



“PERSONAL METHODS” OF THE PHYSICAL TREATMENT OF LYMPHEDEMA AND “EVIDENCE BASED MEDICINE”

Prof. Michael, Földi, M.D.
Foldi Klinik - Hinterzarten

Cheville et al. (1) rightly state, that “combined manual therapy”, often referred as “Complex Decongestive Physiotherapy” (CDT) has emerged as the standard in the treatment of lymphedema”. One of the four constituents of the tetrad of this technique is “Manual lymph drainage” (MLD) which has been devised by the Vodder’s in 1932, however by no means for the treatment of lymphedema. In a “Guide for postgraduate education” entitled “On the track of the lymph vessels” the author Rösler (2) narrates: “The Vodder’s worked in the French Riviera. They had contact with many English people, who, due to the wet and cold climate of their country, have suffered from chronic common cold. Many had swollen cervical lymph nodes... The Vodder’s started to treat them. The result was astounding. By means of careful, turning pumping movements the signs of common cold have vanished forever”. Obviously the Vodder’s can’t be blamed for being, in 1932, unaware of the fact, that the common cold has nothing to do with the climate of the British isles, the author of the post-graduate article, on the other hand should know, that it is a mild, self-limited viral infection.

The first physician, Asdonk, who has tried to treat lymphedema by the massage technique derived by the Vodders, which is highly effective in increasing the lymphangiomotoric activity of healthy lymphatics has observed, that it was inadequate in the treatment of fibrosclerotic – not to mention of elephantastic – lymphedemas, has therefore added what he called “edema-grips”.

As a consequence, a vehement “grips dispute” has broken out between the Vodder’s and Asdonk; henceforth the latter designated the combination of the four grips of the Vodder’s with his “edema grips” as “Vodder-Asdonk-Method”. This term is still used by his pupils. Later on both the heirs of the Vodder’s and Asdonk have complemented MLD by adding compression, remedial exercises and treatment of the skin, employed in the therapy of lymphedema already in the 19th century. Up to now, the two groups advertise their courses they offer to train lymphedema therapists in CDT by designating them “The original technique of Vodder” and “The Method Vodder-Asdonk”. Although not a single study exists which would aim at comparing the efficacy of the two methods according to the principles of “evidence based medicine”, the author of the Guide declared, that Asdonk has “subtilized” Vodder’s technique. One has to admit, that it is easy to perform a study according to the principles of “evidence based medicine” in connection with drugs, but extremely difficult concerning lymphedema and CDT: not only the patients in the trial should form a homogenous group, but the lymphedema therapists, too! Unfortunately, the Casley-Smiths stated, in 1993 at the 14th International Congress of Lymphology held in Washington, that a “Földi-Method” exists, which they have, in

the light of their own findings, “somewhat modified and upgraded”. (3) I emphasize that we did not develop a “Földi-Method of CDT”. In our “Textbook of Lymphology” (4) I have declared:

“I stress that we did not develop any personal method of CDT. This means that there is no Földi method of CDT. What we do in our clinic is to integrate CDT with the broad field of physical medicine and with comprehensive, individualized treatment of the patient.”

What concerns the contended “modification and upgrading” of the non-existing “Földi-Method” attention has to be called to the fact, that neither in their lecture given in Washington, nor in their booklet entitled: “Lymphedema: A guide for therapists and patients” (5) did the Casley-Smith’s explain, in which respect they have “modified and upgraded” the “Földi-Method” which Judith Casley-Smith had the chance to have a look at in our Clinic in the course of a morning. In addition, they have omitted to perform a prospective – randomised study aiming to compare the method which they designated as “the Földi’s” with that they henceforth designated as the “Casley-Smith-method”.

It is a nonsense to train lymphedema therapists by limiting oneself to the technique, to the work to be done by hand; an exhaustive medical knowledge has to be imparted, too. (A conductor has to understand music, it is not enough, if he knows how to slickly fidget with a baton!)

In the native country of CDT, in Germany, a law has been passed which has authorized the federation of the statutory sick-funds to prescribe the members of which occupational groups are allowed to be trained in CDT. The federation has specified the requirements the physicians who give lessons have to fulfil and how the training of lymphedema therapists who work as instructors has to be accomplished. The duration (170 forty-five-minutes lessons), the curriculum and the order of the exams are also specified. Unfortunately, the subjects of the medical curriculum are specified, but not the messages to be imparted. As a consequence, unfortunately at times nonsensical matters are taught.

For example there is a passage in the paper of Rösler, entitled “The impression test as an indicator”. Rösler has been informed by lymphedema therapists working as instructors in one of the accredited CDT-colleges, that there is a correlation between the protein concentration of the edema fluid on the one hand and the period of time it takes for the impression, caused by the pressure of the thumb into the edematous area to disappear on the other. According to them, the test gives

consequences concerning treatment: the higher the protein concentration, the more delayed the therapeutic result! As a consequence, “both therapists and patients have to muster much patience!” The lymphologist-instructor of the same CDT-college has published a book which contains serious professional mistakes. Although it is textbook knowledge, that the essence of chronic venous insufficiency (CVI) in the leg is ambulatory venous hypertension, according to this author venous pressure in CVI is elevated while standing and sitting ! He regards MLD to be indicated in cases of cardiac edemas refractory to treatment. There is not a single textbook of Medicine or Cardiology which shares this opinion! In reality, cardiac edema represents an absolute contraindication for MLD, because, by the elevated myocardial lymphatic preload and afterload the left chamber is also effected: the increase of the blood volume brought about by the uptake of edema fluid into the circulation could trigger a congestive left heart failure. Taking the fact into consideration, that even the reputed “Cecil Textbook of Medicine”(6) contains serious mistakes where it deals with questions of Lymphology [for example the nonsense, that “chronic lymphedemas may be caused by... renal or cardiac failure” (!)], one should strike for an international consensus concerning the subject matter and the relevant message which has to be imparted to students of CDT.

REFERENCES

1. Cheville AL, McGarvey, Petrek JA, Russo SA, Tayler ME, Thiadens SR. *Lymphedema management. Semin Radiat Oncol.*, 13, (2003):290-301.
2. Rösler W. *Den Lymphgefäßen auf der Spur. Physiopraxis* 2, (2004):40-42
3. Casley-Smith, Judith R, Casley-Smith JR. *Lymphoedema Therapy In Australia; Complex Physical Therapy, Exercises & Benzopyrones, on Over 600 Limbs. Progress in Lymphology*, 14,622-626. *Lymphol* 27 (Suppl).
4. *Textbook of Lymphology. Földi M, Földi E, Kubik S, (Eds.), Urban & Fischer, München – Jena, 2004.*
5. Casley-Smith, Judith R, Casley-Smith JR. *Lymphoedema: A guide for Therapists and Patients. Lymphoedema Assoc. Australia, 1992.*
6. *Cecil Textbook of Medicine, 22nd Ed., Saunders, Philadelphia, 2004.*

CONCENTRATION OF TNF- AND IL-1- IN WISTAR RATS SERUM AND LYMPH UNDER PHYSIOLOGICAL CONDITIONS

Brygida Beck, M.D. (1), Marian Ciszek, M.D. (3), Jacek Kosiewicz, M.D. (2), Hanna Duliban, M.D. (1), Ewa Birkner, M.D., Ph. D (1), Konstanty Iusarczyk, M. D., Ph. D (2)

(1) Chair of Biochemistry, Department of General Biochemistry, Medical University of Silesia, Zabrze, Poland.

(2) Chair of Department of Descriptive and Topographic Anatomy, Medical University of Silesia, Zabrze, Poland.

(3) Department of Obstetrics and Gynecology, Regional Hospital, Racibórz, Poland.

Presented : July 2004

Revised : September 2004

Accepted : October 2004

ABSTRACT

TNF- and IL-1- levels both in the lymph collected from thoracic duct and in serum in Wistar rats were determined using immunoenzymatic methods (Bender Med Systems and Endogen, respectively). TNF- concentrations both in the serum and lymph were below sensitiveness threshold of the method (<17 pg/ml). Serum IL-1- concentration was statistically significantly higher ($p<0.005$) – 35.89 ± 3.23 pg/ml compared to lymph concentration (22.50 ± 2.45 pg/ml).

The lymph is an excellent carrier of information about any changes in tissues, whereas the blood delivers only substances which are necessary for the functioning of the organism. It is possible that cytokines are “consumed” during their flow through lymphatic organs and vessels. As a result, the concentration of cytokines in thoracic duct may be lower than in peripheral lymphatics. This may explain a higher IL-1- concentration in blood serum obtained in our study.

KEY WORDS : TNF- and IL-1- – serum - lymph

INTRODUCTION

The lymphatic system, after the nervous and endocrine systems plays a crucial role in maintaining homeostasis. In the last decades an increasing attention has been devoted to the role of lymphatic system in pathomechanism.

The lymphatic system comprises the lymphatic organs, lymphatics and lymphocytes which produce immunoglobulins and cytokines [1, 2, 3].

The cytokines, a group of micromolecular signalling proteins play an important role in immunological responses, acute phase reaction, hematopoiesis and antineoplastic defense. However, cytokines can sometimes cause life – threatening complications [3, 4].

In literature there are only a few reports on cytokines

concentration in lymph. The aim of the present study was to answer the question whether there are any differences between the serum – and lymph concentrations of TNF- (Tumor Necrosis Factor- α) and IL-1- (Interleukin 1- β) in Wistar rats in normal conditions.

MATERIAL AND METHODS

The studies were performed on 20 adult male Wistar rats weighing 180-200 grams each. All the animals were kept in air conditioned room in 12/12 hour light/dark cycle. They were on a standard diet and were supplied with water *ad libitum*. Under pentobarbital anaesthesia the thoracic duct was exposed below the diaphragm and cannulated with 1.2 F hydrophilic elastic catheter (Balton). The abdominal walls were closed and lymph was collected into heparinized test-tube. After an appropriate amount of lymph had been obtained, the blood was collected from the heart. After coagulation the blood was centrifuged. Both in the lymph and in serum the TNF- and IL-1- levels were determined using immunoenzymatic methods (Bender Med Systems and Endogen, respectively).

RESULTS

The TNF- concentrations both in the serum and lymph were lower than 17 pg/ml i.e. below sensitiveness threshold of the method. Serum IL-1- concentration was statistically significantly higher ($p<0.005$) – 35.89 ± 3.23 pg/ml compared to lymph concentration (22.50 ± 2.45 pg/ml).

DISCUSSION

TNF- is one of the main cytokines involved in inflammatory and immunologic responses [5, 6, 7]. In 1975 Carswell identified the factor responsible for tumor neoplastic necrosis. He called it tumor necrosis factor (TNF-). In 1984 a gene encoding the TNF- synthesis was cloned [8, 9]. TNF- co-operating with other cytokines such as IL-1, IL-2, IL-7

enhances thymocytes' proliferation, while with IL-6 it may cause an increase in proliferation and differentiation of B lymphocytes. Together with IL-2 it stimulates the proliferation and cytotoxicity of NK cells and formation of LAK cells. By endo-, para-, and autocrine activity TNF- influences monocytes and macrophages. It also considerably increases cytotoxicity of monocytes, macrophages and NK cells. TNF- increases phagocytic capability of neutrophils and accelerates their release from bone marrow. It may also activate the eosinophils' cytotoxicity in protozoa infection response [5, 10, 11].

TNF- affects the immune system directly and indirectly through release of many cytokines, (e.g. from macrophages are released IL-1, IL-6, IFN- (Interferon-beta), NGF (Nerve Growth Factor), EGF (Epidermal Growth Factor) and from lymphocytes IFN-) [12, 13, 14].

TNF- is capable of inducing the expression of MHC (Major Histocompatibility Complex) class I molecules, but together with IFN- the expression of MHC class II is induced [14]. IL-1 possesses a wide variety of biological activities and is one of the main regulators of immune and inflammatory responses. IL-1 is mainly secreted by monocytes and macrophages from various tissues. Lipopolysaccharides, the main constituents of the Gram-negative bacteria cell wall, are one of the most effective factors which induce the release of IL-1. The inducers of IL-1 are also viruses, saccharomycetes, exotoxins, IL-2, IL-3, IL-12, TNF-, complement fragment C5a, lectins, and IL-2 alone. Besides monocytes and macrophages IL-1 can also be secreted by keratinocytes, chondrocytes, Langerhan's cells, glia cells, mesangium cells, endothelial cells, and even by T and B lymphocytes [3, 4].

IL-1 stimulates IFN- production by thymocytes, and IL-6 by macrophages, fibroblasts and endothelial cells. It also influences the proliferation and differentiation of B lymphocytes. IL-1 induces enhanced production of neutrophils and monocytes, mainly by stimulating release of colony activating factors. It also affects proliferation of fibroblasts and monocytes which is partly the result of the stimulated release of platelet-derived growth factor (PDGF) which acts on these cells both auto- and paracrinically.

IL-1 facilitates the evolution of inflammatory reaction not only as a result of hemotactic attraction of neutrophils and monocytes. It increases histamine release from basophils, degranulation of eosinophils and production of prostaglandins by stimulating phospholipase A2 synthesis. The latter releases arachidonic acid from cell membrane phospholipids. Acting on endothelium IL-1 increases its permeability, induces its procoagulatory activity, stimulates the production of platelet activating factor (PAF) and intensifies adhesion of lymphocytes and neutrophils to endothelial cells [3, 4, 14, 15].

There are two types of IL-1: IL-1 α and IL-1 β . They are products of two different genes. IL-1 α and IL-1 β are in 25% homologous. They are synthesized intracellularly from precursors as well as its activity also as a precursor. Stimulated by LPS monocytes produce mainly IL-1 β , whereas IL-1 α dominates in keratinocytes [2].

The lymph contains proteins which originate from circulating blood, reaching the interstitial fluid through small vessel wall

from where they are exclusively transported to blood circulation by lymphatics [1, 16].

Thoracic duct lymph proteins concentration constitutes about 60% of that in plasma. In the human being about 50% of plasma proteins content (100g) are transported daily through the thoracic duct lymph. In some laboratory animals (such as dogs, cats, rabbits) the total amount of daily transported proteins ranges from 60% to 80% of their plasma concentration.

The concentrations of proteins in lymph are lower than in serum. There are also differences between proportional composition of particular protein fractions in blood and lymph. It is caused by limited transport ability of proteins through the blood vessel walls to tissues and then to lymph. As a result, the lymph concentration of proteins of higher molecular weight is lower than the lymph concentration of lower molecular weight. Moreover, the biological activity of some proteins can be in a considerable degree determined by their occurrence either in blood or in tissue fluid [17].

In normal conditions no active cells and biochemical processes in blood were noted. Contrary to this the active processes in lymph are continuously taking place (e.g. autotransformation of lymphocytes, which begin production of cytokines).

The cells which are present in lymph differ functionally and phenotypically from those present in blood. Lymph contains more lymphocytes and monocytes. There are no granulocytes, whereas the Langerhan's cells, absent in blood, in lymph constitute from 6 to 8%. The lymph is a fluid in which the morphological equivalents of cell cooperation are found. IL-1 is produced by monocytes, T- and B- lymphocytes and Langerhan's cells [13, 14]. Although greater number of these cells is to be found in lymph as compared to blood, in our study we found surprisingly lower IL-1 concentration in lymph than in blood.

It must be emphasized that lymph is an excellent carrier of information about any changes in tissues, whereas the blood delivers only substances which are necessary for the functioning of the organism. The role of blood as a carrier of information has been progressively supplemented by the lymphatic system an evolutionary process [13]. The blood concentration of cytokines is a sum of amounts of cytokines produced by cells present in blood and in lymphatic system as well. Taking into account a dynamic nature of lymph, it is possible to state that cytokines are "consumed" during their flow through lymphatic organs and vessels. As a result, the concentration of cytokines in thoracic duct lymph may be lower than in peripheral lymphatics. This, in turn, may explain a higher IL- concentration in blood serum obtained in our study. What is more the cytokines were determined in the lymph from thoracic duct, i.e. in lymph taken only from a part of the body, which could have additionally influenced lower IL-1 concentration in lymph, as compared to blood.

REFERENCES

1. Beck, B, M Ciszek, R Tarnawski: *Limfa – skąd biochemiczny, znaczenie jej krenia w fizjologii i patologii organizmu. Post. Hig. Med. Dow. 49 (1995), 353.*

2. Janeway, Cr A P, M Walport, M J Shlomchik Jr: *Immunobiology 5th Ed.*, Garland Publishing, New York, 2001.
3. Goldsby R A, Th J Kindt, B A Osborne (Eds.): *Kuby Immunology 4th ed.*, Freeman and Company, New York, 2000.
4. Roitt, I: *Essential Immunology*, Blackwell Scientific Publication, London, Edinburgh, Boston, Melbourne, Paris, Vienna, 1994.
5. Ranges, C., A Zotnik, T Espevi: Tumor necrosis factor- α / cachectin is a growth factor for thymocytes. Synergistic interactions with other cytokines. *J. Exp. Med.* 167 (1988), 1472.
6. Vassali, P: The patophysiology of tumor necrosis factor. *Ann. Rev. Immunol.* 10 (1992), 411.
7. Daniels, HM, A O'Toole, M. J. Hussain et al: TNF gamma 2 stimulates cytokine release by peripheral blood mononuclear cells of patients with chronic hepatitis B virus infection. *J. Hepatol.* 20 (1994), 370.
8. Ostensen, M., D Thiele, P Lipsky. Tumor necrosis factor- α enhances cytolytic activity of human natural killers cells. *J. Immunol.* 138 (1987), 4185.
9. Besedovsky, H O., A del Rey. Immune – Neuroendocrine Network. *Front Horm. Res.* 29 (2002), 1.
10. Ohno T., J. Lau: The “Gold-Standard”, accuracy, and the current concepts: hepatitis C virus genotype and viremia. *Hepatology* 24 (1996), 1312.
11. Scheunich, P, M Thoma, U Ulev et al: Immunoregulatory activity of recombinant human tumor necrosis factor (tnf) mediated enhanced of T cell responses. *J. Immunol.* 138, (1987), 1786.
12. Beutler, BA, N Krochim, IW Milsark et al.: Control of cachectin (tumor necrosis factor) synthesis: mechanism of endotoxin resistance. *Science* 232 (1988), 977.
13. O'Shea ,J J, D M Frucht , C S Duckett. Cytokines and cytokine receptors. In: Rich, R. R., Fleisher Th A, W T Shearer et al. *Clinical Immunology*. Mosby, London, Edinburgh, New York, Philadelphia, St Louis, Sydney, Toronto, 2001. vol. one: 12.1.
14. Arendt, W P. Cytokine inhibitors and receptor antagonists. In. Rich R R, Th A Fleisher , W T Shearer et al. *Clinical Immunology*. Mosby, London, Edinburgh, New York, Philadelphia, St Louis, Sydney, Toronto, 2001, vol. two: 116.1.
15. Boumpas D T, C Prussin, G Uzel, et al. In: Rich, R R, Th A Fleisher, W T Shearer et al. In *Clinical Immunology*. Mosby, London, Edinburgh, New York, Philadelphia, St Louis, Sydney, Toronto, 2001. vol. two: 115.1
16. Messen H: *Lymph vessel system*. Springer – Verlag, Berlin-Heidelberg-New York, 1972.
17. Olszewski W. L.: *Immune proteins, cell interactions and immunoregulatory hormones: lymph versus blood*. *Lyphology* 20 (1987), 239.

CHRONIC LYMPHEDEMA, NO MORE STEPCHILD TO MODERN MEDICINE!

Byung B. Lee, MD, PhD, FACS

Clinical Professor of Surgery Uniformed Services University of the Health Sciences Bethesda, MD

Presented : July 2004

Revised : September 2004

Accepted : October 2004

ABSTRACT

The new concept of total care management based on multidisciplinary approach to accommodate various nonsurgical and surgical therapies has brought substantial progress in the management of chronic lymphedema. The new knowledge in lymphodynamics based on lymphangion as a functional unit of lymphatic circulation provided logical ground to develop more physiologic approach to the chronic lymphedema. Various surgical, reconstructive or excisional, therapies were implemented as adjunct therapy to enhance over-all effectiveness of the CDP (complex decongestive physiotherapy) and/or compressotherapy-based main therapy. New additional role of surgical therapy can improve overall management to deliver better quality of life as the ultimate goal of the management of chronic lymphedema. After all, lymphedema, either primary or secondary, is no more "incurable" disease but manageable if not preventable, when the ignorance and poor compliance should be further overcome.

KEY WORDS : lymphedema management. Global therapeutic approach.

CHANGING CONCEPT

The lymphedema has remained one of obscure condition of limb swelling for so many decades, and did not get enough attention it deserved as one of serious disease entity to need the treatment, remaining as a stepchild in modern medicine(1). It has been simply known as the condition related to the lymphatic dysfunction of various etiologies and benignly neglected as relatively harmless condition only to need to learn to live with. Lymphatic circulation system was also vaguely understood as non-crucial, auxiliary third circulation system only to provide supplemental role to the essential arterial and venous circulation system, even though it has been well documented from earlier centuries(2-4).

However, new hemodynamic knowledges in circulatory system have been rapidly accumulated through earlier decades of 20th century, and once neglected and relatively unknown lymphatic system was finally recognized as crucial last piece of puzzles to be able to answer various important questions on the circulation properly(5,6).

New discovery of "lymphangion", for example, as a

functional unit of lymph transport system through early '60, has served for proper recognition of major differences between normal lymphodynamics and venodynamics, and corrected previous misconception on this system as identical one to the venous system with same hemodynamics(5,6).

Lymphatic circulation is based on active autonomous peristaltic movement to transport lymph from the low pressure to high pressure environment for more than 60mmHg, while venous circulation is based on passive movement from high to low pressure in contrast(7).

Such major discovery in anatomy and physiology of lymphatic system(8) gave new momentum for more rational challenge to the chronic lymphedema to clear its ill reputation as one of last enigma in modern medicine.

Many mysteries in the lymphatic dysfunction (eg. latent edema) have been successfully explained with this new knowledges, and new concept and principle of the lymphedema management have been accordingly well established.

The relationship between the primary and secondary lymphedema became much clear to give proper guide to the each with different etiology for more effective management(9-11), and modified clinical/laboratory staging of lymphedema also gave more room to implement various surgical therapies together with conservative treatment(12,13).

This changing concept was fully implemented to the contemporary management of the chronic lymphedema(9), not only through medical/physical therapy but also through surgical therapy either as an independent or mutually complimentary therapies during the last decades, and whole aspect of chronic lymphedema has made substantial change, resulting in new prospect in its future management.

Old concept of chronic lymphedema as a simple phenomenon of lymph stagnation following obstruction of lymph transport system, has been completely replaced by new concept which accepts the chronic lymphedema not only as a regional (local) problem involving entire soft tissue (e.g. cellulites) in addition to lymphatic system itself (e.g. lymphangitis), but also as a systemic problem (e.g. sepsis) involving immune system as well(14-16).

The chronic lymphedema is no longer considered as a simple lymph fluid collection within the soft tissue by the lymphatic obstruction, but is now viewed as a steadily progressing degenerative disease affecting from skin to entire soft tissue, named as "phenomenon of dermato-lipo-fibrosclerosis"(15). Therefore, critical role of subclinical (latent) infection with serious potential to accelerate the progress of tissue damage from reversible acute condition to the irreversible chronic status, drew new attention lately, especially on prevention point of view. In view of limited ability of the presently available treatment, medical or surgical, modalities with limited success, the

prevention of the development/occurrence as well as progress of chronic lymphedema became new issue for the contemporary management(1, 9).

The secondary lymphedema, mostly owing to the post-surgical/post-radiation lymphedema in developed countries(17-20), has triggered proper attention to its prevention/reduction, and new movement among oncologic surgeons/physicians initiated "second look" to the present policy of cancer management, adopting selective/sentinel lymphnodes biopsies if applicable, before full commitment of radical lymphadenectomy(21-25).

Earliest possible evaluation/ detection/ management of latent edema and/or subclinical infection in postoperative period as well, became increasingly popular in most of leading institutes of surgical/medical oncology.

Collaboration among various specialties involved to the management of chronic lymphedema also became more active in order to accommodate various nonsurgical and surgical therapies through last decade. This effort has resulted in more efficient management by specialized team dedicated only to the chronic lymphedema management based on multidisciplinary clinic in these days.

MANAGEMENT

The manual lymphatic drainage(MLD)-based complex decongestive physiotherapy(CDP)(26-30) has been well proven as a physiologic measurement to restore/compensate malfunctioning lymph collecting system in particular, and established oneself as main stem of the modern therapy becoming major landmark in the progress/development in the management of chronic lymphedema.

The traditional compression therapy for mechanical evacuation of interstitial fluid, also has been evolved to sequential intermittent pneumatic compressotherapy (SIPC) to make it more physiologic(31-34), but its relationship with the CDP has not been clearly understood yet(35-38) and remains one of two major physical therapies together to become mutually supportive to supplement to each other at best. The major difference in their roles at different stages of lymphedema, however, remains to be cleared before proceeding to the further intergration of these two different methods with entirely different mechanisms. In view of ongoing controversy over the long term effect of mechanical evacuation of only liquid component of interstitial fluid by the SIPC, leaving solid component (eg. protein) within tissue to accelerate the tissue damage, further clarification on this particular issue is warranted for more effective implementation to the clinical management.

Various surgical therapies, either independent or supplemental, have been also evolved to essential component of total care management; reconstructive surgery(39-46) to restore lymphatic function, mostly in earlier stage of lymphedema, and excisional surgery(47-50) for the palliation to improve the management and subsequent quality of life, mostly in latter stage toward end stage of lymphedema.

The reconstructive surgery in particular remains one and only therapy to provide chance of "cure" so that it keeps unique position as most ideal form of therapy if applicable.

Reconstruction of lymphatic transportation system with various microsurgical techniques(39-46) has been well established, successfully bypassing the obstruction sites of interrupted collecting vessels to restore lymphatic circulation. Lymphovenous anastomoses with/without lymphatic or venous graft interposition(40), and free transfer of tissue containing lymph vessels and lymphnodes(51-54), have brought excellent long term results, although limited to a few dedicated teams of expert microvascular surgeons.

Eventhough surgical reconstruction can deliver such ideal results of cure, its proper implication warrants earlier stage of lymphatic obstruction/lymphedema while intrinsic contractability of the lymph channels remains to be intact, which also respond very well to the conservative therapy with MLD-based CDP.

Hence, the selection of surgical indication from earlier stage of lymphedema becomes difficult, if not, controversial especially in ethical point of view, since conservative treatment alone is also very effective, although not curative, in same early stage while the peristaltic function of lymphangion is still preserved(55-57). The proper document/evidence to ease this concern over the potential harm of long term failure by the surgical therapy resulting in unnecessary sacrifice of previously healthy lymphatic channels is warranted.

Excisional surgery to remove grotesquely disfigured fibrosclerotic tissue, resistant to the conventional conservative regimen also gained new attention lately to improve the management of late stage to improve efficacy of the CDP/compressotherapy(58,59). But the compliance of the patient to maintain postoperative CDP/compressotherapy remains crucial for the long term outcome, and it warrants careful selection of the candidate through scrutinizing evaluation of mental, psychological and physical condition before the final decision.

We at the Lymphedema Clinic, SamSung Medical Center, Seoul, Korea, therefore, limited the indication for reconstructive surgery only to the patients in early stage of lymphedema which has progressed in spite of adequate management with all available conventional conservative therapies at least for 12 months periods(9). The treatment failure of conservative therapy has been carefully documented by the multidisciplinary team of the Clinic before the selection/decision for the candidates, and additional efforts were made to obtain good compliance from the patient throughout the process.

Same rationale was also implemented to limit the selection of the candidate for the excisional surgery only to the patients who have progressed to the end stage from latter stage of lymphedema with further deterioration of quality of life and increased episodes of sepsis in spite of maximum treatment(9). Excisional surgery was mostly provided to the patient with end stage(clinical stage IV, modified from the I.S.L. staging) to pre-end stage (stage III), in order to change grotesquely disfigured contour of the limb to the normal so that the CDP and/or compressotherapy can be implemented more effectively. Once lymphedema should reach the end-stage, effectiveness and efficiency of CDP is curtailed substantially mainly due to the

difficulty to wrap the swollen extremity properly with non-elastic bandage for the exercise therapy.

High cost of advanced medical care of lymphedema became significant burdening to the patient, family and society, so that the maintenance care following initial physician-initiative in-hospital care has to be based on patient-initiative home-based care to reduce the cost involved.. The role of self-help club, organized voluntarily by the patients and their families, to enhance motivation out of ignorance by chronic nature of the disease and subsequently to improve compliance, has been increased, providing necessary supplemental boost (financial and psychological, etc.) with good maintenance of ever-decreasing compliance(9).

The new role of self-help club as self-imposed surveillance system for the patient-initiative home-care for the maintenance care is increasingly important for the adequate management of lymphedema without extra cost.

CLINICAL EXPERIENCES –DEMOGRAPHIC DATA

Among total of 761 patients, registered at Lymphedema Clinic, Samsung Medical Center and Sungkyunkwan University, Seoul, Korea (1994 September through February 2001), 182(66 males and 116 females with age range from 2 months through 81 years - mean 31.1 years) belonged to primary lymphedema (23.9%); 33 congenital type (18.1%), 110 praxox type (60.4%), and 39 tarda type (21.4%), and 579(26 males and 553 females with age range from 21 through 82 years - mean 53.3 year) to secondary lymphedema (76.1%); mostly postsurgical (536/579) and also combined with radiation therapy postoperatively (458/536).

Among total of 761 patients, 527 had lesions in lower extremity (177 on the right and 222 on the left and 130 on both sides), and 227 patients in upper extremity (99 on the right, 126 on the left and 2 on both sides) and 7 patients with multiple lesions.

Among 182 primary lymphedema, 161 had lesion in lower extremity (46 in the right and 54 in the left, and 28 in both limbs), 14 in upper extremity (4 in the right, 7 in the left, 1 in the both sides), and 7 in multiple sites; head and neck, upper and lower extremities, and abdomen.

Out of total 579 secondary lymphedema patients, 366 had lesions in lower extremity (113 in the right and 156 in the left and 97 in both sides), 213 in upper extremity(93 in the right and 119 in the left and 1 on both sides).

The clinical staging, based on modified I.S.L. staging (clinical stage I through IV) of 761 patients, confirmed 99 at the clinical stage I, 354 at stage II, 224 at stage III and 40 at stage IV. Another 44 patients were deferred for the proper staging due to significant discrepancy with laboratory (image) staging based on lymphoscintigraphic findings of chronic lymphedema although it would belong to the stage III of I.S.L. staging.

CLINICAL EXPERIENCES – RESULTS

Following full investigation of lymphedema status per protocol, 518 out of total 761 patients remained on follow-up protocol

with reasonable compliance and 243 patients were excluded due to various reasons, mainly related to the poor compliances.

However, among 518 patients are able to meet the various criteria to fulfill the condition of then ongoing project. Among 220 patients (clinical stage I-77, II-98, III-29 & IV-16), more effective management results were achieved in earlier clinical stages: 70/77 of Stage I, 84/98 of Stage II, 16/29 of Stage III, and 7/16 of Stage IV during average 4.0 year follow up period.

Progress/deterioration of clinical(C) stage of the lymphedema despite adequate treatment was more frequently noticed among the group accompanying higher laboratory(L) stage based on lymphoscintigraphic evaluation: Among 7 out of 77 in C stage I, which progressed to C stage II or higher, 5 accompanied L stage II or III on initial evaluation. 10 among 14 in C stage II, advanced to C stage III, accompanied higher L stage, III or higher; another 11 among 13 in C stage III, deteriorated to C stage IV, also accompanied L stage IV or higher before the CDP-based treatment was instituted.

Among treatment resistant/failure patients deteriorating from the earlier stage in spite of adequate treatment, 19 patients (19 limbs: 18 females & 1 male: primary-4 & secondary-15: a mean age of 49.0 years) were selected for the venolymphatic reconstructive surgery(VLRS) at clinical stage II (9/19) and early III (10/19).

Sixteen of 19 responded with satisfactory outcome (excellent-8, good-6, and fair-2) on initial evaluation at 6 months following the surgery, but only 8 with good compliance to keep postoperative CDP, were able to maintain initial success to the follow-up assessment on 24 months.

All others with unsatisfactory outcome (3 initial failure and 8 subsequent failure) were mostly (8/11) related to the poor to inadequate compliance for the postoperative CDP maintenance.

Postoperative lymphoscintigraphic evaluation have shown compatible improvement with decreased dermal backflow and/or increased clearance, etc. on 5 among 8 patients with good clinical response.

Among 6 of 7 patients (7 limbs: 5 females & 2 males: primary-5 & secondary-2: clinical stage I-1 & II-6 : mean age - 34 years) with initial success of free lymphnodes transplant surgery(FLTS), only 3 out of 5 available for the first interim assessment (12 months), have shown satisfactory response to the surgery clinically. All 3 have shown viable lymphnodes ultrasonographically and/or functioning status of lymphnodes lymphoscintigraphically to support clinical evidence of improvement.

The results of palliative excisional surgery with modified Homan's operation on 33 limbs of 22 patients (19 females & 3 males: 5 primary & 17 secondary: mean age of 43.2 years: clinical stage III-6 & IV-16), were more striking with closer relationship with the compliance: 28 out of total 33 limbs (22 patients) with good initial (6 months and 12 months) responses, were reduced to 16 during the interim(24 months) follow up assessment period, and further to 6 with good compliance to the final (48 months) assessment. There has been no evidence of lymphatic function improvement lymphoscintigraphically even to the clinically successful patients with the excisional surgery.

DISCUSSION

The limited experiences of multidisciplinary approach to combine the CDP, SIPC, and various surgical therapies, on the basis of new concept of total care management, gave us various preliminary informations to improve future management as following;

CDP-based total care management appears to be the most effective and physiologic treatment of chronic lymphedema available today. It appears to provide consistently better response only on its earlier stage (Stage I to II), but more effective when combined with SIPC on the latter to the end-stage (Stage III to IV) of the lymphedema.

SIPC seems to have more powerful and faster effect of decongestion of the lower (distal) part of the extremity but with limited success due to tendency to push up the fluid mechanically toward torso (proximally) leaving the edema ring. SIPC, therefore, seems to need sequential and/or simultaneous MLD for the further central mobilization of proximally shifted and retained fluid as edema ring out of the extremity to the torso. SIPC is more effective to improve and maintain overall results of treatment especially to the advanced stage and it can enhance its effect with complimentary support by MLD-based CDP.

MLD seems to be more efficient in earlier stage (stage I to II) than later stage (stage II to III) and more efficient on proximal part than distal part of the extremity.

The compliance of the patient and/or the family can not be overemphasized for its critical value since the long-term results of the treatment, either surgical or non-surgical seem to depend on this compliance.

Home maintenance care is as important as initial hospital care to maintain the stabilized results following the in-hospital care, and it will depend on self-initiating motivation with proper commitment by the patients themselves. Therefore, CDP-based treatment should not be started until thorough education convinces the patients of the necessity of life time commitment to the treatment of this mostly incurable disease to maintain maximum control.

To convince them to achieve good compliance, sufficient information about this disease should be provided to the patient and family first, prior to friendly persuasion to improve patient compliance and motivation. Further encouragement of the patient through self-help organization seems to be very effective to maintain the necessary support to each other psychologically and socioeconomically.

Multidisciplinary team of our Clinic has set a strict policy against early implementation of the venolymphatic reconstructive surgery at the clinical stage I, in contrast to other leading groups in this field with different indication. We rather limited its indication only to the unequivocal progression of disease from stage I to II despite all the available therapy implemented and declared as the "failure" by the multidisciplinary team. Therefore, most of our candidates already advanced to the clinical stage II with significant progress of the lymphatic failure/paralysis, particularly resistant to the MLD-based CDP distally along the lower leg to foot.

Local condition among our candidates in general was relatively too advanced to find suitable healthy lymph vessels at the femoral level preoperatively, for the standard approach of microsurgical anastomoses (G. Campisi et al. of Genoa, Italy). Instead, the reconstruction was made at the popliteal(below-knee) level with more healthy vessels, advocated by Professor V. Krylov(Moscow, Russia). Our experiences on the venolymphatic reconstructive surgery are however, very limited with less ideal candidates to restore normal lymphatic function, comparing to those by Campisi's, and its role has been strictly limited as an auxiliary method to supplement the CDP-centered therapy to already damaged lymphatic system in significant degree(9).

The FLTS was originally adopted for the primary lymphedema but extended also to the secondary lymphedema recently as one of reconstructive surgery when the patients should fail to become candidate for the VLRS. Our preliminary results are quite promising, but we are not yet ready to draw a reliable conclusion on the long term outcome of FLTS at this moment(9), and further/final evaluation at least up to the second interim follow-up assessment on 24 months and preferably to the final assessment on 48 months to all the FLTS patients, including subsequently performed another 6 patients, is warranted.

The new role of FLTS as potential substitute of VLRS especially to the patients with relatively advanced stage, and/or with lymphangiodysplasia involving lymphnodes and lymph vessels among primary lymphedema remains to be confirmed through future multicenter studies.

Our results of excisional surgery to the end stage of chronic lymphedema are much better than those of earlier experiences by others, although our indication was strict, remaining in supplemental role to improve the efficacy of CDP/compressotherapy during the limited period of follow up for no more than 4 years(9). However, it seems to be able to provide easier control of end stage of lymphedema with subsequently better quality of life postoperatively with reduced infection rate.

The reconstructive surgery or excisional surgery should be considered as a part of total care management only when sufficient postoperative CDP can be guaranteed with good compliance to enhance and maintain its complimentary effect on over-all total care.

Preventive and/or control of the infection (local/systemic) is utmost important to delay the progress of the disease, and therefore, liberal commitment to the prophylactic antibiotics should be encouraged even indefinitely when the infection should recur frequently or even on the latent sub-clinical status if indicated(14,15).

It was best way to convince the patient and family that the healthcare provider is able to provide only limited role through proper supervision and patients have to learn to take initiative for its own daily home maintenance care.

Therapy regimen should be flexible to accommodate the best-suit treatment to each patient although the MLD-based CDP is

most effective treatment strategy but only to the fully committed patients in earlier stage. The SIPC should be included together with CDP especially to the advanced stage since MLD and SPC seems to hold the mutually complimentary effect as total care..

PROSPECT – PRIMARY LYMPHEDEMA

Although the primary and secondary lymphedema have been treated successfully together in same category of chronic lymphedema, the potential for the future treatment prospect for the primary lymphedema became much clear lately. Therefore, better understanding of these differences in etiology is mandatory for the contemporary management of chronic lymphedema as a whole(9-11,60).

The primary lymphedema represents a clinical manifestation of one of two types of lymphatic malformation (LM). LM is one of various congenital vascular malformation, as the result of developmental arrest occurred in the lymphatic system(10,11). When it should occur in the later stage of lymphangiogenesis, it is classified as the truncular(T) form (Modified Hamburg Classification)(10) and clinically manifested as primary lymphedema. Other form of LM, developed in earlier stage of embryonal life, is classified as the extratruncular(ET) form (e.g. cystic/cavernous lymphangioma) and often combined with other kinds of vascular malformation(e.g. venous malformation)(61-66). Both forms of LM have entirely different characteristics with different clinical behavior so that clear understanding of the relationship between this primary lymphedema as the T form, and other as ET form is essential, since it may exist either alone or together to make the condition more complicated(10).

However, the new prospect of primary lymphedema management is now much bright. Much increased feasibility for the gene manipulation to correct/compensate the genetic defect of lymphangiogenesis as the cause of primary lymphedema will give new opportunity to make fundamental change on our concept to the chronic lymphedema(67-69). And it is also going to give new vision to us for how to lead the management of chronic lymphedema not only for the primary lymphedema but also for the secondary lymphedema (e.g. venolymphangiogenetic manipulation) as well for the future(70,71).

CONCLUSION

The progress of chronic lymphedema, either primary or secondary is no more “incurable” disease but manageable if not preventable, when the ignorance and poor compliance should be overcome together. The new concept of total care management based on multidisciplinary approach to accommodate the new additional role of surgical therapy as adjunct therapy to enhance over-all effectiveness of the CDP-based main therapy, can deliver improved quality of life as the ultimate goal of the management of chronic lymphedema.

REFERENCE

1. Foldi E, Foldi M, Clodius L. *The lymphedema chaos; A lancet.* *Ann Plastic Surg* 1989;22:505-515.
2. Browse N. *The invisible vessels:who saw them first?* In: Sir Browse N, Burnand K, Mortimer P, eds. *Diseases of the Lymphatics.* London, U.K.: Arnold; 2003:3-20.
3. Chauvois L. *William Harvey.* London: Hutchinson, 1957.
4. Wyall H. *William Harvey.* London:Parsons,1924.
5. Horstmann E. *Über die funktionelle Struktur des mesenterialen Lymphgefäße.* *Morpholog Jahrbuch* 1952; 91:483.
6. Horstmann E. *Beobachtungen zur Motorik der Lymphgefäße.* *Pfluegers Archives* 1959; 269:511-19.
7. Mawhinney HJD, Roddie IC. *Spontaneous activity in isolated bovine mesenteric lymphatics.* *Journal of Physiology* 1973;229:339-48.
8. Levick JR, McHale N. *The physiology of lymph production and propulsion.* In: Sir Browse N, Burnand K, Mortimer P, eds. *Diseases of the Lymphatics.* London, U.K.: Arnold; 2003:44-64.
9. Lee BB, Kim DI, Whang JH, Lee KW. *Contemporary management of chronic lymphedema – personal experiences.* *Lymphology* 2002;35 (Suppl):450-455.
10. Lee BB, Seo JM, Hwang JH, Do YS, Kim DI, Byun HS, Lee SK, Huh SH, Hyun WS: *Current concepts in lymphatic malformation (LM).* *J. Vascular & Endovascular Surgery*, 2004 (in press).
11. Lee BB, Kim DI, Hwang JH, Choi JY: *Primary Lymphedema-Angiodysplasia Syndrome.* Abstract, XVIII International Congress of Lymphology, Genoa, Italy, September 3-7, 2001.
12. Bruna J, Miller AJ, Beninson J. *The clinical grading and simple classification of lymphedema.* *Lymphology* 2002;35 (Suppl):160-162.
13. Michelini S, Failla A, Moneta G, Campisi C, Boccardo F. *Clinical staging of lymphedema and therapeutical implications.* *Lymphology* 2002;35 (Suppl):168.
14. Foldi E. *Prevention of dermatolymphangioadenitis by combined physiotherapy of the swollen arm after treatment for breast cancer.* *Lymphology* 1996;29:48-49.
15. Olszewski WL. *Episodic dermatolymphangioadenitis (DLA) in patients with lymphedema of the lower extremities before and after administration of benzathine penicillin: a preliminary study.* *Lymphology* 1996;29:126-31.
16. Bernas MJ, Witte CL, Witte MH. *The diagnosis and treatment of peripheral lymphedema.* *Lymphology* 2001;34:84-91.

17. Hall JG. New possibilities in the pathogenesis of secondary lymphedema. *Lymphology*. 2002 Sep;35(3):129.
18. Rockson SG. Lymphedema. *Am J Med*. 2001 Mar;110(4):288-95. Review.
19. Lammie PJ, Cuenco KT, Punkosdy GA. The pathogenesis of filarial lymphedema: is it the worm or is it the host? *Ann N Y Acad Sci*. 2002 Dec;979:131-42; discussion 188-96. Review.
20. Bunce IH, Mirolo BR, Hennessy JM, Ward LC, Jones LC. Post-mastectomy lymphoedema treatment and measurement. *Med J Aust*. 1994 Jul 18;161(2):125-8.
21. Golshan M, Martin WJ, Dowlathshahi K. Sentinel lymph node biopsy lowers the rate of lymphedema when compared with standard axillary lymph node dissection. *Am Surg*. 2003 Mar;69(3):209-11; discussion 212.
22. Babb RR, Spittell JA Jr, Martin WJ, Schirger A. Prophylaxis of recurrent lymphangitis complicating lymphedema. *JAMA*. 1966 Mar 7;195(10):871-3.
23. Clodius L. Minimizing secondary arm lymphedema from axillary dissection. *Lymphology*. 2001 Sep;34(3):106-10.
24. Coen JJ, Taghian AG, Kachnic LA, Assaad SI, Powell SN. Review Risk of lymphedema after regional nodal irradiation with breast conservation therapy. *Int J Radiat Oncol Biol Phys*. 2003 Apr 1;55(5):1209-15. Review. Erratum in: *Int J Radiat Oncol Biol Phys*. 2003 Jun 1;56(2):604..
25. Pissas A, Rzal K, Math ML, el Nasser M, Dubois JB. Prevention of secondary lymphedema. *Ann Ital Chir*. 2002 Sep-Oct;73(5):489-92.
26. Casley-Smith, Judith R, Casley-Smith JR. *Modern treatment for lymphedema*. Adelaide, Lymphoedema Association of Australia 1994, 245 pp.
27. Foldi E, Foldi M, Weissletter H. Conservative treatment of lymphedema of the limbs. *Angiology* 1985;36:171-180.
28. Hwang JH, Kwon JY, Lee KW, Choi JY, Kim BT, Lee BB, Kim DI: Changes in lymphatic function after complex physical therapy for lymphedema. *Lymphology* 32:15-21, 1999.
29. Hwang JH, Lee KW, Chang DY, Lee BB, Kim DI, Kim SJ, et al. Complex physical therapy for lymphedema. *J Kor Acad Rehab Med* 1998;22:224-9.
30. Johansson K, Albertsson M, Ingvar C, Ekdahl C. Effects of compression bandaging with or without manual lymph drainage treatment in patients with postoperative arm lymphedema. *Lymphology*. 1999 Sep;32(3):103-10.
31. Bastien MR, Goldstein BB, Leshner JL, et al. Treatment of lymphedema with a multi-compartment pneumatic compression device. *J Am Acad Dermatol* 1989;20:853-854.
32. Hwang JH, Kim TU, Lee KW, Kim DI, Lee BB: Sequential intermittent pneumatic compression therapy in lymphedema. *J. Korean Acad. of Rehab. Med.*, 21(1): 146-153, 1997.
33. Richmand DR, O'Donnell TF, Zelikovski A. Sequential pneumatic compression for lymphedema: A controlled trial. *Arch Surg* 1985;120:1116-1119.
34. Zelikovski A. Treatment of lymphedema with a multi-compartmental pneumatic device. *J Am Acad Dermatol* 2990;23:951-952.
35. Boris M, Weindorf S, Lasinski BB. The risk of genital edema after external pump compression for lower limb lymphedema. *Lymphology*. 1998 Mar;31(1):15-20.
36. Callam MJ, Ruckley CV. Hazards of compression treatment of the leg. *Brit Med J* 1987;295:1382.
37. Eliska O, Eliskova M. Are peripheral lymphatics damaged by high pressure manual massage? *Lymphology* 1995;2:21-30.
38. Theys S, Deltombe TH, Scavée V, Legrand C, Schoevaerdt JC. Safety of long-term usage of retrograde-intermittent pneumatic compression in lower limb lymphedema. *Lymphology* 2002;35 (Suppl):293-297.
39. Campisi C, Boccardo F, Zilli A, Maccio A, Gariglio A, Schenone F. Peripheral lymphedema: new advances in microsurgical treatment and long-term outcome. *Microsurgery*. 2003;23(5):522-5.
40. Campisi C, Boccardo F, Zilli A, Maccio A, Napoli F. Long-term results after lymphatic-venous anastomoses for the treatment of obstructive lymphedema. *Microsurgery*. 2001;21(4):135-9.
41. Campisi C, Boccardo F. Role of microsurgery in the management of lymphoedema. *Int Angiol*. 1999 Mar;18(1):47-51.
42. Gloviczki P. Review. Principles of surgical treatment of chronic lymphoedema. *Int Angiol*. 1999 Mar;18(1):42-6.
43. Kim DI, Lee BB, Hwang JH, Lee KW: Clinical Application of CUSA on Venolymphatic Anastomotic Surgery. Abstract, 48th Annual Congress, Korean Surgical Society, November 1996.
44. Krylov V, Milanov N, Abalmasov K. Microlymphatic surgery of secondary lymphoedema of the upper limb. *Ann Chir Gynaecol*. 1982;71(1):77-9.
45. Degni M. New technique of lymphatic-venous anastomosis for the treatment of lymphedema. *J Cardiovasc Surg (Turin)* 1978;19:577.
46. Baumeister RGH, Siuda S. Treatment of lymphedemas by microsurgical lymphatic grafting: what is proved? *Plastic and Reconstructive Surgery* 1990;85:64-74.

47. Auchincloss H. New operation for elephantiasis. *Puerto Rico J Publ Health & Trop. Med* 1930;6:149.
48. Homans J. The treatment of elephantiasis of the legs. *N Engl J Med* 1936;215:1099.
49. Kim DI, Huh S, Lee SJ, Hwang JH, Kim YI, Lee BB. Excision of subcutaneous tissue and deep muscle fascia for advanced lymphedema. *Lymphology* 1998;31:190-194.
50. Servelle M. Surgical treatment of lymphedema: a report on 652 cases. *Surgery*. 1987 Apr;101(4):485-95.
51. Becker C, Bourgeois P, Gilbert A. Free vascularized lymphatic node transplantation for lymphedema. *Surgery of the Skin and Skeleton of the Hand*. 2001.
52. Becker C, Hidden G, Godart S et al. Free lymphatic transplant. *Eur J Lymphol* 1991;6:75-80.
53. Becker C, Hidden G, Pecking A. Transplantation of lymph nodes: an alternative method for treatment of lymphedema. *Progr Lymphol* 1990;6:487-93.
54. Becker C, Hidden G. Transferts lymphatiques libres. *Microchirurgie et Anatomie. Maladies Vasculaires* (Masson: Paris). 1988:119-22.
55. Mortimer PS. Therapy approaches for lymphedema. *Angiology*. 1997 Jan;48(1):87-91.
56. Coget J. Medical and surgical therapies. Their respective indications in lymphedema. *Phlebologie*. 1988 Apr-Jun;41(2):359-69. French.
57. Foldi M. Treatment of lymphedema. *Lymphology*. 1994 Mar;27(1):1-5.
58. Lee BB: Improved efficacy of complex decongestive physiotherapy (CDP) on end-stage chronic lymphedema with supplemental excisional surgery. Abstract, The 4th International Vascular and Endovascular Congress and the 4th BCS International Congress, Beijing, China, October 17-20, 2002.
59. Lee BB: Crucial role of complex decongestive physiotherapy (CDP) for the outcome of excisional surgery on end-stage chronic lymphedema. Abstract, 14th Annual Meeting of the American Venous Forum, California, USA, February 21-27, 2002.
60. Wolfe JH, Kinmonth JB. The prognosis of primary lymphedema of the lower limbs. *Arch Surg*. 1981 Sep;116(9):1157-60.
61. Lee BB, Do YS, Byun HS, Choo IW, Kim DI, Huh SH. Advanced management of venous malformation with ethanol sclerotherapy: mid-term results. *J Vasc Surg* 37(3):533-8, 2003
62. Lee BB, Kim DI, Huh S, Kim HH, Choo IW, Byun HS et al. New experiences with absolute ethanol sclerotherapy in the management of a complex form of congenital venous malformation. *J.Vasc.Surg* 2001;33
63. Lee BB. Critical issues on the management of congenital vascular malformation. *Annals Vasc Surg* 18(3):380-392, 2004.
64. Lee BB: Advanced management of congenital vascular malformation (CVM). *International Angiology* 21(3):209-213, September 2002.
65. Lee BB, Kim DI, Kim HH, Choi JY, Do YS, Choo SW, Kim BT. Hidden risk of the deterioration of the lymphatic function following the management of venous component of the hemolymphatic malformation (HLM). Abstract, 13th International Society for the Study of Vascular Anomalies, Montreal, Canada, May 10-13, 2000.
66. Lee BB, Bergan JJ: Advanced management of congenital vascular malformations: a multidisciplinary approach. *J. Cardiovascular Surgery*, 10(6):523-33, December 2002.
67. Erickson RP. Lymphedema-distichiasis and FOXC2 gene mutations. *Lymphology*. 2001 Mar;34(1):1.
68. Evans AL, Bell R, Brice G, Comeglio P, Lipede C, Jeffery S, Mortimer P, Sarfarazi M, Child AH. Identification of eight novel VEGFR-3 mutations in families with primary congenital lymphoedema. *J Med Genet*. 2003 Sep;40(9):697-703
69. Holberg CJ, Erickson RP, Bernas MJ, Witte MH, Fultz KE, Andrade M, Witte CL. Segregation analyses and a genome-wide linkage search confirm genetic heterogeneity and suggest oligogenic inheritance in some Milroy congenital primary lymphedema families. *Am J Med Genet*. 2001 Feb 1;98(4):303-12.
70. Yoon YS, Murayama T, Gravereaux E, Tkebuchava T, Silver M, Curry C, Wecker A, Kirchmair R, Hu CS, Kearney M, Ashare A, Jackson DG, Kubo H, Isner JM, Losordo DW. VEGF-C gene therapy augments postnatal lymphangiogenesis and ameliorates secondary lymphedema. *J Clin Invest*. 2003 Mar;111(5):717-25.
71. Szuba A, Skobe M, Karkkainen MJ, Shin WS, Beynet DP, Rockson NB, Dakhil N, Spilman S, Goris ML, Strauss HW, Quertermous T, Alitalo K, Rockson SG. Therapeutic lymphangiogenesis with human recombinant VEGF-C. *FASEB J*. 2002 Dec;16(14):1985-7. Epub 2002 Oct 18.

HOW CAN LYMPHEDEMA OF THE UPPER LIMB AFTER AXILLARY DISSECTION DUE TO BREAST CANCER BE MEASURED ? REVIEW OF LITERATURE AND A PROPOSAL OF CLINICAL PAPER

Galli Tiziana

Operative Unit of Rehabilitation Medicine Azienda Ospedaliera "Ospedale di Circolo" di Busto Arsizio (VA). Saronno Hospital (Varese) Italy

Presented : April 2004

Revised : August 2004

Accepted : October 2004

CORRESPONDENCE TO:

tiziana-galli@libero.it

ABSTRACT

BACKGROUND AND PURPOSE: *The lymphedema of the upper extremity is a pathology which can give a severe and permanent physical disability.*

From the clinical picture and the functional assessment we choose the specific rehabilitation plan.

The aim of this study is to propose a Lymphological Medical Record and a Measurement Card. An easy and useful method that could help clinical lymphologist and physical therapist to care these patients.

MATERIALS AND METHOD: *Height, body weight and circumference measurements of both upper extremities are taken by physical therapist at the first treatment.*

The different size of the affected limb and the unaffected limb at various point along the arm are compared.

With computer technology (Microsoft Excel) you can have: the centimetric difference between oedematous limb and non-oedematous limb and its average increase%, the difference after treatment and its average reduction% and from the analyses of these data the lymphedema value % after treatment

PARTECIPANTS: *The study included 10 women with lymphedema of upper extremity after axillary dissection due to breast cancer treated as outpatients.*

RESULTS: *Before treatment oedematous limb of all patients showed average increase of 15,5% compared with non-oedematous limb. At final treatment oedematous limb of all patients showed average reduction of 40,9% compared with their own initial measurement. At final treatment oedematous limb of all patients showed average value of 10,9 % compared with non-oedematous limb*

CONCLUSION: *Standard measurement criteria and data collection are lacking.*

They could be an useful method to assess lymphedema in clinical practice.

KEY WORDS: *lymphedema – measurement – breast cancer*
Lymphedema of the upper limb is one of the most feared side effects of breast surgery due to tumour.

KEY WORDS : Lymphedema monitoring. Limb's Measures.

INTRODUCTION

Thanks to the progress made in surgery, chemotherapy and radiation therapy, women who suffer of breast cancer are able to prolong their life and in many cases to defeat their disease. The axillary dissection as a key surgical act for staging, assessment and subsequent treatment, however, causes a remarkable unbalance in lymph vessels of the upper limb, the remaining part of breast and the thoracic wall, between the quantity of lymph produced and the transportation capacity of the lymph system. In conditions of hypoplasia of the compensation collateral vessels, the lymph system is unable to carry out its task thus causing the lymphedema of the arm. The incidence of lymphedema is reported variably in the various studies as it can develop either early, i.e. soon after surgical intervention, directly connected to the intervention and the radiation therapy, or after some time, often "triggered" by an infection, an acute lymphangitis, or by an even slight trauma. In other cases, after a period of stationary conditions, lymphedema develops rapidly: this worsening in health conditions should lead to a diagnosis of the so-called malign lymphedema. Most lymphedemas are assessed and treated without hospitalization: this is the reason why they are not recorded at national and international level.

Out of the 140 million lymphedemas recorded by the World Health Organization (WHO) in 1994 (latest recorded data), 20 million were post-surgery lymphedemas (caused by the removal of lymph nodes at the root of the limb according to criteria of the surgical treatment), with a greater incidence in the most developed Countries [1].

In a national epidemiological study, carried out by the Italian Society of Lymphangiology between 1997 and 1998 (a year of data recorded by 34 specialist centres located on the national territory), secondary lymphedemas were over 65% and, among this percentage, the post-surgery cases amounted, alone, to about 55%.

According to statistics of the various groups, the incidence of "arm big size" due to post-breast removal or post-quadrantectomy with axillary lympho-adenectomy oscillates around 20-25% (with extreme from 5 to 45%) [2].

If surgery is added to the complementary radiotherapy, the average incidence rises to 35% of cases.

A greater incidence is recorded in patients who underwent quadrantectomy with axillary lympho-adenectomy compared to patients who underwent mastectomy. No significant variations due to seasonal or geographical factors connected to climate were recorded.

The variable incidence depends on an early or late diagnosis is made, on the patient being informed on the possible future problems she might have to face, and on health practitioners who often, in the past, did not care of this pathology. Standard measurement criteria and data collection are lacking. Prevention of lymphedema starts in the pre-surgery phase, with the assessment of functional conditions of the shoulder girdle and neck, muscle tropism, by the measuring of the upper limb size and with special attention to the unilateral extremity of the tumour location.

A lymphangioscintigraphy should be made already in this stage to evaluate lymphatic circulation and drainage through lymph nodes. The co-morbid conditions should be considered, such as: obesity, familiarity to lymphatic disease, metabolic disease, venous insufficiency.

These data allow to define the rehabilitation program tailored to the patient in the post-surgery phase to obtain a rapid functional recovery of the upper extremity. Added to health information on the movement allowed and measures to be taken, these figures represent the essential information that a woman should receive to start her social and/or working life again.

In particular, the arm measurement is essential to recognise and make a diagnosis of lymphedema at its early stage, follow its development and treat the possible side effects.

When an early diagnosis is not made and lymphedema has already developed, measurement is usually carried out by comparing the two upper extremities, taking into account the difference in size that the two arms have in normal conditions. The latter situation is what a physical therapist has often to face with outpatients.

Women who underwent a surgical intervention and realize that their arm has increased in size often turn to the Operative Unit of Rehabilitation Medicine.

It is therefore essential to find a valid measurement method in order to have an accurate diagnosis, to decide the appropriate therapy (Complex Decongestive Physiotherapy), as well as to monitor the disease development to prevent severe and recurring lymphangitic complications.

A study with data bases (PUBMED/MEDLINE, SCIRUS and PEDro) was carried out to find review of literature, consensus conference, guidelines and congress literature which would help to define a valid measurement method for lymphedema. By using key words, i.e. lymphedema-measurement-volumetry-breast cancer, a good number of scientific articles were sorted out, thus proving the great interest that this issue is arising at international level.

A survey at national level was also made on vascular and lymphatic rehabilitation.

A unique, validated and acknowledged method to measure lymphedema is not available yet.

Two primary methods of measuring lymphedema are water displacement volumetric measurements and girth measurement.

The water displacement is based on Archimedes' Principle,

which states that the water volume displaced is equal to the volume of the object immersed in the water.

Water displacement has been considered to be the "gold standard" for its accuracy, with an error of less than 1%, but many researchers chose not to use it because this method is time consuming, expensive and can be unhygienic.

Additionally, the use of water displacement is unsuitable for patients with skin ulcers, in the immediate post-surgery period and doesn't identify the locations of edema on the arm.

Girth measurements, by taking measurements at fixed points, are simple and clinically useful. This method, however should be used avoiding any causes of error: the tension of the tape on the skin, the accuracy in choosing the reference point and the position of the tape with respect to the limb. This method records girth measurements on the oedematous limb, not its volume.

A few years ago the interest of many researchers turned to the calculations of volume on the bases of girth measurements at pre-defined points.

Various geometrical formulas were tested to measure limb volume and the results obtained are then compared with water displacement results to prove the reliability of measurements. Researchers wish to find an accurate, reliable and time-efficient method and which could be used both hospital and with outpatients.

AM Megens et al.(2001) [3] find to determine if two methods of calculating upper extremity volume, the single truncated cone calculations and the summed truncated cone calculation (using arm circumferences), can substitute for water displacement volumetry.

The results of their investigation show that the truncated cone calculation of lymphedema from circumferential measurements cannot be used interchangeably with volume measurements. Both calculated volumes, by the single or summed truncated cone methods, overestimate the volume of the upper extremity by more than 100mL.

The water displacement volumetry is the only method that will provide an accurate estimate of the volume of the upper extremity. Therefore, as the volume of an upper extremity increases, both volumetry and calculated volume measurements will also increase. Volumetry and calculated volume will change in the same direction with one another.

This provides researchers with an alternative method for monitoring upper extremity volume.

Circumferential measurements can be used in other methods of size determination of upper extremity. Direct comparison of the circumference at varying sides on the arm has been used, as well as alternative calculations that have shown agreement with volume measurements in the lower extremity.

Again, water displacement and circumferential measurements do not capture the change of quality of edema. Health care professionals who work with women with lymphedema are attempting not only to decrease the amount of swelling, but also to reduce pain and decrease the hardness in the limb tissues. It is very important to document change in these features.

Sander et al (2002) [4] did not find, in literature, any reports in which geometric volume of the hand was included in the total arm volume measurement.

The purpose of their study was to compare geometric methods of determining upper extremity volumes with water displacement methods.

Geometric volume formulas for a cylinder, frustum, rectangular solid and trapezoidal solid were used to calculate volumes of the arm and hand at different measurement intervals (3, 6 and 9 cm). They wanted to determine an optimal length of segments for use in clinical practice.

They studied only women with lymphedema. Measuring limbs with edema is different from measuring limbs without edema because of the tissue texture change that accompany swelling, such as pitting and fibrosis. Both pitting and fibrosis can respond to external pressure on the skin that may alter the accuracy of girth measurements.

They recommended that the frustum formula be used to calculate volume in both the arm and the hand because the geometric frustum volume had the smallest standard error of measurement. They recommended using a frustum volume calculation with measurements in 3-cm segments for the hand and either 6-cm or 9-cm segments for the arm.

Although strongly correlated, the measurements obtained by the two methods did not agree.

Karges et al (2003) [5] considered water displacement volume the gold standard to determine limb volume. Therefore, the purpose of their study was to determine the concurrent validity of calculated volume derived from circumference measurements and water displacement volume in lymphedematous and non oedematous upper extremities. In their opinion, circumference measurements may be used frequently in the clinic because they are simple and time-efficient.

They calculated the volume using the frustum formula mentioned by Casley-Smith [6]: $\text{Volume} = h(C + C_c + c)/12$ every 4-cm along the arm.

First, they calculated volume of upper extremities with girth measurements in regular intervals from the finger metacarpophalangeal (MCP) joints proximal to the upper arm between the mid-humerus and the axilla.

Second, they determined the upper extremity minus fingers volume by subtracting finger volume from the upper-extremity volume and compared these two kind of measurements.

Third, they compared calculated volume side-to-side differences and water displacement volume side-to-side differences.

However, the differences between the measures indicated that they were highly associated but not interchangeable.

Clinicians or researchers should feel confident in using either the calculated volume or the water displacement volume for clinical and research purposes, but they should not mix or substitute methods with a single patient or in a single study.

Lymphovenous Canada (2002) [7] stated that without scientific protocol and standardized measurements, we cannot truly evaluate the effectiveness of treatments for persons with lymphatic disorders.

Lymphovenous Canada looks at the efforts of two researchers: A. Megens (we just known her study) and N. Piller. Neil Piller was charged by Australasian Lymphology Association to reach a consensus on standards of measurement.

“..You can’t force people to use standards, but the bait to encourage people to use the standard is that you can talk to someone else about how what they are doing compares with what you are doing. Most importantly, you can get a much better quality of result for your patients, you can collaborate in a research sense to in the end achieve a better understanding and better outcomes for the patient”.

Through extensive group discussions, what they came with is hereunder indicated:

- Tape measurements should start from the tip of the middle finger. Measurements should be taken using the narrow tape
- There should be so minimal pressure in using that tape that there is no indent mark
- Only take one measurement should be taken unless therapists feel unsure about the measurement in which case we should take two and then average them
- Measurements should be taken at 10-centimeter measurement intervals
- Calculation of volume was considered to be very important for scientific study. Most respondents thought volume should be calculated from tape measurements of circumference. Some persons thought it should be calculated from immersion in water and perometry if available for the high level of accuracy and repeatability it gives.

Agreeing to these standards in Australia represented a major accomplishment in getting better outcomes for patients.

MC Kenzie DC and Kalda AL (2003) [7] examined the effect of a progressive upper body exercise program on lymphedema secondary to breast cancer treatment. Lymphedema was assessed by arm circumference and measurement of arm volume by water displacement. They also measured quality of life before and after intervention by the Medical Outcomes Trust Short-Form 36 Survey.

No changes were found in arm circumference or arm volume as a result of the exercise program, but they found an increase in quality of life in the exercise group (SF-36).

Percentage difference of arm volume calculated from the two measurements techniques were also correlated, although the means were significantly different.

However, it is impossible with these measurement techniques to know what tissue changes occurred within the upper extremity. Regular exercise is associated with muscle hypertrophy and a loss of adipose tissue. Although arm circumference did not change, we do not know if the level of lymphedema was influenced by the exercise; other tissue changes may have masked any positive effects on lymph accumulation.

Mridha and Odman (1989) [9] some years ago told how volumetry and the surface measurements determines only the degree of swelling in the limb and therefore indicates nothing about the complex changes in the mechanical properties of the tissue due to oedema. The aim of their study was to study the changes in the viscoelastic properties of oedematous tissues with treatment. Oedematous tissue was compressed for 20 sec by a cylindrical head 15mm in diameter to a depth of 4 mm. After withdrawal of the compression head, a depression remained due to the translocation of oedematous limb.

From the analyses of force curves, which was proportional to fluid translocation under compressive deformation, they studied how the curve parameters changed with the treatment of lymphedema.

These indicated that tissues contained less mobile fluid after treatment than before treatment.

Measurement of fluid translocation was useful in selecting and evaluating the effectiveness of lymphedema treatment, as well as in determining the viscoelastic properties of the oedematous tissues.

Recently **Aloisi** (2003) [10] assesses the tissue fluid translocation under the action of deformation with an impression tonometer.

A very important parameter to evaluate lymphedema is its tissue fibrosis.

Subcutaneous pitting edema can be subjectively expressed using the classical clinical test, in which the tissue is indented with the tip of the physicians finger.

With the tonometer, the viscoelastic properties of the tissue in compression can be assessed, and the level of tissue tonicity and its changes can be measured in an accurate and repetitive way. Therefore, interesting information about lymphedema can be taken to determine the changes of lymphedema and its reduction after treatment.

Gerber LH (1998) [11] undertaken a review of literature about measurement of lymphedema.

Many techniques are available for lymphedema assessment:

- circumferential measures of limbs at various points,
- volumetric measures with water displacement,
- skin tonometry in which soft tissue compression is quantified,
- magnetic resonance imaging, computerized tomography and ultrasound described the characteristic of tissue involvement
- lymphoscintigraphy and Doppler venous to evaluate patients with filariasis or in those who are evaluated pre- and post-lymphatic-venous-lymphatic anastomoses

Developing good measures will help in determining the incidence of the problem, its response to treatments and the impact of lymphedema on function. This type of measurement should be easy to use, accessible, no expensive, reliable and quantifiable. Quantitative imaging technique are more sensitive but also less accessible and expensive.

A fruitful area for research and development is to devise a patient-administered questionnaire to assess the degree of swelling and its impact on function. This would give use valuable incidence information as well as understanding of the input lymphedema has on the daily activities and life of the breast carcinoma patient.

From the analysis of international paper, the measurement of upper extremities is still open to questions.

The volumetry and other investigation techniques give high level survey, but they aren't easy to perform and physical therapist needs timely measurement of oedematous limb for treatment.

Girth measurements are one alternative to water displacement volumetry.

The circumferential measurement technique has limitation as well, you can not use it in research setting, but it is practical for clinical purposes, it is time- efficient, easy to perform, no

expensive and you need only a narrow tape.

Rather than determining the volume of the limb with mathematics formulas, I compare both the affected limb and the unaffected limb at various point along the arm for measure the different size. In this way, comparing the affected limb before and after treatment, the level of swelling reduction and the efficacy of treatment can be assessed.

The lymphedema disability isn't only the swelling of the arm, but also the problem that can be caused by it such as lymphangitis, pain, limited range of motion.

The lymphological physical therapist will cure all the body with lymphedema and its impact on function.

The purpose of this study is to propose a Lymphological Medical Record and a Measurement Card.

An easy and useful method that could help clinical lymphologist and physical therapist to care these patients during the Combined Physical Therapy and in the next follow-up.

A type of medical record which considers the ill in her whole clinical picture to prevent severe and recurring lymphangitic complications and prevent the clinical progression of disease. Failure to control lymphedema may lead repeated infections (dermato-lymphangio-adenitis), progressive elephantine tropic changes in the skin and on rare occasions even to the development of a highly lethal angiosarcoma (Stewart-Treves Syndrome).

MATERIALS AND METHODS

The lymphedema of the upper extremity is a pathology which can give a severe and permanent physical disability; for this reason in rehabilitation medicine it have to be considered the whole clinical picture.

It's important to know the clinical history of the lymphedema, its possible reason, how and in which way it has come out. We have also to consider the co-morbid conditions such as obesity, metabolic disease, venous insufficiency and familiarity to lymphatic disease.

The Lymphangioscintigraphy is a modern investigation technique which is essential to evaluate lymphatic circulation and drainage through alternative lymphatic vessels to second level lymph nodes. The study of both deep and surface lymph circulation is useful for therapeutic and prognostic considerations.

Physical examination evaluate the extension of disease, the staging of lymphedema and its fibro sclerotic tissue component. When it's possible it will be interesting to value the fibro sclerotic tissue component with tonometry.

In the Measurement Card is considered the all body area with lymphedema.

The clinical examination values the range of motion and muscular tropism of shoulder girdle and cervical rachis.

Joint limitation associated with muscle hypotrophy don't allow the functional recovery of the upper limb and produce negative effects in lymphedema.

In women underwent to a quadrantectomy is important to assess the partially operated breast for the risk of complications, such as mastitis, and the breast skin changes after radiotherapy.

In the initial assessment is important to observe the skin of the

hand, its hydration and if there are some micro injuries or micro traumatism that could start lymphangitis disease. The cure of the hand is index of the cure women have by herself and the kind of her activity daily living.

We also assess the arm sensibility and if there are paresthesias produced by lymphedema.

From description of patient pain and disability, we can know her way of life, her knowledge about lymphedema and its impact in daily activity.

Height, body weight and circumference measurements of both upper extremities are taken by physical therapist at the first treatment.

The different size of the affected limb and the unaffected limb

at various point along the arm are compared.

From the clinical picture and the functional assessment we choose the specific rehabilitation plan.

With computer technology (Microsoft Excel) you can have:

- the centimetric difference between oedematous limb and non-oedematous limb and its average increase in %,
- the difference after treatment and its average reduction in %
- and from the analyses of these data the lymphedema value in % after treatment

Body weight and circumference measurements are taken by the same physical therapist at the last treatment.

Body weight is controlled every follow-up to avoid false assess of lymphedema.

LYMPHOLOGICAL MEDICAL RECORD

Surname name	age
address	
Telephone number	
Diagnosis	
Clinical history	
Co-morbid conditions	
Surgery treatment	
Post-surgery treatment	
Time lymphedema beginning	
Symptoms	
Complications	
Investigation technique	
Edema thickness	
Clinical examination	
Drug therapy	

MEASUREMENT CARD

Surname name		Age	Date
Body weight	Height	Limb	
Range of motion assessment			
Muscular tropism assessment			
Extension of edema			
Skin description			
Patient pain			

Rehabilitation Plan							
Manual lymph drainage					Pneumatic compression		
Compressive bandage					Low-stretch elastic garment		
Range of motion exercise					Health care education		

Before treatment After treatment							
	Non- edema	oedematous limb	Difference	Increase %	oedematous limb	Difference	Reduction %
MCF joint			0,0	0,0%		0	
Ulnar Styloid process			0,0	0,0%		0	
15 cm down			0,0	0,0%		0	
10 cm down			0,0	0,0%		0	
5 cm down			0,0	0,0%		0	
Elbow			0,0	0,0%		0	
5 cm above			0,0	0,0%		0	
10 cm above			0,0	0,0%		0	
15 cm above			0,0	0,0%		0	
Average reduction %							0,0%
Average increase %				0,0%			
Average lymphedema value % after treatment				0,0%			
Patient Compliance							
Final and functional assessment							
Next Follow up							
Physical therapist							

The Combined Physical Therapy is considered the better therapy of peripheral lymphedema by the International Society of Lymphology.

This methodology generally involves a two-stages treatment program:

the first phase consists of skin care, manual lymph drainage, range of motion exercise and compression, typically applied with multi-layered bandage-wrapping

the second phase (initiated promptly after phase one for maintain and optimize the results obtained) consists of skin care, compression by a low-stretch elastic stocking or sleeve and continued "remedial" exercise.

A prescription for low stretch elastic garments (custom made with specific measurement if needed) to maintain lymphatic reduction after CPT is essential for long-term care.

The physical therapist teach the patients about their pathology, how they can care their limb. Every patient may be the protagonist of her clinical improvement. Great adhesion of patient to the therapeutic protocol allow to obtain the better reduction of arm oedema.

The prevention of lymph stasis is very important to prevent

severe and recurring lymphangitis complications and it can be considered a long-term objective.

Self-lymph drainage technique are taught to woman that demonstrate attention to their therapeutic protocol.

The study was done on 10 outpatient women with lymphedema of upper extremity after axillary dissection due to breast cancer.

The patients had a mean age of 68 years (range 57 to 88).

The patients had undergone different breast cancer treatment, but all of them had axillary node dissection.(tab 1)

KIND OF BREAST CANCER TREATMENT	NUMBER PATIENT	PATIENT POPULATION %
mastectomy	3	30%
quadrantectomy	7	70%
Axillary dissection	10	100%

Table 1: Kind of breast cancer treatment and patient population

Eight patients had undergone post-surgical therapy, two patients had no additional treatment

POST-SURGICAL THERAPY	NUMBER PATIENT	PATIENT POPULATION %
Radiotherapy	6	60%
Radio+chemotherapy	1	10%
Hormone therapy	1	10%
No additional therapy	2	20%

Table 2: Post-surgical therapy and patient population

The time of edema beginning since the surgery treatment was 2,3 years (ranged from 1 month to 7 years).
Edema beginning in different way (Table 3).

REASON	NUMBER PATIENT	PATIENT POPULATION %	TIME BEGINNING SINCE SURGICAL TREATMENT
Post-surgical	1	10%	1 month
Post-trauma (neck homerun fracture)	1	10%	7 years
Without reason (sub acute lymphangitis probably)	2	20%	1 year-18 month
Post- lymphangitis	5	50%	2 years-1years-4years-1years-4 years
After neck lympho-adenectomy	1	10%	2 years

Table 3: Time edema beginning and patient population.
Patients showed lymphedema at different clinical stage (Table 4) [Clinical staging by the Italian Society of Lymphangiology guidelines][13]

CLINICAL STAGE	NUMBER PATIENT	PATIENT POPULATION %	PITTING SIGN TISSUE COMPONENT	FIBRO-SCLEROTIC
I° stage	0	0%		
II° stage	2	20%	present-minimally present	Soft Edema
III° stage	5	50%	absent-minimally absent	Medium Edema
IV° stage	2	20%	Absent	Hard Edema
V° stage	1	10%	absent	Hard Edema

Table 4: Clinical stage and patient population

PROCEDURE

Before treatment all patients underwent measurements of both upper limb and body weight. At the end of the treatment the measurements of oedematous limb and body weight are repeated. If from the beginning to the end of the treatment there are differences about the weight, also the not oedematous limb have to be measured again.

That's an important parameter because body weight changes don't allow to value the result.

The initial and the final measurement was carried out by the same physical-therapist.

It's important that each physical therapist finds to standardize his own measurement method to reduce errors.

All measurements are performed under identical conditions: the therapist uses a narrow tape calibrated in centimetres there should be so minimal pressure in using the narrow tape circumference measurements are taken at fixed point the subject is placed in the supine position with arms resting comfortably at the sides

circumference measurements are taken by the same therapist at the first and a the last treatment

By using this particular method is especially important to have an adequate number of points to be measured .

Sides for measuring upper extremity circumference:

1° level - metacarpophalangeal joint

2° level - ulnar styloid process

3° level - 15 cm down from elbow

4° level - 10 cm down from elbow

5° level - 5 cm down from elbow

6° level - elbow

7° level - 5 cm above elbow

8° level - 10 cm above elbow

9° level - 15 cm above elbow

DATA ANALYSES

Each patient received 17 treatments (range from 10 to 30) of manual lymph drainage, compression bandaging and upper extremities exercises. Four patients received also cervical exercises.

Clinical evaluation of the outcome of therapy showed a decrease in the circumferences of the oedematous limb in all the patients.

All the patients received health care education about lymphedema.

For every measurement level have been calculated:

$\text{Difference before treatment} = \text{oedematous limb} - \text{non-oedematous limb}$

$\text{Increase \%} = \left(\frac{\text{Difference before treatment}}{\text{Non oedematous limb}} \right) * 100$

$\text{Difference after treatment} = \text{final edema} - \text{initial edema}$

$\text{Reduction \%} = \frac{\text{Difference after treatment} * 100}{\text{Difference before treatment}}$

For all these dates have been calculated the average:

$$\text{Average increase \%} = \frac{\text{addition increase \%}}{9}$$

$$\text{Average reduction \%} = \frac{\text{addition reduction \%}}{9}$$

$$\text{Average lymphedema value after treatment \%} = \frac{\text{Medium increase \% less Medium reduction \%}}{9}$$

This is the measure of lymphedema after treatment compared with non-oedematous limb

Table 5: patients dates

PATIENT INCREASE %	AVERAGE REDUCTION %	AVERAGE	AVERAGE LYMPHEDEMA VALUE AFTER TREATMENT %
M.E.	27,2	26,2	20,1
D.C.	23,6	18,1	19,3
G.P.	6,4	60,3	2,5
B.A.	14,4	5,1	13,7
C.MP	3,8	96,9	0,1
C.ML	8,0	46,9	4,2
C.C.	12,6	77,4	2,8
L.F.	10,9	33,6	7,2
P.I.	19,1	34,6	12,5
S.MC.	29,2	10,1	26,3
AVERAGE % OF ALL PATIENTS	15,5	40,9	10,9

Before treatment oedematous limb of all patients showed average increase of 15,5% compared with non-oedematous limb (ranged from 3,8 to 29,2).

At final treatment oedematous limb of all patients showed average reduction of 40,9% compared with their own initial measurement (ranged from 5,1 to 96,9).

At final treatment oedematous limb of all patients showed average value of 10,9 % compared with non-oedematous limb (ranged from 0,1 to 26,3).

Patients dates are compared with their clinical stage.

CLINICAL STAGE	NUMBER PATIENTS	AVERAGE INCREASE %	AVERAGE REDUCTION %	AVERAGE LYMPHEDEMA VALUE AFTER TREATMENT %
II°	2	5,9%	71,9%	2,1%
III°	5	12,68%	42,2%	7,74%
IV°	2	25,4%	22,18%	19,7%
V°	1	29,2%	10,1%	26,3%

Table 8: patients lymphedema modification and clinical stage

Patients with lymphedema at second and third stage have obtained best reduction of girth measurements.

Patients with lymphedema at fourth and fifth stage have obtained less reduction of girth measurements. In spite of these patients felt reduction of heaviness and tension sensation referred before treatment.

The patient with post-trauma lymphedema had tolerated bandage only few hours every day, obtained the smaller average reduction (5,1%).

The patient who obtained the best reduction showed lymphedema at second stage beginning one month after breast treatment. She was treated early and at the final treatment there was no differences between the upper limbs size.

Before treatment the patient at the fifth clinical stage showed the worst average increase (29,2%) and at final treatment her average lymphedema value was 26,3%. She was at her first lymphedema treatment!!!! I take also a photo of the upper-extremities of this patient.

DISCUSSION

The Lymphological Medical Record and the Measurement Card, together with imaging technique, could help the clinician and the physical therapist to care women with lymphedema. They could be an useful method to assess lymphedema in clinical practice.

Girth measurements don't give the arm volume but manage to make evident the lymphedema changes.

However is possible to obtain the "calculated volume" by use of mathematical formulas.

The clinical examination values the range of motion and muscular tropism of shoulder girdle and cervical rachis.

Height, body weight and circumference measurements of upper extremities are taken at the first treatment. From the analysis of these dates you can define the specific rehabilitation plan.

A photo of the upper limb can help to show the lymphedema changes after treatment.

CONCLUSION

Prevention of lymphedema starts in the pre-surgery phase, with the assessment of functional conditions of the shoulder girdle and neck, muscle tropism, and with measuring of the upper limb size, with special attention to the unilateral extremity of the tumour location.

To fight lymphedema it is important an early diagnosis and an early Combined Physical Therapy.

The measurement of upper extremities is still open to questions.

Without a valid and reliable method of measurement, accurate comparisons of treatment effectiveness, of therapeutic modalities remain impossible.

It is desirable that the International Society of Lymphology gives standard indications about how to take circumference measurements, at which fixed point and in which position is placed the subject.

REFERENCES

1. Michelini S: *Epidemiologia dei flebolinfedemi* Atti I° Congresso italiano "Flebolinfedema in Oncologia" 2002 Milano.
2. Michelini S, FAILLA A, MONETA G: *Epidemiologia del linfedema post-mastectomia* Atti Congresso Il linfedema post-mastectomia: non solo un danno estetico 2000 Milano.
3. Megens A, Harris S et al : *Measurement of upper extremity volume in women after axillary dissection for breast cancer.* Arch Phys Med Rehabil Vol 82 Dec 2001; 82(12): 1639-44
4. Sander AP, Hajer NM et al: *Upper-extremity volume measurements in women with lymphedema: a comparison of measurements obtained via water displacement with geometrically determined volume.* Phys Ther 2002;82(12):1201-12
5. Karges JR, Mark BE, Stikeleather SJ, Worrell TW: *Concurrent validity of upper-extremity volume estimates: comparison of calculated volume derived from girth measurements and water displacement volume.* Phys Ther. 2003; 83(2): 134-45
6. Casley-Smith JR: *Measuring and representing peripheral oedema and its alterations.* Lymphology 1994; 27: 56-70
7. Lymphovenous Canada: *Measurement Standard.* 2002
8. McKenzie DC, Kalda AL : *Effect of upper extremity exercise on secondary lymphedema cancer patient: a pilot study.* J Clin Oncol.2003; 21(3):463-6
9. Mridha A, Odman S: *Fluid translocation measurement.* Scand J Rehab Med 1989; 21:63-69
10. Aloisi D: *Valutazione quantitativa della consistenza e della comprimibilità del linfedema con tonometria tissutale* Linfologia Oggi 2003;1:12-15
11. Gerber LH: *A review of measures of lymphedema.* Cancer (suppl) 1998;83 (12):2803-2804
12. Campisi C, Zilli A, Macciò A: *Il linfedema dell'arto superiore secondario a trattamento di carcinoma mammario: attuali possibilità di prevenzione.* Linfologia oggi 2003; 2: 8-11
13. Società italiana di linfangiologia: *Linee guida-EBM sulla diagnosi e terapia del linfedema.* Linfologia Oggi 2003; 4: 7-17 a cura di Campisi C.
14. Bunce IH, Mirolo BR et al: *Post-mastectomy lymphedema treatment and measurement.* Med J Australia 1994; 161: 125-128
15. Harris SR, Hugi MR et al: *Clinical practice guidelines for the care and treatment of breast cancer: 11. Lymphedema.* CMAJ 2001; 164: 191-199
16. Consensus Document of the International Society of Lymphologia. *Linfologia Oggi* 2002; 2: 6-12 traduzione italiana a cura di Michelini S, Failla A, Moneta G
17. Campisi C: *Italian society of lymphangiology guidelines.* Lymphology 2004; 40: 2-12
18. Campisi C, Macciò A: *Dizionario di linfologia* 2003, ed Minerva Medica
19. Michelini S, Failla A, Moneta G: *Manuale teorico pratico di riabilitazione vascolare.* 2000; Edizioni PR
20. Beatrice M, Rusca L, Fanton E: *Disabilità e linfedema. Riflessioni critiche.* Linfologia oggi 2003; 3: 7-10
21. Balzarini A, Sigari C, De Conno F: *Il linfedema nel cancro avanzato.* Linfologia oggi 2003; 1: 7-10
22. Cestari M, Moroni S, De Marchi M: *Studio su un progetto obiettivo per il trattamento del linfedema in un servizio sanitario locale territoriale.* Linfologia oggi 2003; 1:22-24
23. Cestari M, De Marchi M et al: *Linfedema secondario dell'arto superiore: autodrenaggio manuale.* Linfologia oggi 2002; 2: 17-19
24. Basaglia N: *Progettare la riabilitazione, il lavoro in team interprofessionale.* Edi-ermes 2002 Milano.
25. Vitacca M, Porta R: *Come si legge un articolo scientifico.* Riv It Riabil Resp 2002; 1: 16-31
26. Migliorini GB: *Come scrivere un lavoro scientifico.* 2002; 1: 32-35

FACIAL LYMPHEDEMA IN MELKERSSON-ROSENTHAL SYNDROME.

Isabel Forner Cordero (1), Magdalena Querol Giner (1), Montserrat Évole Buselli (2), Miguel Hernandez Marti (3)

- (1) Lymphedema Unit. Rehabilitation Department.
(2) Dermatology Service.
(3) Pathology Service. Hospital Universitario La Fe. VALENCIA. SPAIN.

CORRESPONDENCE:

ISABEL FORNER CORDERO
C/ ANDRÉS MANCEBO 36, 12
46023 VALENCIA
SPAIN
IFORNER@SALUDALIA.COM

Presented : July 2004
Revised : September 2004
Accepted : November 2004

ABSTRACT:

The Melkersson-Rosenthal syndrome is a rare disorder characterized by the triad: recurrent facial edema, facial nerve paralysis and lingua plicata. We present the case of a woman diagnosed of Melkersson-Rosenthal syndrome that started at six years of age with recurrent swelling of the face and lip that has developed a facial lymphedema after several outbreaks. She was treated with metronidazol, estanozolol and systemic corticosteroids with lack of response. Physical therapies for lymphedema will try to reduce the swelling and fibrosis.

KEY WORDS: Melkersson-Rosenthal syndrome; Miescher's cheilitis granulomatosa; Facial edema; Lymphedema.

The Melkersson-Rosenthal syndrome is a rare disorder that was first described in 1928 as a facial edema and paralysis and in 1931 Rosenthal reported the additional feature of lingua plicata, or fissured tongue¹. The complete triad: recurrent facial edema, facial nerve paralysis and lingua plicata is very rare, and monosymptomatic and oligosymptomatic variants are more common, that's why the diagnosis may be difficult.

CASE REPORT:

We present the case of a woman diagnosed of Melkersson-Rosenthal syndrome that has developed a facial lymphedema.
A 25-year-old woman presented a right-sided lymphedema of the face and upper lip to the Lymphedema Unit. Her medical

history was a recurrent angioedema of the face and lip that started at six years of age, with multiples outbreaks that were irregular and often related with herpes simplex virus infection. She also presented with the asymmetric right-sided facial swelling an erytematous eruption that was painless and nonpruritic accompanied with nonpitting edema, as well as right-sided cervical adenopathy (Figure 1). Facial palsy was absent. In the last times, the attacks have become more and more frequent, and now she is having one recurrence per month that stays for 7 to 10 days. After several attacks, facial edema became chronic with a consistence similar to lymphedema that did not reduce after the outbreak. Oral examination revealed a fissured tongue. We were unable to identify evidence to support an allergic or a hereditary cause for the syndrome, the last because she was adopted in childhood and doesn't have any relationship with her biological parents.

The laboratory findings were normal and all the allergy test results were negative. In the dermatology service, the magnetic resonance showed a non hemorrhagic, non ischaemic, non malformative process. Only the edema in the right cheek with a trabeculated fat tissue and cervical adenopathies were identified. The biopsy specimen of the upper lip showed a small non necrotizing granuloma between salivary acini (Figures 3 and 4).

She was treated with metronidazol, estanozolol and systemic corticosteroids with lack of response. Physical therapy was prescribed to try to reduce the swelling and fibrosis, not to prevent a new attack. It consisted in self-drainage, exercises and a compression mask during the night. We find it difficult to assess the results during the remission phase (Figure 2).

DISCUSSION

The prevalence of the syndrome is low and there are near 300 cases reported in the literature. But the incidence must be higher, and many cases lacking the complete triad are misdiagnosed. The syndrome is more frequent in women being the ratio 2:1, according to Zimmerⁱⁱ. The age at onset of the disease varies widely with a mean age of 33 years according to the studies of Greeneⁱⁱⁱ and Zimmer². The Melkersson-Rosenthal syndrome is rarely seen in children^{iv}. The syndrome is generally thought to be more common in Europe than in North America^v.

Etiology

The etiology of this syndrome is uncertain but some authors have suggested an infectious, an autoimmune disorder or a genetic cause. Many infectious agents such *Toxoplasma gondii*, *Treponema pallidum* or mycobacteria^{vi} have been related to Melkersson-Rosenthal syndrome because they are potential causes of the granulomatous response^{vii}, without final conclusions. But the herpes simplex virus have shown some association with facial palsy and with this syndrome. It has been suggested that it can be a manifestation of Crohn disease^{viii, ix, x}, but no evidence of Crohn disease was found in the patients studied by Zimmer², Greene³ or Worsaae¹⁵. Horstein considered Melkersson-Rosenthal as a neuromucocutaneous disorder with micro-neurovascular involvement^{xi}. Autosomal dominant inheritance with variable expression has been well documented in the past^{xii}, with a possible location of this gene most likely at 9p11^{xiii}.

Clinical Manifestations

Orofacial swelling is the most common presentation of Melkersson-Rosenthal Syndrome affecting between 80 to 100% of the patients^{2,3}, and it is the first symptom in 40% of the cases³. In some patients the upper lip was affected with episodic and recurrent swelling and in others it was a permanent edema. The swelling can affect only the lip causing the called Miescher's cheilitis granulomatosa that is the most frequent symptom in the monosymptomatic form of the Melkersson-Rosenthal syndrome. The swelling may extend to the mouth or to the cheek unilaterally or to the infraorbital tissue. The gingival swelling was present in 26% of the patients in Zimmer's study and palatal involvement in 10%². Few cases have been described with eyelid edema^{xiv}. This recurrent episodic edema presents as an attack of erythematous eruption that last some days or weeks without systemic involvement and is always painless, nonpruritic, nonpitting and usually unilateral. Herpeslike attacks associated with outbreaks of the swelling were reported by Worsaae^{xv}. This syndrome may be confounded with angioneurotic edema in the acute phase. After many attacks, facial edema becomes chronic^{xvi}, and does not reduce after the bout, during the intermittent periods of remission³. The skin has a peau d'orange texture due to fibrosis.

Facial nerve paralysis presents as Bell's idiopathic palsy, at first as a mild episodic paresis but with several episodes it results in a complete facial paralysis with synkinesis and myokimia. Sometimes it resolves without sequelae, so the prognosis is variable⁵. It has been proposed that a greater susceptibility of the peripheral nerve to pressure at the fallopian canal triggered by infection or local immunological response may provoke the facial palsy to recur^{xvii}. It may be postulated that the disease may affect other cranial nerve but subclinically^{xviii}. Some features suggesting other cranial nerve involvement as dysesthesias of the tongue, or the face have been described. The facial nerve is affected in 33% to 47% of the cases^{2,3} and it can occur months to years before or after the onset of orofacial edema³.

Lingua plicata, or fissured tongue or scrotal tongue, is the least common and least important finding of the triad that constitutes Melkersson-Rosenthal syndrome, and it is not pathognomonic. It has been reported to be the first symptom of the syndrome in just one case, while 60% of the cases present it with the time in different degrees². Such a nonsevere and frequent complaint is supposed to remain unnoticed to the medical team, and it is probably diagnosed only when other features of the syndrome appear^{xix}.

Laboratory investigations:

Inflammatory activity factors as erythrocyte sedimentation rate were not elevated. Leukocytosis or eosinophilia were not found. Serum biochemical parameters were in normal levels. The immunoglobulins in serum showed no specific alterations. No depression of C-1 esterase inhibitor was seen.

Histologic findings:

Histologically, in the early phase there can be observed dilated lymphatic channels and perivascular aggregates of histiocytes, lymphocytes and plasma cells in a non-specific edema³. In the later stages, nonnecrotizing granulomas are seen as well as edema, lymphangiectasia, and perivascular lymphocytic infiltration (Figures 3 and 4). The absence of the granulomatous changes does not exclude the diagnosis of the Melkersson-Rosenthal syndrome³. Allen found by examining the "vesicles" of the vesicular-appearing lesions by microscopic evaluation that they were actually superficial lymphatic vessels^{xx}.

Treatment:

The persistent edema of the face leads to functional and cosmetic disability. Many therapeutic approaches including systemic and intralesional corticosteroids, antibiotics, radiotherapy and reduction cheiloplasty have been tried to reduce the swelling and control the recurrent episodes, with partial results. The association with Crohn's disease and previous report of good response lead to try Metronidazole⁹ in our patients but without response. Some authors have suggested that an elemental diet with liquid food containing protein as aminoacids, carbohydrate as maltodextrins and sugar, fat as defined oils plus vitamins and minerals should be considered in the treatment of these patients^{xxi}. Stein treated 2 children suffering the syndrome with a combination of prednisone and minocycline proving it was well tolerated and effective⁴. Removal of odontogenic foci seemed to have a good result and shorter duration of the disease¹⁵. Danazol has been used in several patients with variable results. For the treatment of facial palsy surgical approach with nerve decompression has been of some benefit because the oedematous process affects the entire nerve within a tight bony canal causing entrapment neuropathy¹⁸. The treatment can be evaluated by assessing the frequency of attacks or the periods of time of remissions. In our case the Physical Therapy was performed not to prevent the bout, but to reduce the lymphedema and the fibrosis. It



Figure 1. Facial swelling and erythematous eruption in Melkersson-Rosenthal syndrome.

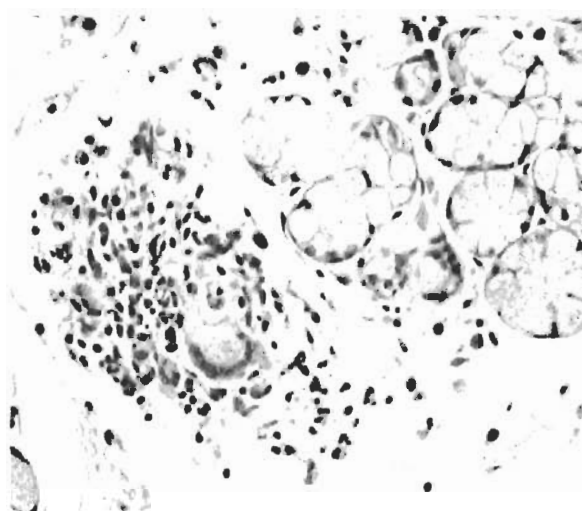


Figure 4. Non-necrotizing granuloma with giant multinuclear cell and perivascular lymphocytic infiltration H&E 40X.



Figure 2. Facial lymphedema after treatment

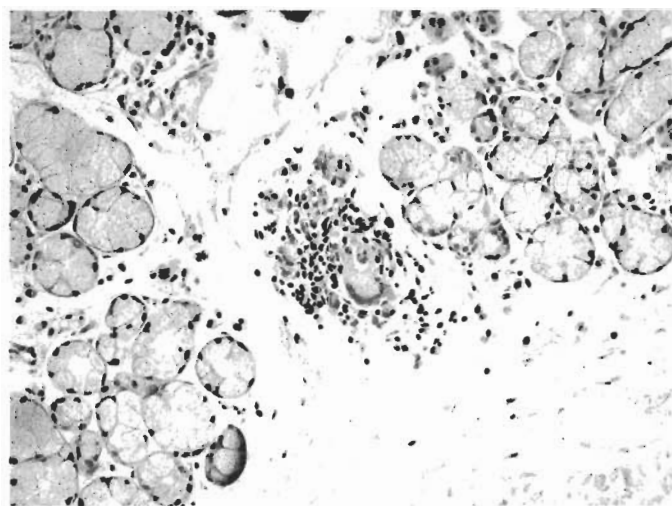


Figure 3. Biopsy specimen. H&E 20X

consisted in training the patient in self-drainage following Földi's indications^{xxii}, exercises and a compression mask during the night. We did not find in the literature any reported case of Melkersson-Rosenthal syndrome treated with Complex Physical Therapy for the lymphedema.

REFERENCES:

1. Browse N, Burnand KG, Mortimer PS. Management of lymphoedema of the head and neck. In: *Diseases of the lymphatics*. London: Arnold; 2003. p. 243-248.
2. Zimmer WM, Rogers RS 3rd, Reeve CM, Sheridan PJ. Orofacial manifestations of Melkersson-Rosenthal syndrome. A study of 42 patients and review of 220 cases from the literature. *Oral Surg Oral Med Oral Pathol*. 1992;74(5):610-9.
3. Greene RM, Rogers RS 3rd. Melkersson-Rosenthal syndrome: a review of 36 patients. *J Am Acad Dermatol*. 1989;21:1263-70.
4. Stein SL, Mancini AJ. Melkersson-Rosenthal syndrome in childhood: successful management with combination steroid and minocycline therapy. *J Am Acad Dermatol*. 1999;41(5):746-8.
5. Cropley TG, Ferry JA. Weekly Clinicopathological Exercises: Case 22-1993: A 22-Year-Old Man With 20 Months Of Progressive Swelling Of The Face. *N Engl J Med*. 1993;328(22):1625-31. Available in: <http://gateway.ut.ovid.com/gw1/ovidweb.cgi> (consulted 9th september 2004).
6. Apaydin R, Bilen N, Bayramgurler D, Efendi H, Vahaboglu H. Detection of *Mycobacterium tuberculosis* DNA in a patient with Melkersson-Rosenthal syndrome using polymerase chain reaction. *Br J Dermatol*. 2000;142(6):1251-2.

7. Rogers RS 3rd. Granulomatous cheilitis, Melkersson-Rosenthal syndrome, and orofacial granulomatosis. *Arch Dermatol.* 2000;136(12):1557-8.
8. Kano Y, Shiohara T, Yagita A, Nagashima M. Granulomatous cheilitis and Crohn's disease. *Br J Dermatol.* 1990;123(3):409-12.
9. Kano Y, Shiohara T, Yagita A, Nagashima M. Treatment of recalcitrant cheilitis granulomatosa with metronidazole. *J Am Acad Dermatol.* 1992;27(4):629-30.
10. Kano Y, Shiohara T, Yagita A, Nagashima M. Association between cheilitis granulomatosa and Crohn's disease. *J Am Acad Dermatol.* 1993;28(5):801.
11. Hornstein OP. Melkersson-Rosenthal syndrome- a challenge for dermatologists to participate in the field of oral medicine. *J Dermatol.* 1997;24(5):281-96.
12. Online Mendelian Inheritance in Man, OMIM(TM). Johns Hopkins University, Baltimore, MD. MIM Number: *155900: 23-8-2002: World Wide Web URL: <<http://www.ncbi.nlm.nih.gov/htbin-post/omim/dispm?155900>> [Consulted October 2004].
13. Smeets E, Fryns JP, Van den Berghe H. Melkersson-Rosenthal syndrome and de novo autosomal t(9;21)(p11;p11) translocation. *Clin Genet.* 1994;45(6):323-4.
14. Cockerham KP, Hidayat AA, Cockerham GC, Depper MH, Sorensen S, Cytryn AS, et al. Melkersson-Rosenthal syndrome: new clinicopathologic findings in 4 cases. *Arch Ophthalmol.* 2000;118(2):227-32.
15. Worsaae N, Christensen KC, Schiodt M, Reibel J. Melkersson-Rosenthal syndrome and cheilitis granulomatosa. A clinicopathological study of thirty-three patients with special reference to their oral lesions. *Oral Surg Oral Med Oral Pathol.* 1982;54(4):404-13.
16. Alexander RW, James RB. Melkersson-Rosenthal syndrome: review of literature and report of case. *J Oral Surg* 1972;30:599-604.
17. Eidlitz-Markus T, Gilai A, Mimouni M, Shuper A. Recurrent facial nerve palsy in paediatric patients. *Eur J Pediatr.* 2001; 160:659-63.
18. Dutt SN, Mirza S, Irving RM, Donaldson I. Total decompression of facial nerve for Melkersson-Rosenthal syndrome. *J Laryngol Otol.* 2000;114(11):870-3.
19. Gonzalez Moles MA, Fernandez Martinez JA, Martinez Lara I. Síndrome de Melkersson-Rosenthal. Presentación de un caso clínico. *Medicina Oral.* 1996;1:44-8.
20. Allen CM, Camisa C, Hamzeh S, Stephens L. Cheilitis granulomatosa: report of six cases and review of the literature. *J Am Acad Dermatol.* 1990;23(3):444-50.
21. Cameron EAB, Middleton SJ. Elemental diet in the treatment of orofacial Crohn's disease. *Gut.* 2003;52:143.
22. Thoma H. Treatment of head and neck lymphedema. In: Földi M, Földi E and Kubik S (Eds). *Textbook of lymphology for physicians and lymphedema therapists.*

LYMPHOLOGY IN MEDICAL AND SURGICAL PRACTICE ITALIAN GUIDELINES LOOKING TOWARDS EUROPE AND THE WORLD

C.Campisi, S.Michelini, F.Boccardo
Italian Society of Lymphangiology (SIL)

Friday, October 29, 2004, by the Department of Surgery of the University of Genoa, a meeting upon **"Lymphatic Microsurgery"** was organized and coordinated by Prof. C.Campisi, in the ambit of the so called *Everest Project*, which aims at creating a real scientific network among distinguished international experts in different surgical fields (Fig.1). During the morning, two surgical operations were carried out of derivative lymphatic-venous microsurgery for the treatment of lower and upper limb lymphedemas. Prof. W. Olszewski, from the Medical Research Center of the Polish Academy of Science of Warsaw, Poland, took part in the first operation, upon the lower limb, together with the Italian surgical team, Prof. C.Campisi and Prof. F.Boccardo. The operation was transmitted to the Auditorium and to the University of Arizona, Tucson (AZ, USA) by 'interactive' teleconference between the two scientific centres.

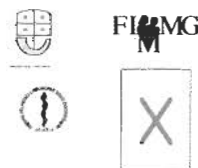
In the Auditorium, the Session was chaired by Prof. M.H.Witte, from the Department of Surgery of the University of Arizona College of Medicine of Tucson, Prof. E.Fulcheri, from the Institute of Pathological Anatomy of the University of Genoa (Italy), and Prof. S.Michelini, from the Neuro-Vascular Rehabilitation Center of S.Giovanni Battista Hospital of Rome (Italy). Among the foreign experts, there were also the President of the International Society of Lymphology, Prof. M.Ohkuma, from Kinki University, Sakai (Japan), Professors Etelka and Michael Földi, from the Földiklinik, Hinterzarten (Germany), Prof. G.Thibaut, from the University Henri Poincaré, Nancy (France), and the therapist J.P.Belgrado, from the Free University of Brussels (Belgium). Prof. A. Pissas, from the Department of Surgery of the Hospital Bagnols-sur-Cèze (France), participated in the second operation, upon the upper limb, together with the same Italian surgical team. From the surgical point of view, it was pointed out that with the advent of Microsurgery, functional and causal therapeutic solutions for lymphedema were investigated and implemented, aiming at draining the lymph flow or reconstructing the lymphatic pathways where they had been obstructed or were missing. Microsurgery techniques have yielded positive and long-lasting results in the treatment of primary lymphedemas - including those in children - as well as in secondary lymphedemas following cancer treatment. Among derivative microsurgery techniques, aiming to resume lymph flow at the obstruction site, through a lympho-venous drainage, multiple end-to-end and end-to-side lymphatic-venous anastomoses are most commonly employed. Conversely, with reconstructive microsurgery techniques, the lymphatic flow is resumed by overcoming the obstruction site through the implant of autologous vein segments between collectors down and upstream the obstruction: lymphatic-venous-lymphatic plasty (LVLA).

Indications for the various microsurgical techniques depend on the presence of a viable lymphatic-venous pressure gradient in the affected limb. Should lymphostatic deficiency be associated with venous insufficiency (a condition mostly found in the lower extremities: varices, venous hypertension, valvular incontinence), derivative microsurgery is not recommended, while only reconstruction techniques can be applied.

Another important item was discussed during the meeting concerning immunohistochemical investigations. Interesting immunohistochemical investigations have recently been conducted on lymphatics-lymph node material taken during the same lymphatic microsurgical operations and on the interstitial matrix. These studies have yielded valuable information on lymphedema pathophysiology. In particular, dysfunctions of lymphatic vessel walls and of lymph nodes have been identified and classified. They progressively develop and evolve in parallel with lymphedema progression and, more specifically, proportionally with lymphedema duration. These observations have confirmed that, for a proper treatment of this disorder, whenever lymphatic drainage is lacking or obstructed, it is essential to resume its good functioning, as soon as possible. In this way, successful and long-lasting results will be obtained, through the preservation of a good autonomous lymphatic pump performance linked with smooth muscle fibrocells that are normally present in lymphatic pre-collectors and collectors, as well as in lymph node capsules. With disease progression, smooth muscle cells are gradually lost and replaced by non-dynamic fibrosclerotic tissue.

Moreover, on Saturday 30 October 2004, a meeting on the **Italian Guidelines on "Diagnosis and Treatment of lymphedema"** was organized and coordinated by Prof. C.Campisi, with the participation of distinguished experts in the field of Lymphology coming from all over Europe, the United States, and Japan. It was a good occasion to update and integrate the guidelines upon different items such as: classification and staging, diagnosis, non operative and operative treatment, prevention, angiodysplasia-lymphedema syndromes, immunohistochemical findings (Fig.2). Furthermore, the clinical and research activities of various lymphological centers throughout the world were also reported. The Italian Guidelines, like the Consensus Document of the International Society of Lymphology, include different diagnostic and therapeutic protocols carried out worldwide and adapted to the socio-economic and sanitary situation of our Country. With these considerations, these guidelines represent an evidenced based tool to approach patients affected from peripheral lymphedema and at the same time is continuously updated on the basis of wide discussions at local, national and international meetings in Lymphology and related disciplines.

Stampato in proprio
Stampo e grafica*
Marina Dall'Asta



Il corso è stato registrato presso il Ministero della Salute ai fini dell'accreditamento ECM



groupe ment européen de lymphologie

XXXI

CONGRESS

XXXI

CONGRESS

President: S. Michelini (Rome)
Vice-President: F. Boccardo (Genoa)

Topics:

- ✓ Anatomical and clinical aspects of lymphedema
- ✓ Lymphedema and Disability
- ✓ Lymphedema Prevention
- ✓ Oncology and Lymphology
- ✓ Angiodysplasias and Lymphedema
- ✓ Functional lymphedema
- ✓ Phlebolympedema
- ✓ Physical rehabilitative project
- ✓ Drugs and lymphedema
- ✓ Surgery: from prevention to therapy
- ✓ Lymphedema Management

Congress Secretary: Easycontact
Ph. +393488745662 • e-mail carla@econtact.it

Abstract typing instructions:

Arrange the abstract in the following order:

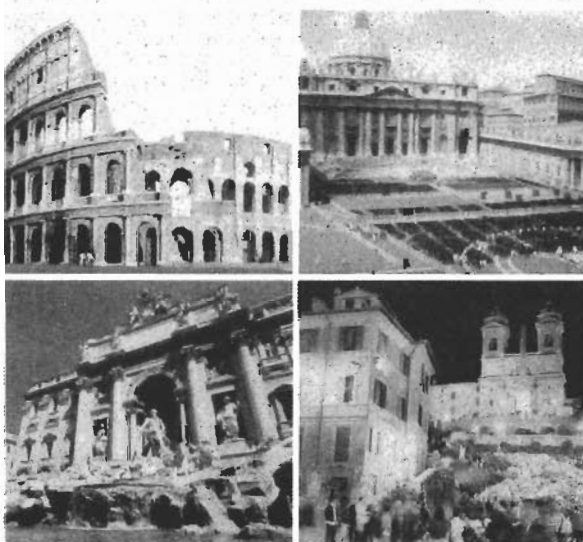
- Title (in capital letters)
- Author(s) first name and last name
- Underline names of authors presenting the paper
- Origin of work, city, country
- Purpose
- Methods
- Results
- Conclusions

Type size should neither be smaller than 10 point nor larger than 12 point, true-type setting must be used.

The abstract has to be send exclusively by e-mail to the congress secretary.

Deadline for the abstract presentation:

15 April 2005



XX International Congress of Lymphology

I Congresso Brasileiro de Linfologia

I Congreso del Capal




President: Mauro Andrade (Brazil) - *Honorary President:* Robert Cluzan (France)

Congress dedicated to the memory of Charles L. Witte (USA) and Rubens C. Mayall (Brasil)

September 26 to October 1 st. 2005
Salvador - Bahia Othon Hotel - Brazil
lymphology2005@uol.com.br

Deadline for abstract submission Jan 31, 2005



**XX INTERNATIONAL
CONGRESS OF LYMPHOLOGY**

Preliminary Program

Sep 26/Mon
 Opening ceremony
 Conference: R. V. Cluzan
 Welcome Brazilian Party

Sep 27/Tue
 New insights on basic lymphology
 - Anatomy
 - Physiology/Physiopathology
 - Immunology and Infectious diseases
 Epidemiology of lymphatic diseases

Sep 28/Wed
 Molecular lymphology: where will it lead us?
 - Genetics
 - Lymphangiogenesis
 - Angiodysplasias
 Special free paper on basic lymphology (Charles Witte Presidential Award)

Sep 29/Thu
 Treatment of lymphatic disorders. State of the art.
 - Clinical treatment
 - Surgical options
 - Compression
 Alternative therapies
 Special free paper on clinical lymphology (R.C. Mayall Presidential Award)

Sep 30/Fri
 Frontiers in lymphatic disorders.
 - Phlebolympology
 - Oncolymphology
 Lymphatic Imaging
 Consensus on idiopathic lymphedema

Oct 1/Sat
 Special course on physical therapy of lymphedemas
 General Assembly

CALENDAR

11-13 March 2005, Bologna, Italy

7th INTERNATIONAL CONGRESS OF PHLEBOLOGY AND LYMPHOLOGY

Varicose veins and phlebolympoedema: lights and shadows

ref: <http://www.valet.it/7flebolgia/7flebo.html> - congresso@valet.it - www.cavezzi.it

Tel.: 051 6388334 – Fax: 051 326840

• • •

MASTER IN “LYMPHOLOGY”

I° Level, opened to: Nurses, Physiotherapists, Obstetricians, Podologists, Orthopedic Technicians, Sanitary Assistant, Professional Educator

Application must be addressed before March 21, 2005 !

ref: Phone/Fax: 55-11-3341-2980 / 3207-8241 E-mail: lymphology2005@uol.com.br

ref.: Prof. C. Campisi Phone: 0039 3381718067-0039 3356073246

Fax: 0039 010811465 – 0108461057 - E-mail: campisi@unige.it - campisicorradino@tin.it

• • •

MASTER IN “LYMPHOLOGIC CLINICS, LYMPHATIC SURGERY AND MICROSURGERY”

I° Level, opened to: Physicians

Application must be addressed before March 21, 2005 !

ref: Phone/Fax: 55-11-3341-2980 / 3207-8241 E-mail: lymphology2005@uol.com.br

ref.: Prof. C. Campisi Phone: 0039 3381718067-0039 3356073246

Fax: 0039 010811465 – 0108461057 - E-mail: campisi@unige.it - campisicorradino@tin.it

• • •

9-10 June 2005, Parma, Italy

I° INTERNATIONAL SYMPOSIUM LYMPHATIC MICROCIRCULATION AND NEOPLASTIC METASTASIS

ref: info@newteam.it - www.newteam.it

• • •

11-12 June 2005, Rome, Italy

XXXI g.e.l. ROME CONGRESS

E-mail: carla@eceasycontact.it

• • •

6th MEETING OF THE EUROPEAN VENOUS FORUM

24-25 June 2005, Crete, Greece

President: Professor Asterios Katsamouris

ref: Tel/Fax: +44 (0) 20 8575 7044 - E-mail: evenousforum@aol.com

Website: www.europeanvenousforum.org

• • •

26-30 September 2005, Salvador-Bahia, (BRA)

20th ISL INTERNATIONAL CONGRESS OF LYMPHOLOGY

ref: Phone/Fax: 55-11-3341-2980 / 3207-8241 E-mail: lymphology2005@uol.com.br

• • •

2-7 October 2005, Rio de Janeiro, (BRA)

XVth WORLD CONGRESS - INTERNATIONAL UNION OF PHLEBOLOGY (UIP)

ref.: www.flebologiabrasil.br

mediven® flat-knitted product range

Confidence through strength.

mediven® maxi

mediven® mondi

mediven® 550

mediven® flat knitted care products

Powerful arguments
for mediven® mondi, 550 and maxi

- powerful, active-breathing and elastic two-way stretch fabric guarantees pleasant wearing comfort
- wide range of special models ensures individual care
- maximum pressure stability – for high degree of efficacy
- robust material vouches for extreme durability

Powerful accessory products



Lymphpads



mediven®
Gel & Creme



mediven®
Spray



mediven®
Butler

medi

I feel better.