Lymphology 14 (1981) 69–76

The Problems of Lymphatic Microsurgery for Lymphedema

L. Clodius[1], N.B. Piller[2] and J.R. Casley-Smith[3]

[1]Plastische und Wiederherstellungschirurgie, Universitätsspital, CH 8091 Zürich, Switzerland
[2]School of Health Professions, Sturt CAE and Flinders Medical Centre, Bedford Park, South Australia
[3]Electron Microscope Unit, University of Adelaide, Box 498, G.P.O. Adelaide, South Australia

Summary

The problems of microsurgery for lymphedema consist of the discrepancy between the excellent technical possibilities, especially of microsurgical lympho-venous shunts and the subsequently insufficient reduction of the lymphedematous tissue fibrosis and sclerosis. Generally, the lymphatic surgeon considers the lymphatic system to be a canalicular system of drainage tubes, of lymph collectors. Bypassing a lymph block through peripheral lympho-venous shunts should therefore solve the problem of lymphstasis, present in each type of lymphedema. In chronic lymphedema however, not only the canalicular lymphatic system, but also the tissues, an integral part of the lymphatic system, are affected. In chronic lymphedema, canalicular repair, for reasons of quantitative lymph drainage, exceptionally only provides a "restitutio ad integrum" of the tissues, altered by lymph stasis.

Lymphedema, an easy microsurgical problem?

With the advent, perfection and popularisation of microsurgical techniques, for many microsurgeons the problem of lymphedema seemed to be amenable to an easy solution. Nature, which provides lympho-venous anastomoses in the neck and in the periphery, is copied and shunts are contstructed in the periphery of the lymphedematous extremity, between the lymphatic circulation and the venous circulation. *Danese* (17, 18) as early as 1968, in secondary arm lymphedema, had reported one case, in which he performed an anastomosis between a proximal and a distal lymph collector for bridging a lymph block following axillary dissection. In 1979, *O'Brien* (36) published his latest series of patients, in whom, however, he is adding tissue resections to the microsurgical lympho-venous shunts. *Yamada* (49), who introduced the different techniques of shunting lymph-collectors to veins: end-to-end, end-to-side anastomosis as well as end-to-end, end-to-side implantation (Fig. 1) achieved patency rates of 44.4% after six months in cases of his experimental lymphedema. This was controlled by lymphangiography. Recently, *Puckett* et al. (45) demonstrated a patency rate of their lymphovenous shunts in dog legs with secondary lymphedema of 100% at seven days. From this they conclude, that these anastomosis are feasible, but report occlusion of all anastomoses at 21 days. If all the anastomoses are patent at one week, the endothelium has grown across the suture lines and a 100% success can be claimed for the technical aspect of microsurgery. In the following, we present and discuss some factors which offer an explanation for the discrepancy between the technical possibilities and the fact, that today only a few lymphatic surgeons use the microsurgical approach for lymphedema.

Lymphedema; Surgery vs. conservative therapy: Result control

In order to exactly evaluate the benefits of surgical results on a long term basis, they must be compared with a baseline, which would be the course of lymphedema, if left untreated.

This paper is dedicated to the Sixtieth Birthday of *Michael Földi*

0024–7766/81 1400–0069 $ 02.00

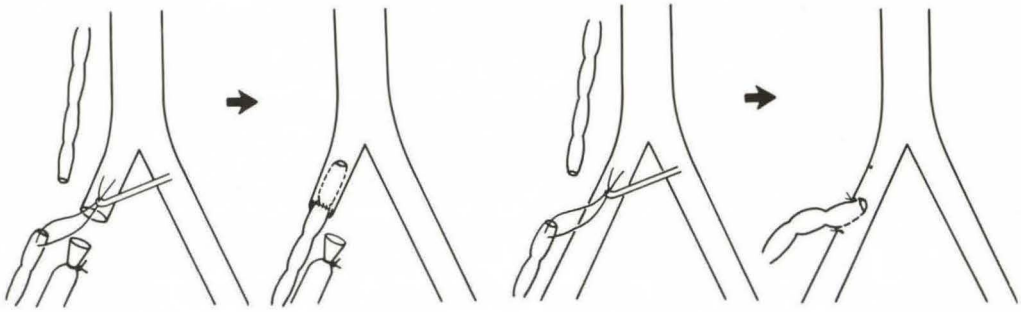

Fig. 1 The types of lymphatico-venous anastomoses after *Yamada*
a) On the left end-to-end implantation and on the right end-to-side implantation of a lymphcollector into a vein is demonstrated

In practically all published series of surgically treated lymphedemas (2, 25, 34, 35, 47), the patient post-operatively is fitted with an elastic compressing stocking. However, mostly because the patient wants instant relief and because conservative therapy is time-consuming, cumbersome and may be expensive, the patients of these series did not benefit of the full possibilities of conservative therapy before operation. In addition, any surgical result should be compared with the results that modern conservative therapy can achieve (3, 12, 22, 50). In a series involving conservative therapy, *Clodius* and *Piller* (13) showed 68% of of 92 patients, who were originally to be considered surgical candidates, to be moved into the group needing no surgery. (The normal criteria for surgery is that the arm circumference is greater by 8 cm or more than the normal one.)

When a patient with incipient primary lymphedema is seen for the first time by his physician, he will not be able to predict, in this

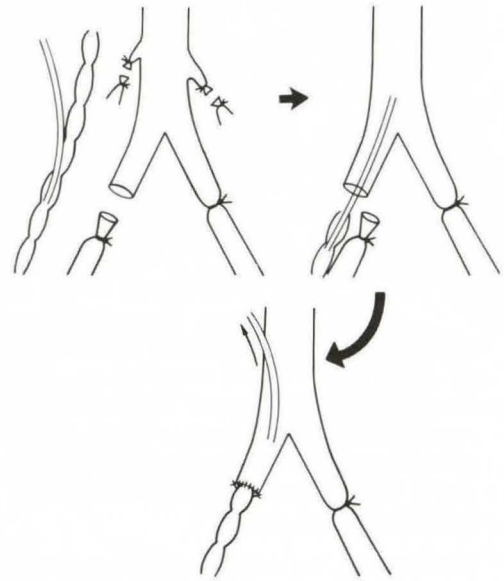

Fig. 1b End-to-end anastomosis of a lymphcollector to the saphenous vein of a dog, using a small catheter as a splint

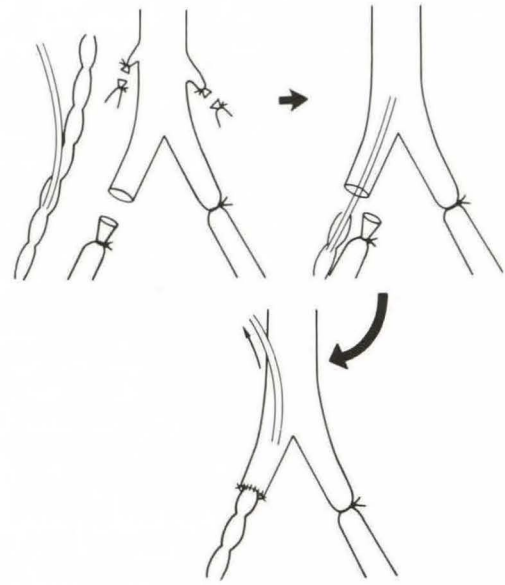

Fig. 1c End-to-side anastomosis of a lymphcollector to the saphenous vein of a dog, using a small catheter as splint

patient, the pace of its progression, as there are no long term control data available. However, in secondary post-mastectomy lymphedema of the arm, *Clodius* and *Piller* (12) have been able to follow its progression. This was done in two ways, namely by circumference measurement and by tonometry.

In 41 control patients it was found that the circumference of the affected arm increased by an average of 1 cm per year for the first six years, thereafter there was very little significant change. Other authors have critisized the measurement of circumference as a means of determining the progression of lymphedema, and we refer you to their works (3, 23, 31). While we still use circumference measurement for its rapidity and simplicity, we have developed a means of determining numerically the state of the tissues (14, 40). This involves the use of an instrument called a tissue tonometer which is based on a similar principle to the tonometer used in ophthalmology. In the above mentioned 41 untreated control patients, tonometry was able to indicate numerically the occurrence of a number of important events. The first was that there were changes in the compressibility of the tissues even before lymphedema was clinically discernable i.e. in the "latent" phase. This amounted to a gradual increase in resistance to compression. At the end of the latent phase, as lymphedema became manifest at an average of 1 cm/year (as detailed above), the resistance of the tissue to compression became less. Then after 6 years, they again hardened. (For a detailed discussion of these events, we refer to *Clodius* and *Piller*, 12). Unfortunately there are no tissue tonometry controlled series available in primary lymphedemas of the lower extremity, or of the surgically treated patients.

Lymphatics, lymphodynamics, lymphedema

For keeping the protein balance of the tissues intact, the task of the lymphatic system as a circulatory system is to recycle the lymphatic load: the amount of large molecular plasma proteins, with their osmotically associated water, from the interstice back to the venous junction in the neck. This canalicular function is supplemented by a function of the tissues: the extra-lymphatic mastering of plasma proteins, through the macrophage system. According to *Mayerson* from 50 to 100% of the circulating plasma proteins leave the blood vascular system in 24 hours. Most of the quantitative aspects of the lymph formation are unknown.

The amount of the capillary filtrate depends on the number and the state of function of continuous, non-fenestrated and tunnel or fenestrated capillaries. It varies considerably, and arterial and venous limbs of the capillaries are only statistical concepts (5, 6).

Since lymphedema is also a quantitative lymph-drainage problem, it would be most important to know these parameters. Only recently, the lymphatic clearance flow rates per tissue fluid volume have been assessed for the hind legs of dogs (34), amounting to 0.233 ± 0.077 ml/hr/per 100 ml tissue fluid volume. The difficulty of interpretation in these studies is outlined by *Földi* (22). How much, how many percent of the capillary filtrate becomes lymph, varies from tissue to tissue, from its state of activity, from the amount of the capillary filtrate and on the nature of the capillaries.

The lymphatic transport capacity depends on the number of lymph collectors and their state of activity. The lymph collectors as determined by lymphangiography, removing the lymphatic load, vary to a great extent in number and in position (27). But, as pharmaco-lymphography demonstrated (29), conventional lymphography, using an oily or aqueous contrast medium, never demonstrated all the lymph collectors. The amount of lymph, measured in a superficial lymph vessel of the lower leg of a normal man, varied between 0.78 to 5.5 ml per hour (19). It is the total cross section of the lymph vessels times the lymphokinetic forces (force pumps of the initial lymphatics, intrinsic lymphatic muscle pumps, lymphatic pulse (38), function of lymphatic valves, pulsatile blood flow, extrinsic muscle pump, respiratory movements.

Unfortunately, for the microscurgeon, lymphedema is not a problem of canalicular lymph-drainage. Since lymph is formed in the tissues,

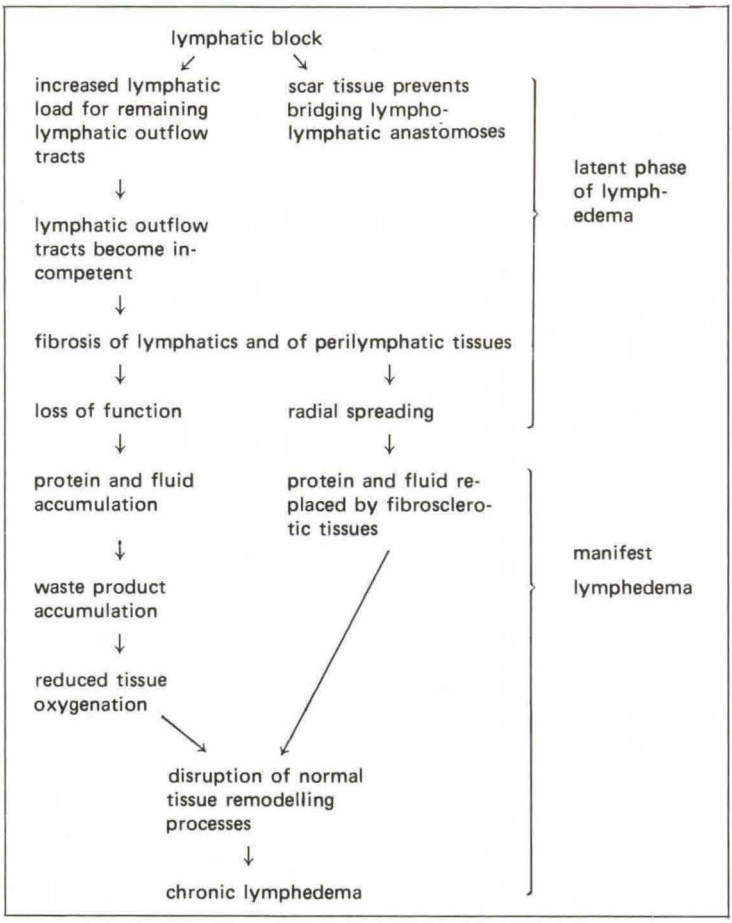

Fig. 2 The course of events from a lymphatic block, through the invisible latent phase, to manifest lymphedema

lymphedema may be considered primarily a tissue problem. Edema is defined as visible tissue swelling due to fluid accumulation. In generalized low protein edemas (renal, cardiac), the restoration of osmotic pressure will return the tissues to normal and leave no trace of edema in them. Localized, high protein edema however, gradually "poisons" the tissues (Fig. 2). This is a process unfortunately not visible to the clinician's eye. Following a lymph block, only after all the safety factors of the microcirculation, of the lymphatic system have been decompensated, and only after the mononuclear phagocytic system has decompensated (1, 42, 43), lymphedema as a clinical symptom becomes apparent. Tissue tonometry proves this; already during the latent phase, resistance to compression rises (12), lymphangiograms demonstrate lymphstasis, and incompetency of inter-endothelial junctions are visualized (7, 37). During chronic manifest lymphedema, there is further radial spreading of fibrosclerotic tissues, starting from the lymph collectors. The accumulating proteins raise the colloidal osmotic pressure and attract water. As a consequence of changes in tissues, biophysical parameters such as oxygenation, pH etc., the cells of the mononuclear phagocytic system – the tissue scavengers – are depressed in their activity levels. The balance between deposition and lysis of collagen is shifted towards the former, and the fibrosclerotic induration gradually progresses (39).

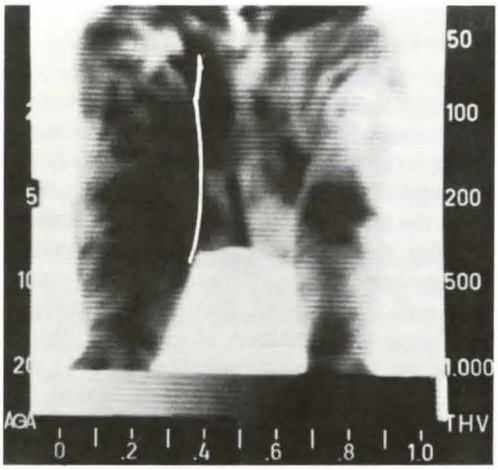

Fig. 3 Thermography of both arms and anterior chest wall. The right arm, affected by secondary arm lymphedema, is up to 1 °C warmer than the left

When operating on lymphedematous extremities, in patients as well as in the experimental animal, excessive bleeding was frequently observed. When measuring the surface humidity of the skin of lymphedematous and normal arms, the skin of the lymphedematous arm in approximately 70% of the patients was found to be dryer than the normal one. A patient gave the explanation to one of us (L. C.): "my swollen arm is warmer than the other, therefore the skin is dry". Thermographies of lymphedematous arms documented this (Fig. 3). Lymphedematous legs were found to have an increased temperature of up to 2 degrees Celcius. Figs. 4a and 4b demonstrate such a patient with primary hypoplastic lymphedema of his left leg.

Corrosive preparations of extremities of dogs with chronic lymphedema demonstrate the markedly increased vascularity, leading to the temperature differences (Fig. 5). There is evidence that the former may be a consequence of changes in macrophage activity (43).

In the face of these tissue alterations, the question for the micro-surgeon arises: to what degree will the creation of lymphovenous shunts revert these tissue changes?

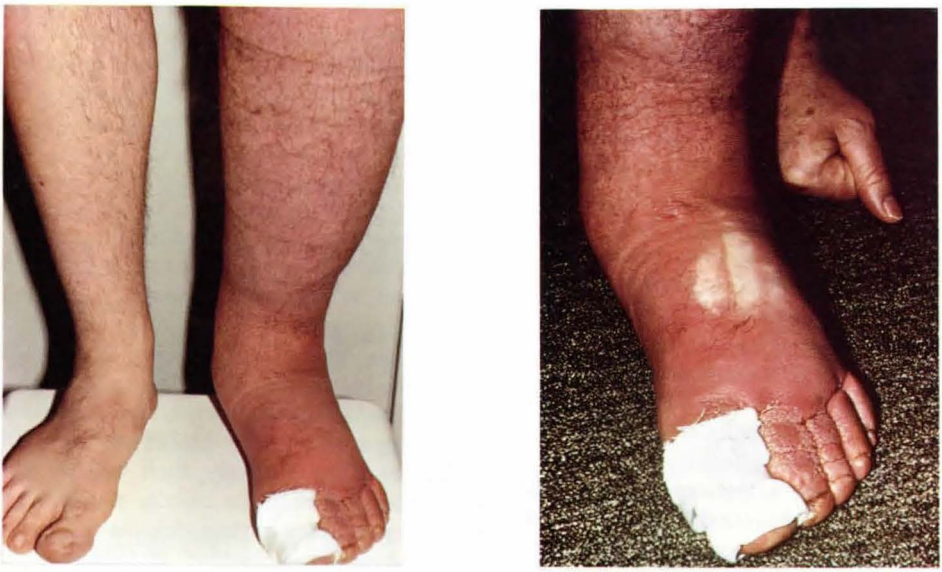

Fig. 4 Patient with primary hypoplastic lymphedema of the left leg. This patient does not suffer from erypsipelas
a) Comparativ view of right and left lower leg, indicating the color differences
b) Close up view, indicating the increase in capillary filling as demonstrated by the blanching of the skin under pressure by the examiners hand

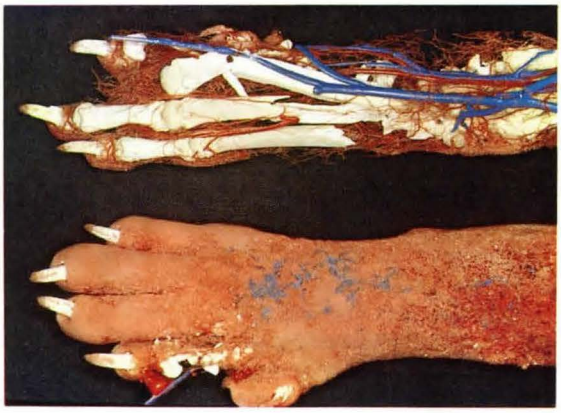

Fig. 5 Corrosive preparation of both hind legs of a dog with secondary lymphedema of left leg (Type 2: Clodius, 8), of three years duration. The corrosive materials were injected into the distal aorta and inferior vena cava, thus under equal pressure for the vascular systems of both legs. This demonstrates a marked difference in vascularisation of the skin and subcutaneous tissues

Lymphedema, the law of quantitative lymph-drainage

As outlined above, from a pathophysiological standpoint, lymphedema is the disturbance of the equilibrium between the lymphatic load on one side, and the transport capacity of the lymphatic system and the extra-lymphatic mastering of plasma proteins on the other side. From the lymphvascular point of view, every lymphedema, congenital or aquired, is a mechanical lymphdrainage insufficiency: whereas the lymphatic load is normal, the transport capacity of the lymphatic system is reduced (20, 22). Following surgical reduction of the lymphatic outflow tracts (lymph node dissection), the remaining lymph collectors increase their lymphflow, their output. But gradually, these normal lymph collectors decompensate – even when they are not affected by surgery and/or radiation, or situated in surgically or radiologically undisturbed tissues (8). The lymph collectors used for lymphovenous shunts in the experimental (45) and clinical (35) series were dilated superficial lymph collectors. In contrast to the collector of the deep system, into which they normally drain, they handle a smaller lymphatic load. Therefore, it doesn't seem surprising that, following an initial period of function they become occluded.

The problem for the microsurgeon is therefore not only to establish some new outflow tracts, e.g. through lymphovenous shunts, but to provide an adequate number of new outflow tracts. In addition, once lymphedema has progressed from the latent phase into manifest clinical swelling, the remaining lymph collectors used for anastomoses are altered in their structures: their wall is thickened, their valves incompetent, their flow reduced. In our mind, this explains the findings of *Puckett* et al. (45), in which the calculated steady state relative lymph flow for the edematous legs was between 0.21 and 0.87 as normal. If the surgically created additional lymphatic transport capacity is rather limited, recurrence will be early.

The superficial and the deep lymphatic systems im lymphedema

For more than a century the traditional concept for the surgeon dealing with lymphedematous extremities consisted of the belief that only the epifascial lymph system was affected by lymphedema (28, 32, 44, 46, 47). It was therefore considered that draining the epifascial lymphatics into the subfascial lymphatics across the barrier of the deep fascia represented a physiological approach. By clinical lymphangiography, and by experiment, it was demonstrated that this concept, certainly for secondary lymphedema, was wrong (8, 11, 16, 25, 48). In secondary lymphedemas, by which most patients of the published series are affected, the deep lymphatics are removed at the root of the extremities. The partially or totally interrupted deep outflow must be compensated by the epifascial lymphatics. However, under normal conditions, due to the unidirectional flow provided by the lymphatic valves, the epifascial lymph drains into the deep lymphatic system. Following a deep lymph block, the deep lymph collectors dilate massively, their wall becomes edematous, between the cellular elements and the collagen fibres protein rich material, leading to fibrosis, is embedded. Multiple thrombi occupy the lumen of the lymph collectors (1, 36). This is unfortunate, because all or most of the lymph must be drained through the

superficial lymphatics, which as the typical lymphogram reveal, become irregular, tortuous and dilated. There is dermal backflow of the contrast medium, which stagnates. Unless "lymphedema" is operated "prophylactically", using deep lymphatics (9), microsurgical shunts must be performed with "diseased" superficial lymphatics.

A further problem when shunting superficial lymph collectors, is the concept of lymphatic skin territories (30), which are drained only by specific collectors. Only from the margins between such skin zones or "skin lymphotomes" can lymph drain towards two neighbouring collectors. If collaterals between congested and uncongested skin zone form, and how many of them are able to compensate a lymphblock of one skin lymphotome, and whether they are capable of sufficient drainage, is unknown.

Can surgery for lymphedema achieve a restitutio ad integrum? Complete restitutio ad integrum, following a lymphatic blockade leading to manifest lymphedema, was observed by one of the authors (L.C.) only in cases of temporary self inflicted lymphatic obstruction (15). A final reason, why shunts should be done prophylactically, consists in the activation of the clotting mechanisms in the plasma (and in the lymph) by diseased tissues. The more numerous the surgically created lymphovenous shunts, the slower will be the flow and the lower the pressure gradient across the anastomoses. Considering these aspects, microsurgical lymphovenous shunts for chronic lymphedema are problematic.

Acknowledgement

The authors are grateful to Dr. *F. Heinzel*, Director of the Institutes for Nuclear Medicine of the Zürich City Hospitals, for the thermography. The experimental part of the paper was subsidized by the Swiss National Fund.

References

1 *Altorfer, J., Chr. Hedinger, L. Clodius:* Light and electron microscopic investigation of extremities of dogs with experimental chronic lymphoedema. Folia Angiol. 25 (1977) 141
2 *Barinka, L.:* The technique of the excisional operation for lymphedema of the lower extremity using a new instrument. In "Lymphedema" (ed. L. Clodius). Thieme, Stuttgart 1977, p. 139
3 *Beninson, J.:* Post-mastectomy lymphedema: 20 years of medical therapy. In "Lymphology, Proc. VI. Int. Cong. Lymphology" (eds. P. Malek, V. Bartos, H. Weissleder and M.H. Witte). Thieme, Stuttgart 1979, 400
4 *Casley-Smith, J.R.:* The functioning and interrelationships of blood capillaries and lymphatics. Experientia 32 (1976) 1
5 *Casley-Smith, J.R.:* Functional fine structure of lymphatics. Experientia 32 (1976) 818
6 *Casley-Smith, J.R., M.A. Sims:* Protein concentrations in regions with fenestrated and continuous blood capillaries and in initial and collecting lymphatics. Microvascular Res. 12, 245
7 *Casley-Smith,J.R., L. Clodius, N.B. Piller, M. Földi:* A model of lymphoedema in the rabbit's ear. The effects of the benzo-pyrones. Chirurgia Plastica 4 (1977) 5
8 *Clodius, L.:* The experimental basis for the surgical treatment of lymphedema. In "Lymphedema" (ed. L. Clodius). Thieme Stuttgart 1977, 43
9 *Clodius, L.:* Secondary arm lymphedema. In "Lymphedema" (ed. L. Clodius). Thieme, Stuttgart 1977, 147
10 *Clodius, L.:* Microlymphatic surgery. In "Reconstructive Microsurgery" (eds. R.K. Daniel and J. K. Terzis). Little, Brown, Boston 1978
11 *Clodius, L., W. Wirth:* A new experimental model for chronic lymphedema of the extremities. Chirurgia Plastica (Berl.) 2 (1974) 115
12 *Clodius, L., N.B. Piller:* Conservative therapy for postmastectomy lymphoedema. Chirurgia Plastica (Berl.) 4 (1978) 193
13 *Clodius, L., N.B. Piller:* Das sekundäre Armlymphödem: Spontanverlauf, Resultate konservativer und operativer Therapie. Therapiewoche 30 (1980) 5182
14 *Clodius, L., L. Deak, N.B. Piller:* A new instrument for the evaluation of tissue tonicity in lymphoedema. Lymphology 9 (1976) 1
15 *Clodius, L., H. Köhnlein, N.B. Piller:* Chronic limb lymphedema produced solely by blocking the lymphatics in the subcutaneous compartment. Brit. J. Plast. Surg. 30 (1977) 156
16 *Crockett, D.J.:* Lymphatic anatomy and lymphedema. Brit. J. Plast. Surg. 18 (1965) 12
17 *Danese, C., R. Brower:* Experimental anastomoses of lymphatics. Arch. Surg. 84 (162) 6
18 *Danese, C., A.N. Papaioannou, L.E. Morales, S. Mitsuda:* Surgical approaches to lymphatic blocks. Surgery 64 (1968) 821
19 *Engeset, A., B.Hager, A. Nesheim, A. Kolbenstved:* Studies on human peripheral lymph. Lymphology 6 (1973) 1
20 *Földi, M.:* Physiologie und Pathophysiologie des Lymphgefäßsystems. In: „Handbuch der Allgemeinen Pathologie", Springer Verlag, Berlin 1972
21 *Földi, M.:* Basic Lymphology. Folia Angiologica Suppl. vol. III, Haupt & Koska, Berlin 1974

22 *Földi, M.:* Physiology and pathophysiology of lymph flow. In: "Lymphedema" (ed. L. Clodius). Thieme, Stuttgart 1977, 1
23 *Földi, M.:* Die konservative Therapie des Lymphödems. Therapiewoche 30 (1980) 5162
24 *Földi, M., N. Klüken, M. Collard:* Praxis der Lymphgefäß- und Venenerkrankungen. G. Fischer, Stuttgart 1974
25 *Gibson, T., S. Tough:* A simplified one stage operation for the correction of lymphoedema of the leg. Arch. Surg. 71 (1955) 809
26 *Gregl, A., H. Poppe, H. Pöhls, J. Kienle, Th. Schwartz, J. Stelzner:* Häufigkeit, Pathogenese und klinische Symptomatik des Armödems bei Mammakarzinom. W. de Gruyter, Berlin 1971
27 *Jungblut, R.:* Klinisch-experimentelle Studie zur Armlymphographie unter besonderer Berücksichtigung des Mammakarzinoms. W. de Gruyter, Berlin 1971
28 *Kondoleon, E.:* Operative Behandlung der elephantastischen Oedeme. Zentralbl. Chir. 39 (1912) 1022
29 *Krajnovic, P.:* Die Verwendung von Venalot in der Lymphographie. In: "Lymphographie und Pharmakolymphographie" (ed. A. Gregl). G. Fischer, Stuttgart 1975
30 *Kubik, St., W. Wirth:* Histology, anatomy and lymphographic appearance. In: "Atlas of lymphography" (ed. M. Viamonte and A. Rüttimann). Thieme, Stuttgart 1980
31 *Kuhnke, E.:* Die Volumenbestimmung entrundeter Extremitäten aus Umfangsmessungen. Z. Lymphologie 2 (1978) 35
32 *Lanz, O.:* Eröffnung neuer Abfuhrwege bei Stauung im Bauch und unteren Extremitäten. Zentralbl. Chir. 3 (1911) 3
33 *Mayerson, H.S.:* Physiologic importance of lymph. In: "Handbook of Physiology, Circulation II". (Eds. W.F. Hamilton and P. Dow), Waverly Press, U.S.A., 2 (1963) 1035
34 *Miller, S., J.B. Laines, J.M. Howard:* Lymphatic pressures in extremities of dogs. Arch. Surg. 87 (1963) 193
35 *O'Brien, B.:* Microvascular Reconstructive Surgery. Churchill Livingstone, Edinburgh, London N. Y. 1977
36 *O'Brien, B., B.B. Shafiropp:* Microlymphaticovenous and resectional surgery in obstructive lymphoedema. World J. Surg. 3 (1979) 3
37 *Olszewski, W.:* Pathophysiological and clinical observations of obstructive lymphedema of the limbs. In: "Lymphedema" (ed. L. Clodius). Georg Thieme Publishers, Stuttgart 1977, 79
38 *Olszewski, W.:* Surgical lymphovenous shunts for the treatment of lymphedema. In: "Lymphedema" (ed. L. Clodius) Georg Thieme Publishers, Stuttgart 1977, 103
39 *Olszewskik, W., A. Engeset:* Intrinsic contractility of leg lymphatics in man. Lymphology 12 (1979) 81
40 *Piller, N.B.:* The induction of controlled proteolysis in high protein oedemas by coumarin. Z. Lymphologie 1 (1977) 39
41 *Piller, N.B., L. Clodius:* Conservative treatment of acute and chronic lymphedemas with benzopyrones. Lymphology 9 (1976) 132
42 *Piller, N.B., L. Clodius:* Lymphoedema of the rabbit ear following partial and complete lymphatic blockade: its effect on fibrotic development, enzyme types and their activity levels. Brit. J. exp. Path. 59 (1978) 319
43 *Piller, N.B., L. Clodius:* The blood-tissue-lymph system in lymphoedema: an examination of the role of the mononuclear phagocytic system and its relationship to observed histopathological changes. Folia Angiologica – in press. (1980)
44 *Poirier, P., B. Cueno, G. Delamare:* The Lymphatics. Constable, London 1973
45 *Puckett, Ch. L., G.R. Jacobs, J.S. Hurvitz, D. Silver:* Evaluation of lymphovenous anastomosis in obstructive lymphedema. Plast. Reconstr. Surg. 66 (1980) 116
46 *Sappey, M.P.C.:* Anatomie, physiologie, pathologie des vaissaux lymphatiques considerés chez l' homme. Paris 1894
47 *Thompson, N.:* The surgical treatment of advanced post-mastectomy lymphoedema of the upper limb. Scand. J. plast. Surg. 3 (1969) 54
48 *Watson, T.A., A.F. Bond, A.J. Phillips:* Swelling and disfunction of the upper limb following radical mastectomy. Surg. Gynaecol. Obstet. 116 (1963) 99
49 *Yamada, Y.:* Studies on lymphatic venous anastomosis in lymphoedema. Nagoya. J. Med. Sci. 32 (1969) 1
50 *Zelikovski, A., M. Manoach, Sh. Giler, I. Urda:* Lymphapress. Lymphology 13 (1980) 68

L. Clodius, Plastische und Wiederherstellungschirurgie, Universitätsspital, CH-8091 Zürich, Switzerland