

ARE PERIPHERAL LYMPHATICS DAMAGED BY HIGH PRESSURE MANUAL MASSAGE?

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ABSTRACT

Massage of the foot in men and the hindpaw in dogs was performed by applying external pressures of 70-100 mmHg for a period of one, three, five, and ten minutes with a frequency of 25 strokes per minute. This protocol was performed on individuals without edema, on dogs with experimental lymphedema and men with post-thrombotic venous edema.

After ten minutes of forceful massage, focal damage of lymphatics was present. In a group of dogs with lymphedema and men with post-thrombotic venous edema, the alteration of lymphatics was greater than in normal individuals and evident only after 3 to 5 minutes of massage. At first, the forceful massage affected the endothelial lining of the initial lymphatics. Alterations of lymphatic collectors were visible later. The fluid in lymphedema was translocated by massage using high pressure from the interstitium into the lumen of lymphatics by means of the open junctions and by artificial cracks that develop from injury to the lymphatic wall.

Vigorous massage in lymphedema also produces loosening of subcutaneous connective tissue, formation of large tissue channels and release of lipid droplets that enter the lymphatics. By this mechanism, massage helps reduce the amount of fat cells in the lymphedematous leg.

A common and proven method of conservative treatment of lymphedema is

manual lymph massage or drainage (1,2). In the last few years, this method has been facilitated by the aid of pneumatic pumps (3-8). The pressures attained in some of these pneumatic pumps reach up to 200 mmHg (3,4). Whereas some therapists (6-9) have suggested that pressures exceeding 60 mmHg alter microvascular integrity, morphologic evidence for this position is scarce. From preliminary communication (10), hyperthermia together with gentle massage seems to open interendothelial junctions of the initial lymphatics. We decided to examine if manual lymph massage performed with an external pressure of 70-100 mmHg leads to destruction of the wall of lymphatic vessels. Ultrastructure of lymphatics in the normal state (11-19), and in the different types of lymphedema (20-27) has been well described.

MATERIALS AND METHODS

The investigation was performed in accordance with the animal and human ethical rules of the University on lymphatics of the lower leg of patients and the hindpaw of dogs. The patients and dogs were divided into two groups.

Group I - Hosts without peripheral edema. Six patients (age 25 to 75 years) and eight dogs of both sexes.

Group II - Hosts with edema. Four dogs with lymphedema of the right or left hindpaw and two patients (males, age 40 and 46 years) with post-thrombotic venous edema of the

lower leg. The duration of edema was two and a half to four months in the dogs and three and ten years in the patients.

Lymphedema was produced in 4 of 12 dogs by repeated injection (three or four times) of the lymphatics of the hindpaw with UF lipiodol and India ink or a mixture of 4% gelatin with India ink over a period of two months. The site of injection was invariably proximal to the part where the massage was later performed. From the dorsal part of the foot of patients and the hindpaw of the dogs of both groups, samples were taken of dermal and subdermal lymphatics, before and after massage, for light and electron microscopy. Operative procedures and manipulations on dogs were carried out under sodium pentobarbital anesthesia (25 mg/kg).

Technique of Manual Lymph Massage

Lymphatics of the dorsal part of the foot and paw were visualized by injection of patent blue into interdigital clefts of the leg or hindlimb. The skin with blue translucent lymphatics was massaged for a period of 1, 3, 5, and 10 minutes using external pressures of 70 to 100 mmHg.

The pressure used during compressive loading was measured by the technique of Miller and Seale (9). We modified this method by providing contact of the known weight device on the skin of the massaged leg by placing the weight device on top of the fingers of the physiotherapist. The weight of the device which generated a pressure of 100 mmHg was calculated for the area of fingers which were performing the massage. As a control, the massage was done by two methods: In one, the weight device was set directly on the skin of the massaged leg and drawn across the skin. In the other method, the weight device was placed on top of the fingers of the physiotherapist performing the massage. The results of both methods were similar.

The length of the massaged skin area was 10 to 13 cm, with a frequency of 25 strokes per minute. The massage was carried out by two fingers in the direction of lymph flow. The procedure was performed by only one person to keep the pressure of the massage on the skin constant and minimize the differences between single strokes.

Technique of Sampling for Electron Microscopy

From each patient and dog before and after massage, the skin above the lymphatics was cut and tissue with lymphatics fixed into special forceps (28). The forceps preserved lymph vessels in the same orientation and state as they were situated in the tissue. The tip of the forceps with the lymphatics was plunged into Karnovsky fixative (29). The tissues were postfixed in 2% osmium tetroxide solution and embedded in araldite. Semithin sections were stained with toluidine blue, thin sections were contrasted with uranyl acetate and lead citrate and observed with a JEM 1200 EX electron microscope. Samples taken from contralateral non-massaged legs were used for morphologic control.

RESULTS

Group I - Hosts (without edema)

A. Before massage

No pathological changes were found on initial lymphatics, precollectors and collectors.

B. Changes after 1, 3 and 5 minutes of massage.

Endothelial lining: interendothelial junctions were both open (*Fig. 1*) and closed. Between these two states a partial dilation of interendothelial junctions was present. The

Fig. 1. Open "end-to-end" junction of lymphatic collector (arrow) in a healthy male (34 years) after three minutes of manual massage. Orig. mag. x8000.

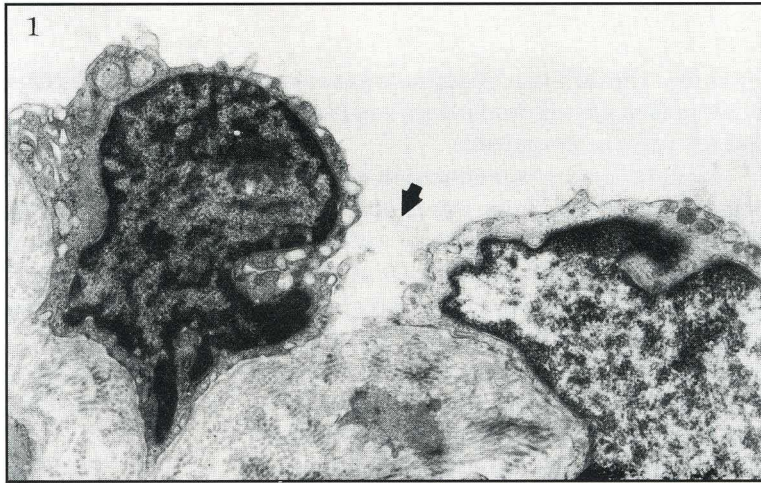
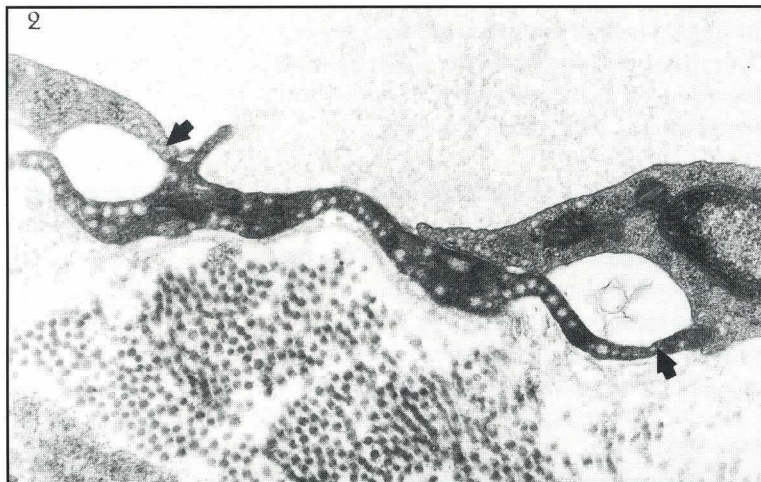


Fig. 2. Dog without lymphedema, one minute after massage. Overlapping interendothelial junctions of an initial lymphatic are partially open. Cavities and tiny channels between opposing membranes of the junctions are visible (arrows). Orig. mag. x13000.



closed interendothelial junctions became dilated from 20-30 nm up to 2 μ m but remained firmly attached to the places of the punctuate condensations of opposing membranes corresponding to tight junctions (Fig. 2). Therefore, large cavities or channels were created that provided direct communications between the lumen of the lymphatics and interstitial tissue. Dilated cavities and channels were irregular and occupied different large parts of the interendothelial cleft (Fig. 2). With increasing time of massage the number and enlargement of the interendothelial cavities was increased. Numerous micropinocytotic vesicles in endothelial cells were detected.

Subendothelial collagen fibers including anchoring ligaments reached to the discontinuous basal membrane of the endothelial cells. In only one dog was there separation of endothelial cells from the underlying basal membrane after three minutes of massage in some areas where interendothelial cavities (canals) opened into interstitial tissue. Electron microscopy of collagen fibers and smooth cells did not reveal pathological changes.

C. Changes after ten minutes of massage

The endothelial lining of initial lymphatics precollectors and collectors was

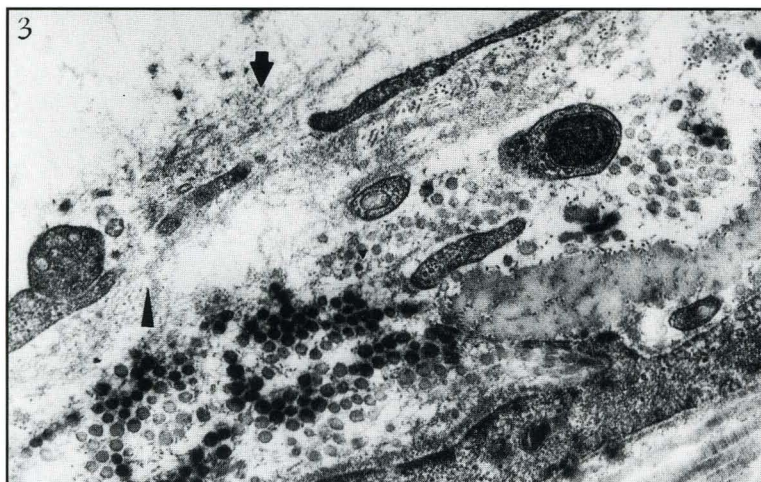


Fig. 3. Dog without lymphedema after 10 minutes of massage. Focal destruction and denudation of the endothelial lining of the pre-collector (arrow). Interstitial tissue (fine fibrillar material) protrudes into lumen of lymphatic (arrow-head). Orig. mag. x15000.



Fig. 4. Desquamation of endothelial cells of lymphatic (arrow) in a healthy 70 year old woman after ten minutes of massage. Orig. mag. x2500.

focally damaged (Fig. 3,4). The following phenomenon occurred to different extents:

- 1) The attenuation of endothelial cells.
- 2) Focal destruction of endothelial lining.
- 3) Desquamation of endothelial cells.

The subendothelial interstitial space directly connected with the lumen of the lymphatics and in some instances the interstitial tissue protruded into the lumen of the lymphatics. Nevertheless, not all lymphatics of the massaged area exhibited ultrastructural damage. The lymphatics in the depth of the subcutaneous tissue or running along and behind the larger subcutaneous veins remained intact.

In the cytoplasm of some smooth

muscle cells of the lymphatic collectors, numerous pinocytotic vesicles were seen.

Group II - Hosts with edema

A. Before massage (dogs with lymphedema)

Lymphatics in the skin and the subcutaneous tissue were uniformly dilated and the endothelial cells were extremely flat. Interendothelial junctions were both open and closed. The interdigitating and overlapping interendothelial junctions were partly dilated but not to the extent of that seen after massage (see Group I). The cytoplasm of endothelial

Fig. 5. Dog with three months of lymphedema. Lymphatic precollector after five minutes of massage. Large cavities (2-7 μm in diameter) between the opposing membranes of junctions have formed (X-X). Orig. mag. x5000.

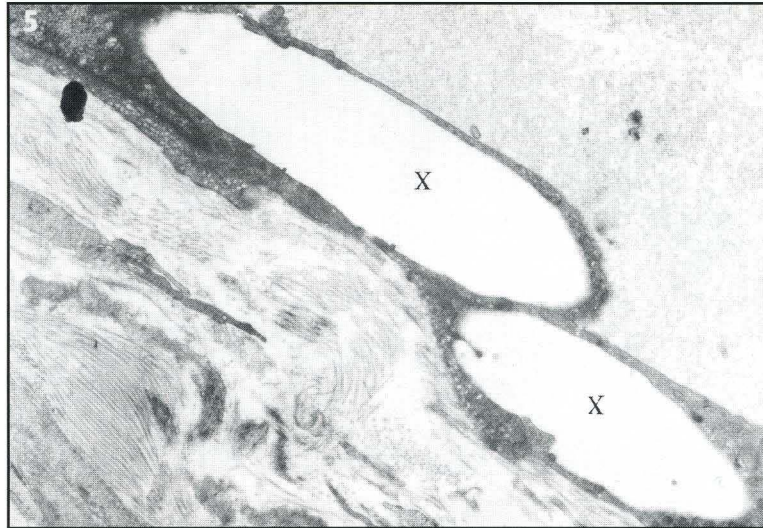
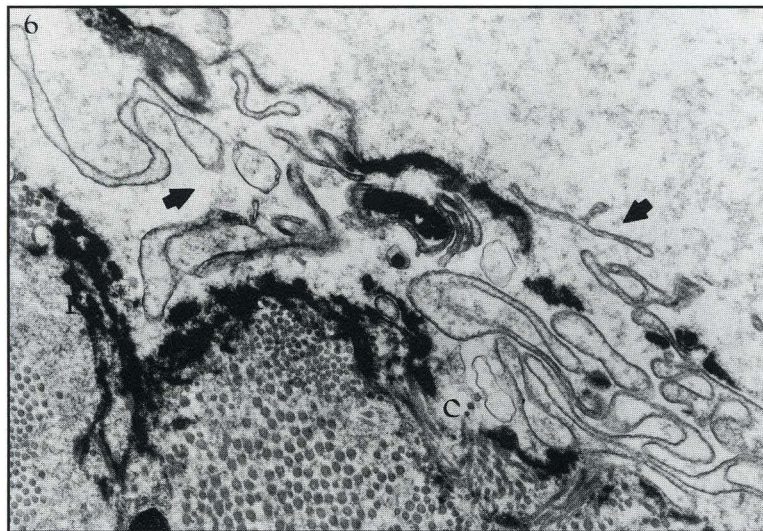


Fig. 6. Dog with three months of lymphedema after ten minutes of massage. Endothelial cells of initial lymphatics are damaged and exfoliated (arrows) in the form of free membranes in the lumen of the initial lymphatics. Fibrinoid mass (F), disintegration of collagen fibers (C) and loss of basal lamina are also seen. Orig. mag. x15000.



cells showed pinocytotic vesicles, occasionally dividing mitochondria and lamellar bodies. The basal lamina of the initial lymphatics was typically discontinuous but structurally unchanged. Along the wall of the lymphatics, many activated fibroblasts and macrophages with phagosomes and phagolysosomes were visible.

The wall of some precollectors and collectors was edematous. A small amount of edema was found in lymphatics located between dense collagen fibers.

B. After massage

After 3 to 5 minutes of massage, the space between opposing membranes of the interendothelial junction of the lymphatics was larger (1-8 μm in diameter) (Fig. 5) than in non-massaged lymphedematous paws. A pronounced irregularity of the collagen fibers in the subendothelial space, edema between smooth muscle cells in lymphatic collectors and focal desquamation of endothelial lining in initial lymphatics were evident.

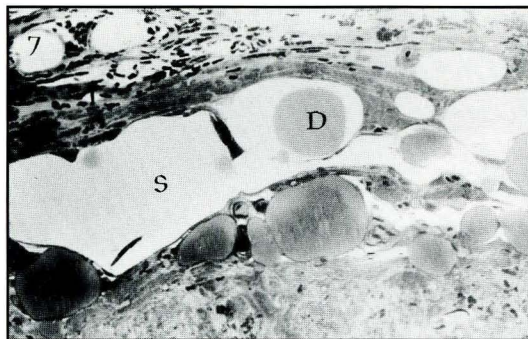


Fig. 7. Dog with lymphedema after ten minutes of massage. Interstitial clefts and spaces (S) of subcutis are filled with free lipid droplets (D). Semithin section, toluidine blue. Orig. mag. x45.

After ten minutes of massage, desquamation of the endothelial lining of the initial lymphatics was extensive (Fig. 6). The desquamated endothelial cells forming free membranes were detached from the basal lamina, fragmented, and coiled. The subendothelial space was packed with dense amorphous material forming sporadic myelin figures. Fibrinoid deposits in the wall of the initial lymphatics were present. As a result the perivascular space was directly connected with the lumen of the lymphatics to a wide extent. These changes were less pronounced in lymphatics running in the depth of subcutaneous tissue and along large blood vessels.

Interendothelial clefts in the venules and small veins were patent but endothelial cells contained many vacuoles and micropinocytotic vesicles.

In the subcutaneous tissue after massage, large clefts and spaces filled with free lipid droplets appeared in the edematous subcutaneous connective tissue (Fig. 7) and these lipid droplets entered the lymphatics (Fig. 8).

Other findings were of the same magnitude after 3 and 5 minutes of massage.

C. Before massage (patients with post-thrombotic venous edema)

In some areas the lymphatic structure

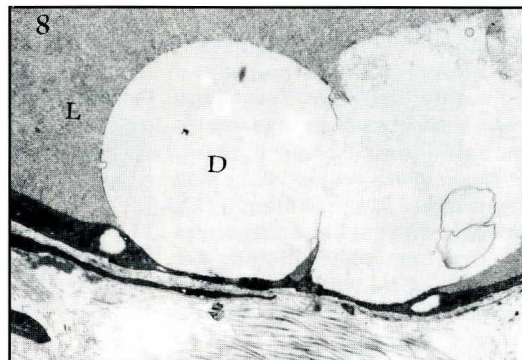


Fig. 8. Dog with lymphedema. Lipid droplets (D) during massage enter the lymphatics (L). Orig. mag. x5000.

was well preserved but in other areas there was pronounced attenuation and atrophy of the endothelial cells with wide interendothelial gaps (Fig. 9a). The wall of the lymphatics was edematous and contained considerable fibrinoid material. Some smooth muscle cells were transformed into fibroblast-like cells. Stasis of erythrocytes in postcapillary venules with accumulation of polymorphonuclear cells in the wall was evident.

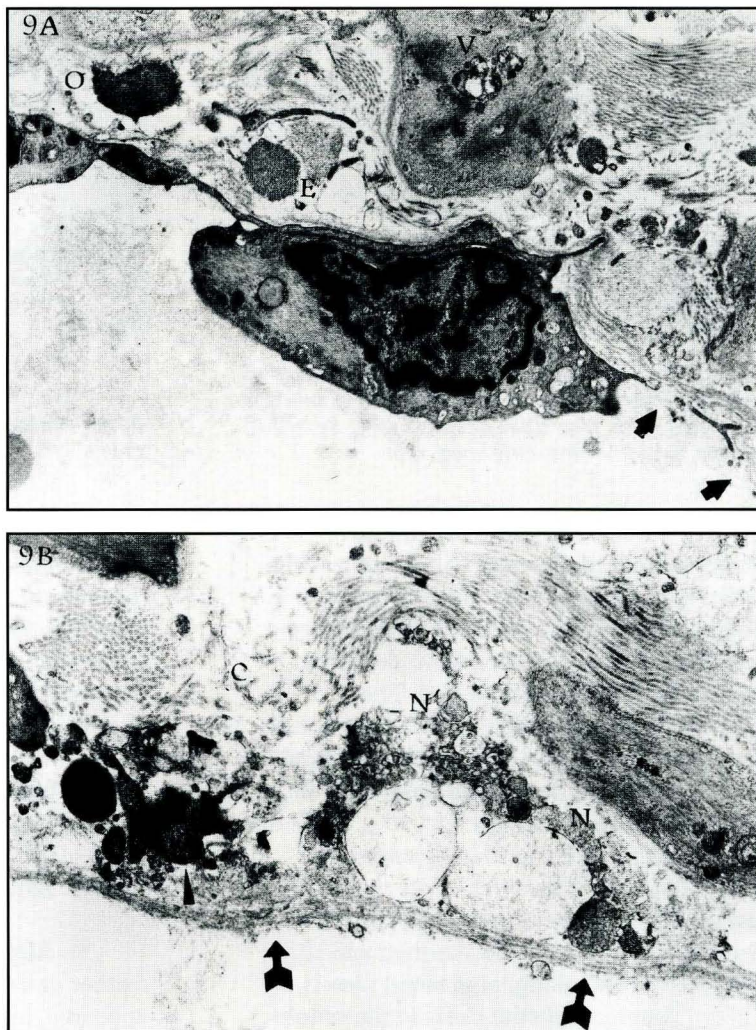
D. After massage.

After 3 to 5 minutes of massage further destruction of the lymphatics appeared, including marked desquamation of the endothelial lining, disruption of collagen and elastic fibers with the deposition of fibrinoid material, tissue debris and erythrocytes in the wall of the lymphatics (Fig. 9b).

DISCUSSION

The morphological findings we obtained before massage in lymphatics of individuals without edema (dogs and patients) and in those with lymphedema were near identical to those reported by others previously. Our results extend these observations and report that in non-edematous individuals (dogs and patients) manual massage performed for ten minutes with a frequency of 25 strokes per

Fig. 9. Male (46 years), post-thrombotic venous edema lasting ten years. **A)** Before massage—extremely atrophic lymphatic endothelium with gaps (arrows). The wall of the lymphatic is altered by edema alone—edema of the wall (O); vacuoles in myofibroblasts (V); probably the rest are erythrocytes (E). Orig. mag. x4000. **B)** After five minutes of massage. The denudation of endothelium (arrows), debris of necrotic tissue (N) and disorganization of collagen fibers (C) are visible. Apoptotic cell (arrowhead). Orig. mag. x6000.



minute by pressures of 70 to 100 mmHg caused focal damage of lymphatics, mainly of the endothelial lining. In the patients and dogs with lymphedema and longstanding post-thrombotic venous edema, the damage of lymphatics was even greater and was already apparent after only 3 and 5 minutes of massage.

At first, massage affected the endothelial lining of the initial lymphatics which was followed by damage of the lymphatic collectors. Collagen and elastic fibers and smooth muscle cells were more resistant to increased pressure of massage (Figs. 2-4,10).

Mechanisms of the Action of Massage

Massage widely opens the interendothelial junctions. The junctions with “end-to-end” connections open completely. In the interdigitating and overlapping junctions interstitial fluid propelled by massage in most instances dilates only a part of the junction and creates large cavities and channels between opposing membranes of the junction (Fig. 10).

However, microscopy failed to explain why some interendothelial junctions in lymphatics of the massaged area remained wide open whereas others remained closed.

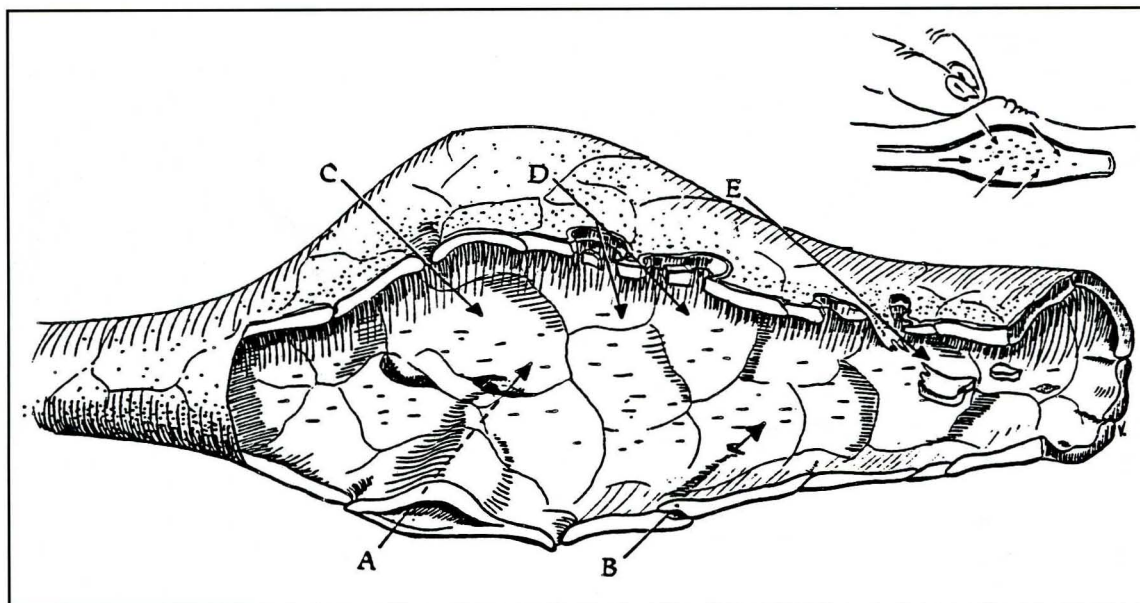


Fig. 10. Schematic diagram of structural changes that likely develop in lymphatics after manual massage with a pressure of ~100 mmHg. In the lower border of the cut lymphatic are opening of interendothelial junctions in the form of small channels (A,B). In the upper border is an opening of the "end-to-end" type junction (C), focal damage to the endothelial lining (D) and desquamation of endothelial cells (E).

Vesicles in endothelial cells of the lymphatics in both groups were seen before and after massage. Although the vesicles were not statistically evaluated, there did not appear to be a remarkable decrease or increase with and without massage. Most likely, vesicular transport is not a key mechanism for transport of fluid from the interstitium into the lymphatics during massage, a concept indirectly supported by others (16,30). The functional significance of these vesicles for lymphatic endothelial cells perhaps acts as a means for fluid uptake rather than for fluid transport.

The fact that wide clefts in interendothelial junctions were seen in subcutaneous veins after vigorous massage, suggests that under these artificial circumstances interstitial fluid may gain access into the venous system as well as the lymphatic apparatus (2).

Accumulation of fat is common in lymphedema (31,32), and vigorous massage in lymphedema produces loosening of connective

tissue, formation of large tissue channels and releases lipid droplets into initial lymphatics. These phenomena were also observed by manual lymph massage performed with pressures of 40-50 mmHg.

Post-thrombotic Venous Edema

In longstanding post-thrombotic venous edema, the lymphatics are deranged either directly by inflammatory process or indirectly by elevation of venous pressure and failure of edema safety factors (33-37). Thus, increased postcapillary venous resistance leads to increased microvascular hydrostatic pressure and greater net capillary filtration and accordingly a greater lymphatic waterload. When functional reserves of lymphatic drainage are overwhelmed, dynamic insufficiency of lymph flow emerges and edema ensues. A morphological picture of the partial destruction of lymphatics in the two male patients corresponds with this view.

When manual massage was applied on such affected lymphatics, their damage appeared earlier and was more extensive. The damage of these lymphatics by massage seems to depend on both the level of the pressure applied and on its duration.

In long-lasting edemas, lymphatics are partly damaged by two mechanisms: first and foremost by the edematogenic process and second by overvigorous massage. Massage performed with high pressure, favors the escape of fluid from the interstitium by the opening of endothelial junctions and through the artificial defects of the partly damaged wall of the lymphatics.

For a physiotherapist, it is difficult to maintain the same pressure during manual massage using just hand on skin.

In more severe longstanding edema, the pressure for massage to be effective is sometimes higher (70-100 mmHg) than usually performed (40-60 mmHg). In some instances, it is likely that physiotherapy partly damages superficial lymphatics but at present no other effective non-operative treatment of lymphedema exists. We suggest that after finishing the massage and application of bandages and elastic supports, that lymphatics depleted of fluid overload be given time for partial recovery. This proposal is supported by our findings that where lymphedema subsides most of the alterations on lymphatics are expected to gradually resolve.

The massage performed in this report (25 strokes per minute) was quick and was especially adapted for our research work. Typically, massage performed by a clinical physiotherapist is much slower (8-12 strokes/minutes). Therefore, changes in lymphatics are likely to appear in patients somewhat later, i.e., after 20-30 minutes of massage.

The issue of injury to the lymphatic endothelial lining needs further research. It has even been recently suggested that removal of the lymphatic endothelial lining had no effect on lymphatic pumping (38) although these experiments were in the larger lymph collectors.

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