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SUMMARY

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Comparative aspects concerning skin healing in patients with primary lymphedema (PL) and postthrombotic syndrome (PTS)

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ABSTRACT

Normally, healing of the skin wounds is more difficult on the inner part of the calves, compared to other areas of the body. A coexisting PTS makes the healing of this region even more difficult than normally.

We have studied and compared, from the clinical point of view, the healing of the skin on the inner aspect of the calves in 20 patients with PL (who previously underwent lympho-venous anastomosis in this area) and in 25 patients with PTS (on whom the COCKETT ligation of the veins was performed).

The skin wounds healed after 5 days in patients with PL ; in patients with PTS, some unhealed spots were still present after 12 days. Almost 80 % of the wounds in PL regions led to keloid scars. We noted important morphological differences between the aspect of the skin in the PL and PTS patients : thickness, trophicity, vascularisation, hair, etc., they all explain the specific features of healing.

When impairement of the lymphatic circulation on the affected side occurs in patients with PTS (following reiterated erysipelas, inguinal adenitis, etc.), the ulcers of the inner aspect of the calves heal rapidly.

RÉSUMÉ

Normalement, la guérison de plaies cutanées est plus difficile au niveau de la face interne des jambes que de toute autre région. Un syndrome postthrombotique (SPT) coexistant peut entraîner des difficultés supplémentaires en ce qui concerne la guérison locale.

Nous avons étudié et comparé du point de vue clinique la guérison cutanée au niveau de la face interne de jambes chez 20 patients avec lymphœdème primaire (LP) (qui ont été auparavant le sujet d'anastomoses lympho-veineuses pratiquées dans cette région) et chez 25 patients avec SPT (qui ont été soumis à une ligature veineuse selon COCKETT).

Les plaies cutanées ont guéri en 5 jours dans le cas des patients avec LP, alors que les patients avec SPT présentaient des endroits non-épithalisés après 12 jours. Environ 80 % des plaies situées dans la région du LP ont guéri avec des cicatrices keloïdes. Nous avons remarqué des différences morphologiques importantes de l'aspect cutané en LP et SPT : épaisseur, trophicité, vascularisation, pilosité, etc. Ces différences expliquent les traits principaux de la guérison.

Quand un trouble lymphatique survient sur la région malade d'un patient avec SPT (après érysipèle récidivant, adenites inguinales, etc.), les ulcères de la région interne des jambes guérissent rapidement.

Key words : lymphoedema, leg ulcers, relapsis, erysipelas, keloid scars.

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INTRODUCTION

Large shank skin lesions healing is difficult even in healthy people. Shank skin scarring in patients with venous diseases of this region is much more difficult. In the presence of such venous diseases, trophical and hypodermal disturbances are represented by pigmentation and thickening of skin, thick and rarefied hair, hypotrophy of skin and subcutaneous tissue, shank ulcerations and appearance of enduring subulcerative hypotrophic processes. In such conditions, almost any wound has a difficult cure, even with a correct and competent medical assistance : recumbency (with decreases venous pressure), compressive bandages in orthostatic position (which intends to achieve the same purpose), general and local antiseptics, vasodilatatory drugs (Pentoxifiline), etc.

MATERIAL AND METHOD

Over a periode of almost 3 decades (1963 - 1992), we have studied healing ang skin aspects in more than 1000 patients with PL of the inferior extremity, about 200 patients with secondary lymphedema of the inferior limbs, 150 patients with secondary lymphedema of the upper limbs and more than 400 patients with PTS, shank ulcerations and advanced trophical disturbances. We have used clinical examination, phlebographical, lymphographical and morphological examinations, studies of the composition

of edema liquid, of the resorption of labelled macromolecules, etc. From this large and polymorphous number of cases, we have selected for presentation 20 representative patients with PL (6 male, 14 female - 4 having large and sinuous lymph vessels (Fig. 10) with stasis (Fig. 11) and the other 15 having reduced number of lymph vessels (Fig. 12) and 25 patients with PTS (Figs. 1, 2, 3, 4, 5, 6). We have operated the selection according to the period of evolution and patient's agreement to the experiment. During the last period of time, we have also studied shank skin healing in patients with chronical venous failure, where the healing of leg ulcusses on the internal aspect of the calf is difficult and ephemeral. We have observed a group of 5 patients in whom a lymph-flow disorder (involving regional lymphnodes) was added to the chronical venous failure. Lymph-flow disturbances were due to prolonged festering in thigh. Though edema worsened, we noted an improvement in the evolution of shank ulcusses, which healed more rapidly and for a long time as well as an improvement in skin trophicity and hyperpilosity (Fig. 13). As the local lymph-flow recovered, edema decreased, but the hypotrophic ulcusses also relapsed. Such improvement in skin trophicity in patients with chronical venous failure correlated to an increase in edema volume was noted after several episodes of relapsing erysipelias, as well.

RESULTS

Clinical observations are presented in the near-by pictures (Fig. 1, 2, 3), and are expected to confirm the following hypothesis : in lymphedema patients, healing occurs with hypertrophical scars (Fig. 14). In lymphedema, patient shank ulcusses do not appear ; in chronical venous failure patients, the healing of shank ulcuses takes place in a slow and difficult manner.

The interstitial liquid proteins were below 7,7 g/1000 in PTS patients and over 50 g/1000 in PL patients.

Lymphangiographically, we observed 2 kinds of aspects in PL patients : large, sinuous and varicous lymph vessels in which lymph and Lipiodol last for days and weeks in 10 - 15 % of cases (Fig. 10, 11) and another kind of patients with thin lymph vessels in reduced number including a subgroup of about 20 - 30 % of cases in which we did not identify lymph vessels on the dorsal side of the foot. The most suggestive aspects appear in several cases with huge lymphedema developed on skin graft, 15 years after the operation (Fig. 15, 16), cases in which we have removed all the subcutaneous tissue and aponevrosis and we covered the muscles with split epidermal teguments (removed by dermatome (Fig. 15, 16). Even the cases in which the muscles have been covered with total teguments had an unsatisfactory evolution, with unestethical monstruous aspects, appearing after a longer period (several years) (Fig. 17).

As a first conclusion, we can state the difference between the hypertrophical skin healing in patients with PL and slow, difficult and usually temporary healing of the internal inferior third of shanks in PTS patients. As an unusual observation, we can remember the absence of trophical disturbances on the dorsal side of foot in patients with PTS (Fig. 1, 2, 3) - though at this level we can notice a difficult skin healing as well.

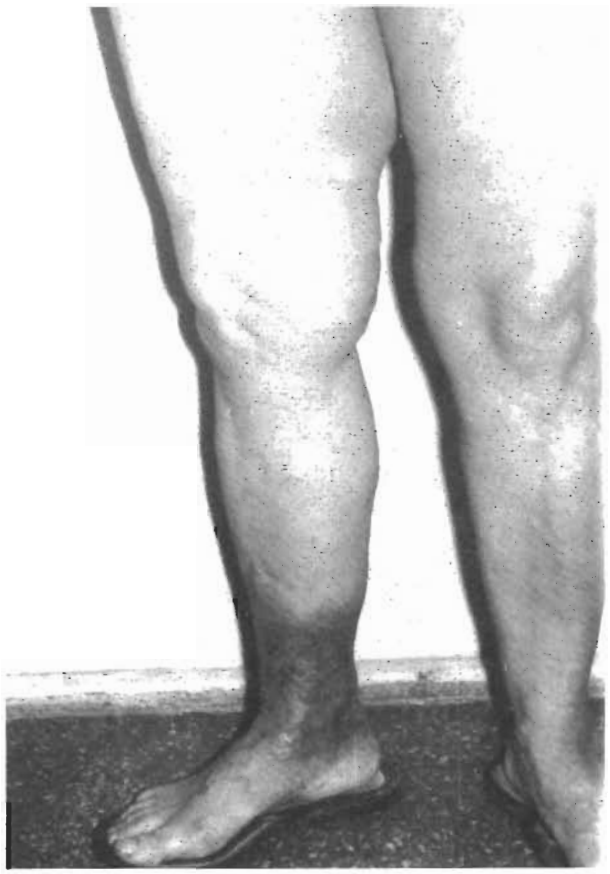


Fig. 1

PTS - leg ulcus.

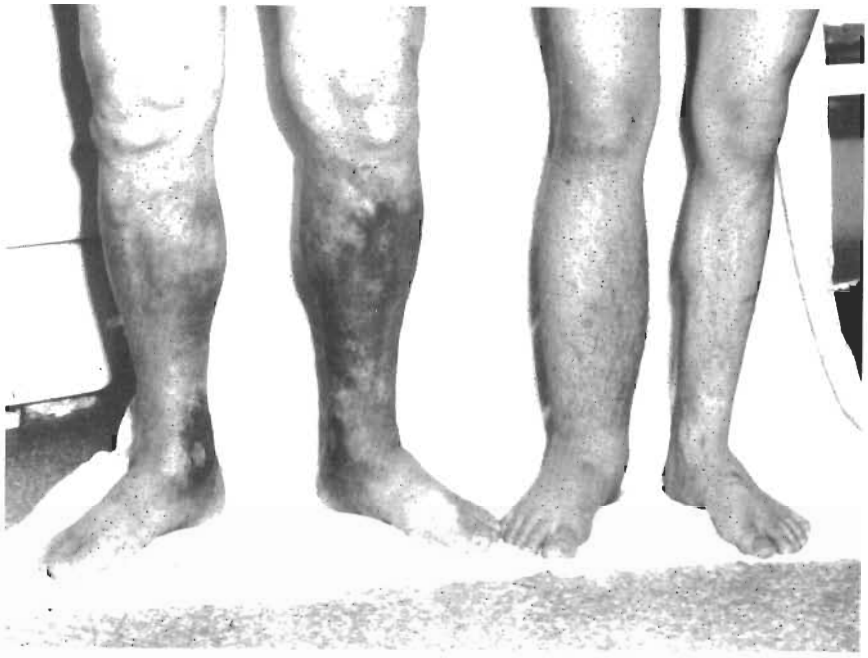


Fig. 2

Clinical aspect of PTS and PL (front view).

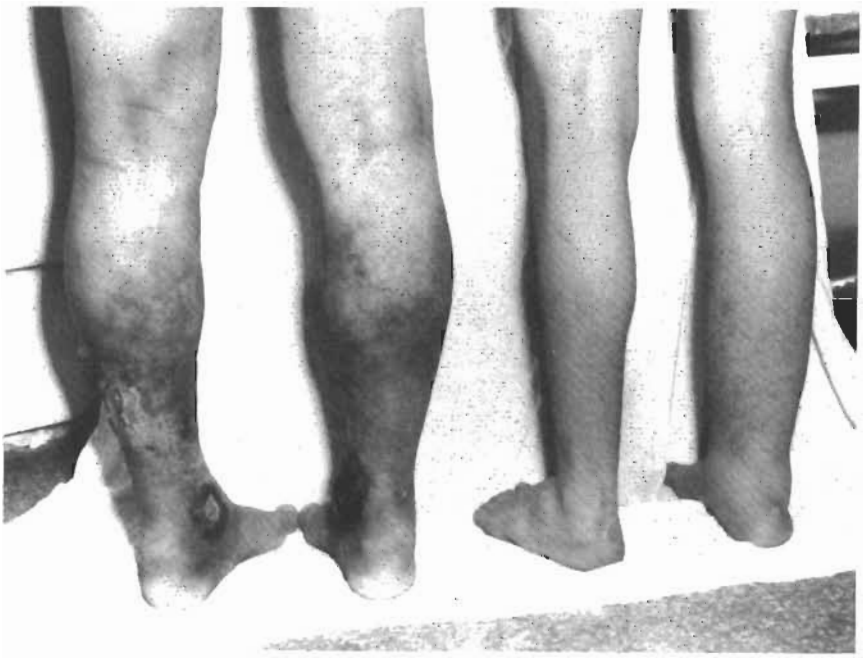


Fig. 3

Same aspect (backside).

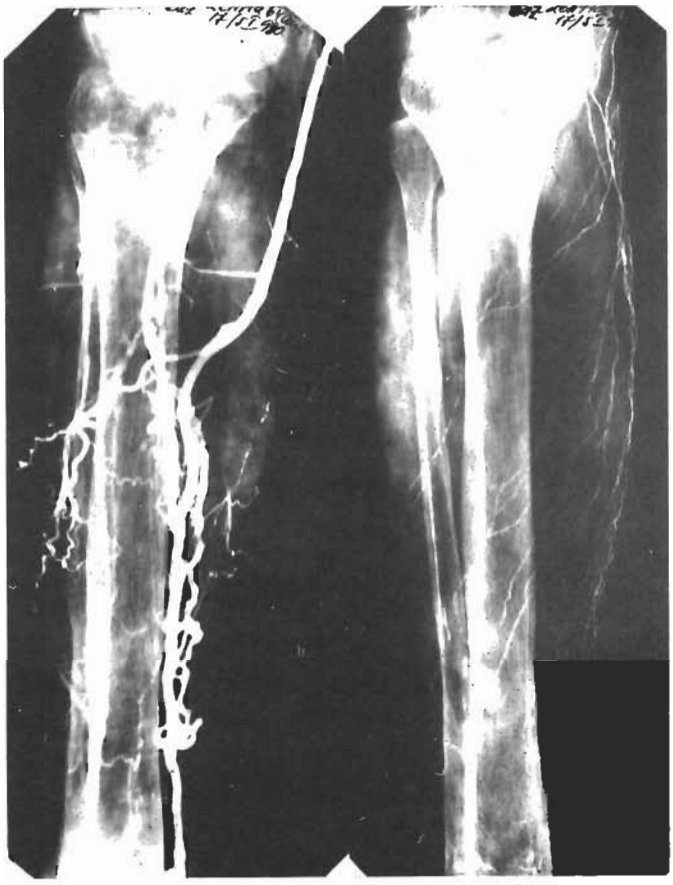


Fig. 4

PTS - Phlebography, lymphangiography in shank (disturbances in lymphvessels in the vicinity of the leg ulcus).

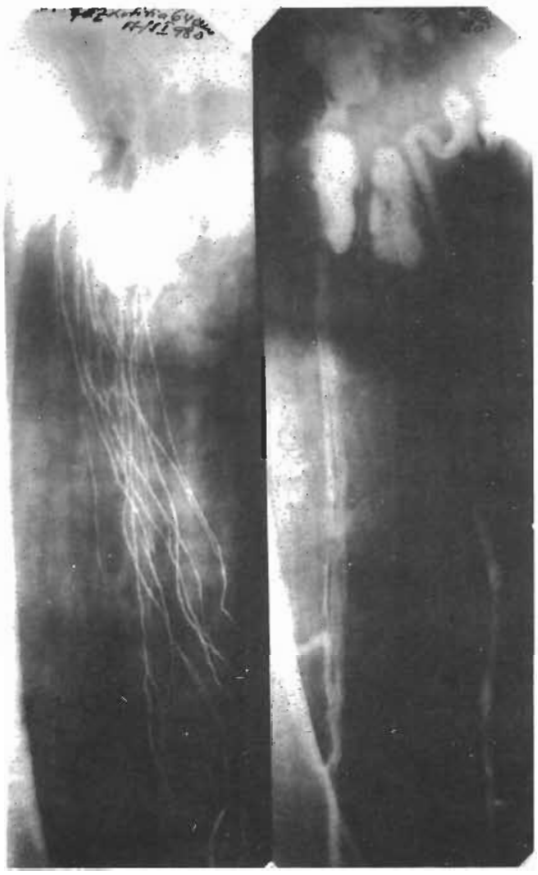


Fig. 5

PTS - Thigh lymphography (a triple number of vessels are opacified, there is no lymphostasis) - Phlebography.

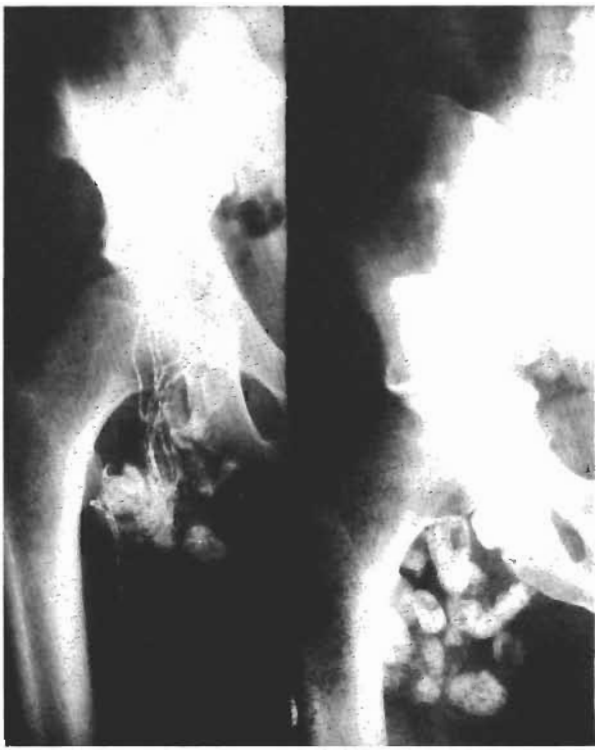


Fig. 6

PTS - precocious and belated lymphangiography - lymphonodal hypertrophy without lymphostasis.

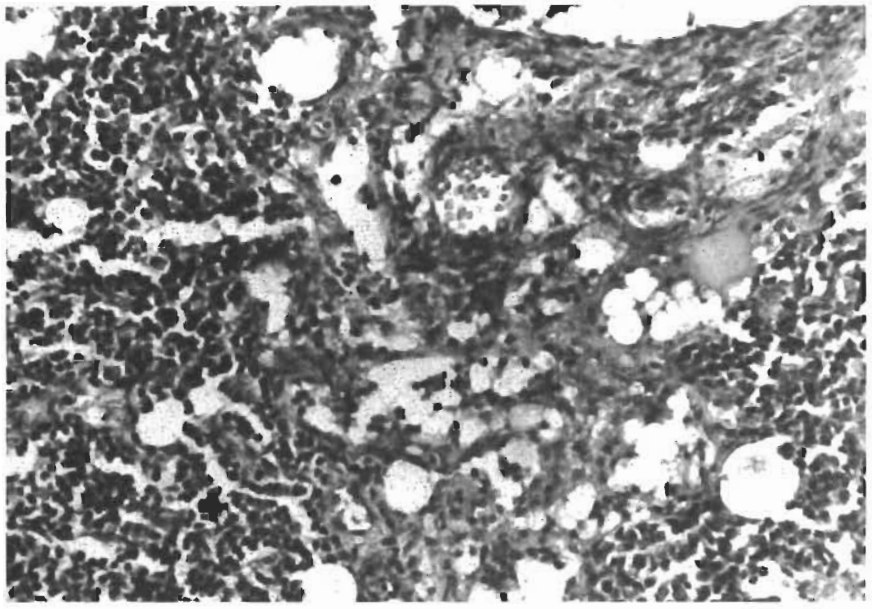


Fig. 7

PTS - Morphopathological exam (MPE) inguinal lymphnode hypercellularity.

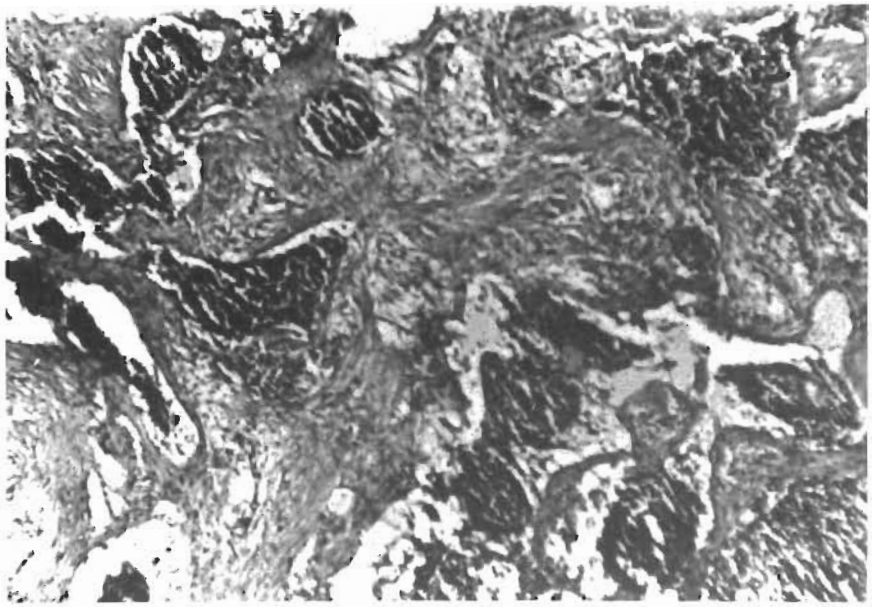


Fig. 8

Lymphnode MPE - fibrosclerosis hypercellularity in the absence of any blockage.

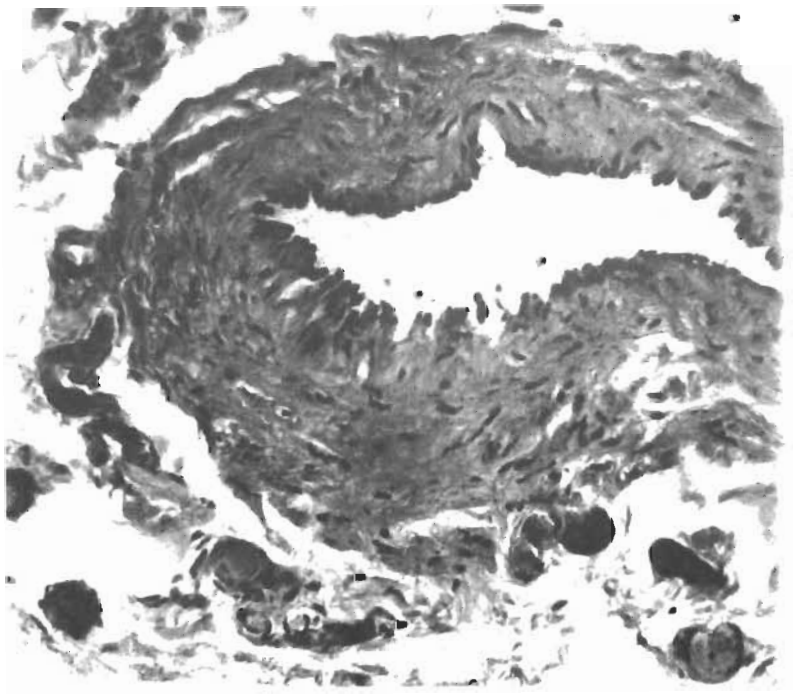


Fig. 9

PL - Lymphvessel MPE - monstruous fibrosclerosis.

DISCUSSION

Primary lymphostasis is always located (Fig. 2, 3, 9, 10, 11, 12, 14, 15) and presents 3 main lymphangiographical aspects (8, 3) :

1) large, sinuous lymph vessels with prolonged stasis and massive parietal alterations (Fig. 8, 9, 10, 11) ;
2) thin, rare lymph vessels with a medium volume edema ;
3) lymphedema with lymphangiographically undetectable lymph vessels in the affected region (lymphedema which develops usually to a large volume, similarly to one of the first category).

Lymphangiography is an invasive exploration method, without therapeutical effects, except for the cases in which in the same operation, a lympho-venous termino-lateral anastomosis is performed (7). We consider that ultrafluid Lipiodol lymphangiography did not reveal yet all its pathogenic secrets.

Cases in which we cannot identify lymph-vessels on lymphangiography may present alteration of the anchoring filaments of lymph capillaries to the connective tissue cells or other elements of this tissue.

The high, abundant protein concentration in the interstitial fluid is responsable for generating the hypertrophical keloidal healing (Fig. 11, 12). The hypoproteic edema generates healing by hypotrophic scars (Fig. 6, 7). Deep hypotrophical hypoderma fibrosclerosis generates atone ulceration, which are difficult to treat and have very ephemeral therapeutical results (Fig. 1, 2, 4, 5, 8, 9, 10).

These essential differences in skin trophicity between patients with PL and PTS have a double background : lymphatic pathology generates hypertrophic scars, hyperpilosity, monstruous, keloid scars (Fig. 2, 14, 16, 17), while venous pathology generates hypoplasy of skin (involving derma, hypoderma), of hairs, and a hypotrophical fibrosclerosis in hypoderma (Fig. 1, 2, 3).

The absence of trophic disturbances on the dorsal region on foot in patients with PTS seems to be contradictly (Fig. 1, 2, 13). Histo-angeic trophicity on the dorsal region of foot is not significantly altered, as it is on the inner side of shanks, where the histo-angeic complex is deeply affected by disturbances considered as secundary to an increase in the hydrodynamic pressures (1, 2, 5, 9). We consider that these statements made by mechanicists do not bear a strong enough physiopathological support. A blockage in the transmission of hyperpressure from the underfascial sector in the superficial subcutaneous sector gives unsufficient results. Compressive bandages seem to provide a subcutaneous hystoangeical compensation which cannot be generated by recumbant positions aiming to the improvement in the venous flow and in the edema (10, 4, 3).

As a conclusion, we can affirm that a hyperproteic edema generates skin healing in conditions of subcutaneous massive fibrosclerosis. In antithesis, the skin of PTS patients remains hypotrophical even after the improvement of the hypoproteic edema. The hypodermal changes are also different in both of these diseases, lymphatic and venous.

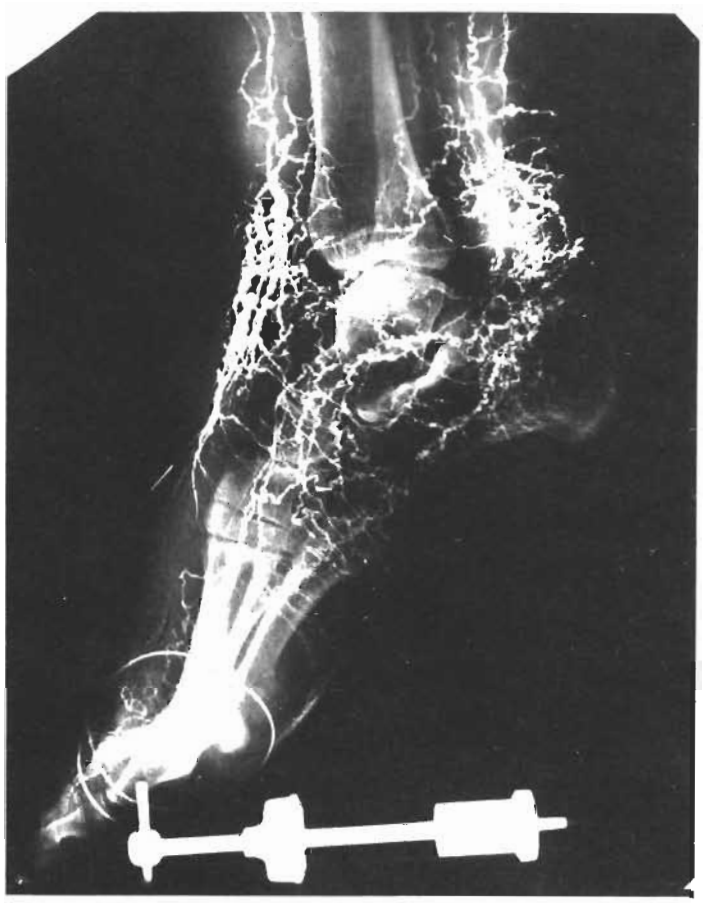


Fig. 10

PL - Lymphangiography - large number of opacified lymphvessels with backflow hyperplasic vessels.

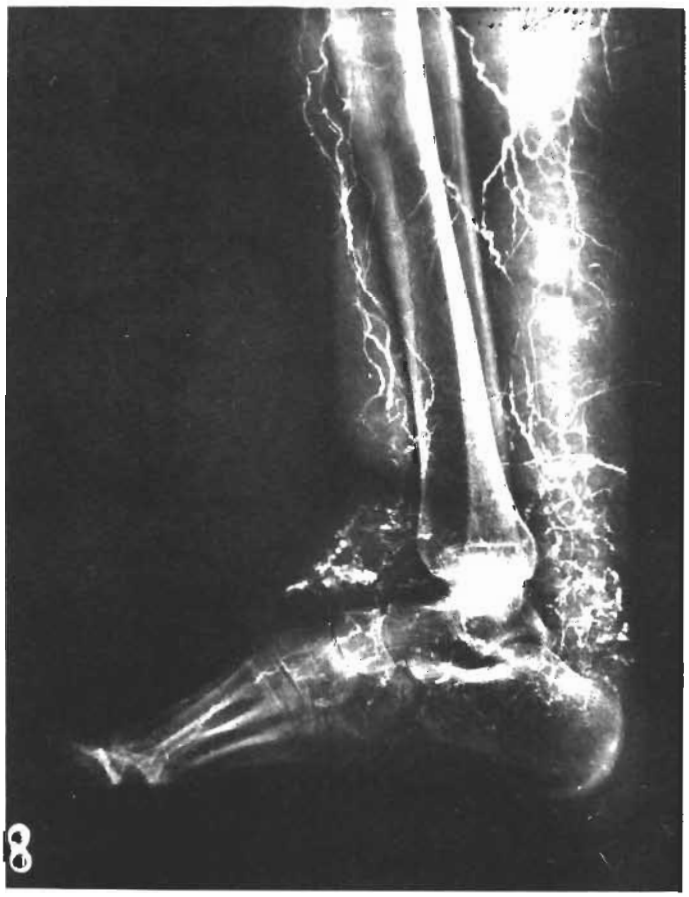


Fig. 11

PL - Lymphangiography of the case in fig. 10 performed 72 hours after the injection of dye : distal lymphostasis without lymphonodal blockage.

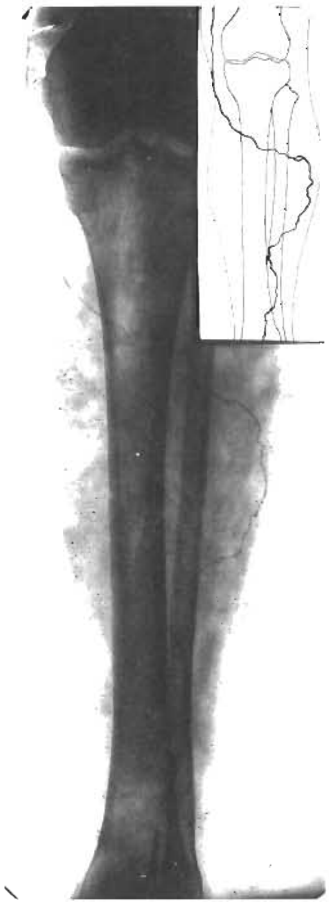


Fig. 12

PL - Lymphangiography - hyperplastic aspect.

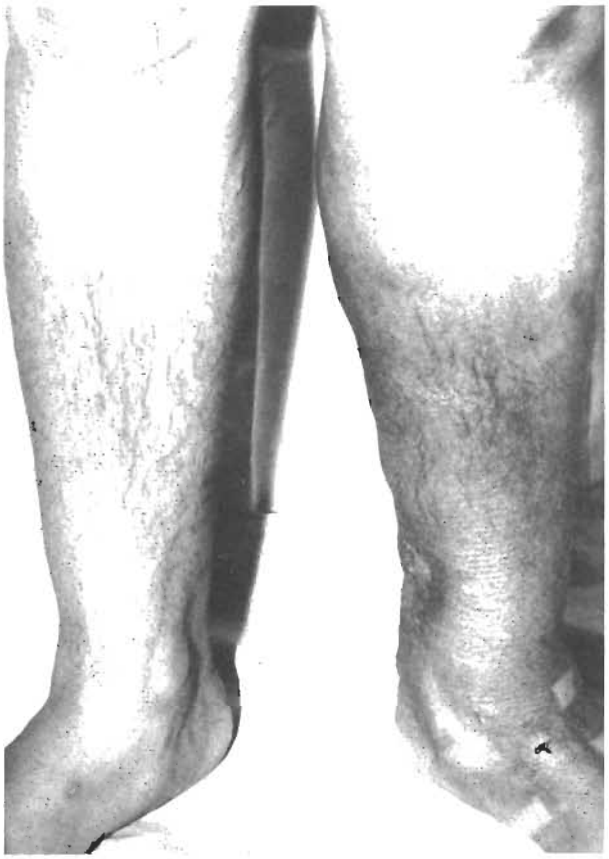


Fig. 13

In PTS patients who had erysipelias, skin becomes thicker, hair grows both thicker and more dense, leg ulcusses heal, edema becomes more voluminous.

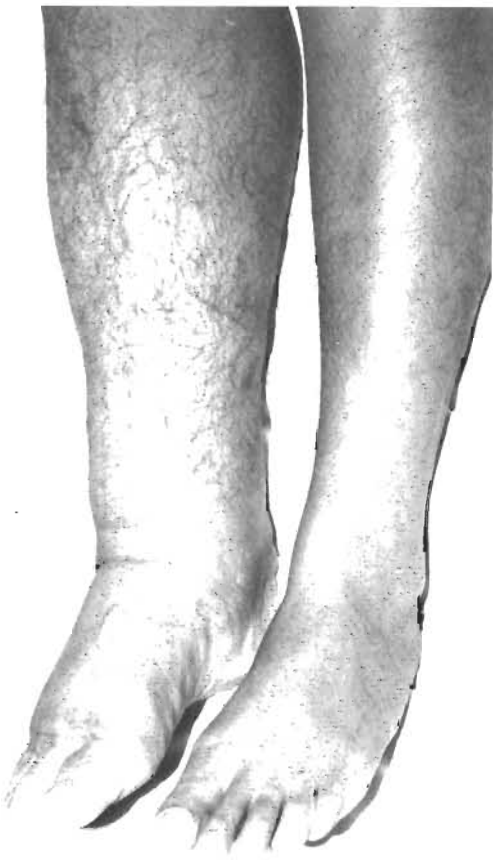


Fig. 14

PL - Clinical aspect : hair, hyperthropical scar, hard edema, etc.

Fig. 15

Clinical aspect of an elephantiasis after cutaneo-subcutaneous excision and split-skin graft.

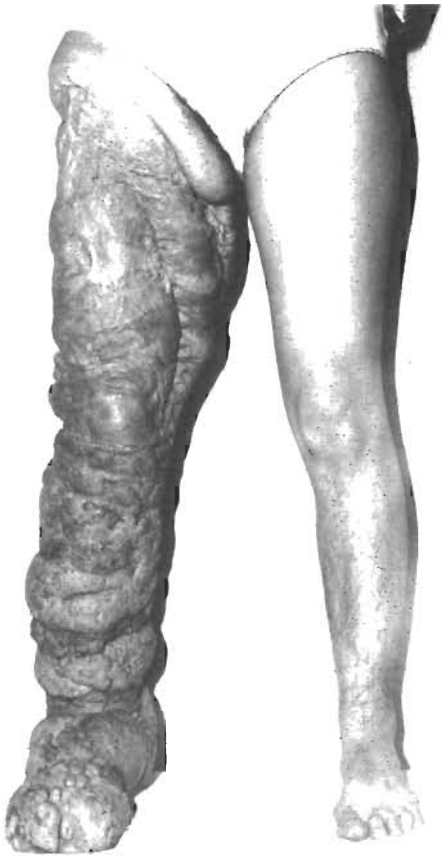


Fig. 16

Some cases. 10 years later - monstruous hyperkeratosic scarring.

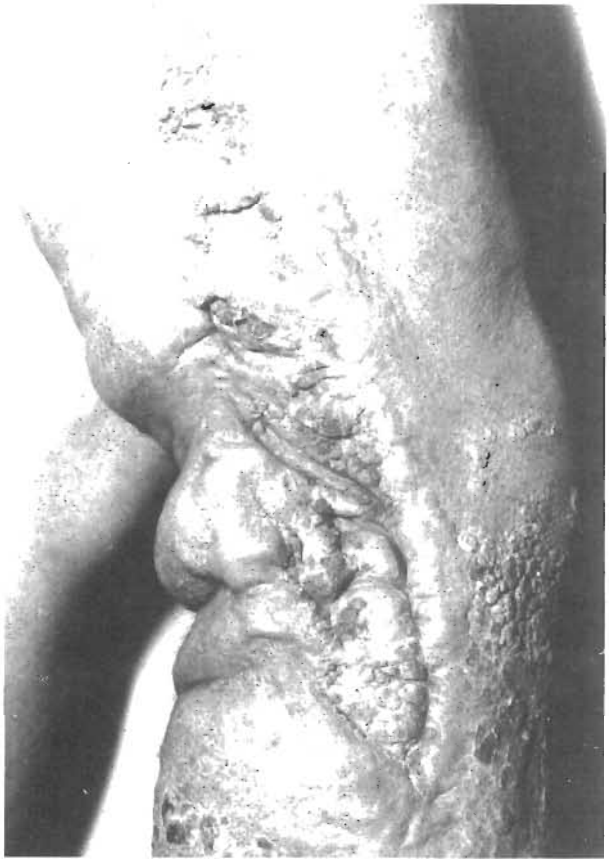
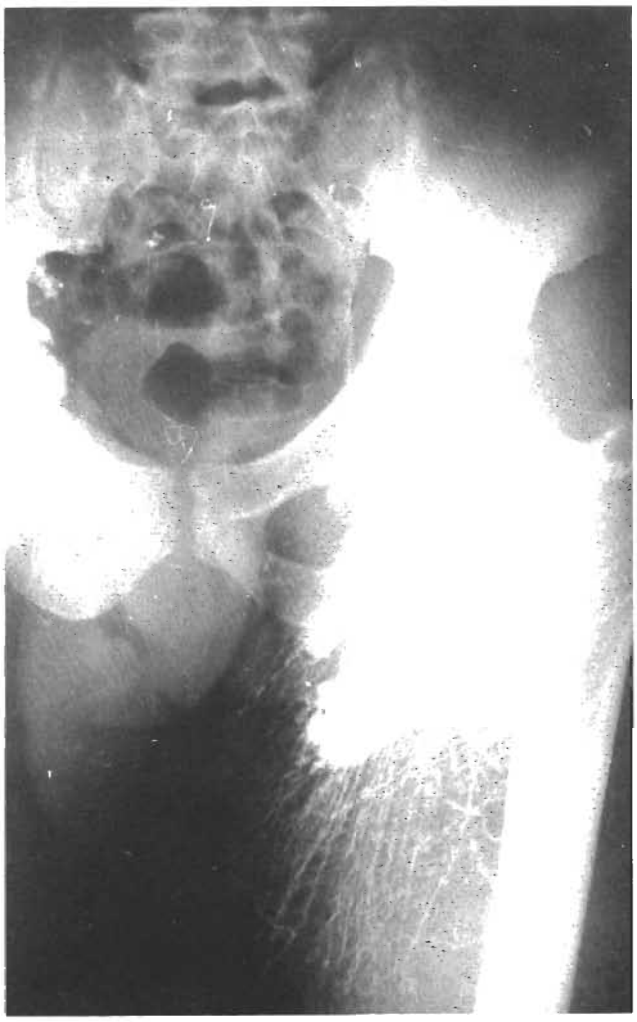
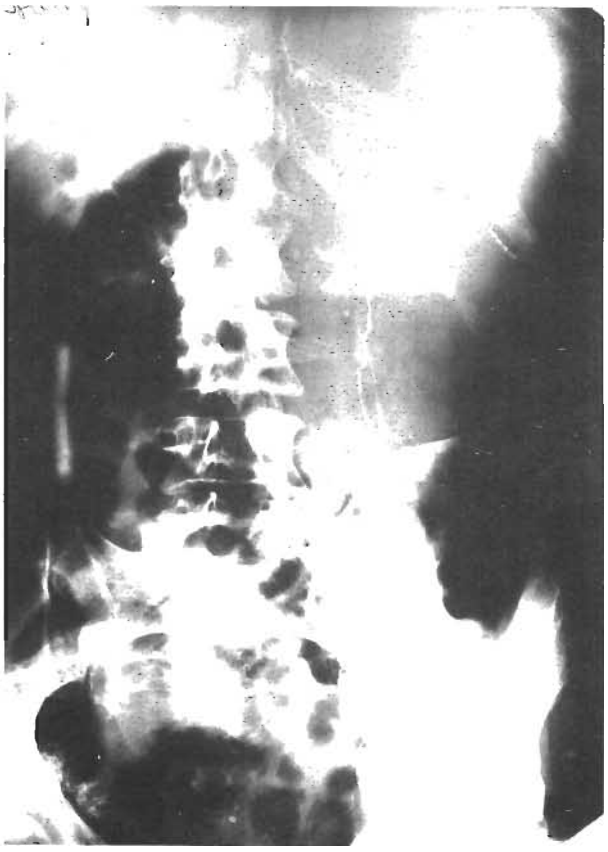


Fig. 17

Monstruous hyperkeratosic scars on suture line 8 years after Servelle operation.





▲ *Fig. 19 - Colateral lymphatic circulation in presence of lymph-nodal obstacle.*

◀ *Fig. 18 - Secundary lymphoedema (after radiotherapy) - lymphangiography proximal lymphostasis, inefficient collateral circulation.*

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Lymphatic drainage of the upper limb.
Substitution lymphatic pathways.

Drainage lymphatique du membre supérieur.
Voies lymphatiques de dérivation.

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RÉSUMÉ

Des études cliniques ont montré l'existence de voies lymphatiques de suppléance. Ces voies sont susceptibles de détourner le cours de la lymphe.

Les auteurs ont étudié l'existence des voies de suppléance à partir de 300 cadavres humains.

L'échantillonnage est composé de 269 fœtus (de 7 à 9 mois), de 8 enfants (de 1 à 3 ans) et de 23 cadavres adultes (de 35 à 71 ans).

Les voies de dérivations qui ont été isolées sont représentées à la face antérieure par la voie céphalique ou de Mascagni (70 % des cas) et à la face postérieure par la voie tricipitale ainsi que les voies dorsales.

La voie tricipitale ou voie de Caplan se rend à un secteur ganglionnaire scapulaire superficiel tandis que les voies de dérivation par la face dorsale du tronc se rendent respectivement aux secteurs supra-claviculaires homo- (36 %) et contro-latéral (20 %) ainsi qu'au secteur axillaire contro-latéral (56 %).

INTRODUCTION

The present study was undertaken with the purpose of providing better anatomical basis to the clinical care of upper limb lymphoedema which is one of the most important postoperative complication of breast surgery. In several cases, lymphoedema can reach such severe forms that it provokes partial or complete invalidation of the affected limbs. Physical therapy undoubtedly represents the most classical treatment of that affection thanks to different techniques enabling a better lymph flow in residual pathways, not affected by the intervention (4).

Key words : Lymphatics, lymphatic drainage, upper limb.

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Previous in vivo studies performed in animals have provided good evidence for the possible existence of substitution pathways capable of diverting the normal course of lymph (4). With the purpose of disclosing substitution lymphatic pathways of the upper limb, we have therefore decided to examine the possible existence of anastomotic channels between the normal lympohatic pathways of the upper limb and those of dorsal cutaneous areas of the shoulder and posterior thoracic regions. The knowledge of such substitution pathways may be essential to human pathology since they can either prevent oedema formation or contribute to the regression of an already established lymphoedema.

MATERIAL AND METHOD (1, 3, 6)

The experiments have been performed on 300 human bodies including 269 fetuses (from 7 to 9 months), 8 children (from 1 to 3 years old) and 23 adults (from 35 to 71 years old). In 250 of them, injections were made in different superficial and deep topographic areas of the upper limb ; 50 were injected in cutaneous dorsal areas of the posterior scapular and upper thoracic regions.

The right side was injected in 136 cases and the left side in 164 cases. Formalin-fixed bodies have been avoided since they usually don't provide good results.

All observations have been gathered in the Department of Motor Revalidation of the Faculty of Medicine and Pharmacy of the " Vrije Univertsiteit Brussel " and in the Anatomical Research Department of the 2d chair of Normal Anatomy of the Faculty of Medicine of the University of Buenos Aires.

TECHNIQUE OF INJECTION

A. The dye

The dye is the same as that recommended by GEROTA (1), but without ether addition. Several other dyes have been used such as the emerald green and the scarlet red.

Each dye is dissolved into terpentine and the solution is filtered twice. A few minutes before injection, the staining mass is heated up to about 40°C in a double boiler.

B. **The syringes**

Two different kinds of syringes have been used : insulin injection - like glass syringes and metallic syringes with a carpule as those used by odontologists. The latter have our preference.

C. **Pretreatment of the material**

As the unfixed material used is nearly always frozen, the injection areas have first been thawn out through 20 to 30 minutes exposure to a 200 W lamplight placed at a distance olf 10 to 20 cm from the skin. More recently, the use of infra-red lamps have permitted quicker results.

D. **The injection areas**

Most injections in the upper limb have been made in cutaneous areas of the digits, in joints and in a few cases in muscular structures. In the back, the injection was made along a vertical paracostovertebral line extending from the second to the tenth rib. When two injections are made in the back of the same subject, different dyes have been used in order to distinguish the lymphatic pathways of either sides and to be able to detect crossed pathways.

The injection was always performed slowly and gently in order to prevent the rupture of lymphatic channels. A slight massage with the tip of the fingers helps the diffusion of the staining mass through the interstitial space.

E. **The amount of injected mass**

One to two ml. according to the subject's shape have been found sufficient for a successful preparation. When it is performed in superficial areas, a successful injection is immediately followed by the staining of a dense network of fine capillaries.

F. **Fixation of the injected material**

After checking that the injection has been successful as revealed by the presence of stain in the lymph vessels and ganglia, the preparation is dipped into 40 % formalin, which precipitates the dye within the lymphatic network and allows an easier observation. It is then transfered for 12 to 24 hours into hydrogen peroxyde (100 volumes) which bleaches all tissues with the exception of the stained parts.

RESULTS

1) **The lymphatic system of the upper limb**

The lymph vessels and ganglia of the upper limb can be divided into superficial and deep systems running on either sides of the superficial aponeurotic sheat. The superficial or supraaponeurotic system contains a great number of collecting vessels (7, 8). Well protected by the subcutaneous fatty tissues, they run aside the superficial blood vessels and finally reach the ganglionic groups of the axilla and, for some of them, the supraclavicular or the posterior scapular ganglia. The lymph vessels of the deep or subaponeurotic systems are less numerous and run along with the deep neurovascular channels of the upper limb. They end generally in the different ganglionic groups and chains of the axilla.

Only the superficial lymph system will be examined here : only them contract anastomotic relationship with the " posterior " or " posterior scapular " pathways and therefore may contribute to create substitution pathways.

A. **Classification**

All lymph vessels originate in regional networks present in the dermis and superficial aponeurosis which therefore represent the walls of the superficial lymphatic space where the collecting vessels run in parallel with the supraaponeurotic blood vessels. Two lymphatic pathways can be recognized in that space : a subdermal pathway composed of numerous very fine and delicate collecting vessels which can be easily ruptured by unexperienced investigators and a subaponeurotic pathway composed of larger collecting vessels located beneath the aponeurosis, not or poorly visible through the skin but which can be easily dissected out.

Four well-defined primary pathways run from the hand to the elbow where they divide into four secondary terminal pathways : 3 anterior and 1 posterior.

The four primary lymphatic pathways (2 anterior and 2 posterior) become divided into :
a) anterior radial or anterolateral pathway ;
b) anterior ulnar or anteromedial pathway ;
c) posterior radial or posterolateral pathway ;
d) posterior ulnar or posteromedial pathway.

The four secondary lymphatic pathways (3 anterior and 1 posterior) themselves divide into :
a) anterior or bicipital pathway ;
b) medial or basilic pathway ;
c) lateral or cephalic pathway ;
d) posterior or tricipital pathway.

Each pathway will now be submitted to detailled descriptive analysis.

B. **Descriptive analysis**

B.1. ***Primary pathways***

a) *The anterior radial or anterolateral pathway*

It runs obliquely from the proximal part of the hand to the elbow, parallel to the vena radialis superficialis. There the anterolateral pathway divides into 3 terminal secondary pathways : medial, anterior and lateral. No ganglion could be found along this collecting pathway which drains the skin of the thumb, of the thenarian area and of the anterolateral part of the forearm. In the middle and superior part of its course, the anterolateral pathway is joined by the posterolateral or posterior radial pathway.

b) *The anterior ulnar or anteromedial pathway*

This pathway extends from the hypothenar eminence to the elbow where it divides into 2 to 3 secondary terminal pathways running on the medial and anterior aspects of the arm. Less obliquely oriented than the anterior radial pathway, the anterior ulnar pathway accompanies the vena basilica and regularly presents a ganglionic group located in the proximal one third of the forearm. The anteromedial pathway drains the skin of digit V, of the hypothenarian area and of the anterolateral territory of the forearm. In its middle and superior parts it receives numerous collecting vessels from the posteromedial or posterior ulnar pathway.

c) *The posterior radial or posterolateral pathway*

Extending from the proximal part of the dorsal aspect of the fingers, the posterior radial pathway runs through the anterior aspect of the forearm, elbow and arm where it contributes to form 2 out of the 3 terminal secondary pathways : the lateral and the anterior.

Together with the posteromedial pathway, the posterolateral pathway forms the secondary posterior pathway of the arm. The number of its collecting vessels varies from 5 to 12.

The posterolateral pathway represents the only lymphatic outflow which realizes a true anastomotic network between the dorsum of the hand and the proximal part of the forearm ; there it divides into 2 posterior pathways. It receives the lymph from the skin of all five fingers, from the dorsum of the hand and from the posterolateral territory of the forearm. No ganglion was observed along its course.

d) *The posterior ulnar or posteromedial pathway*

Similarly with the posterolateral one, the posteromedial pathway starts from the proximal end of the dorsal aspect of the fingers, runs through the dorsum of the hand and wrist and reaches the proximal one third of the forearm. Thence, both posterior pathways of the forearm continue in the direction of the anterior aspect of the forearm and arm where they join the anteromedial or anterior ulnar pathway which, in the elbow area contributes to the formation of 2 to 3 secondary terminal pathways (anterior and medial). The posterior ulnar pathway is usually well developed, the number of its constituant vessels varying from 5 to 14. Like the posterolateral pathway, it gives origin to the posterior lymphatic outflow of the arm.

B.2. ***The secondary lymphatic pathways***

B.2.1. Anterior pathways

a) *The anterior bicipital pathway*

In relation with the anterior aspect of the muscle biceps brachii, the anterior bicipital pathway drains four primary lymphatic pathways originating from the hand and forearm. It is composed of 8 to 15 collecting vessels. Obliquely directed from lateral to medial, it extends from the elbow up to the basis of the axilla. There it goes through the superficial aponeurosis and joins the different axillary lymph chains.

A single ganglion located 2 cm below the axillary basis on the anteromedial aspect of the superior one third of the arm was found in one case ; to the best of our knowledge, it was never mentioned before.

b) *The anteromedial or basilic pathway*

Closely related to the basilic vein and to the medial bicipital groove, the anteromedial pathway receives the anterior and posterior ulnar primary pathways originating from the arm and forearm. In a few cases, the anterior and posterior radial outflows were also found ending in the basilic pathway. The basilic pathway is usually represented by 3 to 6 collecting vessels. Their course may follow two different ways. The first one accompanies the basilic vein in the canalis brachialis and reaches the deep ganglia of the axillary region by running parallel to the humeral blood vessels ; the ganglia of the basilic chain or of the humeral chain are frequently found along that pathway. The vessels following the second course run superficially in the medial bicipital groove and cross the superficial aponeurosis of the axillary basis where they also join the axillary ganglionic chains. In one case, they were found associated with a single ganglion superficially located in the angle between the muscles triceps (*capsut longum*) and *latissimus dorsi*. This ganglion had so far never been described.

c) *The anterolateral or cephalic pathway*

Closely associated with the cephalic vein, the anterolateral or cephalic pathway prolonges the antero- and posterolateral primary pathways originating from the hand and forearm. It is a constant lymphatic channel which starts in the inferior one third of the arm, successively runs in the lateral bicipital and deltopectoral grooves before reaching the trigonum clavipectoralis. There the collecting vessels may follow three different routes : (1) along the cephalic vein towards the ganglia of the axillary chain, (2) a superficial one which crosses the outer aspect of the clavicle and reaches the transverse cervical ganglionic chain (this route was described by MASCAGNI (5) and later on by SAPPEY (10) (fig. 1) ; (3) another route ending in the clacivulopectoral group of the cephalic chain near the deep bending of the vein ; some of its collecting vessels follow the cephalic vein and end in the axillary ganglia, others reach the superclavicular ganglionic chain after crossing the clavicle superficially. The variants (2) and (3) play a decisive role in the surgery of the breast cancer, they ought to be spared during complete or subtotal mastectomy and surgical exploration should be avoided in that area.

Similarly, if the patient receives pre- or postsurgical radiotherapy, the deltopectoral area should be protected, if possible, by lead plates in order to avoid the destruction of the unique possibility of lymph drainage of the upper limb. This drainage can contribute to suppress or alleviate the lymphoedema which might appear thereafter.

B.2.2. The posterior or tricipital pathway (fig. 2)

Closely associated with the muscle triceps brachii, this pathway starts from the upper one third of the back of the forearm ; according to the case it may be a continuation of the posterior ulnar, of the posterior radial or of both of this primary lymphatich pathways. It is obliquely directed from the lateral to the medial part of the dorsal aspect of the arm and reaches the axillary ganglia. In four cases, however, the tricipital pathway followed the deltotricipital groove and reached a ganglion located on the muscle teres major belonging to the inferior scapular chain. In one single case, a lymphatic vessel was found running from that ganglion to the posterior scapular chain. A ganglion so far not mentioned was found along that pathway in the angle between the muscles triceps brachii and latissimus dorsi. In another case, a direct lymphatic communication was found between the superficial dorsal network of the arm and that of the posterior thoracic region.

The knowledge of the tricipital pathway is of tremendous importance in the interpretation of the lymphatic drainage after mastectomy.

2) **The subcutaneous lymph vessels of the dorsal thoracic wall**

A. **Homolateral lymphatic pathways** (figs. 3 and 4)

Two different kinds of well defined lymphatic pathways have been revealed after injection of GEROTA's (1) mass along the spinal border of the scapula between the second and the tenth rib : homolateral and contralateral pathways. They can be distinguished by their topographically distinct regional and extraregional courses.

Four homolateral pathways can be recognized and were named according to their course :

1) the axillary pathway,
2) the supraclavicular pathway,
3) the dorsal or dorsososcapular pathway,
4) the posterior intercostal pathway.

They can be described as follows.

1) ***The axillary pathway***

It is the main superficial lymph outflow and was found constrant. Seven to 12 collecting vessels are converging toward the axilla where they reach different ganglionic chains, particularly the external mammary chain (92 %), the inferior subscapular chain (84 %) and the axillary chain (32 %).

2) ***The supraclavicular pathway***

It represents the second substitution pathway of the superficial and deep lymphatic drainage originating from the dorsal cutaneous component of the upper thorax. It was found present in 36 % of the cases and generally includes 1 to 4 collecting lymph vessels running towards the neck either superficially or through the muscle trapezius. In either case, they end in the deep transverse cervical chain located in the supraclavicular area. One or two ganglia are usually found associated with the superficial vessels and take place in front of the muscle at the level of the 7th cervical vertebra.

3) ***The dorsal or dorsoscapular pathway***

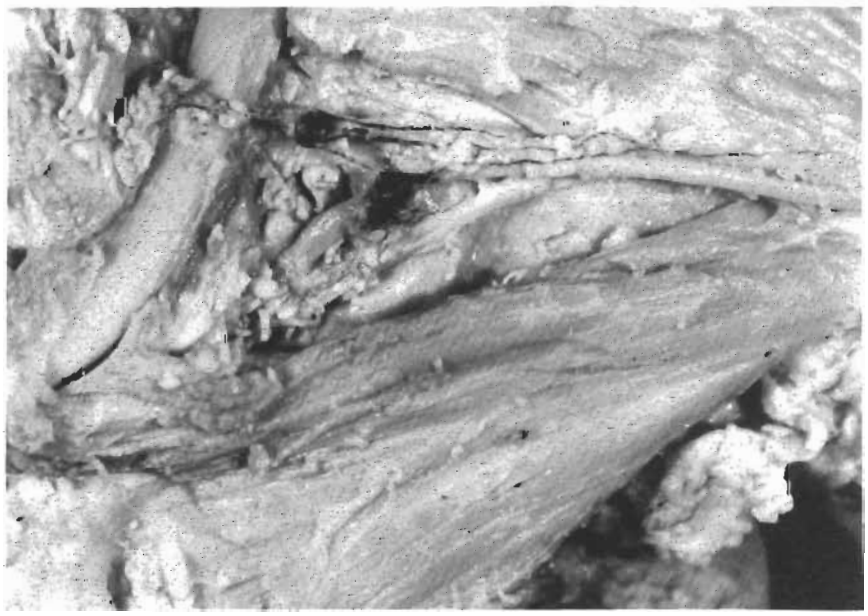
It is the third substitution pathway of the deep lymphatic network in this area. Observed in 36 % of the cases, it is composed of 1 to 4 collecting vessels which after a short subcutaneous course penetrate across the superficial aponeurosis and run within the muscle trapezius between the 2d and 5th thoracic vertebrae. They may then follow one of the two following routes : the subtrapezian or the subrhomboidal ones.

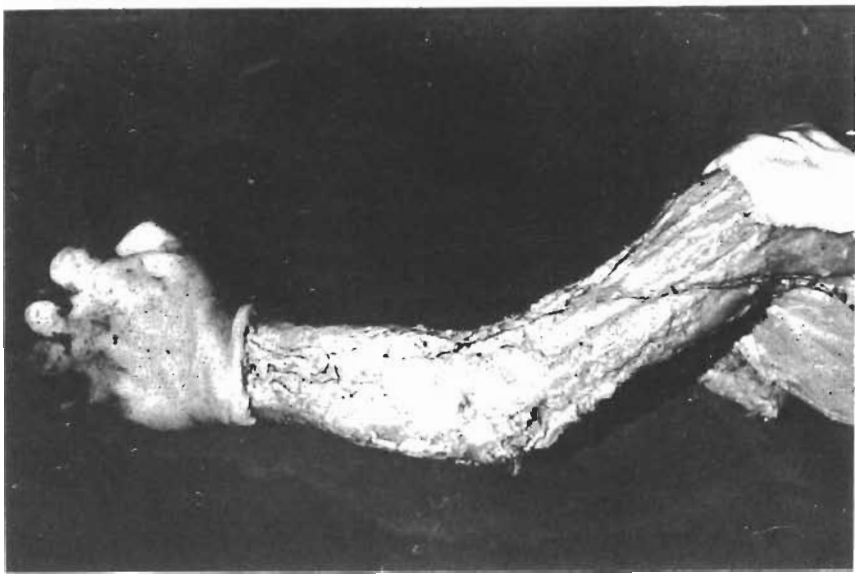
Fig. 1 a

Fig. 1 b

Possibilities described by MASCAGNI :
a. directly to the transverse cervical ganglionic chain ;
b. indirectly along a preclavicular node.

Possibilités décrites par MASCAGNI :
a. directement à la chaîne ganglionnaire cervicale transverse ;
b. indirectement à travers un ganglion préclaviculaire.





◀ *Fig.2*

The tricipital pathway
or the " CAPLAN's pathway ".

This proposal was introduced by
Profs CUICCI and LEDUC A.
during the Int. Congr. of Phlebology
and Lymphology in Tucuman
(Argentine 1993)
and was accepted.

La voie tricipitale ou " voie de CAPLAN ".

Cette proposition introduite par les
Prof. CUICCI et LEDUC a été acceptée
lors du Congrès International de Phlébologie
et Lymphologie
de Tucuman (Argentine, 1993).

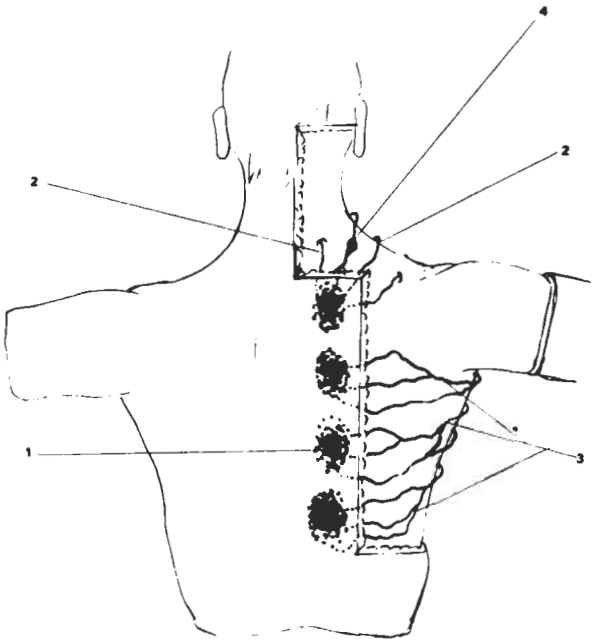


Fig. 3

Homolateral superficial lymphatic pathways

1. *injection*
2. *supra-clavicular pathway*
3. *axillary pathway*
4. *superficial lymphnode.*

Voies lymphatiques superficielles homolatérales

1. *injection*
2. *voie supraclaviculaire*
3. *voie axillaire*
4. *ganglion superficiel*

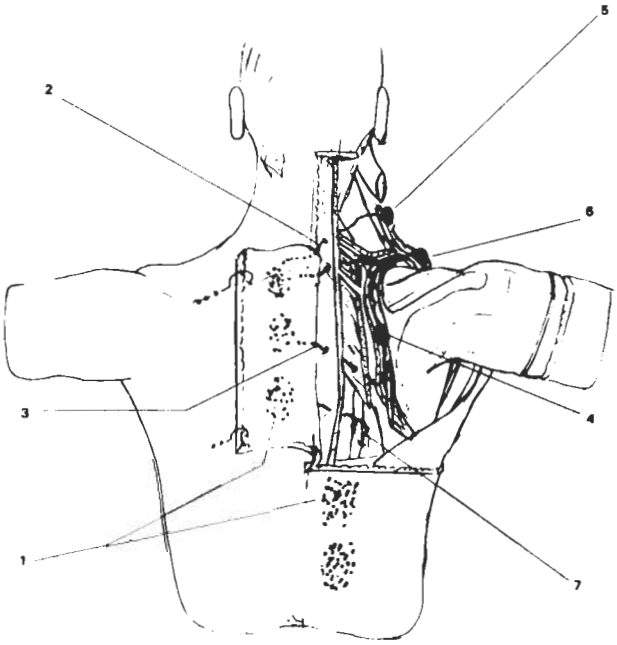


Fig. 4

Homolateral deep lymphatic pathways

1. *injections*
2. *supraclavicular pathway*
3. *dorso-scapular posterior pathway*
4. *scapular chain*
5. *jugular node*
6. *deep transverse cervical chain*
7. *posterior intercostal pathway.*

Voies lymphatiques profondes homolatérales

1. *injection*
2. *voie supraclaviculaire*
3. *voie dorsoscapulaire postérieure*
4. *chaîne scapulaire*
5. *ganglion jugulaire*
6. *chaîne normale transverse profonde*
7. *voie intercostale postérieure.*

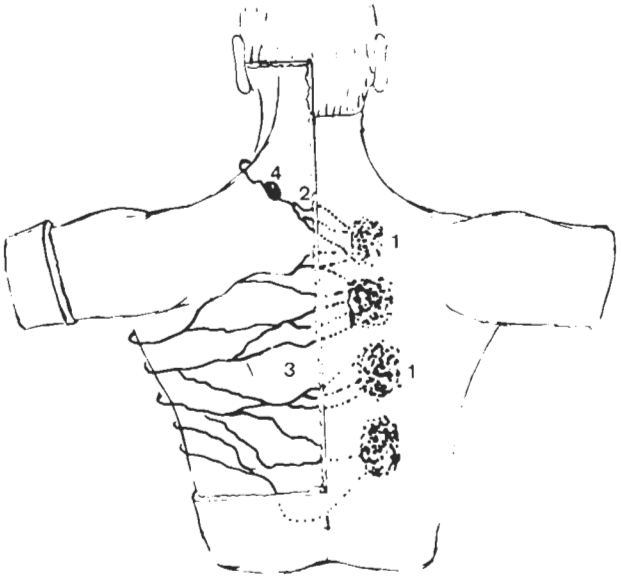


Fig. 5 a

Superficial contro-lateral pathways

1. *injections*
2. *supraclavicular pathway*
3. *axillary pathway*
4. *superficial node.*

Voies contralatérales superficielles

1. *injection*
2. *voie supraclaviculaire*
3. *voie axillaire*
4. *ganglion superficiel.*

Fig. 5 b

Supraclavicular pathway - Voie supraclaviculaire

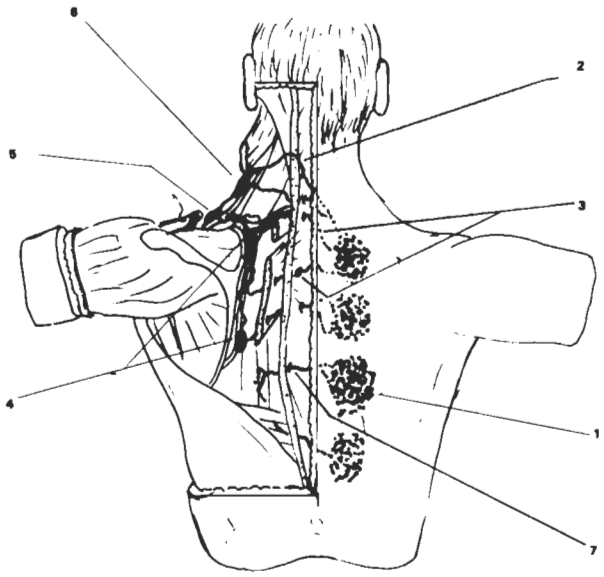


Fig. 6

Deep controlateral pathways - Voies contralatérales profondes

1. *injection*
2. *supra-clavicular pathway*
   voie supraclaviculaire
3. *dorso-scapular pathway*
   voie dorsoscapulaire
4. *posterior scapular chain*
   chaîne scapulaire postérieure
5. *deep transverse*
   chaîne transverse profonde
6. *cervical jugular node*
   ganglion cervical jugulaire
7. *posterior intercostal pathway.*
   voie intercostale postérieure.

(a) ***The subtrapezian pathway*** runs ***behind the muscle*** trapezius and ***in front of*** the muscles rhomboid and levator scapulae, along with the dorsal superior artery, a branch of the cervical transverse artery. It is followed by 1 or 2 collecting vessels which may end in the posterior scapular or in the deep transverse cervical chain. They may also reach the fossa supraspinata through the posterior scapular chain. One or 2 ganglia have been observed in a few cases along the superior dorsal or the subtrapezian chain.

(b) ***The subrhomboidal pathway*** is followed by one or two collecting vessels which in different places were found crossing the muscles trapezius and teres major before ending in the scapular chain satellite of the posterior scapular vessels. The latter runs along the spinal border of the scapula. This chain receives the lymph from the inferior scapular ganglia representing the posterior lymphatic drainage from the upper limb through the third substitution pathway. This route is only rarely used.

4) ***The posterior intercostal pathway***

It represents the fourth deep drainage route from the posterior cutaneous thoracic region extending from the 6th to the 12th rib. Present in 24 % of the cases, its collecting vessels rapidly go across the muscle trapezius or sometimes across the muscle rhomboid major before penetrating the deep intermuscular spaces between the thoracic portions of the muscles longissimus, iliocostalis and semispinosus. They usually accompany the dorsal perforating branches of the posterior intercostal vessels. Once in the intercostal space, the vessels end in the posterior intercostal chain which itself reaches the thoracic duct. One or two ganglia have been found associated with the dorsospinal perforating vessels.

B. **Controlateral pathways**
(figs. 5 and 6)

In 76 % of the cases collecting lymphatic vessels originating from the posterior cutaneous thoracic region were found crossing the midline and reaching one of the following 4 controlateral substitution pathways : the axillary pathway, the supraclavicular pathway, the dorsoscapular pathway or the posterior intercostal pathway. They can be described as follows.

1) ***The axillary pathway***

It is the most important controlateral pathway. Present in 56 % of the cases, it is represented by 2 to 10 collecting vessels which cross the dorsal midline superficially and reach the lateral boundary of the posterior axillary wall. There they penetrate the axillary basal aponeurosis and join preferentially the inferior scapular and external mammary chains or, less frequently, the chain of the axillary vein.

2) ***The supraclavicular pathway***

Present in 20 % of the cases, it is represented by 1 or 2 collecting vessels which after crossing the dorsal midline reach the basis of the neck and continue in front of the muscle trapezius. One or two ganglia can be found along their course at the surface of the muscle. They finally reach the controlateral supraclavicular area where they come to end either in the superficial transverse cervical chain, in the posterior jugular chain or in the deep transverse cervical chain. In 10 % of the cases, one or two collecting vessels of the supraclavicular pathway run through the muscle trapezius and join the deep transverse cervical chain.

3) ***The dorsal or dorsoscapular pathway***

This deep controlateral pathway was found present in 16 % of the cases. It is represented by 1 or 2 collecting vessels which go across the dorsal midline, penetrate the heterolateral muscle trapezius (thoracic part) and then follow either a subtrapezian or a subrhomboidal course. The ***subtrapezian*** course is generally composed of 1 or 2 collecting vessels which accompany superior dorsal vessels and join the deep transverse cervical chain. One or two ganglia were frequently found along their intermuscular course.

The ***subrhomboidal*** pathway goes through the space between the muscle rhomboides major and minor and reaches the posterior scapular chain along with the posterior scapular vessels near the spinal border of the scapula. Its collecting vessels drain the lymph from the inferior scapular chain which itself receives that from the dorsal aspect of the upper limb through the third substitution pathway. This latter situation is inconstant.

4) ***The posterior intercostal pathway***

The controlateral posterior intercostal pathway was found present in 4 % of the cases and therefore appears as the less frequent deep controlateral lymphatic pathway of the dorsal thoracic wall. It was represented by one single collecting vessel which goes across the dorsal midline and successively penetrates the muscles trapezius and rhomboid major (sometimes) before entering the intermuscular space between the muscles longissimus thoracis and semispinalis thoracis, along with dorsospinal perforating vessels originating from the posterior intercostal vessels. It finally ends into the posterior intercostal chain.

CONCLUSIONS

Numerous potential substitution lymphatic pathways capable of collecting the lymph from the upper limb have been detected in this study. They are preferentially locatred on the dorsal aspect of the shoulder and represent interlymphatic anastomoses between the dorsal aspect of the arm and the posterior thoracic wall. These substitution pathways drain the lymph to homo- and controlateral ganglionic chains or to the thoracic duct, which represent normal lymphatic pathways.

After complete or partial axillary ganglionic removal, the substitution pathways can take in charge the whole lymphatic drainage from the upper limb. The " replacement " of normal by substitution pathways is not always immediate. It is often necessary to help the opening of anastomotic vessels through increasing the intralymphatic hydrostatic pressure by careful manipulation. The homo- and controlateral substitution pathways are usually represented by numerous collecting vessels grouped into definite pedicles.

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Ultrastructure of dermal lymphatic vessels in chronic venous insufficiency of the human leg

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ABSTRACT

Morphological and ultrastructural changes of dermal lymphatic microcirculation in Chronic Venous Insufficiency (CVI) of the lower limbs are reported. Skin biopsies from adult subjects suffering of IVC of the limbs associated with skin changes, suggestive for the so called stasis dermatitis were excised from the lower areas of the leg. Biopsies from normal subjects were also performed.

The most important morphological changes in dermal lymphatic vessels were : i) collapsed lumen of lymphatic capillaries located in the papillary area of the derma ; ii) numerous and elaborated interdigitations between the surface of contiguous endothelial cells with consequent absence of open junctions ; iii) scanty micropinocytotic vesicles. The connective tissue surrounding the lymphatic vessels appeared to be organized in bundles of collagen fibers arranged in packed assemblies. The elastic fibers were very abundant around the lymphatics ; the anchoring filaments that usually may pull open the lymphatic lumen, often were not seen or were separated from the endothelial wall by a dense basement membrane. These results suggest that the dermal lymphatic microcirculation in the IVC may be involved in the decreased capability of the lymph formation because of abnormal organization of the connective tissue.

Key words : lymphatic vessels, human skin, venous insufficiency, ultrastructure, lower leg.

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RÉSUMÉ

Nous avons étudié les modifications morphologiques et ultrastructurelles des vaisseaux lymphatiques dans l'Insuffisance Veineuse Chronique (IVC) des jambes. Nous avons utilisé des biopsies cutanées de jambes de patientes avec IVC et de volontaires sains. Les principaux changements ont été : i) " collapse" des vaisseaux lymphatiques dans les papilles dermiques ; ii) nombreuses et compliquées interdigitations entre les cellules andothéliales et absence des " jonctions ouvertes " ; iii) rares vésicules micropinocytotiques près de la paroi endothéliale. Le tissu conjonctif entourant les vaisseaux lymphatiques apparaissait être organisé en faisceaux de fibres collagènes arrangés en assemblages serrés. Les fibres élastiques étaient très abondantes autour des vaisseaux. Les " filaments d'ancrage " qui tiennent ouvert le vaisseau lymphatique faisaient souvent défaut ou étaient séparés de la paroi andothéliale par une épaisse membrane basale. Ces résultats suggèrent que la microcirculation lymphatique de la peau des jambes dans l'IVC est impliquée dans la réduction de la formation de la lymphe suite à une organisation anormale du tissu conjonctif.

RIASSUNTO

Nella presente indagine sono state descritte la modificazioni morfologiche ed ultrastrutturali del microcircolo linfatico nell'Insufficienza Venosa Cronica (IVC) degli arti inferiori. Sono state utilizzate biopsie cutanee dell'arto inferiore di soggetti adulti sofferenti di Insufficienza Venosa Cronica (IVC) e di soggetti normali. Le principali alterazioni morfologiche riscontrate nei vasi linfatici dermici sono state : i) marcato collassamento dei capillari linfatici nelle aree papillari del derma ; ii) numerose e complesse interdigitazioni tra cellule endoteliali contigue e assenza di " giunzioni aperte " ; iii) scarse vescicole di micropinocitosi alla superficia luminale ed abluminale delle cellule endoteliali. Il tessuto connettivo xirxonstante appariva caratterizzato della presenza di densi fasci di fibre collagene mentre abbondanti fibre elastiche erano strettamente associata alla parete dei vasi. I filamenti di ancoraggio che normalmente mantengono aperto il lume del vaso risultavano spenso assenti oppure erano separati della parete endoteliale da una spessa membrana basale. Tali risultati potrebbero suggerie che il microcircolo linfatico cutaneo nella IVC sia coinvolto in una diminuita o mancata capacità di formare la linfa a causa dell'anormale organizzazione del tessuto connettivo.

INTRODUCTION

Chronic Venous Insufficiency (CVI) refers to modifications occurring on the blood defluxion in the lower regions of the legs. It is a frequent disease often linked to skin lesions, subcutaneous fibrosis and non-inflammatory edema.

In the past years, morphological and ultrastructural changes of the dermal capillary network in CVI were described : they consisted mainly in dilatation and leakage of blood capillaries (11, 6, 10, 3). In CVI, there is clinical evidence for physiological changes of the lymphatic microcirculation, but no recent morphological studies have been made on the lymphatic network draining the dermal interstitial fluid. The present investigation reports on the light microscopy and ultrastructural features of the lymphatic vessels seen in the skin of patients affected by CVI of the lower regions of the leg. Our purpose was to show the ultrastructural changes occurring in the lymphatic endothelial wall and in the surrounding connective tissue related with the functional conditions of the skin area involved in this pathology.

MATERIAL AND METHODS

Skin biopsies from 6 healthy subjects (40 to 60 years old) and from 10 female patients (50 to 65 years old) affected by CVI of the limbs and with skin changes suggestive for the so called stasis dermatitis, were taken from the lower leg. Small pieces of the skin were fixed in a mixture of glutaraldehyde (2,5 %) and paraformaldehyde (2 %) in a sodium cacodylate buffer 0,1 M (pH 7,4) for 4 h and postfixed in 1 % OsO_4 in collidine buffer pH 7,4 for 2 h. Then they were dehydrated and embedded in Epoxy resin. Semithin sections (0,5 - 0,7 μm) stained with toluidine blue, were observed and recorded at the light microscope. Ultrathin sections (40 - 100 μm) contrasted with uranyl acetate and lead citrate, were observed and recorded at the electron microscope Zeiss EM10 : some ultrathin sections were contrasted with orcein in aqueous solution (2 %) to detect the elastic fibers.

RESULTS

Light Microscopy.

From the semithin section examination, the dermis of the control subjects was characterized by a very loose connective matrix : small bundles of collagen and elastic fibers surrounded the blood and lymphatic vessels. The blood capillaries were numerous and the lymphatic capillaries were characterized by a distended wall that appeared thin and indented ; the wide lumen was often filled with dense and amorphous material, probably coagulated lymph (fig. 1). In the diseased skin, the connective tissue was characterized by fibrosis : the collagen fibers were very numerous forming wide and dense bundles ; the amorphous component of connective matrix was very scanty. The small blood and lymphatic vessels were scarse. Particularly, the blood capillaries showed a thick cuff of amorphous dense material. Lymphatic capillaries were difficult to recognize at the light microscope because most of them were characterized by occluded lumen (fig. 2).

Electron Microscopy.

In the normal control, the capillary wall of blood capillaries was regular in shape and the endothelial cells showed no degenerative appearance. The lymphatic wall appeared thin and flattened and, in some areas, it was attenuated by open junctions between contiguous endothelial cells (fig. 3). Dense bundles of elastic and collagen fibers surrounded the endothelial wall. The external side of the endothelial wall was joined to the connective matrix by the anchoring filaments (fig. 4).

Most endothelial cells of blood capillaries from diseased skin were swollen and they protruded in the vessel lumen as far as their occlusion ; the nuclei were indented and picnotic (fig. 5) and the basement membrane often appeared to be thick and multiplied into several lamellae (fig. 6).

In the lymphatic capillaries of subjects with CVI, the endothelial cells protruded into the lumen and often joined together so that the vessel lumen was obstructed in some areas (fig. 7). The connection between contiguous endothelial cells were characterized by complex interdigitations (fig. 7) ; rarely " end to end " junctions were present and open junctions were virtually almost absent. Few micropinocytotic vesicles were present along the luminal and abluminal side of the endothelial wall. Around the vessels numerous bundles of elastic fibers were seen (fig. 8). In much lymphatics from diseased skin, the anchoring filaments did not reach the external wall of the endothelial cell ; they were instead separated from it by a dense amorphous material (fig. 8).

DISCUSSION

In the CVI, because of the increase in the arterial pressure as a result of to a defective blood defluxion at the deep levels, a stagnation of the venous circulation extends to the whole capillary network. After stagnation is set up, it produces a change at the level of capillary network. Particularly, the venular hypertension provokes morphological and functional modifications of the superficial microcirculation or rather of the capillary network. Consequently, the surrounding connective tissue showes some trophic lesions i.e. sclerosis and fibrosis losing its reabsorbing and metabolising capacity. These changes could also involve the lymphatic system that can not drain the interstitial fluid thus causing both venous and lymphatic insufficiency. In CVI, the blood and lymphatic microcirculation undergoes some modifications strictly connected with those of the connective matrix that surrounds the vessels. The CVI develops according to several phases : early, because of increased permeability of blood capillaries and venules, a stasis edema with erythrocyte extravasation is evident. This is followed by inflammation with the participation of lymphocytes and plasma cells ; in addition, the abundant interstitial fluid promotes fibroblast proliferation. At the end, the chronic inflammation gives rise to fibrosis characterized by large and dense bundles of collagen fibers. When this fibrosis is severe, the interstitial matrix shows a decrease in cell concentration ; the collagen fibers pressure the blood vessels and the nutritional exchange fail. In the past years the blood capillary morphology has been described in CVI (11, 10, 2, 3). The authors enpohasized the dilatation and leakage of blood capillaries ; the pericapillary connective tissue appears to get edematous and inflamed because of the presence of lymphocytes and macrophages. At the ultrastructural level, the main findings are a dilated lumen of the vessels and numerous intercellular clefts between the contiguous endothelial cells (11, 6). This feature is evidence of an increased permeability of endothelial cells of blood capillaries and venules. On the contrary, in our cases a restricted lumen of the vessels and no gaps between andothelial cells were detectable. These differences are probably due to a severe degree of disease characterized by a remarkable interstitial fibrosis (indurative edema). This edema could squeeze the vessel causing endothelial cell necrosis. The enlargement and splitting of the basement membrane into several lamellae can not be considered as a pathological finding because it is a common finding in cutaneous capillaries (5). On the other hand, it has been demonstrated (9) that the multiplication of basement membrane is an arteriosclerotic phenomenon connected to non-vascular disease.

From our observations, the lymphatic capillaries of diseased skin show a collapsed lumen : according to same authors (4, 7), this is a common feature also in normal conditions. Nevertheless, at the

Figure 1

A large lymphatic vessel from normal control skin is characterized by a distended and thin wall (a).
A lymphatic vessel (arrows) from diseased skin shows an occluded lumen (b).
(× 800)

Un large vaisseau lymphatique dans la peau d'un sujet sain est caractérisé par une paroi mince et distendue (a).
Un vaisseau lymphatique (flèches) de la peau d'un sujet avec IVC paraît collapsé (b).
(× 800)

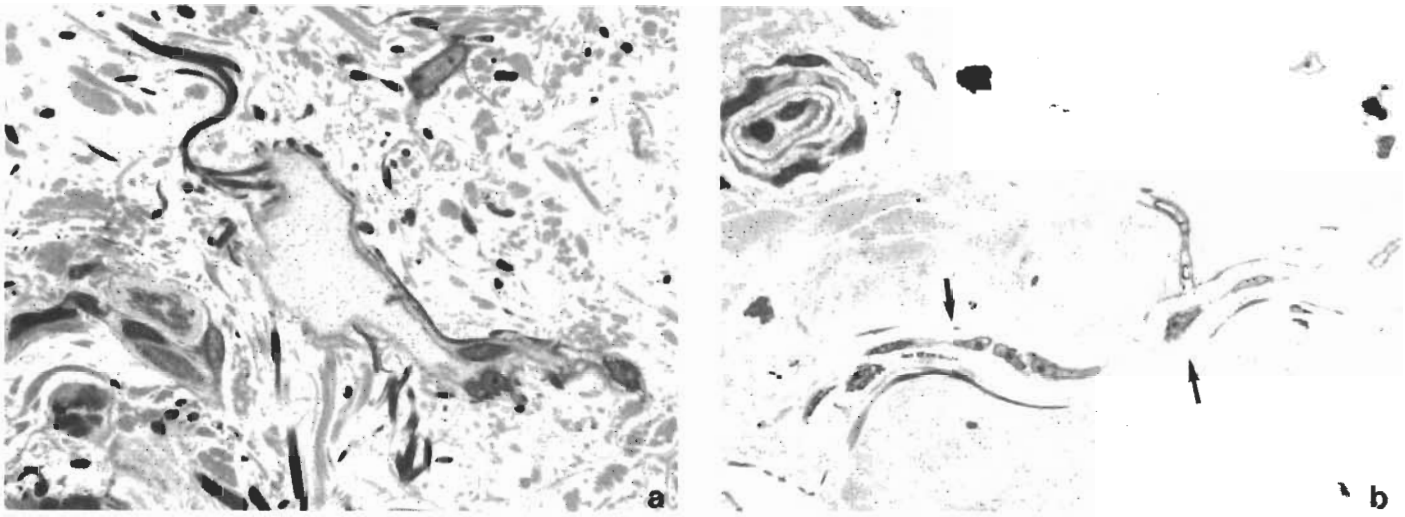


Figure 2

Lymphatic capillary from normal control skin :
a) the lymphatic endothelial wall shows an open junction between contiguous cells ;
b) the lymphatic wall is characterized by the presence of anchoring filaments (arrows) joining the endothelial cells to the collective tissue. (× 18.500)

Vaisseau lymphatique de la peau d'un sujet sain :
a) la paroi du vaisseau montre une " jonction ouverte " entre deux cellules endothéliales ;
b) la paroi du vaisseau est entourée par des filaments d'ancrage (flèches) qui joignent les cellules endothéliales au tissu conjonctif. (× 18.500)

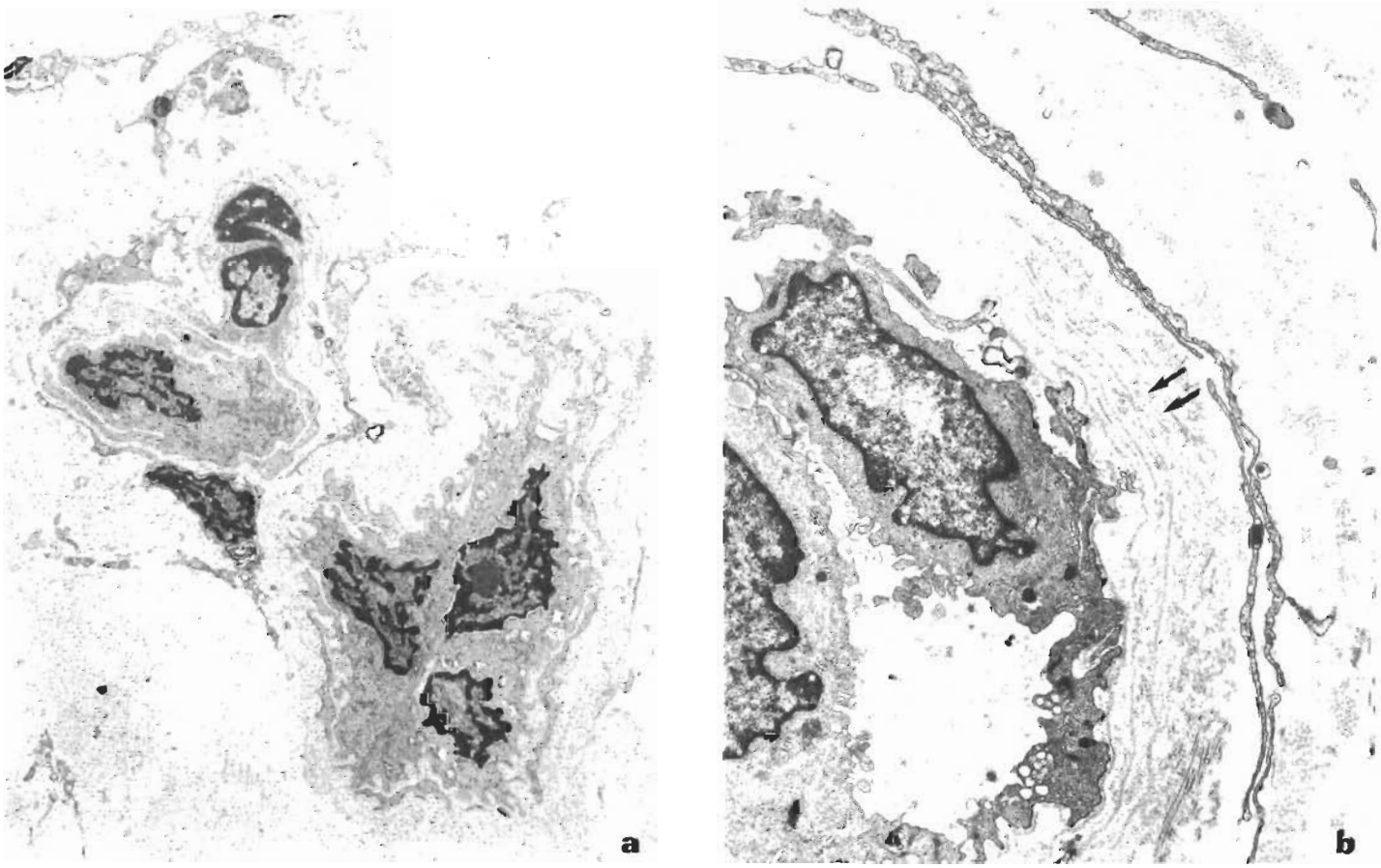


Figure 3

Blood capillaries from diseased skin :
a) the blood capillary is characterized by occluded lumen and by swollen endothelial cells (× 4.000).
b) the basement membrane appears to be thick and reduplicated into several lamellae (arrows) (× 7.500).

Capillaire sanguin de la peau d'un sujet avec IVC :
a) la paroi du vaisseau est collapsée et les cellules endothéliales sont enflées (× 4.000) ;
b) la membrane basale paraît multipliée (flèches) (× 7.500).

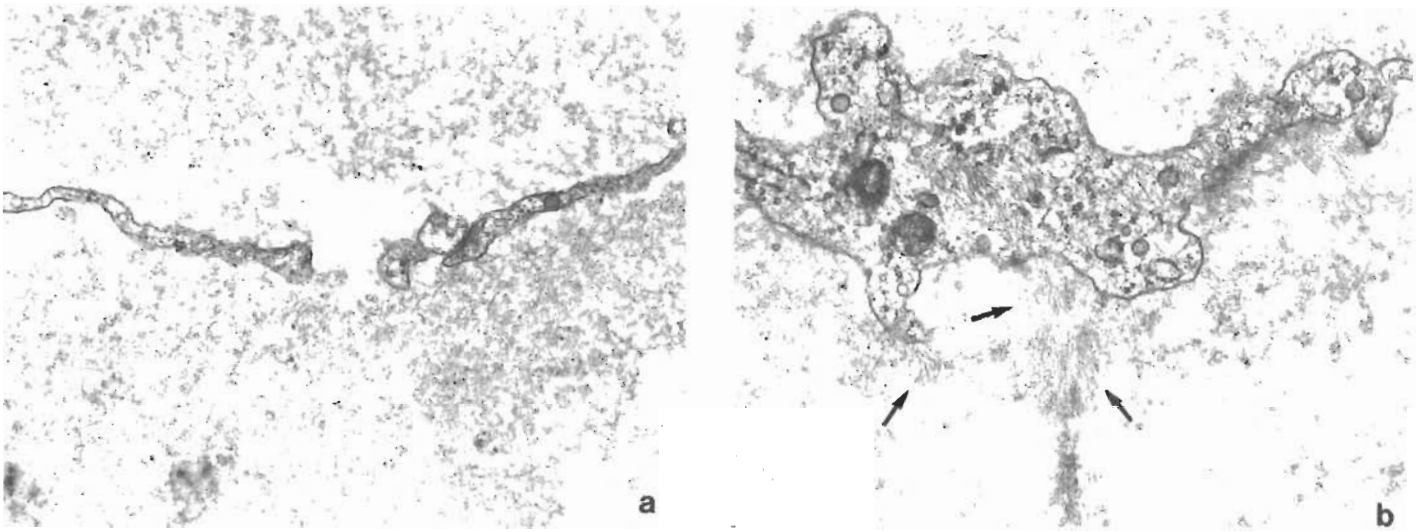
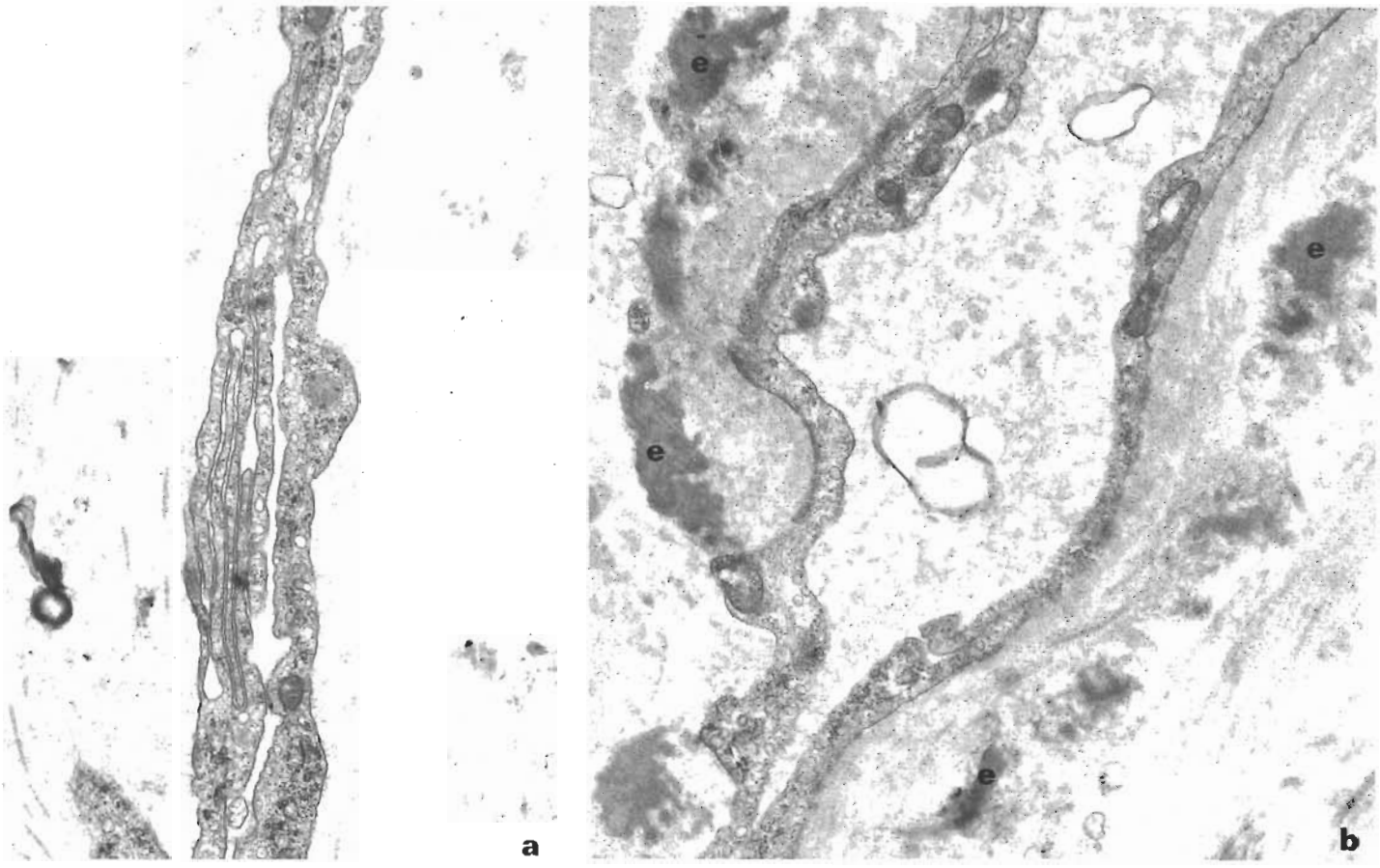


Figure 4

Lymphatic capillaries from diseased skin :
a) the endothelial wall is very collapsed and complex interdigitations characterize the junction between two contiguous endothelial cells ;
b) a dense basement membrane surrounds the endothelial wall.
Abundant elastic fibers are also present in the connective tissue (e) (× 12.000).

Vaisseau lymphatique de la peau d'un sujet avec IVC :
a) la paroi du vaisseau est collapsée et de nombreuses interdigitations caractérisent les jonctions entre cellules endothéliales ;
b) une épaisse membrane basale entoure les cellules endothéliales : de nombreuses fibres élastiques sont rangées dans le tissu connectif (e).
(× 12.000)



ultrastructural level, we observed some changes that could be ascribed to an impaired function of the lymphatics. These changes concern especially the endothelial wall and its connections with the surrounding connective tissue. In normal conditions, open junctions and the intercellular channels are the most important ways to enter into the lymphatic vessels (8, 7). In our cases, these structures were scanty : the endothelial cells were connected especially by complex interdigitations. In addition, under normal conditions, the endothelial wall is joined to neighbouring elastic and collagen fibers by the anchoring filaments that are necessary to keep open the lumen during the filling phase of the vessel (1). From our observations, the anchoring filaments were often separated from the endothelial wall by a thick basal lamina. An increase of the basement membrane has been observed in conditions that provide a raise of the intralymphatic pressure particularly in the venous diseases of the lower leg (7). The scanty anchoring filaments and the thick basal membrane observed on our lymphatic vessels could be responsible for the slowing or the stopping of the substance passing into the vessel lumen from the interstitium. This hypothesis is supported by the severe fibrosis of the dermis : the lymphatic vessels as the blood vessels, could be compressed by the bundles of collagen fibers characterizing the extracellular matrix. In conclusion, our morphological findings on the skin in CVI show changes both in blood microvasculature and also in the lymphatic capillaries. We hypothesize that they reduce the capability of lymph formation because of collagen fiber compaction and of interstitial fluid decrease even if they do not stop functioning.

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The lymphatic drainage of the esophagus.
Le drainage lymphatique de l'œsophage.

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ABSTRACT

We studied 65 cadavers : 50 adults and 15 newborns. The esophagus was injected at four levels : cervical (16), upper thoracic (18), middle thoracic (30) and lower thoracic (21).

The injected lymphatic vessels were considered : short, when they ended in lymph nodes at the same level ; half-long, when they ended in lymph nodes at the contiguous levels ; long, when they ended in lymph nodes two levels away from the injection site ; and very long, when they ended in lymph nodes more than two levels away from the injection site.

At the cervical level, 24 lymphatic vessels were injected ; 12,5 % were long, ending in the azygotic arch nodes.

At the upper thoracic level, 27 lymphatic vessels were injected : more than half were half long, and two (7,5 %) were long, ending in the regional nodes of the pharynx one, and of the cardia once.

At the middle thoracic level, 37 lymphatic vessels were injected ; 11 % were half long and 27 % were long or very long, ending in the abdomen (70 %) or in the neck (30 %).

At the lower thoracic level, 21 lymphatic vessels were injected ; 50 % were half long, and 15 % were long ending in cervical lymph nodes.

The results of this anatomical study concur with oncological findings and support total esophagectomy with extensive lymph node dissections in the surgical treatment of carcinoma of the esophagus.

Key words : Lymphatics, lymphatic drainage, esophagus, anatomy.

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RÉSUMÉ

L'étude a porté sur 65 cadavres : 50 adultes et 15 nouveaux-nés. L'œsophage a été injecté à 4 niveaux : cervical (16), tiers supérieur de l'œsophage thoracique (18), tiers moyen (30) et tiers inférieur (21). Les vaisseaux lymphatiques injectés ont été étiquetés courts quand ils se rendaient aux lymphonœuds du même niveau, demi-longs quand ils se rendaient aux lympho-nœuds des niveaux voisins, longs s'il s'agissait des lymphonœuds d'un deuxième niveau à partir du point d'injection et très longs au delà de deux niveaux.

Au niveau cervical, 24 vaisseaux lymphatiques ont été injectés : 12,5 % très longs se rendaient aux nœuds de la grande veine azygos.

Au tiers supérieur du thorax, 27 vaisseaux ont été injectés : plus de la moitié étaient demi-longs et deux longs (7,5 %) se rendaient au pharynx dans un cas et au cardia dans l'autre.

Au tiers moyen du thorax, 37 vaisseaux ont été injectés : 11 % étaient demi-longs et 27 % longs ou très longs se terminant dans l'abdomen (70 %) ou au cou (30 %).

Au tiers inférieur du thorax, 21 vaisseaux ont été injectés : 50 % étaient demi-longs et 15 % très longs se rendaient aux lymphonœuds cervicaux.

Les résultats de cette étude anatomique concordent avec les données carcinologiques et militent en faveur de l'œsophagectomie totale avec curages ganglionnaires extensifs en cas de traitement chirurgical du cancer de l'œsophage.

La première étude anatomique sur les lymphatiques de l'œsophage a été réalisée par SAKATA (10) chez 15 fœtus. Ses découvertes ont expliqué les particularités des métastases ganglionnaires dans le cancer de l'œsophage et ont été corroborés par les constatations cliniques de AKIYAMA (1, 2).

Depuis SAKATA, peu de travaux anatomiques ont porté sur le drainage lymphatique de l'œsophage à cause des difficultés techniques rencontrées pour injecter cet organe. Nous rapportons une étude portant sur 65 cadavres.

Lymphatic drainage of the esophagus was first investigated by SAKATA (10) in an anatomical study of 15 fetus. His findings explained the peculiarities of lymphatic metastasis from cancer of the esophagus and were corroborated by the clinical findings of AKIYAMA (1, 2).

Since SAKATA's study, few anatomical studies were devoted to the lymphatic drainage of the esophagus because of the technical difficulties encountered in the injection of this structure. We report a study of 65 cadavers.

MATERIAL AND METHOD

The study was carried out on 50 adult and 15 newborn cadavers.

After removal of the sternum and anterior ribs, thoracic organs were eviscerated in keeping in the plane of the prevertebral ligament. The whole viscera was placed in pronation on the abdomen and the posterior aspect of esophagus was exposed. A blue or green modified Gerota medium was injected in the esophageal wall, at different levels :

— between the lower border of the cricoid cartilage and the jugular notch (fig. 1 A) (cervical esophagus) ;

— between the jugular notch and the Azygotic Arch (fig. 1 B) (upper thoracic esophagus) ;

— between the Azygotic Arch and both the inferior pulmonary veins (fig. 1 C) (middle thoracic esophagus).

— between those veins and the cardia (fig. 1 D) (lower esophagus).

After injection, the dissection of the mediastinum was carried out in situ, and the injected lymphatics were followed as far as their connection with the veins. From the injected sites, the colored medium reached different nodes stations in the mediastinum but also in the neck and in the abdomen. We considered that the collecting vessels were " short " when they joined nodes located at the same level, " half long " when they reached the nodes of the adjacent levels, long at the level after and very long when they exceeded three levels of nodes and injections.

We also noticed the number of collecting vessels we found, their location within the wall of the esophagus (submucosal or muscular), the different nodes interested by the injection.

RESULTS

The location of the involved nodes is given in figure 1 ; 85 injections in 65 cadavers were successful.

A. **Results according to the level injected.**

1) **Cervical esophagus** (fig. 6) :
16 cadavers, 24 lymphatic vessels (L.V.).

No epiesophagal lymph node (L.N.) was observed.

Of the 24 L.V. injected :
- Only one was submucous : half long, it ended at the base of the tongue.
- 20 ended in the cervical nodes, including one after a relay in one node at the left lower pole of the thyroid.
- 3 directed caudad, ended in the azygotic arch nodes.

2) **Upper thoracic esophagus** (fig. 3) :
18 cadavers, 27 lymphatic vessels.

One epiesophagal node was injected in only one case.

Of the 27 L.V. injected :
- Only one was submucous and very long, ended in a paracardial node.

MATÉRIEL ET MÉTHODE

L'étude a porté sur les cadavres de 50 adultes et de 15 fœtus et nouveaux-nés. Après ablation du plastron sternocostal, les organes intra-thoraciques étaient éviscérés en restant dans le plan du ligament prévertébral. L'ensemble des viscères était placé en pronation sur l'abdomen ce qui exposait ainsi la face postérieure de l'œsophage. Une masse de Gerota modifiée (bleue ou verte) était injectée dans la paroi de l'œsophage à différents niveaux :

— entre le bord inférieur du cartilage cricoïde et le confluent de Pirogoff (fig. 1 A) : œsophage cervical ;

— entre le confluent et la crosse de la veine (2) Azygos (fig. 1 B) : tiers supérieur de l'œsophage thoracique ;

— entre le bord supérieur de la veine Azygos et les veines pulmonaires infértieures (fig. 1 C) : tiers moyen de l'œsophage ;

— entre ces veines et le cardia (fig. 1 D) : bas œsophage.

Après l'injection, la dissection du médiastin était effectuée in situ et les vaisseaux lymphatiques injectés étaient suivis jusqu'à leurs abouchements veineux. A partir de l'injection, le colorant atteignait différents lymphonœuds dans le médiastin mais aussi dans le cou et l'abdomen. Nous avons considéré que les vaisseaux étaient " courts " quand ils rejoignaient des lymphonœuds situés au même niveau, " demi-longs " quand il s'agissait des nœuds d'un niveau adjacent, " longs " au niveau après et " très longs " quand les vaisseaux injectaient des nœuds au delà du deuxième niveau, à partir de l'injection.

Nous avons également noté le nombre des vaisseaux injectés, leur siège à l'intérieur de la paroi de l'œsophage (sous-muqueux ou musculaires), les différents lymphonœuds intéressés par l'injection.

RÉSULTATS

Le siège des lymphonœuds (L.N.) injectés est représenté dans la figure 1 ; 85 injections ont pu être réalisées chez les 65 cadavres.

A. **Résultats selon le niveau d'injection.**

1) **Œsophage cervical** (fig. 2) :
16 cadavres, 24 vaisseaux lymphatiques (V.L.) injectés :

Aucun L.N. epiœsophagien n'a été observé.

Parmi les 24 V.L :
- seulement un était sous-muqueux : " demi-long ", il se terminait au niveau de la base de la langue ;
- 20 se rendaient aux lymphonœuds cervicaux, dont un après un relais dans un L.N. situé au pôle inférieur du lobe thyroïdien gauche ;
- 3 descendants allaient aux L.N. de la veine Azygos ;

2) **Tiers supérieur de l'œsophage thoracique** (fig. 3) :
18 cadavres, 27 vaisseaux lymphatiques.

Un L.N. épiœsophagien était injecté dans un cas.

Parmi les 27 V.L. :
- un seul était sous-muqueux : " très long ", il se rendait aux L.N. du cardia ;
- 17 se rendaient aux L.N. du médiastin : deux injectaient le canal thoracique après relais dans un L.N. à son contact ;
- 7 se rendaient aux L.N. cervicaux dont 2 après relais dans un L.N. au pôle inférieur du lobe droit de la thyroïde ;
- 1 se terminait à la base de la langue.

- 17 ended in mediastinal L.N. : 2 of them injected the thoracic duct after a relay in a LN in the vicinity.
- 7 ended in the cervical nodes including 2 after a relay at the right lower pole of the thyroid.
- 1 ended at the base of the tongue.

3) **Middel thoracic esophagus** (fig. 4) :
30 cadavers, 37 lymphatic vessels.

Epiesophagal nodes were observed 2 times.

Of the 37 L.V. injected :
- 3 observed in adults were submucous : two long ended in the paracardial nodes and one very long joined the base of the tongue.
- the injected L.V. ended in :
  - the neck : 2 times.
  - the abdomen : 7 times (including 1 celiac L.N.).
  - the mediastinum : 28 times including 8 times in the thoracic duct (TD), 5 times directly, 3 times after a relay in its vicinity.

4) **Lower thoracic esophagus** (fig. 5) :
21 cadavers, 21 lymphatic vessels.

Of the 21 L.V. injected :
- 3 very long, submucous, were directed cephalad to the pharynx.
- 7 ended in the abdomen. The only one of them submucous injected the lymphatic vessels of the fundus.
- 11 ended in the nodes of the mediastinum.

B. **Pertinent findings.**

1) **In the fetus and newborns** :
15 cadavers, 21 levels, 25 lymphatic vessels.

Only one submucosal L.V., no epiesophagal L.N. and no junction into the thoracic duct were evidenced.

2) **In the adults** :
50 cadavers, 64 levels, 85 lymphatic vessels.

Submucosal L.V. were observed 9 times (10 %) and were preferentially long or very long ending in the cardia or the pharynx.

Of the 13 L.V. who injected the thoracic duct, 5 did so directly without relay into L.N.

Epiesophagal lymph nodes were rarely injected (6 cases).

Injections ended in the first reached node station in all cases except 4 (fig. 3, 4, 5) and those already quoted cases injecting TD (8) and relaying in lower pole of the thyroid (3).

COMMENTS

After SAKATA's work, a lot of publications refered to what he said (3, 5, 8, 9) and no anatomical research, even recently (12, 13) achieved a sufficient number of subjects. However, two particularities of the lymphatic drainage of the esophagus were noted in those former anatomical studies and confirmed in our larger series :

– first, the presence of a submucous lymphatic plexus and of long lymphatic channels ;

– second, the frequent injection as a first relay of nodal stations for away from the injection level of the esophagus.

Both of them were found whatever the esophagal level injected. These particularities were corroborated by clinical studies of cancer of the esophagus (2, 4, 11).

The first particularity explains some of the multifocal forms of cancer of the esophagus through submucous lymphatic permeation. One case of intragastric submucous metastases from a

3) **Tiers moyen de l'œsophage thoracique** (fig. 4) :
30 cadavres, 37 vaisseaux lymphatiques.

Deux fois existaient des L.N. épiœsophagiens.

Parmi les 37 V.L. :
- 3 rencontrés chez l'adulte étaient sous-muqueux : deux " longs " se rendaient aux L.N. du cardia et un " très long " à la base de la langue.
- Les V.L. injectés se rendaient :
  - au cou : 2 fois.
  - à l'abdomen : 7 fois (dont une fois au tronc cœliaque) ;
  - au médiastin : 28 fois, dont 8 fois au canal thoracique (directement dans 5 cas et après relais dans un L.N. à son contact dans 3 cas.

4) **Bas œsophage** (fig. 5) :
21 cadavres, 21 vaisseaux lymphatiques.

Parmi les 21 V.L. injectés :
- 3 " très longs " sous-muqueux se rendaient au pharynx ;
- 7 se rendaient dans l'abdomen : le seul d'entre eux à être sous-muqueux injecte les V.L. du fundus gastrique.
- 11 se terminaient dans les L.N. du médiastin.

B. **Constatations complémentaires particulières.**

1) **Chez les fœtus et nouveaux-nés** :
15 cadavres, 21 niveaux injectés, 25 vaisseaux lymphatiques.

Seulement un V.L. était sous-muqueux ; aucun L.N. épi-œsophagien et aucun abouchement dans le canal thoracique n'ont été observés.

2) **Chez les adultes** :
50 cadavres, 64 niveaux, 85 vaisseaux lymphatiques injectés.

Des V.L. sous-muqueux ont eté observés 9 fois (10 %) : ils étaient longs et demi-longs et se rendaient au cardia ou au pharynx.

Parmi les 13 V.L. qui se rendaient au canal thoracique, 5 le faisaient directement sans aucun relais dans un L.N.

Les L.N. épi-œsophagiens (au contact même de la paroi œsophagienne (12), étaient rarement rencontrés (5 cas).

Les injections se terminaient dans les premiers L.N. rencontrés sauf dans 4 cas (fig. 3, 4, 5) et ceux déjà cités injectant le canal thoracique (8) et ceux faisant relais à un L.N. du pôle inférieur d'un lobe thyroïdien (3).

COMMENTAIRES

Après les travaux de SAKATA, de nombreuses publications se référèrent à ce qu'il avait dit (3, 5, 8, 9) et aucune recherche anatomique , même les plus récentes (12, 13), n'a pu réunir un nombre suffisant de cas.

Cependant, deux particularités du drainage lymphatique de l'œsophage furent notées dans ces précédents travaux anatomiques et confirmées par notre série plus large :

– premièrement, il existe des vaisseaux lymphatiques sous-muqueux et des vaisseaux lymphatiques longs et très longs ;

– deuxièmement, le premier lymphonœud rencontré est fréquemment situé à distance du niveau injecté sur l'œsophage.

Ces deux particularités furent constatées quel que soit le siège étudié sur l'œsophage et furent corroborées par la recherche clinique sur le cancer de l'œsophage (2, 4, 11).

La première particularité explique certaines des formes plurifocales du cancer de l'œsophage liées à des nodules de perméation à partir des lymphatiques sous-muqueux ; un cas de métastases gastriques sous-muqueuses d'un cancer du tiers inférieur

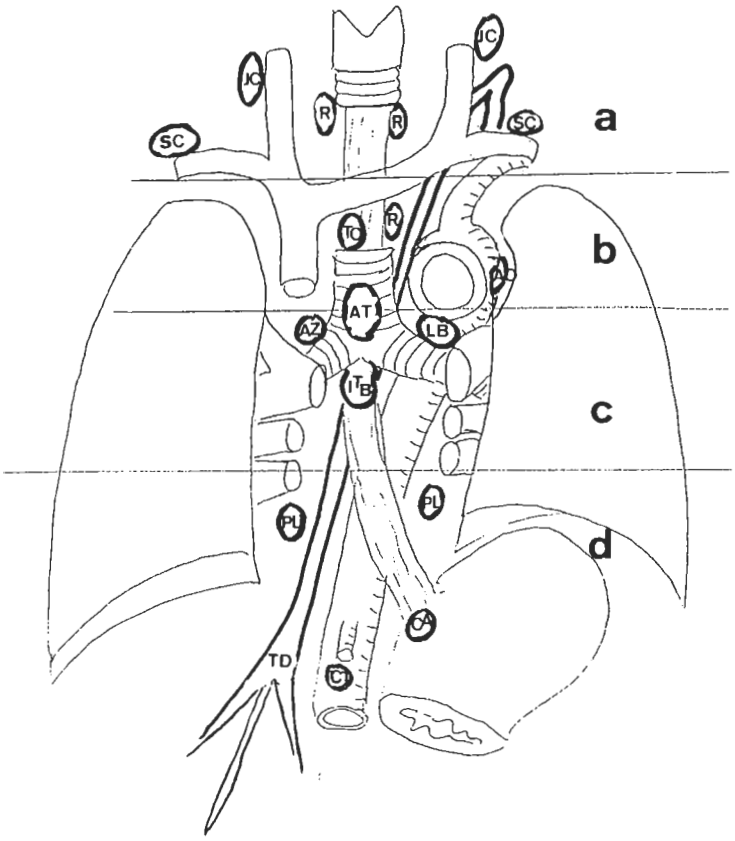

Fig. 1

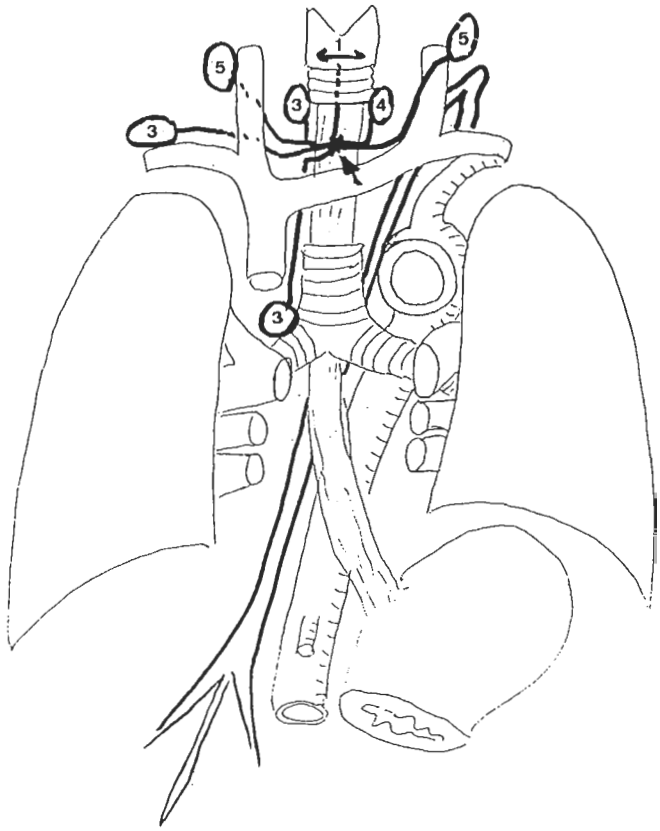

Fig. 2

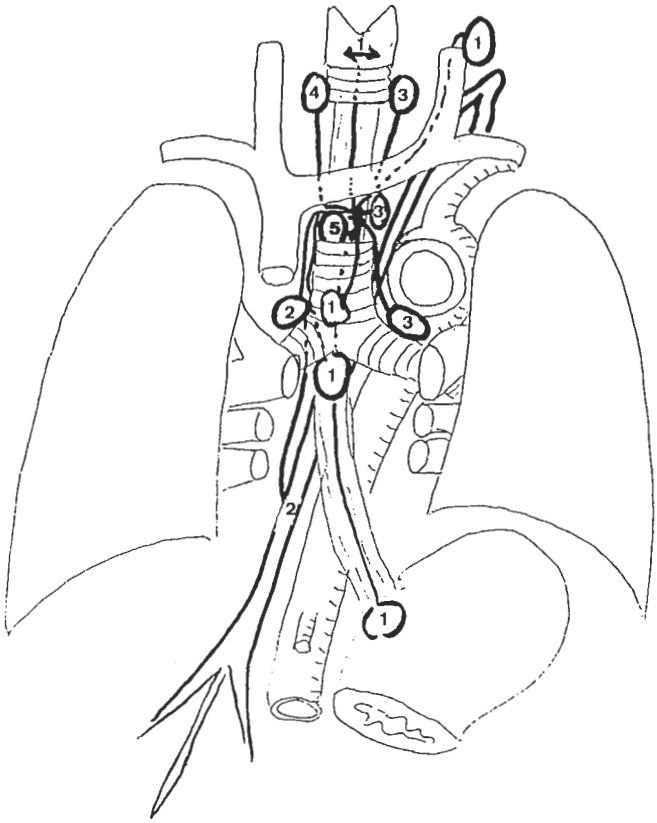

Fig. 3

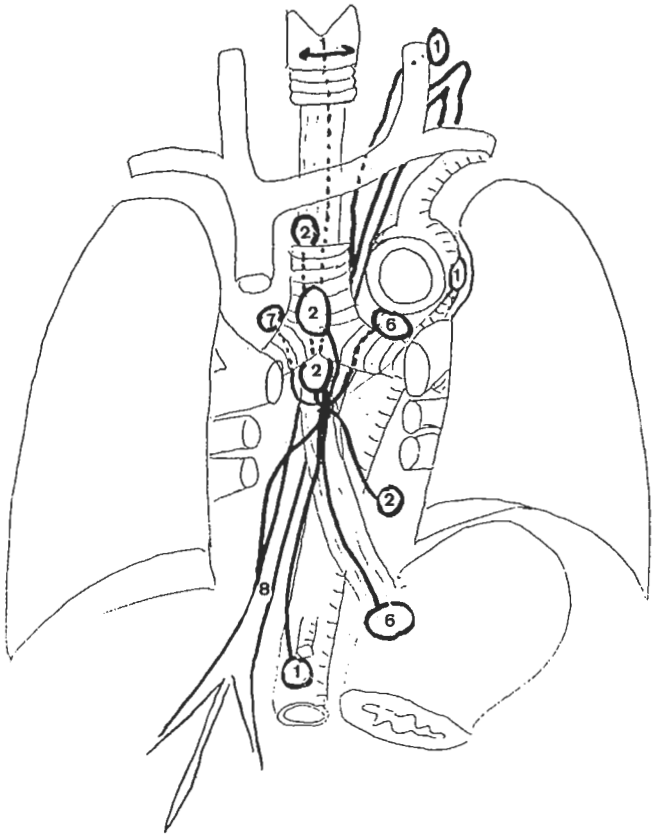

Fig. 4

carcinoma of the lower third of the esophagus was reported (7) and we observed a submucous lymphatic channel injecting the lymphatics of the fundus...

The second particularity emphasizes the necessity for systematic lymphatic dissection of all nodal stations possibly involved in the neck, mediastinum and upper abdomen (1, 6).

Both of them support the concept of total esophagectomy with extensive lymphatic dissection in the surgical treatment of the cancer of esophagus.

Endly, we observed that epiesophagal nodes were not as frequent as noted by SARRAZIN (12) and their injection was rarely observed, and that the thoracic duct was injected in a substantial number of cases, sometimes directly.

de l'œsophage a même été rapportée (7) et nous avons observé un cas où les vaisseaux lymphatiques sous-muqueux injectaient les lymphatiques du fundus...

La seconde particularité souligne la nécessité de reséquer systématiquement toutes les chaînes ganglionnaires susceptibles d'être atteintes tant au niveau cervical, médiastinal ou abdominal (1, 6) en cas de cancer.

Ces deux particularités militent en faveur de l'œsophagectomie totale avec curages ganglionnaires extensifs lors du traitement chirurgical du cancer de l'œsophage.

Enfin, nous avons observé que les lymphonœuds épiœsophagiens n'étaient pas aussi fréquents que le pensait SARRAZIN (12) et sont rarement injectés, et que le canal thoracique par contre est injecté dans un nombre de cas important, parfois même directement sans relais aux lymphonœuds.

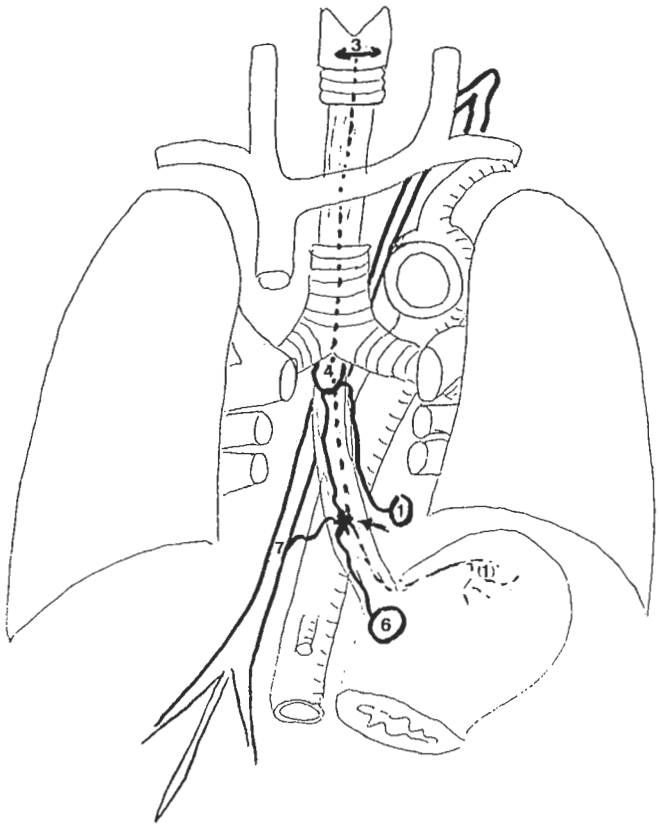

Fig.5

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The absorbing lymphatic vessels of trachea and oesophagus in guinea pig : a histotopographic and ultrastructural study.

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ABSTRACT

The only systematic study of the absorbing lymphatic vessels of the trachea and oesophagus was performed by light microscopy. The aim of this study was to verify the histotopography of the lymphatic absorbing network of the guinea pig trachea and oesophagus and to define their ultrastructural features by transmission electron microscopy. The lymphatic vessels were located deeper in both organs than the blood capillaries. A rich lymphatic network was present in the mucous and submucous coats of the oesophagus. Absorbing lymphatic vessels were also found in the muscle coat of this organ. These vessels were probably en route to the fibrous coat. Tracheal lymphatic absorbing vessels were located in the mucous and submucous coats, often in close association with glands. Some lymphatic vessels with values but still absorbing ultrastructure were found near tracheal cartilage. No ultrastructural differences were detected between the absorbing plexuses of the inner coats of these two organs and the initial effluent lymphatics. This confirms the peculiarity of the visceral district also in the trachea and oesophagus. There are no morphologically distinct outflow routes comparable to the so-called precollectors of the superficial districts.

Key words : Lymphatic vessels, trachea, oesophagus, ultrastructure, guinea pig.

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INTRODUCTION

Little information is available in the literature on the absorbing lymphatic vessels of the trachea and oesophagus. To our knowledge, the only systematic study on the subject is a light microscopy study by BASTIANINI and SACCHI (1968) in the guinea pig. These authors, using lymphagogue substances to visualize the lymphatic vessels, report the presence in the oesophagus of two distinct plexuses, one of which is located in the mucous membrane and the other in the submucous coat. They report that the muscle coat lacks an absorbing lymphatic network of its own. The lymphatics of the trachea run longitudinally along the internal side of cartilage rings or annular ligaments to reach the posterior wall where they drain into efferent collectors.

The aim of this study was to investigate the histotopography of the lymphatic absorbing network of the trachea and oesophagus in the guinea pig and to verify by transmission electron microscopy (TEM) the morphological features of these vessels and their exact relationship with the other wall components of these organs.

MATERIALS AND METHODS

Five guinea pigs weighing 250 - 300 gr. were either anesthetized and given 200 U/kg. i.v. heparin. Two minutes later the animals were bled by cutting the abdominal aorta. Trachea and oesophagus were removed in block, washed in saline and cut into pieces. The oesophagus was divided into 4 segments : cervical, thoracic, diaphragmatic, and abdominal to evaluate whether the distribution of absorbing lymphatics differed in these segments. All samples were fixed in 2.5 % glutaraldehyde in 0.1 M cacodylate buffer, pH 7.35 for 3 h at 4°C, postfixed 2 h at 4°C in OsO_4, dehydrated in acetone and embedded in Epon 812. Semithin sections were stained with 1 % toluidine blue and observed under a Zeiss Axioplan microscope. All lymphatic vessels observed under light microscopy were checked by electron microscopy to distinguish lymphatics from blood vessels. Ultrathin sections, obtained with an LKS ultratome were observed in a Philips 201 electron microscope operating at 60 kV.

RESULTS

Light microscopy.

There was a rich absorbing lymphatic network in both organs. Under light microscopy the absorbing lymphatic vessels could be differentiated from blood capillaries and venules by their morphology : their larger size, thinner walls and extremely fine and irregular endothelial profile with folds and digitations. Electron microscopy confirmed that these vessels were indeed lymphatics. Light microscopy however was invaluable for defining the histotopography of lymphatic absorbing vessels and their distribution.

The **oesophagus** possessed an absorbing lymphatic network in the tunica propria of the mucous coat (fig. 1). These lymphatic vessels, wide and sparse, were located in the vicinity of arterioles in a deeper position than blood capillaries which were mainly subepithelial, smaller and more numerous. Larger absorbing lymphatic vessels were found in the more external coats of the oesophagus wall. We also observed lymphatic vessels that moved in the muscle coat (Fig. 2). These vessels were located in large connective shoots together with arteries and veins and were often encountered at the boundary between the internal circular and the external longitudinal muscle layer. These vessels joined those of the fibrous coat which in turn joined together to form the efferent collectors of the organ. The lymphatic absorbing network was not equally distributed in the different segments of the oesophagus. It was particularly abundant in subepithelial position in the cervical segments where the muscolaris mucosae is only slightly developed, whereas it was less abundant in the lower segments where the muscolaris mucosae becomes more robust and conspicuous. The reduction of lymphatic vessels in the lower segments of the oesophagus was not accompanied by changes in the distribution of blood capillaries : these were equally numerous in all segments.

The absorbing lymphatic network of the **trachea** was less developed than that of the oesophagus. Large absorbing lymphatic vessels were located in the mucous and submucous coats. It should however be noted that they constitute one plexus extending from the tunica propria of the mucous coat to the internal side of the cartilage rings. Lymphatic vessels near cartilage rings sometimes contained fine valves (Fig. 3). In the submucous coat, lymphatic vessels were often closely associated with glands (Fig. 4). As in the oesophagus, the absorbing lymphatic vessels were always deeper than blood capillaries, the latter being mainly subepithelial.

Transmission electron microscopy

The wall of all lymphatics examined consisted solely of a thin layer of endothelial cells with a discontinuous basement membrane (Fig. 3). Anchoring filaments extended between the abluminal side of endothelial cells and the surrounding connective tissue. Endothelial cell cytoplasm contained an abundance of rough endoplasmic reticulum, free ribosomes, well developed Golgi apparatus, lysosomes, mitochondria and pinocytotic vesicles. The endothelial cells were connected by three types of intercellular contacts : interdigitating (Fig. 6), overlapping and end to end. Occasionally, open junctions were also observed (Fig. 7).

The lymphatic vessels of the muscle coat of the oesophagus (Fig. 8) were devoid of valves and showed the same ultrastructural features as the above.

The absorbing lymphatic vessels of the tracheal submucous coat were narrower than the oesophageal vessels. Their connective environment was rich in fibroblasts and mastcells (Fig. 9). Their close association with glands in the submucous coat (Fig. 9) and with cartilage rings was confirmed by TEM.

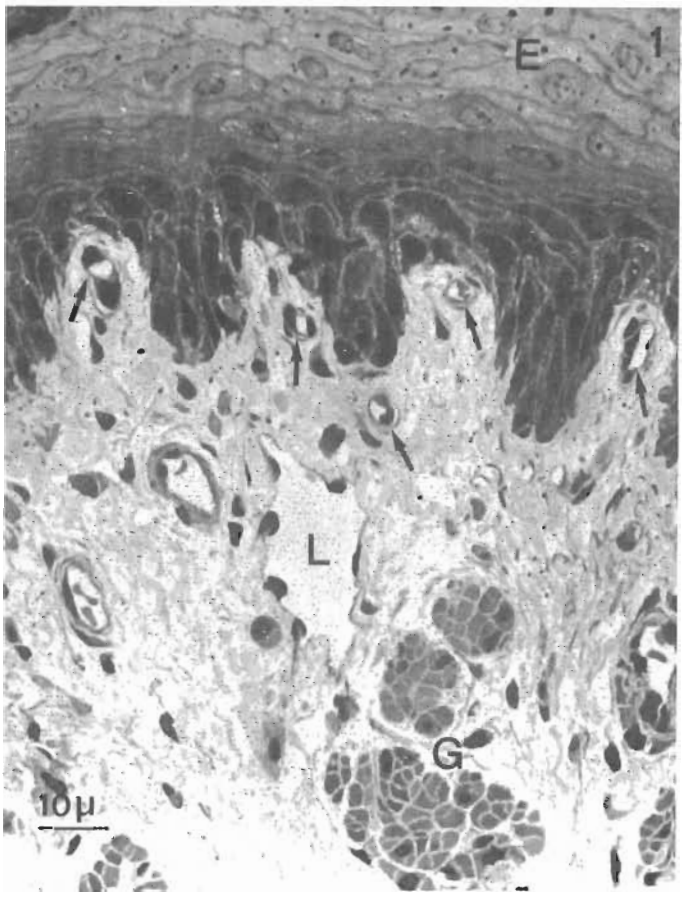

Fig. 1

Oesophagus. A lymphatic vessel (L) in the mucous coat. Subepithelial blood capillaries (arrows). E = epithelium. G = glands. Original magnification : × 40.

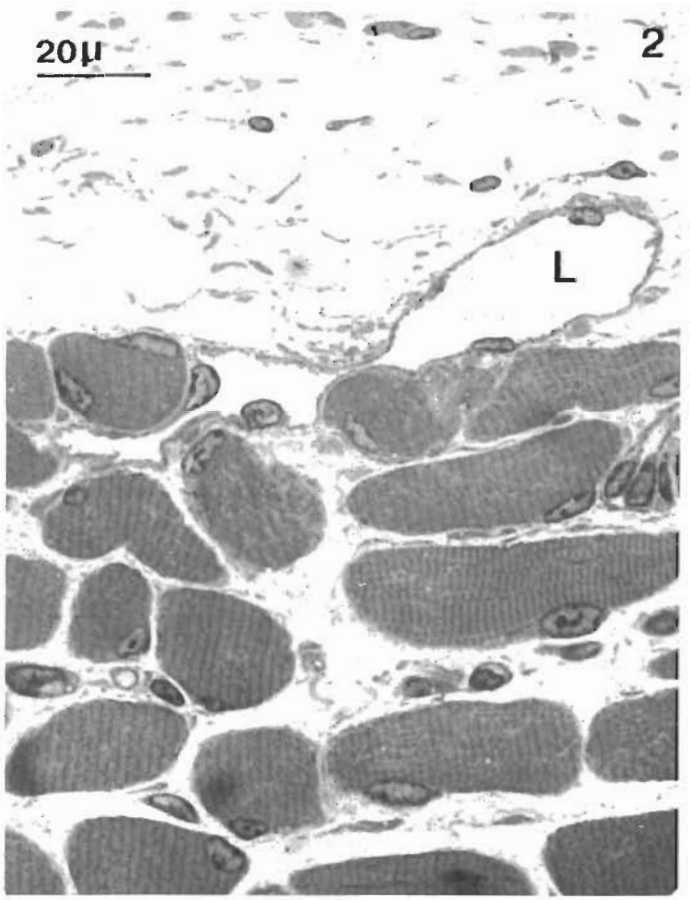

Fig. 2

Oesophagus. A lymphatic vessel (L) passing from the submucous into the muscle coat. Original magnification : × 63.

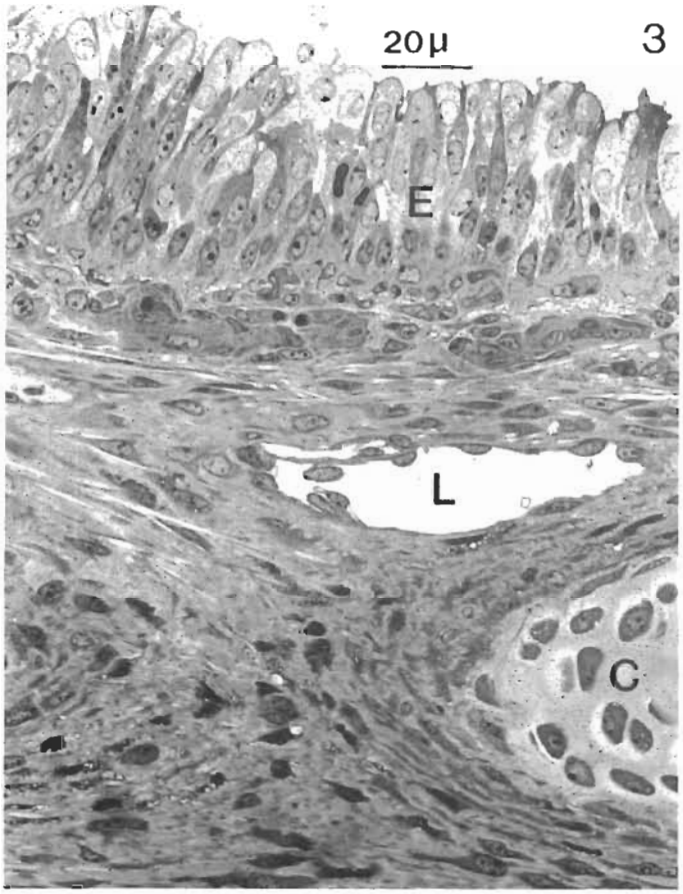

Fig. 3

Trachea. A lymphatic vessel (L), with a valve between the epithelium (E) and cartilage (C). Original magnification : × 63.

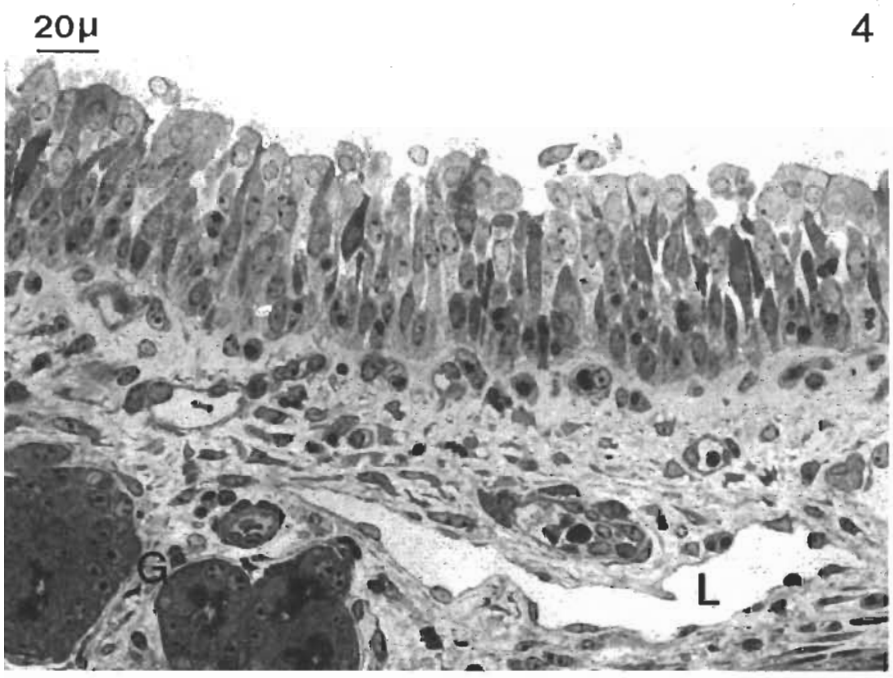

Fig. 4

Trachea. A large lymphatic vessel (L) in the submucous coat near glands (G). Original magnification : × 40.

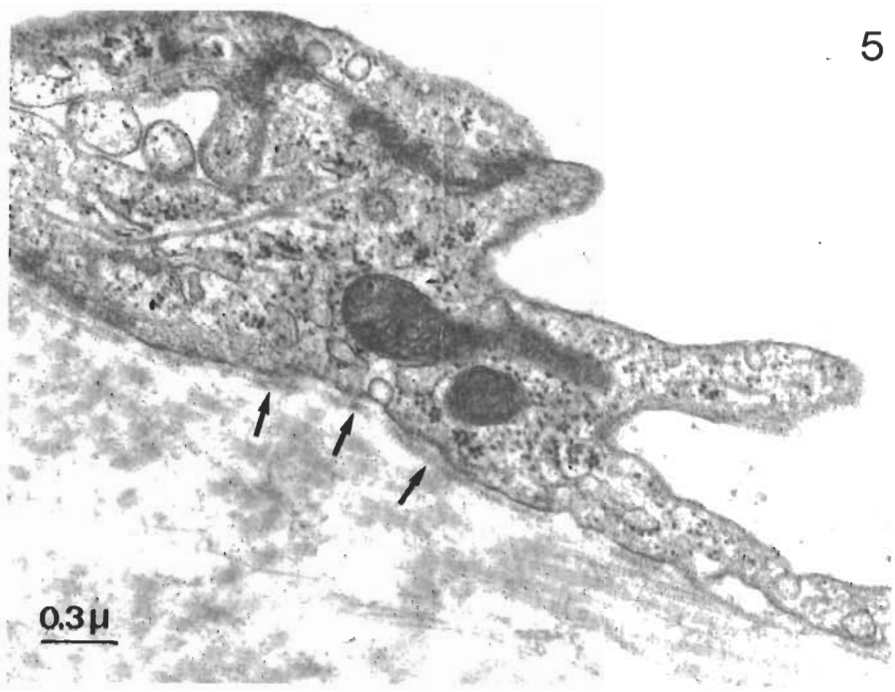

Fig. 5

Two tracheal lymphatic endothelial cells with discontinous basement membrane (arrows). Original magnification : × 20,000.

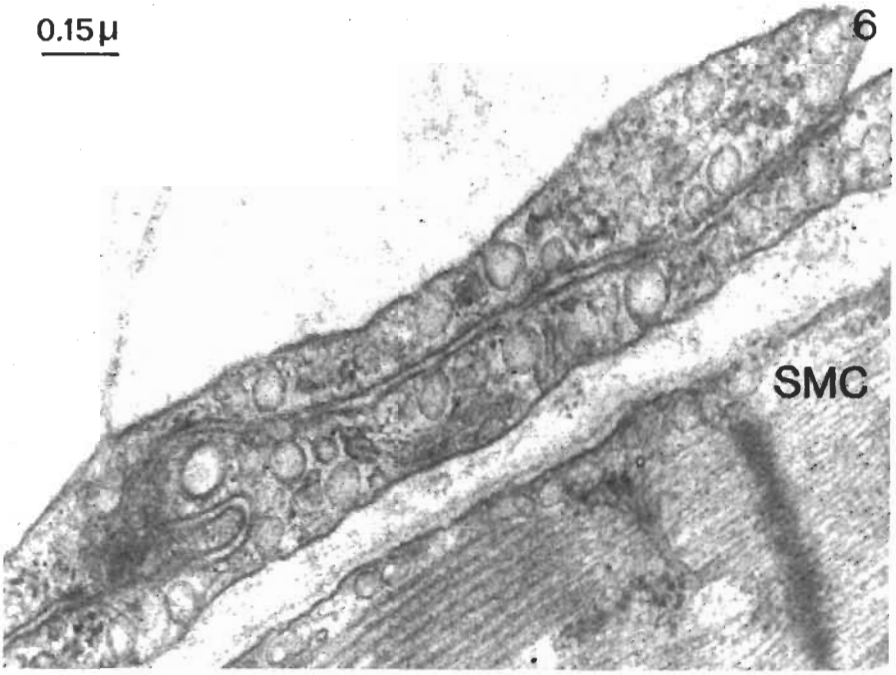

Fig. 6

An interdigitating junction between two endothelial cells at the boundary between the submucous and muscle coat of the oesophagus. The endothelial cells contain several pinocytotic vesicles. SMC = smooth muscle cell. Original magnification : × 45,000.

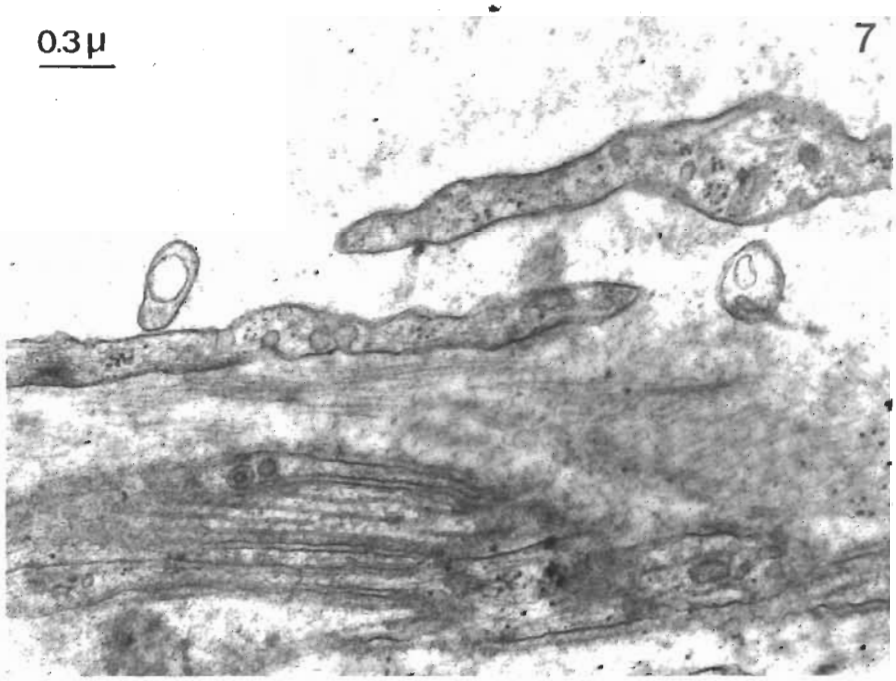

Fig. 7

An open junction between two endothelial cells in a tracheal lymphatic vessel. Original magnification : × 20,000.

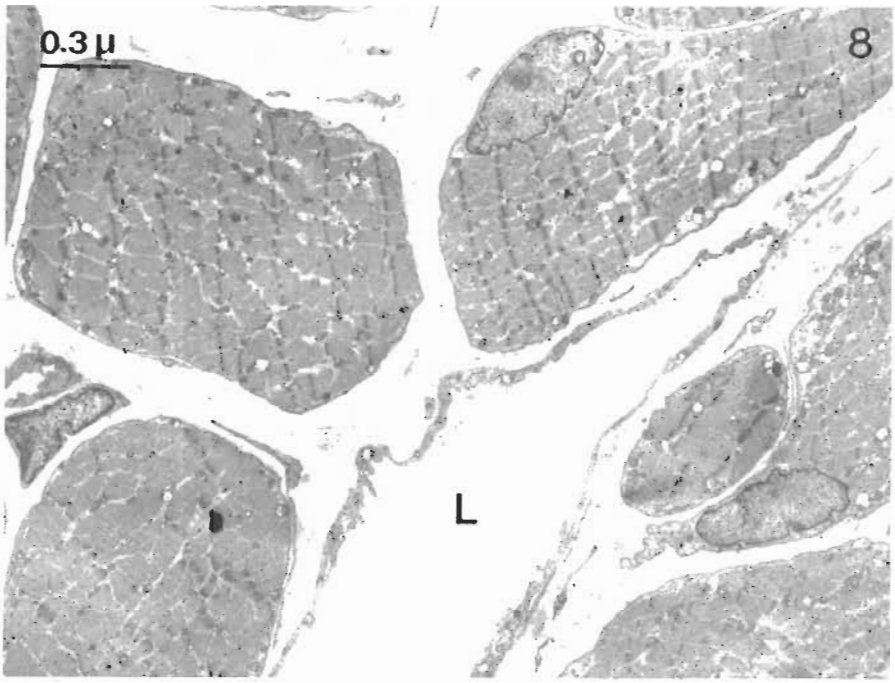

Fig. 8

A lymphatic vessel (L) in the muscle coat of the oesophagus.
Original magnification : × 1,500.

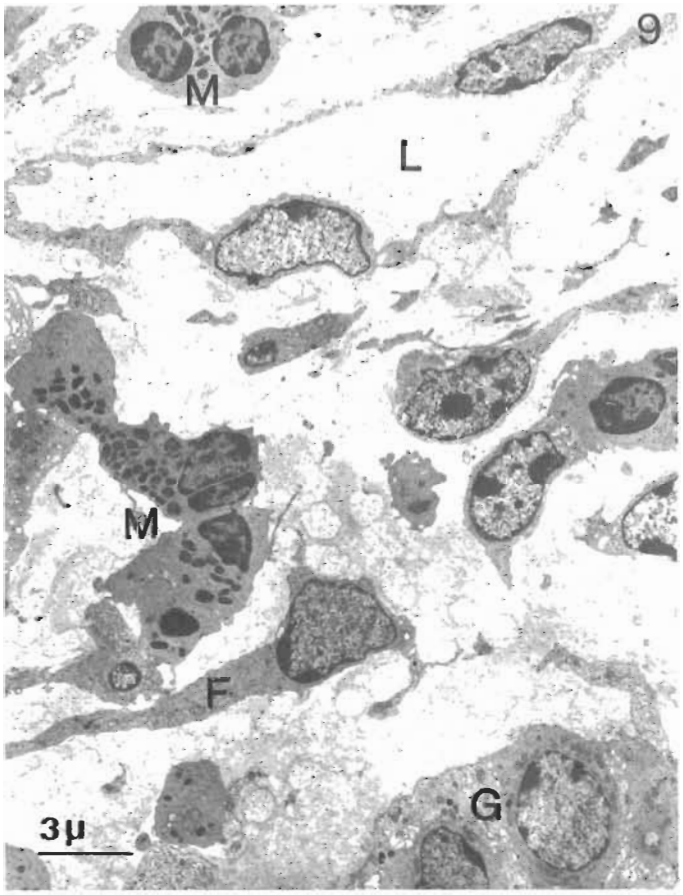

Fig. 9

A lymphatic vessel (L) in the submucous coat of the trachea.
The surrounding connective tissue is rich in mast cells (M)
and fibroblasts (F).
A gland (G) is visible in the lower right corner.
Original magnification : × 1,500.

DISCUSSION

The present findings confirm those previously reported (BASTIANINI and SACCHI 1968). In both organs, the absorbing lymphatic vessels were localized in the inner layers of the walls, the mucous and submucous coats. Larger lymphatics, still with an absorbing ultrastructure, were found in the fibrous coat.

All the absorbing lymphatic vessels observed by light microscopy were confirmed to be lymphatics by their typical ultrastructural features (LEAK and BURKE, 1965 ; LEAK, 1976 ; MARCHETTI et al., 1987 ; GERLI et al., 1990).

The oesophageal muscle coat, previously reported to be devoid of a lymphatic network of its own, did contain some lymphatics. These lymphatics, located in the connective shoots together with arteries and veins, should be interpreted as vessels passing from the inner to the outer coats. The quantitative differences in the distribution of lymphatic absorbing vessels in the four oesophageal segments (cervical, thoracic, diaphragmatic and abdominal) seemed strictly related to the presence or absence of a well developed muscularia mucosae. We have no explanation for this phenomenon.

Tracheal lymphatics were distributed throughout the organ wall from the mucous coat to the cartilage rings, forming a single plexus of large, sparse lymphatics. The larger lymphatics in the proximity of the cartilage rings possessed valves and showed the same ultrastructural features as the smaller inner ones.

In superficial districts (NIIRO et al., 1986 ; NIIRO and O'MORCHOE, 1986 ; O'MORCHOE et al., 1987), the lymphatic vessels that join the absorbing periphery with the effluent routes of collectors, the so-called precollectors, have a more complex wall that distinguishes them from the absorbing lymphatic vessels (COMPARINI, 1962) by virtue of the presence of smooth muscle cells. It is interesting that all the lymphatic vessels located in the wall of these two organs, whether this subepithelial or larger vessels, even those with valves (NAVAS et al., 1991), showed the same ultrastructural simplicity as absorbing lymphatic vessels.

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