COMMENTARY

REMARKS CONCERNING THE CONSENSUS DOCUMENT (CD) OF THE INTERNATIONAL SOCIETY OF LYMPHOLOGY "THE DIAGNOSIS AND TREATMENT OF PERIPHERAL LYMPHEDEMA"

M. Földi

Földiklinik, Hinterzarten, Germany

1. Introduction
According to my understanding the Consensus Document (CD) should confine itself to supply physicians and lymphedema therapists with **practice guidelines and to leave out consideration of hotly debated questions concerning definitions**. "Practice guidelines have been defined by the Institute of Medicine as systematically developed statements to assist practitioner ... decisions about appropriate health care for specific clinical circumstances. Guidelines can be developed based on informal consensus ... Evidence-based guidelines are the most rigorously developed. There should be a focused clinical question, and a systematic approach to the retrieval, assessment of quality and synthesis of evidence should be followed." (2)

2. The CD states: "*Lymphedema is an external manifestation of lymphatic system insufficiency and deranged lymph transport*"

To my mind this definition is wrong, because there are various forms of lymphatic system insufficiencies, because lymphedema can be caused not only by deranged lymph transport, but by the incapability of the initial lymphatics to form lymph, too, and because lymphedema is characterized not only by ***"external manifestations"***; **internal** manifestations exist, too!
Every author has his own definition; the definition has no relevance for practitioners and therapists; the Executive Committee of the Society is not authorized to commit the authors to employ the proposed definition!

3. The same holds true for the statement, that: *"Swelling is produced by accumulation in the extracellular space of excess water, filtered plasma proteins, extravascular blood cells and parenchymal cell products."*

It is textbook-knowledge, that plasma proteins are not only **filtered**; they leave microcirculation by **diffusion**, too. The word "filtered" has to be deleted.

4. According to the CD: *"Because lymphedema is a chronic, generally incurable ailment, it requires, as do other chronic disorders, lifelong care and attention along with psychosocial support. The continued need for therapy does not mean a priori that treatment is unsatisfactory, although it is less than ideal."*

Lifelong care is **not** always necessary! I recommend the formulation "... chronic disorders, in most cases lifelong ...".

"*Often less than ideal"* is not a scientific formulation! The CD should state, that no method of

lymphedema treatment exists, which would have been analyzed according to the rigorous criteria of "evidence based medicine" and, that no such studies will be available in the foreseeable future, because these criteria can't be fulfilled. It would be necessary to:
Select a homogenous group of patients considering, i.e.

- Stage of the disease, the
- age of the patients,
- accompanying diseases, the
- compliance, the
- geographical area (2) etc.

It would be necessary to allocate the patients randomly in groups, for example:
- No treatment at all;
- Combined Decongestive Therapy (CDT);
- Intermittent compression;
- Thermotherapy;
- Microvascular Surgery, as the creation of lympho-(nodo-)venous shunts, lymph vessel transplantation, vein-transplantation;
- Debulking operations;
- Liposuction.

The problems of
- Small area and volume outcome variations (homogenous groups not only of patients, but also of therapists and of physicians) have to be considered

The end-point of the study could not be before 10 years. Regular checkups would be mandatory.

What concerns CDT: in its homeland, Germany, it has become, several decades before "evidence based medicine" has been codified, the routine treatment, payed for by Social Security! This fact excludes the possibility that a group of patients would receive no treatment at all or could be allocated to some other form of treatment.

5. According to the CD: *"Patients with chronic venous insufficiency require lifelong external compression therapy to minimize edema, lipodermatosclerosis and skin ulceration."*

In CVI compression **prevents** these alterations, if applied immediately when ambulatory venous hypertension appears! If the alterations are already present, CDT eliminates edema and lipodermatosclerosis; skin ulcerations disappear.

6. According to the CD: *"The compliance and commitment of the patient is also essential to an improved outcome."*

The word *"also"* and the term *"improved outcome"* are false. **Compliance is a "conditio sine qua non"** in CDT. It is mandatory for the **maintenance** and for the **optimization** of the results of its "Phase one".

7. The CD states: *"With chronic venous insufficiency, poor patient cooperation may be associated with progressive skin ulceration, hyperpigmentation, and other trophic changes in the lower leg."*
In CVI, poor patient cooperation (= no compression!) **is the cause** of trophic changes; good compliance

prevents them.

Hyperpigmentation is **not** a trophic change; it is the consequence of the well-known "stretched pore phenomenon".

8. According to the CD: *"Stage I represents an early accumulation of fluid relatively high in protein content (e.g. in comparison with venous edema) and subsides with limb elevation. Pitting may occur. Stage II signifies that limb elevation alone rarely reduces tissue swelling and pitting is manifest. Late in Stage II, the limb may or may not pit as tissue fibrosis supervenes. Stage III encompasses lymphostatic elephantiasis where pitting is absent and trophic skin changes such as acanthosis, fat deposits and warty overgrowths develop. Within each Stage, severity based on volume difference can be assessed as minimal (< 20% increase) in limb volume, moderate (20 – 40% increase), or severe (> 40% increase).*
These Stages only refer to the physical condition of the extremities. A more detailed and inclusive classification needs to be formulated."

It is a mistake to regard "venous edema" as an example of a low-protein edema: **in the final Stage of CVI it is a high-protein edema**! An adequate example would be the anasarca in the nephrotic syndrome with a protein concentration of around 0.1 gr%!

The description of the stages is wrong. Correctly:
Stage I: Pitting; elevation reduces the swelling.
Stage II: No pitting (brawny); elevation is without effect.
Fat deposits develop already in Stage II.

Severity cannot be based on volume differences alone! For example: the presence, or the absence of erysipelas attacks (cellulitis, dermatolymphangiodermitis) is much more important. In addition, the figures are based on personal appraisals, they lack any scientific substance.

It is not the task of the CD, to express a view concerning future Stage-classifications. They will automatically arise if new facts become established. Presently, based on our experience gained from seeing about hundred thousand patients suffering from lymphedema, we are quite happy with the stages as described above.

9. The CD states: *"Direct oil contrast lymphography, which is cumbersome and occasionally associated with minor and major complications, is usually reserved for complex conditions such as chylous reflux syndrome and thoracic duct injury. Non-invasive duplex-Doppler studies and occasionally phlebography are useful for examining the deep venous system and supplement or complement the evaluation of extremity edema. Other diagnostic and investigational tools used to elucidate lymphangiodysplasia/lymphedema syndromes include magnetic resonance imaging (MRI), computed tomography (CT), ultrasonography (US), indirect (water soluble) lymphography (IL) and fluorescent microlymphangiography (FM). DEXA, or bi-photonic absorptiometry, may help classify and diagnose a lymphedematous limb but its greatest potential use may be to assess the chemical component of limb swelling (% fat, water, lean mass) before and after treatment, IL and FM are best suited to depict initial and terminal lymphatics and accordingly have limited clinical usefulness. US has found its most practical value in depicting the dance of the living adult worms in scrotal lymphatic filariasis."*

It is most deplorable, that the authors of the CD ignore the international statistics which have been presented at the first Congress of the Society in 1966 by Köhler (3). Out of 16,501 oil contrast

lymphographies 18 resulted in the death of patients – death is more than a "major complication" – the number of serious complications amounted to 198. In marked contrast to the view expressed in the book "Diseases of the Lymphatics" (4), I regard oil contrast lymphography as absolutely contraindicated as a tool in the diagnosis of lymphedema!

Phlebography is only used, if, based on duplex-Doppler studies, the decision concerning treatment of the phlebopathy really necessitates it.

There is no difference between "initial" and "terminal" lymphatics; the terms are synonyms.

US is important in the diagnosis of lymphangiomas, too!

10. According to the authors of the CD: *"Limb elevation is helpful to virtually all patients undergoing treatment."*

This is not true. **It is useless and without any effect in Stages II and III of lymphedema.**

11. *"Physical therapy...a. Combined physical therapy (CPT) (also known as Complete or Complex Decongestive Therapy (CDT) or Complex Decongestive Physiotherapy (CDP) among others) is backed by longstanding experience and generally involves a two-stage treatment program that can be applied to both children and adults. The firt phase consists of skin care, light manual massage (manual lymph drainage), range of motion exercise and compression typically applied with multi-layered bandage-wrapping. Phase 2 (initiated promptly after Phase 1) aims to conserve and optimize the results obtained in Phase 1. It consists of compression by a low-stretch elastic stocking or sleeve, skin care, continued remedial exercise, and repeated light massage as needed."*

Due to the fact, that "*massage"* means *"the action of rubbing and pressing a person's body with the hands"* (5) *"manual massage"* is false. In addition, *"manual lymph drainage"* and *"light massage"* are not synonyms.

12. *"Prerequisites of successful combined physiotherapy are the availability of physicians (i.e., clinical lymphologists), nurses and therapists highly trained and educated in this method, acceptance of health insurers to underwrite the cost of treatment, and a biomaterials industry willing to provide high quality products. Compressive bandages, when applied incorrectly, can be harmful and/or useless. Accordingly, such multilayer wrapping should be carried out only by professionally trained personnel. Newer manufactured devises (e.g. CircAid, Reid sleeve) to assist in compression (i.e. pull on, velcro-assisted, quilted, etc.) may relieve some patients of the bandaging burden and perhaps facilitate compliance with the full treatment program. Some clinics find that patient self-care and risk reduction strategies help maintain edema reduction."*

Instead of *"nurses and therapists" ,"lymphedema therapists"* has to be written. In the homeland of MLD, nurses are not allowed to perform MLD.

"Highly trained" is a nebulous concept. The qualification of the teachers, the curriculum and the duration of the courses, the regulations concerning exams, etc. have to be described.

A scientific Society cannot state in a CD, that *"newer manufactured devices ...* ***perhaps*** *facilitate compliance." "Perhaps"* means a pure guesswork. Either yes, or no, to be answered by the meta-analysis of studies.

The formulation, that "*some clinics find, that patient self-care and risk reduction strategies help maintain edema-reduction*", falls into the same category. Although these are standard prerequisites of CDT, no up to date study exists which would have compared the long-term results of two homogenous groups of patients, one with a good and the other one with an inadequate compliance.

13. "*CDT may also be of use for palliation as, for example, to control secondary lymphedema from tumor-blocked lymphatics. Treatment is typically performed in conjunction with chemo- or radiotherapy directed specifically at producing tumor regression. Theoretically, massage and mechanical compression could promote metastasis in this setting by mobilizing dormant rumor cells, although only diffuse carcinomatous infiltrates which have already spread to lymph collectors as tumor thrombi might be mobilized by such treatment. Because the long-term prognosis for such an advanced patient is already dismal, any reduction in morbid swelling is nonetheless decidedly palliative.*"

The view, that by mobilizing dormant tumor cells, for example by massage, metastases can be triggered, is obsolete. The ability, to detach from the primary tumor mass, to invade nearby tissue and then metastasize, is acquired only by an elite few cells. These elite cells metastasize, regardless of whether they are pushed or not by massage. The molecular biological condition of dormant tumor cells is inappropriate for the formation of metastases.

14. *"A prescription for low stretch elastic garments (custom made with specific measurement if needed) to maintain lymphedema reduction after CPT is essential for long-term care. Preferably a physician should prescribe the compression garment to avoid inappropriate usage in a patient with medical contraindications such as arterial disease, painful postphlebitic syndrome or occult visceral neoplasia. Generally the highest compression level tolerated (» 20 – 60 mmHg) by the patient is likely to be the most beneficial."*

The formulation *"preferably a physician should prescribe the compression garment"* reflects the situation in the USA. In Germany only the physician **is allowed** to prescribe them.

"*Painful postphlebitic syndrome"* is by no means a contraindication for compression, quite to the contrary!

15. According to the CD, classical massage "**may** damage" lymphatics. The much more drastic *"Tuyautage"* is only "**probably"** injurious to it. Such subjective points of view don't belong in a CD.

16. *"Thermal Therapy. Although a combination of heat, skin care, and external compression has been advocated by some practitioners in Europe and Asia, the role and value of thermotherapy in the management of lymphedema remain unclear."*

Thermal therapy is described in an unjust manner. It has been used in China for centuries and has been introduced in modern Chinese medicine not by "some practitioners", but by a distinguished professor of the Shanghai University. His papers are of top quality. Two distinguished members of the ISL, Fox and Olszewski – and not **some European** practitioners - have confirmed the results of Prof.. Chang. **A careful meta-analysis of the literature is imperative!**

17. *"Elevation. Simple elevation of a lymphedematous limb often reduces swelling particularly in the early stage of lymphedema. If swelling is reduced by antigravimetric means, the effect should be maintained by wearing of a low-stretch, elastic stocking/sleeve."*

The text is not correct. *"Simple elevation"* reduces swelling **only** in Stage I.

18. *"Drug therapy...Diuretics. Diuretic agents are occasionally useful during the initial treatment phase of CPT. Long-term administration of diuretics, however, is discouraged for it is of marginal benefit in treatment of peripheral lymphedema and potentially may induce fluid and electrolyte imbalance. Diuretic drugs may be helpful to treat effusions in body cavities (e.g., ascites, hydrothorax) and with protein-losing enteropathy."*

Based on which studies the CD declares, that diuretic agents are "occasionally" useful? What is the numerical value of "occasionally"?

19. *"Benzopyrones. (oral benzopyrones), which are thought to hydrolyze tissue proteins and facilitate their absorption while stimulation lymphatic collectors, are neither an alternative nor substitute for CPT. The exact role for benzopyrones (and related rutin and bioflavonoid compounds) as an adjunct in primary and secondary lymphedema treatment including filariasis is still not definitively determined including appropriate formulations and dose regimens."*

If the authors of the Document *"thought"* that *"benzopyrones hydrolyze tissue proteins"*, they went astray. They should read the paper of Piller (6). The formulation "the exact role for benzopyrones and related rutin and bioflavonoid compounds" shows, that the authors of the CD are not aware of the fact, that

Rutin is a bioflavonoid and that

Bioflavonoids are benzopyrones!

20. *"Mesotherapy. The injection of hyaluronidase or similar agents to loosen the extracellular matrix is of unclear benefit."*

What does *"unclear benefit"* mean? The CD should, by careful meta-analysis, comment on the quality of the published papers! Mesotherapy has no place whatsoever in the treatment of lymphedema!

21. *"Immunological therapy. Efficacy of boosting immunity by intraarterial injection of autologous lymphocytes is unclear."*

The word *"unclear"* has no place in a CD. The authors have to describe the result of the meta-analysis of the pertinent literature!

22. *"Restricted fluid intake is not of demonstrated benefit. In chylous reflux syndromes (e.g., intestinal lymphangiectasia), a diet low in long-chain triglycerides (absorbed via intestinal lacteals) and high in short and medium chain triglycerides (absorbed via the portal vein) is of benefit especially in children."*

The sentence "restricted fluid intake is not of demonstrated benefit" is false. One should state, that **fluid intake has to be ad libitum**!

The diet has to be **free** (not ***"low"***) of long-chain fatty acids!

23. *"Operative treatment"*

This chapter should be started by calling attention to the fact, that two forms of indications for operative treatments exist, **relative** and **absolute (vital)** indications and that there is only one absolute indication for surgery in lymphedema: angiosarcoma. All the other indications are relative.

24. *"Debulking is probably useful in treatment of advanced fibrosclerotic lymphedema (elephantiasis)."*

What does *"probably"* mean? The CD has to express a view which is based on the careful study of the literature! Is debulking useful? Yes or no! [Unfortunately, it is unavoidable in tropical countries of the "third world" and in those countries of the "first world" in which Social Security and health insurance companies refuse to pay for CDT. It is shocking to see Figure 10.9 on page 185 in the book "Diseases of the lymphatics" (4): Charles reducing operation is performed "when the swelling on the dorsum of the foot is excessive". The swelling in this case can be abolished by "Phase I" of CDT.]

25. *"Omental transposition, enteromesenteric bridge operations, and the implantation of tubes or threads to promote perilymphatic spaces (substitute lymphatics) have not shown long-term value."*

This is a very slapdash approach to this important question. There is not a single word about mortality! The CD should explicitly warn against these methods, which, unfortunately, are described in detail in (4)!

26. *"Liposuction has been reported successfully modified in specialized clinics to treat non-pitting, non-fibrotic upper extremity lymphedema due to excess fat deposition (which has not responded to non-operative therapy) as, for example, after treatment of breast cancer. At this time, results are encouraging but long-therm management requires strict patient compliance with dedicated wearing of a low-stretch elastic compression sleeve. This operation should be performed by an experienced team of plastic surgeon, nurses and physiotherapists to obtain optimal outcomes."*

I urge the authors of the CD to inform the Society, which are the *clinics* which have reported to have modified liposuction successfully! I am aware of only one such Clinic, namely that of Brorson!

How biased the Document is, demonstrates the fact, that its authors find the results of liposuction, based on the papers of one single author, *encouraging*; the value of thermal therapy, which has been confirmed by two prominent authors, on the contrary is, for them *unclear*! This smacks of cronyism! The complications of liposuction are not mentioned at all!

Brorson's warning, not to use liposuction in the treatment of lymphedemas of the lower extremities, is not mentioned. The sentence *"This operation should be performed by an experienced team of plastic surgeons, nurses and physiotherapists to obtain optimal outcomes"* is useless. One has to believe in miracles to suppose, that a plastic surgeon or a dermatologist will regard himself inexperienced!

27. *" Microsurgical procedures...This operative approach is designed to augment the rate of return of lymph to the blood circulation. The surgeon should be well-schooled in both microsurgery and ..."*

It should be mentioned, that approximately 250 million people suffer from lymphedema worldwide and that according to Olszewski less than 100 microsurgical operations are performed per annum!

28. *"Derivate methods...Experience with these procedures over the last 20 years suggests that improved and more lasting benefit is forthcoming if performed early in the course of lymphedema."*

Personal experiences can't motivate a scientific Society, to express the view, that these methods are *"of*

more lasting benefit ... if performed early". Evidence based medicine necessitates a controlled-randomized long-term study: early cases; one group treated by some conservative method, the other by derivative surgery!

REFERENCES

1. The diagnosis and treatment of peripheral lymphedema. Consensus Document of the International Society of Lymphology. Lymphology 36 (2003), 84-91.
2. Norton, JA, RR Bollinger, SF Lowry, et al: Surgery. *Basic Science and Clinical Evidence*. Springer, New York, 2001.
3. Köhler, PR: In: *Progress in Lymphology*, Rüttimann, A, et al (Eds.), Thieme, 1967, page 306.
4. Browse, N, KG Burnand, PS Mortimer: *Diseases of the Lymphatics*. Arnold, London, 2003.
5. *Oxford Advanced Dictionary*, Oxford University Press, Oxford, 2000.
6. Piller, N: Macrophage and tissue changes in the developmental phases of secondary lymphedema and during conservative therapy with benzopyrone. Arch. Histol. Cytol. 53 Suppl. (1999), 209-218.