbacher

mistake lipohypertrophy for lipedema. Experienced professionals can clearly diagnose and differentiate obesity from lipedema as we palpate the tissue and find nodules and other markers of fibrotic tissue. Delayed or inaccurate diagnosis of lipedema contributes to the physical and psychological pain and suffering experienced by many women. We can reduce this pain by pushing for earlier diagnosis and treatment, including screening younger women. In addition, readers should be aware that inappropriate language towards patients has been used in the articles by Bertsch and Erbacher including this statement when discussing weight gain with people with lipedema: "It is laborious and time-consuming to convince patients that they are misinformed and that there are other factors that lead to an increase in weight, and it is certainly not due to lipoedema." This statement has no proof, suggests that the patient is always at fault, and closes the door to any further research into weight gain in association with the development of lipedema.

The third issue is the statement "mental health issues were present before the onset of symptoms typically associated with lipedema and that these issues have an influence on the patient's perception of pain".9 The authors state that women with lipedema develop mental health issues prior to the symptoms of lipedema developing, especially pain.¹⁶ The idea that mental health diseases such as depression and anxiety can increase the perception of pain is not new. Reports of rates of depression and other mental health disorders in lipedema are not inconsistent with patients with other chronic pain disorders.¹⁷ We want to make it clear that women can develop lipedema tissue well before pain develops, and that this can result in the development of depression and anxiety as they see themselves different than their peers. We also want to be clear that mental health issues are not the sole source of pain in women with lipedema. However, mental health disorders can hinder the ability to cope with chronic pain.18

The fourth issue that we feel requires clarification is the following statement by Klose: "There is a common misperception that liposuction can eliminate lipedema and along with it, a patient's emotional and psychological burdens. Although liposuction can reduce the size of a limb, there are grave risks..." There is no misconception that liposuction will eliminate lipedema. Liposuction removes diseased fat in

the areas of liposuction but the patient still has lipedema and has to continue appropriate exercise and diet. There are now studies that demonstrate the long-term benefits of liposuction not only on tissue reduction but improved quality of life. 19-23 Mobility, function and pain are decreased after liposuction which has a positive effect on the patients psyche and also enables patients to participate in activities they may not have been able to do prior to liposuction. If liposuction is performed

by a skilled surgeon, there are no grave risks.

We advise caution in reading the articles by Drs. Erbacher and Bertsch because they put at risk the progress we and others in this field have made towards improving our understanding of lipedema and the lives of women with lipedema. To simply state that lipedema is obesity that can be solved by treatment methods aimed solely at obesity, neglecting the etiology of lipedema and the fibrotic nature of the lipedema tissue which requires a

different treatment paradigm is not progress and certainly not a new paradigm.

Find more here: 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.

A full set of references can be found at www.lymphedemapathways.ca

In Response to Herbst's Letter to the Editors of Pathways

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We are responding to the letter to the editors of Pathways from Karen Herbst and her colleagues ("the authors"). Their statements made, are only superficially directed to the contribution to Pathways made by Klose, but essentially are directed to the lead authors of the recently published International Consensus Document on Lipedema.¹ Therefore, it is only appropriate that the following is a joint response by Bertsch, Erbacher and Klose. The statements made by Herbst and colleagues provide an opportunity to clarify essential aspects regarding lipedema. On one hand, readers of Pathways are able to see the perspective of Herbst and her colleagues. On the other hand, there is the International Consensus on Lipedema which was summarized by both Bertsch and Klose in the Fall and Winter issues of Pathways—and which is supported by renowned experts from 10 European countries, as well as from key opinion leaders from the U.S. and Australia.^{1,2} Below, we respond to and debunk the four disputed points put forth by the authors.

1) Unfortunately, the authors confuse three diseases - lymphedema, lipedema and obesity. Although many of our patients with lipedema additionally present with obesity³ and, in cases of severe obesity, obesity-related lymphedema⁴, it is essential to consider all three diseases individually, and with their own specific pathophysiology.

In the first two paragraphs of their letter, Herbst and her colleagues correctly describe the situation we see in patients with lymphedema – but not in patients with lipedema. All the sources mentioned in these paragraphs refer to lymphedema – not

to lipedema. In the third paragraph, Herbst and colleagues write: "In support of edema in lipedema as bound fluid, as fat tissue increases on the body, so do proteoglycans in the interstitial space." The reference the authors cite is NOT an article about lipedema; in fact, the term lipedema is not mentioned at all. That reference is an article about proteoglycans in obesity-induced dysfunction. In other words, none of the sources refer to lipedema.

There is no scientific evidence for the claim that lipedema is marked by edema. If it were the case (hypothetically) that there was relevant edema in lipedema, and furthermore, that this mild edema would be the cause of the pain of our patients, as Herbst claims in other articles (e.g.⁵), then patients with lymphedema would also have pain. We all know that this is not the case.

Furthermore, Herbst and colleagues write: "Using the very powerful imaging modality, magnetic resonance lymphography, there is clearly free fluid present in lipedema tissue..." However, the authors' reference is an article by Cellina et al. In contrast to the claim of the Herbst group, only patients who suffered from lymphedema, in addition to their lipedema, showed—of course—free fluid in the tissues. Cellina et al., who investigated patients with lipedema by magnetic resonance lymphography, stated: "The fat tissue was homogeneous, without any signs of edema in patients with pure lipedema."

Moreover, Herbst and her colleagues claim: "Lymphatic dysfunction has also been documented in early and late stages of lipedema." The authors reference an article by Forner-Cordero et al. Let us

quote the authors cited: "...because of a lack of a test of diagnostic certainty of lipedema, we may have included patients with lymphedema instead of lipedema." Additionally, to this very essential scientific incertitude, the investigated patient population in the study by Forner-Cordero was old (up to 80 years of age). It is well established and documented that lymphatic function declines with age - even in healthy people.⁶

In addition, there is definitely no "new marker of lymphatic disease ...for people with lipedema," as Herbst and her colleagues claim. To debunk this, we refer to an article by Bertsch and Erbacher in which this issue is discussed in detail.⁷

To be clear, edema is defined as an "abnormal accumulation of fluid" in the tissue8. Neither clinical examination, nor imaging techniques like those mentioned above, could ever prove relevant edema in patients with pure lipedema. 9,10 Reich-Schupke et al. wrote in their pioneering article in 2012: "The term 'lipedema' is actually misleading, since it is not an edema in a sense of accumulation of fluid in the tissue". 11 This was confirmed by the authors of the Dutch lipedema guidelines, in which they described lipedema as an "unfortunate term," as it suggests fluid in the tissue where no fluid can be found.12 Finally, the European Lipedema Forum an international group of high-ranking experts from various European countries—summarized in a highly-recognized consensus paper: "There is **no** [emphasized in the original] scientific evidence that lipedema is an 'edema problem'".2

To reiterate, there are patients who, in addition to

Thank you!

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their lipedema, also suffer from lymphedema—e.g. primary or obesity-induced lymphedema. Others (not only patients with lipedema) experience orthostatic edema after long periods of standing or during the hot summer months. But there is no scientific evidence that lipedema is the cause of any relevant edema—an edema that necessitates treatment.

2) We reply to the following statement from Herbst and her colleagues: "The authors from the Foeldi Clinic in Germany primarily care for women with obesity." The Foeldi Clinic in Germany is in fact the largest and most prestigious hospital for patients with lymphedema and lipedema from all over the world. The Foeldi Clinic is not an "obesity clinic".

Herbst and her colleagues continue: "But not all women with lipedema are obese though the majority of women in the Foeldi Clinic may have obesity; the Foeldi Clinic population does not represent all women with lipedema." We agree that, not all; but the majority of patients with lipedema are obese (BMI > 30 kg/m²) and around 50% are even morbidly obese (BMI > 40 kg/m²). 14,19 These are not only numbers from the Foeldi Clinic but also from several other European centers. 3, 13-17 We found data by Karen Herbst herself in which she described that 76% of her patient population in the U.S. is obese. 18 It is obvious that the patient population at the Foeldi Clinic is very representative.

Furthermore; it is not "part of the definition of lipedema is fat that resists loss by diet, exercise and bariatric surgery." Apart from the fact that there is no scientific basis for this claim, this statement by Herbst and her colleagues contradicts the daily clinical experience at the Foeldi Clinic since the 1970's with these patients. Moreover, what is the pathophysiological concept behind this statement? When you lose weight, why should you lose weight everywhere but not in the legs? The references the authors used to support their statement are case studies by Bast (consisting of one patient) and Pouwels (consisting of two patients). At the same time, Herbst and her colleagues ignore the data that the Foeldi Clinic published in collaboration with the University of Freiburg, Germany last year. This data shows the tremendous impact of bariatric surgery on patients with lipedema—particularly on the volume of the legs.19

Regarding the term "lipohypertrophy," we, once again, refer to the publication by Bertsch and Erbacher in which we already explained the well-established European concept in response to another letter to the editor by the Herbst group.

Regarding the "inappropriate language" that (at least in the view of the Herbst group) Bertsch and Erbacher have used in their articles when discussing weight gain "that the patient is always at fault," this statement is surprising. In all their articles, Bertsch and Erbacher emphasize that obesity is a disease, a disease with multiple causes and definitely not a matter of fault.^{3,4} Moreover, Karen Herbst personally attended several lectures given by Bertsch in Dallas, Denver, and Chicago, during which he emphasized exactly this issue. To maintain that the opposite is true is really remarkable.

3) We are glad that Herbst and her colleagues accept the important role of mental health issues in patients who are diagnosed with lipedema, as well as the data by Erbacher et al.¹⁴ that indicates these mental health disorders usually exist prior to the development of lipedema symptoms. The claim of the authors that depression and anxiety could also be the result of disproportionate fat tissue in the legs is conceivable. Unfortunately, the authors didn't provide any scientific evidence for this statement.

4) Herbst and her colleagues criticize Klose's cautions about lipedema, claiming: "There is no misconception that liposuction will eliminate lipedema." We recommend that readers take a look at the references the authors cited in support of their statement. Surgeons who perform liposuction write nearly all these sources mentioned by the authors themselves—and who earn a great deal of money with this procedure. Does anyone expect results other than those supporting liposuction from these surgeons?

The only study mentioned by the authors that is not conducted by surgeons is a recent review directed at healthcare providers in Canada which came to a completely different result: "The findings have to be interpreted with caution, given that they are from single-arm, non-randomized studies based on patients' self-assessment data collected using tools that have not been validated for the assessment of lipedema-related complaints".²⁰ The same

conclusions were obtained by Bertsch, Erbacher, and Torio²¹ as conveyed in Part 4 of their article series about the myths and facts about lipedema. To put it in a nutshell, studies regarding liposuction in patients with lipedema are poorly conducted, and the results are biased.

Furthermore, the authors ignore the only prospective randomized study addressing this issue in which women with disproportional adiposetissue presentation demonstrated accumulation of abdominal adipose tissue following thigh liposuction to an extent that offset the initial body-fat loss in the thigh region.²² In our view, patients who are interested in liposuction must be fully informed of these important facts.

In conclusion: In our contributions to Pathways, we didn't express our individual opinions. Rather, we know that our statements are consistent with high-quality scientific studies and the International Consensus on Lipedema. Renowned Lymphology and Lipedema Experts from ten European countries, as well as experts from beyond Europe, support this consensus, which constitutes a paradigm shift in lipedema. The Foeldi Clinic in Germany, as the most renowned clinic in this field worldwide, already successfully treats patients with lipedema according to this new therapeutic concept.

Nevertheless, we have to acknowledge that, as always when things change, there is resistance to these changes. Ultimately, however, this clinging to the "old lore" by Herbst and her colleagues must also be understood as a concern, a concern about change. But exactly this change, this paradigm shift, is urgently needed. As health professionals we have to focus on the real suffering of our patients with lipedema which is definitely not edema—but which is pain, weight gain, psychosocial issues, and a lack of self-acceptance, not least because of the current beauty ideal.

In their final sentence Herbst and her colleagues referred to yet another Letter to the Editors of Phlebologie by her that was published in Phlebologie 2020. The response by Bertsch and Erbacher to that letter is our reference #7.

A full set of references can be found at www.lymphedemapathways.ca



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Response to "Therapy for Lipedema Incorporating New Clinical Guidelines"

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Letters to the Editor

In Response to Herbst's Letter to the Editors of *Pathways*

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Further reading:

International Lipedema Consensus which is now published and supported by KOLs from 10 European countries.

https://www.magonlinelibrary.com/pb-assets/JOWC/JWC_Consensus_Lipoedema.pdf