

## Physiology and Microsurgery of Lymphatic Vessels in Man

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### Summary

Personal experience in surgical treatment of lymph stasis with lympho-venous shunts has been presented. A brief summary of results of physiological studies on lymph flow in human legs is preceding the chapter on diagnostic procedures, indications and contraindications for surgery, surgical techniques of lymph node and lymph vessel to vein anastomoses.

#### *Physiological considerations:*

1. Lymph flow and proteins in normal leg during lying, getting up, and walking.
2. Effect of increased ambient temperature on leg lymph flow and composition.
3. Immune proteins in leg lymph.
4. Lymph flow in human legs — intrinsic vessel contractility as a determinant of flow.
5. Cells in human leg lymph.

#### *Microsurgical methods of treatment of lymph stasis:*

1. Lymphangiographic criteria for selection of patients for lymphovenous shunts.
2. Lymphangiographic contraindications for lymphovenous shunts.
3. Phlebography.
4. Other investigations.
5. Indications for lymph node-vein shunt in lower limbs.
6. Technique of operation of lymph node-vein shunt.
7. Lymph vessel-vein shunt.
8. Cannulation of lymphatics of human extremities.

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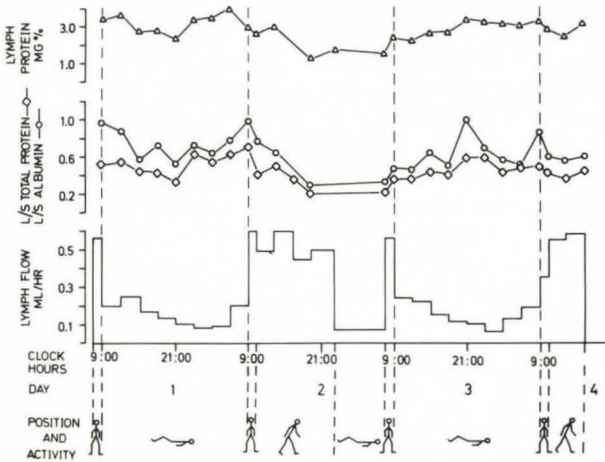
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### *Physiological considerations*

Lymph flow and proteins in normal leg during lying, getting up, and walking — safety factors against edema formation.

The rate of formation, flow and composition of lymph in human leg depends mainly on the position of the extremity, its muscular activity and ambient temperature. Change of position from the horizontal to the upright is accompanied by a rise in venous hydrostatic pressure. Walking causes an increase in blood flow through the leg tissues and capillary filtration, and muscle pump promotes lymph flow. Ambient temperature may influence lymph formation by dilatation or constriction of skin microcirculation. All the three described physical factors may, to different degrees affect lymph volume, protein concentration and lymph/serum protein ratios. Also, while studying the lymph flow rate the individual factors should be taken into consideration. These are the size of the cannulated vessel and individual differences in local lymph production. Lymph flow rate and protein concentration in vessels of the same size and topography in two individuals are usually different.

Leg lymph flow and protein concentration in normal men undergo major 24-hr variation dependent on the position of the body and type of activity (Fig. 1) (5, 19). During rest in a horizontal position lymph flow is low. In one series of our studies during the night rest it was  $0.24 \pm 0.056$  ml/hr. Mean protein concentration was  $2.16 \pm 0.12$ , g%, but in some cases reached the level above 3.0 g%. The lymph/serum ratio reached after a prolonged rest in a



**Fig. 1** Lymph flow, protein concentration and lymph/serum (L/S) protein concentration ratio in the leg in a normal man during 3 days of continuous observation. Note that lymph flow is high upon assuming upright position (9.00 hr) and decreases fast in a horizontal position to reach the lowest level during maximum relaxation at night (24.00–6.00 hr). During walking lymph flow is 3–5 times higher than during rest and slightly falls down during hours of walking. The protein L/S ratio is high during prolonged rest and decreases during walking. This is due to changes in protein concentration in lymph, since serum protein level remains relatively stable (20).

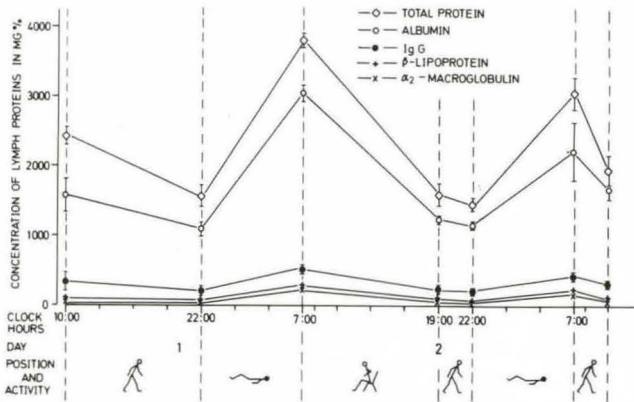
horizontal position the value of 0.55. There were only minor variations in the flow rate during the prolonged rest lasting for 24 hr, with the lowest flow recorded between 24.00 and 6.00 hours during sleep and maximum relaxation of muscles (20). The low lymph flow in a horizontal position is due to decreased capillary filtration and probably also increased reabsorption of excess of water and solutes from the tissue space. There is also a reduced muscular activity which decreases the rate of passage of free tissue fluid to the initial lymphatics.

Assumption of the upright position after prolonged rest was, in our studies, followed by a 3 to 5-fold rise in the mean lymph flow (Fig. 1). This effect lasted for about 1 hr, and then a slight decrease was observed. Lymph/serum protein concentration did not decrease for the first hour. Later it started to decrease steadily, reaching by the end of the day values as low as 1.2 g% and the L/S ratio of 0.25. Assuming the upright position several mechanisms become effective which bring about squeezing and washing out the preformed free tissue fluid and lymph and filling initial and collecting lymphatics. An increase of venous pressure and expansion of the capacitance vessels elevates the total tissue pressure and also to some extent the free fluid tissue pressure. Muscular movements drive, by raising total tissue pressure, tissue fluid into the initial lymphatics. An increase

in capillary filtration surface occurs due to opening of capillaries, closed at low pressures, and stretching of capillaries evokes „stretch pore effect“ increasing capillary filtration rate and lymph formation.

Walking considerably increases lymph flow. The flow rate differs between individuals and may range from 0.1 ml/hr to above 1.0 ml/hr per vessel. In a group of volunteers studied by us, the mean flow was  $0.74 \pm 0.26$  ml/hr (27). Comparatively, in the same group of individuals lymph flow was during rest in a horizontal position  $0.25 \pm 0.04$  ml/hr, during foot and calf contractions  $0.57 \pm 0.15$  ml/hr, and in a standing position  $0.41 \pm 0.21$  ml/hr. Taking into account that there are at least 10 lymph vessels in the foot and calf, the estimated total flow over a 24 hr period should range between 10–25 ml at night and 70–140 ml during the day in an upright position. The total protein output from the lower limb over the 24 hr period should be 2 to 4 g.

An inverse relationship between protein L/S ratio and lymph flow is observed during longer periods of lying or standing or walking. Changing of position from lying to standing or vice versa is characterized by lack of that inverse relationship. A high flow of concentrated lymph is observed in a standing position during the first hour, and a low flow of lymph with low protein concentration for at least 3 hr when lying. These findings suggest



**Fig. 2** Changes in leg lymph concentration of proteins of different molecular weight during various daily activities. Low molecular proteins like albumin, comprising above 60% of all lymph proteins, undergo major variation of concentration, increasing or decreasing tissue fluid oncotic pressure, thus preventing accumulation of excess of free interstitial water. Large molecular proteins reveal minor fluctuations. Values are means of samples obtained from 5 normal men  $\pm$  S.E. (24).

that the high initial protein output upon assuming standing position is due to the "squeeze out" of interstitial fluid and lymph by sudden venous expansion and muscular pumping rather than to increased capillary filtration. If the rise in lymph protein output were primarily caused by a sudden increase in capillary filtration, a decrease in lymph protein concentration and L/S total protein concentration ratio would have been evident what was not observed. Enhanced permeability of capillaries upon assumption of upright position also does not seem responsible for the increased protein output, because a decrease in ratio between L/S total protein to L/S albumin concentration does not occur.

A continuous decrease in lymph protein concentration observed while in the upright position may be explained by the wash-out of proteins accumulated in the lymph space during periods in the horizontal position. Moreover, some dilution of the interstitial and lymph proteins by the low protein capillary filtrate accumulating in the enlarged lymph space may also occur, bringing about a decrease in oncotic pressure.

It may be concluded that the rapid and increased lymph flow immediately after assuming the upright position helps to remove fluid and protein from the interstitium. Together with the continuous wash-out of protein during the day while upright, and dilution of pro-

teins, both resulting in lowering of oncotic pressure of tissue fluid, it provides a safety factor against formation of edema in the skin and subcutaneous tissue of the leg.

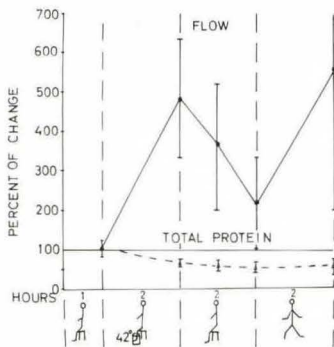
Proteins exerting most of the osmotic pressure are those of low molecular weight. Measuring the concentration changes of these proteins in lymph provides information concerning oncotic conditions in the tissue fluid. We found (24) evident differences in concentration in lymph of proteins of different molecular weight.

The rate of changes of concentration during various activities corresponds to the molecular weights of individual proteins. The lower the m.w. the less pronounced are these changes (Fig. 2). The differences in concentration between different proteins are small during lying, to increase significantly after prolonged walking or sitting. For example, the mean L/S ratio of low m.w.  $\alpha_2$ -HS-glycoprotein was 0.43 in the morning, dropped to 0.23 after 12 hours of walking, rose to 0.51 during the night rest, dropped again to 0.21 after 12 hours of sitting, and rose again to 0.45 after the 2nd night. The albumin L/S ratio changed from 0.38 to 0.24 respectively, then rose to 0.81 to drop to 0.2 and rose again to 0.57. The high m.w.  $\alpha_2$ -macroglobulin changed from 0.17 to 0.07, to rise to 0.46, to fall again to 0.06 and rise again to 0.41. The drop in the L/S of low m.w. proteins was not so rapid and profound

as of high m.w. proteins. Since albumin and other low m.w. proteins constitute around 75% of the total lymph protein pool, a decrease in concentration of these proteins by 60–70%, occurring after prolonged walking or sitting, considerably reduces the interstitial fluid oncotic pressure, thus opposing the edema formation. The estimated mean lymph oncotic pressures changed from 72 mmH<sub>2</sub>O in the first morning to 43 mm H<sub>2</sub>O by the end of day 1, rose to 149 mm H<sub>2</sub>O after night rest, dropped after 12 hours of sitting to 37 mm H<sub>2</sub>O, to rise again to 104 mm H<sub>2</sub>O, after night rest.

#### *Effect of increased ambient temperature on lymph flow and composition*

We studied in a group of normal subjects lymph flow and protein concentration of different molecular weight when the limb was placed in a 42 °C water bath. Warming of the limb produced within several minutes a 3- to 5-fold rise in flow (Fig. 3) and a parallel decrease in concentration of all protein components, irrespective of their molecular weight.



**Fig. 3** Changes in lymph flow and protein concentration in leg lymph during and after warming of the foot. An increase in flow occurred within the first 30 min after starting warm water bath, to decrease fast after its completion. Protein concentration decreased steadily irrespective of the lymph flow rate, most likely due to accumulation of protein-poor fluid in the lymph space during the period of warming. Data are means from 5 normal men  $\pm$  S.D. The curves had a similar shape in all, but some individuals responded to warming with abundant lymph flow.

The output of proteins increased by an average of 200%. Cooling of the limb at room temperature brought about a drop in flow, but the concentration of proteins remained low. This was probably due to accumulation of diluted lymph in the lymph space during the period of enhanced capillary filtration. A certain period of time was needed for replacement of that lymph by a new, more concentrated capillary filtrate and tissue fluid. Lack of higher increase in output in lymph of large molecular weight proteins like alpha-2-macroglobulin or IgM than of small molecular weight, indicates that there was no increase in capillary permeability. The increase in total lymph volume was caused by expansion of the filtration surface area, most likely due to dilatation and opening of new capillaries.

#### *Immune proteins in human peripheral lymph*

Proteins found in the peripheral lymph originate from 3 sources: a) plasma, b) tissues from which lymph is drained, c) free floating lymph cells. The prevalent mass of proteins comes from plasma through the capillary wall by diffusion, filtration and vesicular transport. The net volume of transported protein depends also on the capillary membrane permeability of the tissue. Leg skin, subcutaneous tissue and perimuscular fascia have a low permeability coefficient. This may explain the low lymph protein concentration usually observed. Only a small fraction of leg lymph protein could be an admixture of locally produced immunoglobulins and complement. The free-floating cells in lymph can produce IgG and IgM upon antigenic stimulation, but this applies mostly to efferent and not afferent lymph. Also skin macrophages can produce, when studied in vitro, C3 component, but the number of these cells in afferent lymph is extremely small. The concentration of immune proteins in lymph is low. We have found that the concentration of IgG, A and M compared with serum was 17, 16 and 7.4%, respectively (21, 22). Lymph C1q level was 12% of that of serum, C1s 21%, C4 22%, C3 14%, C9 24%, and C3PA 19%. The mean L/S ratio for total hemolytic complement was found 0.275, for C1H50 0.138, C4H50 0.105, C2H50 0.279, C3H50 0.063,

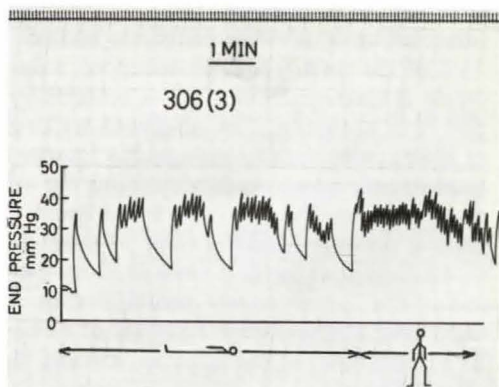
C5H50 0.266, C6H50 0.145, C7H50 0.25, C8H50 0.244, C9H50 0.253. The L/S ratio for total hemolytic complement was closely approaching the L/S ratio of globulin (CH50 0.275, globulin 0.3). However, the ratios of C1H50, C4H50, C3H50 and C6H50 were much below the globulin L/S ratios.

The titers of immune adherence (IA) capacity of lymph ranged from 1:16 (7 samples with 0 capacity), of serum 1:8 to 1:256. The difference in titers significantly exceeded the difference in globulin concentration between lymph and serum, what may be caused by existence in lymph of factors inhibiting IA.

The protein concentration and biological activity of C1 inactivator (C1INA) and C3b inactivator (C3bINA or KAF) were measured simultaneously in lymph and serum (28). The mean C1INA concentration in lymph was 9.76 mg%, in serum 42.6 mg%, the L/S ratio 0.236. The concentration of C1INA in lymph per g of globulin was 18.8 mg, whereas in serum only 14.7 mg, the L/S ratio 1.28. The functional evaluation of C1INA in an assay for inhibition of hemolytic activity of C1 revealed that its activity in lymph was about 3 times lower than in serum.

The C3b INA protein concentration in lymph was 33.4 u/ml, in serum 133.8 u/ml, the L/S ratio being 0.238. The concentration calculated per g of globulin was in lymph 6625 u, in serum 4568 u, the L/S ratio 1.45. The functional assessment of C3bINA in the immune adherence inhibition assay revealed its activity in lymph to be 4 times lower than in serum. Although the concentration of complement inhibitor proteins and their biological activity were lower in lymph than in serum, when expressed as a function of globulin concentration, they exceeded the serum values. This study has shown that the interstitial fluid and lymph contain complement inhibitors in sufficient amounts to prevent activation of complement once it has left the intravascular space.

The low concentration of immune proteins in peripheral lymph, found under physiological conditions, indicates that the defense reaction in the lymph space may in the first period af-



**Fig. 4** Intralymphatic end pressures in a man in a horizontal and upright position. Changing the position brought about only a slight increase in mean pressure but higher pulse frequency. No hydrostatic component was noted in the lymph vessel in a standing position (23).

ter invasion of a foreign antigen be weaker than in the serum.

#### *Lymph flow in human leg – intrinsic vessel contractility as a determinant of flow*

In man, spontaneous intrinsic rhythmic contractions of lymph vessels are a major determinant of lymph flow in limbs (23, 26, 27). To study the efficiency of intrinsic contractions of lymphatics in propelling lymph the end and lateral pressures and lymph flow were measured in prenodal lymphatics in legs of above 30 normal men in a horizontal and upright position, during rest and contractions of foot and calf muscles. The effect of venous congestion, warming of the limb and external massage of the foot on lymph pressures and flow was also evaluated.

In a horizontal position at rest the end systolic pressures (with obstructed flow) remained in the range of 20 to 50 mmHg, the diastolic pressures between 5 and 25 mmHg (Fig. 4). The lymphatic pulse amplitude ranged between 3 and 35 mmHg and pulse frequency between 2.5 to 10/min. Voluntary flexing of foot in a horizontal position did not increase the systolic pressure, but slightly increased the pulse frequency. The foot and calf muscle contractions did not produce any intralymphatic pressures in the calf vessels.

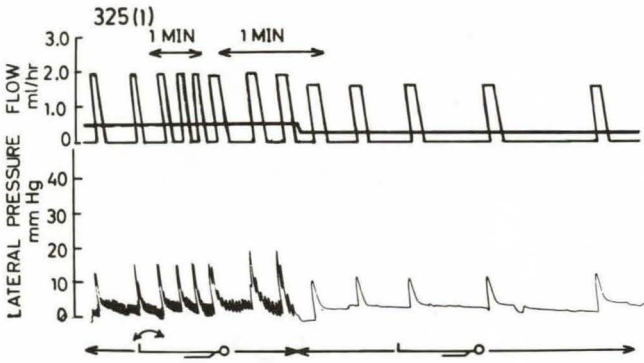


Fig. 5 Same legend as to Fig. 4

Changing from the horizontal to the upright position did not cause any elevation of the end systolic or diastolic pressures. The mean end systolic pressure in 10 investigated men was  $44.7 \pm 19.0$  mmHg. The pulse frequency rose slightly. Raising on the toes had no effect on the systolic or diastolic pressures, however, it increased pulse frequency. It can be inferred from our observations that in an obstructed lymph collector the maximum pressures generated by intrinsic contractions, are about 50 mmHg. The contracting segment of the lymphatic vessel will not be able to propel lymph if the pressure in the proximal segment exceeds that level.

Lymphatic pulsation is a permanent process. We recorded in 4 normal men the end pressures continuously over a period of 18 hours. The frequency of pulsations decreased during the first hour, later it began to rise, and in one case there was continuous pulsation without resting intervals.

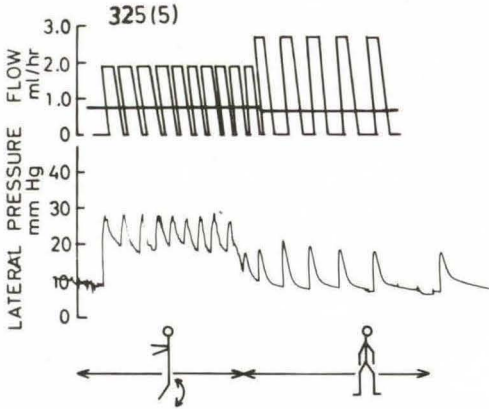
Voluntary stopping of respiration did not affect the pressure pattern, neither did the elimination of pulsation. These findings support the notion of an autonomous mechanism of lymphatic contractility. Appearance of pulse waves after intralymphatic fluid injection or downstream massaging of lymph vessels strongly suggests that the spontaneous contractility is myogenic in origin.

Lateral systolic pressures (with free flow) in a horizontal position at rest, were considerably lower than the end pressures (Fig. 5).

They ranged between 7 and 30 mmHg with a mean of 13.5 mmHg. The diastolic pressures were usually 0 mmHg, mean 8.8 mmHg, and the pulse frequency 0.6–6/min, mean 2.4/min. Foot and muscular contractions in the horizontal position did not cause any significant rise of mean diastolic pressure, however, the pulse amplitude and frequency increased evidently. Changing from the recumbent to the standing position did not bring about any rise in the systolic or diastolic pressures. An increase in pulse frequency has occurred. Raising on toes was followed by a rise in systolic but not diastolic pressure, from a mean of 15.2 mmHg to 23.8 mmHg, and an evident acceleration of pulsation with relatively high pulse amplitude. The muscle contractions of the foot did not generate any significant lateral lymph pressures.

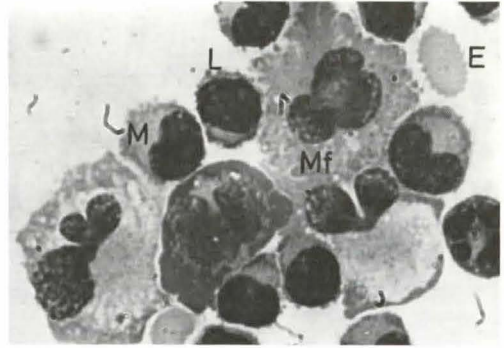
Lymph flow occurred during rest of the extremity as well as during foot and leg movements only when the intrinsic pulse waves were observed. There was no flow in the periods between pulse waves (Fig. 6). The pressure waves produced by limb muscular contractions had an amplitude of 1–3 mmHg and were too weak to produce any lymph flow. The stroke volume of pulse remained at rest in a recumbent position as well as upright position within limits of 1–2 ml/hr, during contractions of leg muscles it had a tendency to rise slightly.

As already mentioned, contractions of foot and calf muscles did not produce any movement of lymph in calf vessels. Lymph flow



**Fig. 6** Intralymphatic lateral pressure tracings and lymph flow rate in a normal man in an upright position during raising on toes and resting. Mean pressure, pulse frequency and mean flow higher during movements than the following resting period. For details see Fig. 5 (23).

occurred, as in rest, only during intrinsic contractions of lymphatics. The volume of lymph transported along the superficial system in a human lower limb can be roughly estimated to approximately 120 ml/24 hours. Eighty per cent of that volume flows through the superficial collectors, the rest through the deep vessels. The lack of an efficient transport mechanism of such a volume would result in formation of edema in just a few days. Since this does not happen and the foot and calf muscles do not propel lymph in the superficial collectors, the intrinsic contractions remain the only mechanism responsible for lymph transport in most of the lower limb. However, the mean lymph flow was during muscular contractions higher than during the resting period. This might be due to an increased formation rate of lymph, which in itself would stimulate lymphatic contractions independent from any effect muscle movement may have on massaging lymph along lymphatics. It is also possible, that contracting striated muscles increase the total tissue pressure which is transmitted to the initial lymphatics, thus driving the fluid from these vessels to the more proximal segments. This has been partially proven by us in the group of subjects with external massaging of the



**Fig. 7** Cells in a normal leg lymph. L – lymphocyte, MF – macrophage, M – monocyte, E – erythrocyte (6, 7).

foot, where the external pressure exerted on the tissue had the same effect on lymph flow as muscular contractions.

Filling of the lymphatics with lymph by external massaging or retrograde injection of fluid evoked intrinsic contractions. The pressure threshold for eliciting contractions varied in different subjects. It was interesting to find that intraluminal pressures as low as 5–10 mmHg were sufficient to elicit contractions, which makes the lymph vessels a very efficient transport system of even very small volumes of fluid.

Venous stasis produced by inflation of a sphygmomanometer cuff placed around the thigh to 50 mmHg, brought in most cases a several minutes lasting disappearance of lymphatic pulsations and lymph flow. Warm water bath (42 °C) of the foot caused, within some minutes, an increase in pulse frequency and lymph flow. This was most likely, a result of higher capillary filtration rate and lymph formation, since the local heating of the investigated segment of lymph vessel did not increase the pulse frequency.

#### *Cells in human leg lymph*

Peripheral lymph comprises 80 to 90 percent

of small lymphocytes. The other cells are monocytes, granulocytes and some large lymphocytes (Fig. 7). The cells arise from the blood capillaries. They migrate through the endothelium in the postcapillary venules into the interstitial space and initial lymphatics. Also a certain number of erythrocytes is always found in the prenodal lymph. In contrast to leucocytes which migrate actively through the blood capillary wall, the passage of erythrocytes to the interstitial fluid and lymph must be a passive process.

Our studies showed that there is a great variation in cell output from prenodal lymph in man, depending on the position of the body and physical activity (6). It does not, however, mean that these factors influence the tempo of migration of lymphocytes across the capillary wall. That tempo remains, most likely, stable. The variation in output of lymph cells is rather caused by accumulation of cells in the expanded interstitial space and initial lymphatics and then a sudden evacuation due to action of physical factors promoting lymph flow. According to our studies the mean lymphocyte output in night lymph was  $81 \pm 19 \times 10^3$ /hr, erythrocyte output  $20 \pm 7 \times 10^3$ /hr, monocyte output  $5 \pm 1.2 \times 10^3$ /hr. Granulocytes were present in samples from the first experimental day accounting for 2–5% of all nucleated cells. At later interval granulocytes were not found. During everyday activity the highest output of lymphocytes, erythrocytes and monocytes was observed in the early morning sample when the mean output was 80, 40 and 43 times, respectively, of that of the night. During subsequent walking there was a marked drop in the output of all cell types.

The high output of cells in the morning after getting up, which we observed in our studies, is probably caused by a washout of cells which have accumulated in the lymph space during night rest, when lymph flow is extremely low. The relatively high output also of erythrocytes in these samples showed that some erythrocytes pass through the capillary wall even during the complete rest when physical traumatization of the foot vessels during walking has been eliminated. The mechanism

of the passage of lymphocytes through the capillary wall to the lymph space is probably different from the mechanism regulating erythrocyte passage to the lymph. This is clear from the fact that lymphocyte erythrocyte ratio in blood is less than 1/3000 while the ratio in peripheral lymph is about 4/1. The difference can not be caused by peripheral flow of leucocytes in the blood vessels versus central flow of erythrocytes because the migration takes place in the narrow blood capillaries where both lymphocytes and erythrocytes have a close contact with the endothelium. It must depend on differences in cell properties such as motility and stickiness to the endothelial cell.

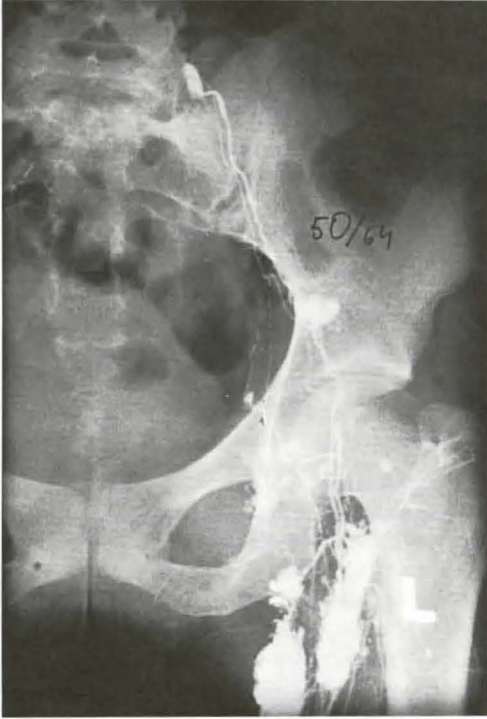
The populations of leucocytes in prenodal lymph in man differ considerably from those of peripheral blood. In lymph, there is a higher percentage than in the blood of E-rosette forming cells, but lower of EA- and EAC-RFC (9). This may indicate that B cells have a limited tendency toward leaving the blood circulation and migrating through the non-lymphoid tissues.

Leg lymph lymphocytes cultures in vitro reveal a high autotransformation rate. They respond more strongly with DNA synthesis to concanavalin A than to phytohemagglutinin, in an opposite way as the blood lymphocytes (8). The natural cytotoxicity of lymph lymphocytes against tumor cells (K562) tested in vitro was found on the average 6 times lower than in the blood (9).

#### *Microsurgical methods of treatment of lymph stasis*

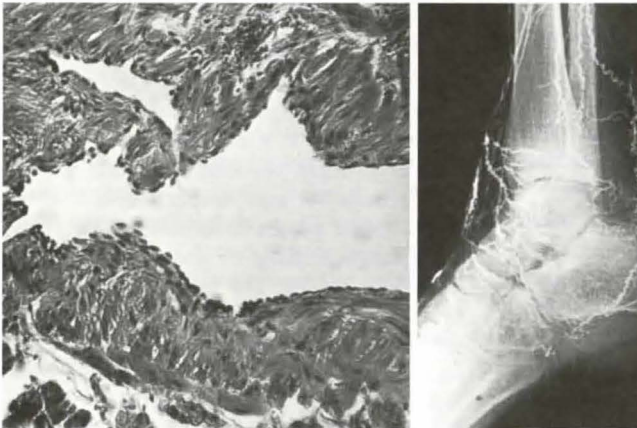
The diagnosis of lymphedema is based on the clinical, lymphangiographic and phlebographic findings. Measuring of lymph pressures and flow is strongly advocated. Among the clinical findings the most important is to establish whether edema is limited to the skin and subcutaneous tissue or also effects the muscular compartment. The latter strongly suggests a venous type of edema. An X-ray picture of soft tissues will allow to measure the thickness of tissues and compare with the normal leg. Thickening of calf subcutaneous tissue





**Fig. 8** Lymphangiogram in a female patient with lymphedema of left lower limb, 2 years after hysterectomy and radiotherapy. Blockage of the contrast medium flow in the pelvis

with a foot of normal shape suggests the existence of lipedema, a condition so frequently mistaken with lymphedema.



**Fig. 9** Lymphangiogram and histological appearance of foot lymphatics in a patient with hyperplastic type of lymphedema. Note multiple, dilated, tortuous lymph vessels. The lumen of the vessel enlarged, thick muscular layer in the wall

### *Lymphangiographic criteria for selection of patients for lympho-venous shunts*

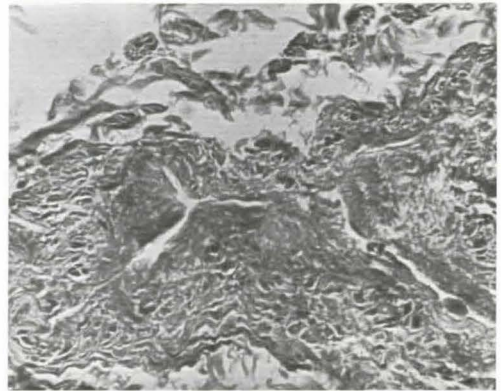
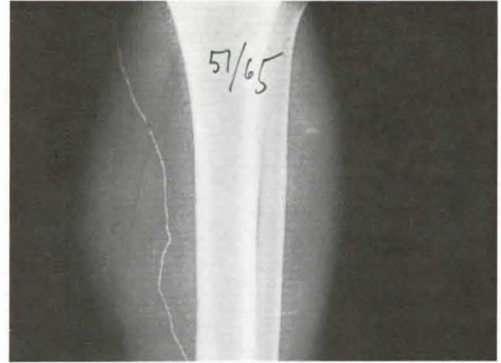
Two to three ml of Lipiodol-U-fluid are injected into the foot lymphatics of each leg. Both legs should be investigated. Not infrequently identical lymphangiographic patterns are found in the edematous and normal legs. This may indicate that lymphedema of the non-swollen leg is in a latent phase (16, 18). Also, an extralymphatic etiology of edema should be taken into consideration of the lymphangiographic pattern reveals only minor changes.

The radiograms should be made: a) on the table immediately after completion of injection, 2) after walking of "100 steps", 3) after 3, 4) 24, and 5) 72 hours. Only patients with: a) an evident block for Lipiodol flow in the pelvis (Fig. 8), retention of the contrast medium in pelvic or thigh lymphatics, dermal backflow in the thigh, collateral circulation in pelvis or thigh, b) dilated and tortuous lymphatics changing their diameter on serial radiograms (contracting!) – typical for hyperplastic type of lymphedema (Fig. 9), and c) radiological signs of chylous reflux (Fig. 10) are suitable for surgical treatment with lymphovenous shunts.

A number of operations of lympho-venous shunt performed in various centers in patients with doubtful indications prompted us to establish the lymphangiographic contraindications for the lympho-venous shunts.



**Fig. 10** Lymphadenogram in a patient with chylous reflux. Multiple large and small lymph nodes in the groin, pelvis and retroperitoneal area. Some stagnant contrast medium in dilated vessels



**Fig. 11** Lymphangiogram and histological appearance of the calf lymph vessel in a patient with the so-called hypoplastic lymphedema. Single, tiny vessel in the calf. On histology a narrow lumen of the vessel with thickening of intima. Accumulation of collagen fibers in all layers. The case not suitable for LNVS

#### *Lymphangiographic contraindications for lympho-venous shunts*

a) A single, tiny lymphatic in leg and thigh (Fig. 11), b) Retention of Lipiodol in the foot and lower leg lymphatics for 24 hours and no contrast medium in the thigh (Fig. 12), c) Network of small lymphatics in the foot and lower leg with contrast medium retention (Fig. 13), d) Tortuous, moth-eaten outline, partly narrowed partly dilated, interrupted lymphatics (postinflammatory changes) (Fig. 14), e) Extravasations of Lipiodol (Fig. 15), f) single, small inguinal lymph node.

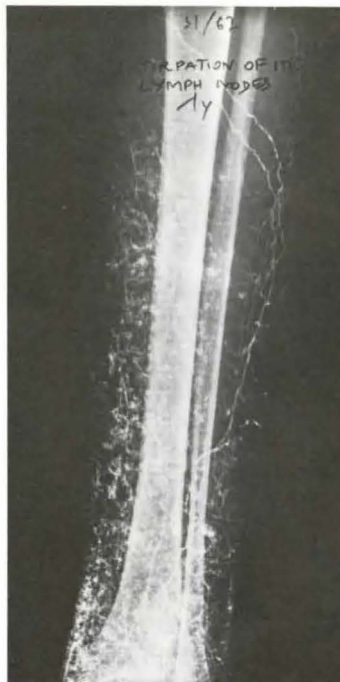
#### *Phlebography*

Phlebography of the lower leg, thigh and iliac vein helps to exclude the venous factors in the pathomechanism of lymphedema.

It should however be remembered that minor phlebographic changes may be observed in around 50% of cases of obstructive lymphedema and 20% of primary idiopathic lymphedema (15). There are also cases of mixed pathology where venous thrombosis increases lymph flow, leading subsequently to an overloading of lymphatics. Infected leg ulcers in time cause secondary changes in lymphatics and lymph nodes (13). Major venous changes are a contraindication to LVS, but every case should be thoroughly evaluated before any decision is made. Thrombosis of the iliac vein, evident hypertension in the femoral vein, and an active thrombotic process in the extremity are contraindicative factors. There is an interesting observation that in cases of chronic deep vein thrombosis the great saph-



**Fig. 12** Lymphangiogram of a patient with hypoplastic lymphedema complicated by lymphangitis. After walking "100 steps" retention of the contrast medium in the multiple, thin, partly interrupted lymphatics of the foot and calf. The case not suitable for LNVS



**Fig. 14** Lymphangiogram of a female patient with postinflammatory lymphedema of unknown etiology. A dense network of filated small lymphatics in the skin. Retention of the contrast medium for several days. The case not suitable for LNVS



**Fig. 13** lymphangiogram of a patient with lymphedema which developed after three operations for congenital hip luxation. Retention of the contrast medium in multiple, tortuous lymph vessels, partly interrupted with uneven outline. Deformities of lymph vessels most likely caused by inflammation complicating lymph stasis. The case not suitable for LNVS



**Fig. 15** Lymphangiogram in a female patient with hypoplastic lymphedema. Single, tiny lymph vessel with extravasations of the contrast medium. Retention of Lipiodol after a "100 steps" test. The case not suitable for LNVS

nous vein remains patent in its proximal part. Some authors have reported successes with LVSs between the superficial inguinal node and the saphenous vein in cases of obstruction of the femoral vein.

#### *Other investigations*

Measuring of lymph pressure and flow seems to be a very promising method in differentiation of lymphedema with other types of limb swellings. It also gives an insight into the pumping capacity of lymph vessels. The intralymphatic pressure pattern allows to evaluate the contractile force of the vessels segment, which might be decreased in a fibrotic vessel. It also helps to evaluate the function of valves. Hydrostatic pressure can not be recorded when the valves are competent, since there is no hydrostatic component in normal lymph vessels. With the valves destroyed the pressure of lymph column from the foot to the thigh will be recorded. The pressure wave by tapping of the proximal segment of lymph vessel is not transmitted in a retrograde fashion unless valves are incompetent. High lymph flows and frequent pulsations characteristic for an excessive lymph production would point to a non-lymphatic etiology of edema, e.g. venous stasis, nephrotic edema etc.

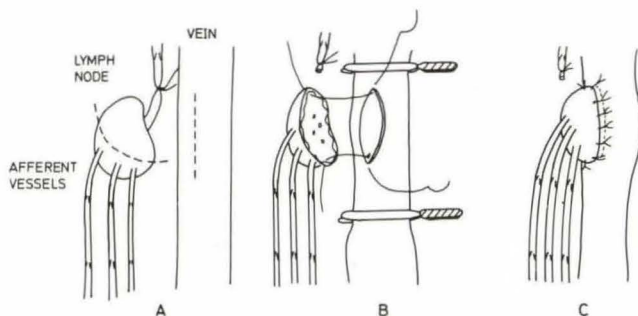
#### *Indications for lymph node-vein shunts in lower limbs*

a) Secondary postsurgical lymphedema of the lower limb: The most numerous group of patients suitable for LNVS has been women after radiotherapy and/or hysterectomy for cancer of the uterus, developing lymphedema several months to years after the treatment. There is usually an obstruction to the lymph flow in the pelvis. The inguinal lymph nodes are not affected by the tumor or radiotherapy. Their sinuses are dilated and the lymphoid tissue undergoes atrophy. Technically, suture of the capsule of the node to the vein is easy to perform. Care should only be taken not to damage any different vessels, which leads to a persistent leakage of lymph into the wound. If the femoral or iliac veins are narrowed or occluded LNVS may be performed with the great saphenous vein.

b) Primary hyperplastic lymphedema of lower limbs: This is a condition affecting young patients at the age of 6–18 years. The whole limb is swollen and on lymphangiography multiple dilated tortuous lymphatics with incompetent valves are seen. There is also a retrograde flow of Lipiodol. The contrast medium may be found in the foot lymphatics even several days after the injection. In many of these patients peristaltic movements of lymph vessels, and in some of them conglomerates of contracting lymphatics may be seen on radiograms (14). On histology there is an evident hypertrophy of muscular fibres of the vessel wall. LNVS in the groin is highly recommended and the long-term results are often good.

c) Chylous reflux to the lower limbs. Diagnosis is made on finding chyle in the subepidermal vesicles or surgically exposed small lymphatics. The operation consists of LNVS or anastomoses of proximal segments of lymph vessels end-to-end with small veins, and ligation of vessels medially and laterally from the site of anastomosis. End-to-end lymphatico-venous shunts (LVS) have also been performed by us in the mesentery.

Only the early, non-advanced cases of lymphedema are suitable for LNVS. The difference in lower leg circumference should not exceed 8 cm as compared with the normal side or calculated circumference of a normal leg. Patients with a difference in leg circumference of over 8 cm usually reveal major hyperkeratotic, fibrotic and irreversible changes of the skin and are much more suitable for plastic reducing procedures. Good results may be obtained in cases with soft, pitting edema alleviated by night rest. Patients with persistent hard edema have a bad prognosis and are not good candidates for LNVS. Recurrent lymphangitis strongly limits the indications for LNVS. The persistent inflammatory process in the lymphatics brings about major changes in the skin, vessel and nodes. The results of treatment in this group are rather unsatisfactory. Patients should be kept on antibiotic therapy for at least 6 months before any type of surgery is considered. Depot penicillin in high doses is the drug of choice. However, a single incidence of lymphangitis in a patient with an early stage of lymph-



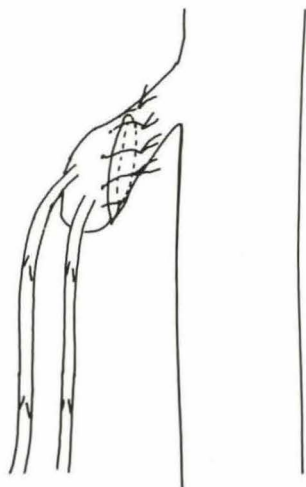
**Fig. 16** Diagram of the technique of a lymph node-vein shunt. For details see the text

edema may be an indication for LNVS. Persistent bursting pain in the swollen leg may constitute an indication for LNVS irrespective of the intensity of skin changes.

#### *Technique of operation of lymph-vein shunt (LNVS)*

Principles of the technique have been presented on Fig. 16 and 17 (11, 12, 25). Some additional points should be mentioned.

- (a) The groin skin should be shaved and disinfected 48 hours before the operation and kept under a sterile dressing until the day of operation.
- (b) Patient should be given depot penicillin at least 3–5 days before the operation and continued every 3rd day for 1–2 months.



**Fig. 17** Diagram of the technique of a lymph node to vein anastomosis, by invagination of the distal part of the cut node to the vein

(c) Special care should be taken during lymph node dissection not to damage the afferent lymph vessels and the lymph node capsule.

(d) Blood supply to the lymph node should be preserved.

(e) The lymph node should be cut transversely across its long axis between the first distal and second third.

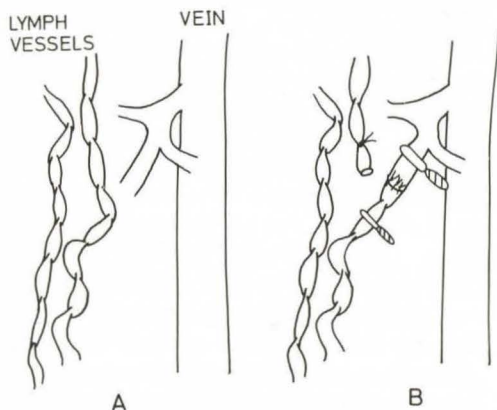
(f) Care should be taken to avoid kinking of the vein at the time of its mobilization. Only the anterior wall of the vein should be made free.

(g) Delicate vascular clamps should be used to avoid vein wall damage. After venotomy the lumen of the vein should be rinsed with heparin saline solution, the distal and proximal segments of the vein must also be filled with heparine saline.

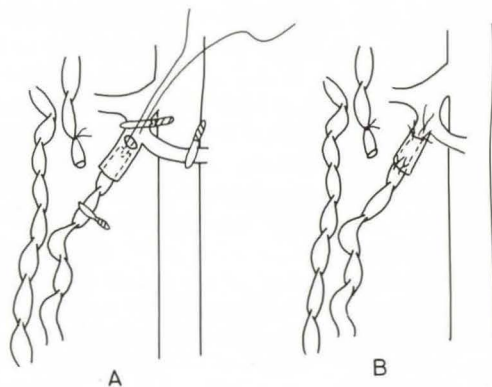
(h) Bleeding points on the cut surface of the lymph node must not be coagulated, as this procedure may obliterate lymphatic sinuses.

(i) Only the capsule of the node without parenchyma should be stitched to the vein wall, interrupted 6–0 or 7–0 Dexon being the most suitable suturing material. Absorbable polyglycolic acid sutures produce less foreign body reaction than the non-absorbable ones. This is of a great importance for avoiding the narrowing or even closure of the lymphatic anastomoses. An operating microscope and magnification  $\times 8$ –12.5 during dissection and suturing should be used.

(j) After release of vascular clamps a slight massage of the distal part of the limb should be instituted to increase the lymph flow through the anastomosis.



**Fig. 18** Diagram of the technique of a lymph vessel-vein end-to-end anastomosis. Only large lymph vessels are suitable for this type of shunting. A 7-0 or 8-0 Dexon interrupted suture with curved tape needle used. The operation can be performed in the groin, iliac region and even the mesentery



**Fig. 19** Diagram of the technique of lymph vessel to vein anastomosis by invagination of the lymphatic into a small vein. For fixing the vessel and sealing off the anastomosis absorbable 7-0 Dexon sutures used. A, B-stages of the operation

(k) Systemic heparinization is contraindicated because of bleeding from the suture line. Thrombotic complications have, so far, not been observed.

(l) All bleeding points in the wound should be ligated or coagulated to avoid hematoma formation. Suction drainage of the wound should be instituted for 48 hours.

(m) Elastic stockings or bandage should be put on the operated limb immediately after completion of the operation. Ambulation as soon as the patient awakes from the anesthesia is indispensable. Walking increases the lymph flow and prevents blood stasis in the veins.

#### *Lymph vessel-vein shunt (LVS)*

According to our experience, this type of anastomosis should be performed in cases with dilated lymph vessels, easily dissected (chylous reflux, hyperplastic type of lymphedema), or when no suitable lymph node is available. Clinical and lymphangiographic indications, as well as contraindications are the same as for lymph node-vein shunts. Two types of operative techniques have been presented on

Fig. 18 and 19. One is an end-to-end anastomosis of dilated lymph vessel with a vein of the same caliber. To avoid a stricture at the site of anastomosis, a short tubing can be inserted into the lymph vessel and vein for the time of suturing and removed immediately before completion of the anastomosis through an incision in the proximal part of the vein.

Technically more simple is the procedure of invagination of the lymph vessel into the vein. Tension should be avoided. Sutures sealing the gap between the lymph vessel and vein should not go through the whole cross section of the wall. In all types of LVS a special care should be taken not to deprive the lymph vessel of its blood supply (!). The lymphatic vasa vasorum can easily be seen under magnification.

Other types of LVS (1, 2, 10) have been presented in this issue in an article by *Degni*.

#### *Postoperative evaluation and long-term results of surgical lymphovenous shunts*

The following parameters should be taken into account in evaluation of the results of LVS: (a) foot, leg and thigh circumference; (b) alleviation of leg pains; (c) decreased limitation of

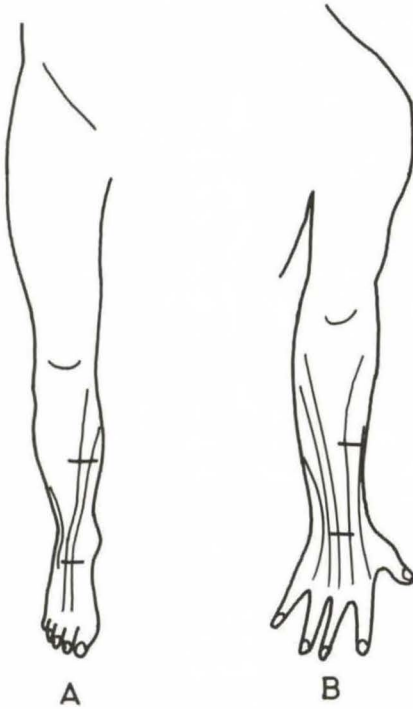


Fig. 20 Sites of cannulation of lymph vessels in the lower (A) and upper (B) extremity

movements in knee and ankle joints; (d) decreased incidence of lymphangitis. A follow-up period not shorter than 6 months is necessary for the primary assessment. A favorable cosmetic result with a visible decrease in leg circumference is what the surgeon intends to achieve. One should however remember that the usual sequela of lymphedema is skin and subcutaneous tissue fibrosis. These changes are irreversible. Thus, a slight decrease in circumference with disappearance of leg pains and no recurrence of lymphangitis may be considered a good result. So, in evaluation of results all the above-mentioned parameters together should be taken into consideration.

#### *Cannulation of lymphatics of human extremities*

Indications for cannulation of lymphatics of extremities are: (a) measuring of lymph pressure and flow for establishing the diagnosis of lymphedema and differentiation with other

types of edema (b) intralymphatic infusion of drugs in certain types of tumours, (c) collection of lymph for cellular studies in neoplastic diseases, (d) collection of lymph for studies of kinetics of drug distribution in the extravascular space. The lymph obtained from the extremity is suitable for physiological investigations as it originates from a rather homologous tissue, the influence of physical (capillary and venous pressure, external pressure, temperature), nervous and hormonal (nervous stimulation, hormones, drugs), and immune (infection, antigenic stimuli) factors on water and protein transport as well as cell migration can be studied. It should be pointed out that collection and *in vivo* studies of lymph and interstitial fluid must be carried out under uniform and strictly defined conditions. Factors such as location of the tissue from which fluid is derived in regard to heart level metabolism, passive and active movements of the tissues, ambient temperature and the temperature of the tissue itself, local and systemic nervous stimuli, drugs, water and electrolyte balance, and trauma, even the time of the day, may considerably affect the volume and composition of lymph and interstitial fluid.

The method for cannulation of lymphatics of the leg has been worked out by *Engesal et al.* (3). *Olszewski* cannulated thigh and foot lymphatics in patients with pathological alterations of the peripheral lymph vessels. Lymphatic cannulation can be performed in connection with lymphography, extra surgical intervention is then not necessary. Leg lymph can be easily obtained by cannulation of the superficial lymphatic trunks on the dorsum of the foot medial group of calf vessels, in the thigh and groin. For chronic cannulation, however, the lower part of the calf seems to be most suitable (Fig. 20).

After injection of Patent Blue in the same way as for routine lymphography, the lymph vessel is exposed. Patent Blue coloration of the lymph may, however, influence the results of biochemical studies when the colorimetric methods are used; lymph cells may also be damaged. It is preferred to use no dye if lymph composition studies are planned. With experience lymphatic trunks can be

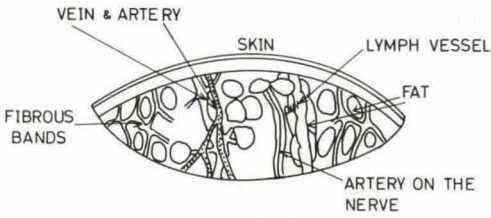


Fig. 21A

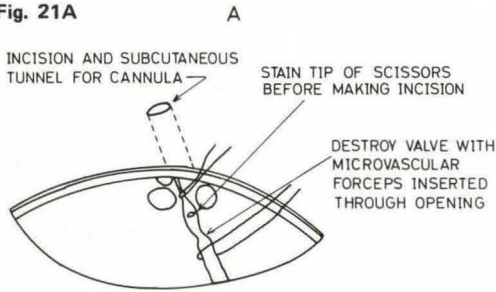


Fig. 21B

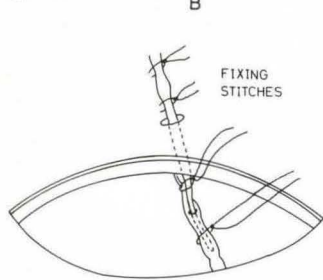


Fig. 21C

**Fig. 21** Diagram of the technique of cannulation of lymphatics in human extremities. A, B, C-stages of the operation. For details see text

found easily, without coloration. The cannulation is carried out under strictly sterile conditions. Skin is anesthetized with 1% Xylocaine, and a 2 to 3 cm long incision made at the front aspect of the calf about 15 cm above the ankle. The largest lymph vessels can be found deep on the muscular fascia. The vessel is exposed, an opening made and a sterile, siliconized polyethylene Clay-Adams P60 tube with a conical tip, filled with heparin saline solution is inserted distally (Fig. 21). Contamination of the tube tip with wound content should be avoided in order to prevent formation of clot in the tube after it has been introduced into the lymphatic vessel. A fine thread

is put around the vessel containing the tube and tied gently so that lumen is not occluded. The tube is additionally fastened to the surrounding tissue in the wound with 1 to 2 sutures. Another tube can be inserted into the proximal portion. The wound is closed and the tube fixed to the skin with adhesive tape. The external tip of the tube is inserted into a sterile disposable syringe through its needle outlet. The plunger is displaced distally so that the whole syringe can be gradually filled with lymph. The use of syringes has the advantage over the other methods because it protects the sterility of lymph and allows accurate measurement of volume in the course of collection. The danger of lymph evaporation is also avoided since the tube almost occludes the needle outlet of the syringe. According to the requirement, heparin solution, culture media etc. can be placed in the syringe. The syringe is fixed to the leg with adhesive tape. Patients are allowed to walk and there is practically no danger that the tube will slip out. Collection of lymph can be carried out continuously for several days. Special care should be taken to avoid contamination of the wound and tube during the change of syringes. The temperature of lymph collected in syringes fixed to the calf skin is 27 °C to 31 °C. Cannulation of the upper limb lymphatics is practically the same as that described for the lower limb.

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