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Lymphatics of Blood Vessels

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Lymphatics of blood vessels

In recent years a number of investigations of the anatomy of the vasa vasorum of major blood vessels have been made (1, 2, 3, 4), but few observations of the lymphatic component of vasa vasorum have been recorded. Investigations of lymphatics of blood vessel walls were reported nearly one hundred years ago (5), and the anatomical findings apparently were unclear which resulted in considerable debate among contemporary investigators regarding what had been observed. Most of the controversy

seemed to center about whether intercellular spaces were being interpreted as lymphatic capillaries. Some investigators at that time even denied that lymphatics existed within or about the walls of the blood vessels. In recent years there have been only a few reports specifically on the subject (6, 7, 8, 9, 10).

The present study describes results of a preliminary investigation to determine the anatomical relationships of lymphatics to the walls of blood vessels. No effort was made to delineate specific lymph drainage pathways.

Material and methods

Studies were made on portions of aorta, pulmonary artery, vena cava, pulmonary vein, and coronary artery and vein obtained from dogs, pigs, and humans. The specimens from healthy swine approximately six months of age were obtained from a local abbatoir; specimens from dogs were furnished by the experimental surgical laboratory at the time animals were sacrificed. Human specimens were obtained at random from autopsies of adult patients dying from various causes. Several older patients had severe arteriosclerosis of the aorta with aneurysms. Specimens were obtained from 15 of each of the species.

Lymphatics were demonstrated by injection of India ink (diluted 1 : 10) through a 27-guage needle, attached to a five or ten cc syringe. Identification of lymphatics was made on the basis of morphological characteristics which have been described previously (11, 12, 13). Several techniques of injection were applied; 1. The needle was advanced carefully through the adventitia at the medial junction. As the needle passed through small vessels, ink was drawn into them by capillary action; then gentle pressure on the syringe completed filling of the plexus of vessels. The pattern formed by lymphatic plexuses is characteristic and can be distinguished by the naked eye from plexuses of blood capillaries. Because of the delicate structure of lymphatic capillaries, they rupture easily and only small areas can be injected at any one time. 2. The aorta and vena cava specimens obtained from pigs and dogs were removed with much of the perivascular structures intact. Ink injected into large paravascular lymph nodes flowed into the cisterna chyli or thoracic duct which was closely related to the aorta. By clamping both ends of this vessel with hemostats, ink injected directly into it filled a number of lymph ducts and plexuses of lymphatics on the aortic wall. 3. Small lymph nodes were identified in the deep adventitia surrounding the aorta, particularly in specimens from humans. These were injected gently with ink which resulted in retrograde and antegrade filling of adventitial plexuses of regional lymphatics. All three methods of injection were utilized whenever possible, but in general the method of injecting into the deep adventitia usually was more rewarding.

All specimens were injected while fresh, then fixed in 10 per cent formalin and cleared by the Spalteholz method (1). After clearing, specimens were observed through a stereomicroscope and photographed with a 35 mm Exacta camera back attached to one ocular of the microscope. Exposure time was determined with a photometer

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attached to the other ocular. The light source for dissection and photography was a standard 35 mm slide projector equipped with a 500-watt bulb (13).

Results

Aorta and Pulmonary Artery in Pigs and Dogs. The large lymphatic channel (3–5 mm in width) in dogs and pigs demonstrated by injecting ink into the para-aortic lymph nodes was assumed to be the thoracic duct though it was not traced to its termination. It was located at the adventitial-medial junction and often one or two smaller channels (1–2 mm in width) were present which anastomosed with the larger vessel prior to its exit near the aortic arch. Smaller vessels (50–300 microns in width) in the deep and superficial adventitia joined the thoracic duct along its course. Some of these channels had characteristics of blood vessels with uniform margins and no evidence of valves, while others appeared as typical lymphatics with a bulbous contour (Figure 1). This observation was suggestive of lymphatic-blood vascular communications. The deep and superficial adventitial lymphatic channels (30–100 microns in width) are arranged in a network surrounding the aorta but do not penetrate into the media (Figure 2). Collecting channels from the adventitial plexuses join regional adventitial and para-aortic lymph nodes (Figure 3) and in some instances join the thoracic duct directly as mentioned above.

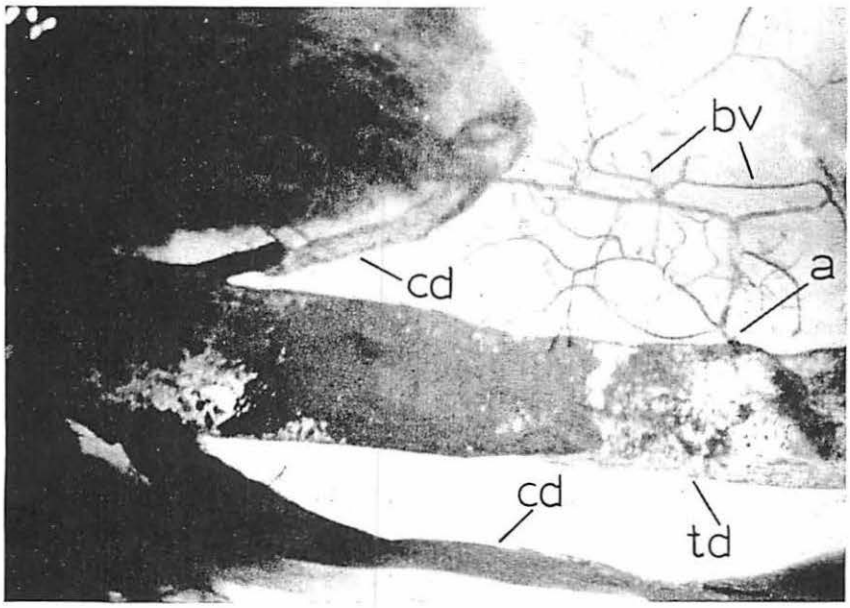

Fig. 1 Illustration of thoracic duct (td) and accompanying vessels at the adventitial-medial junction of the aorta from a pig. The thoracic duct (4 mm in width) and adjoining lymphatic collecting ducts (cd) course along the longitudinal axis of the aorta. The thoracic duct (td) has been injected with India ink (see text) which has entered the blood vessel network (bv) overlying the media of the aorta through anastomosis (a). The lymphatic collecting ducts (cd) were filled concomitantly. Magnification x12.

Lymphatics in the adventitia of the ascending aorta were in continuity with the subepicardial lymphatics of the left ventricle, but the denseness of the network over the aorta was less than that of the subepicardium (13).

The arrangement of lymphatic channels in the superficial and deep adventitia of the pulmonary artery was similar to that seen about the aorta and the lymphatic vessels did not penetrate the media (Figure 4). Drainage channels into regional nodes of the pulmonary artery were not observed since these regional tissues were detached at the time the specimens were obtained.

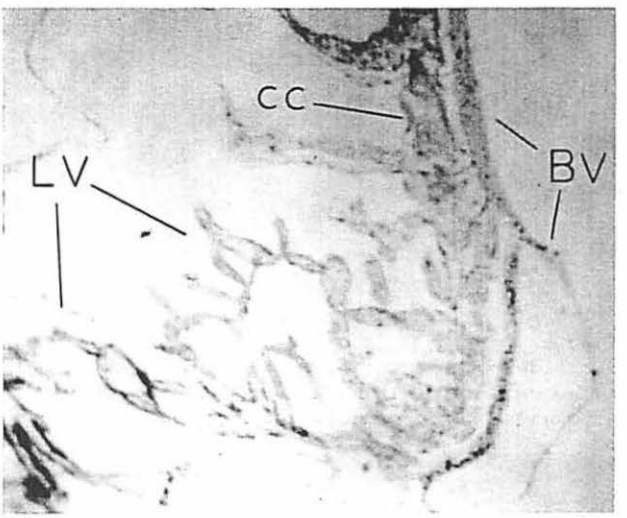

Fig. 2 Plexus of lymphatic vessels (LV) approximately 30–50 microns in width at the adventitial-medial junction of aorta from a pig. These small channels converge toward a lymphatic collecting channel (cc) 300 microns in width. A blood vessel (BV) measuring approximately 150 microns in width is noted to the right of the lymphatic collecting channel. Magnification x15.

Lymphatics were not demonstrated on the endothelium or subjacent areas in any of the arterial specimens.

Human Aorta. Most specimens of human aorta were obtained from elderly patients and three of these with severe arteriosclerosis had undergone previous surgery for aneurysm of the abdominal aorta. As much as possible of the perivascular tissues was preserved during removal of the specimens, but apparently the thoracic duct was detached and could not be demonstrated.

Plexuses of lymphatic channels (30–70 microns in width) were demonstrated in the deep and superficial adventitia and in general were similar to those seen in dogs and pigs. In several specimens of thoracic and abdominal aorta, a fine network of lymphatic vessels (15–50 microns in width) was observed at the adventitial-medial junction (Figure 5). This was not a consistent finding in all specimens and it could not be correlated with the degree of arteriosclerotic involvement. This pattern was not seen in the pigs and dogs studied.

Small lymph nodes in the adventitia of the aorta of humans were more numerous than in the other two species. Many of these nodes ranged from 1 to 2 mm in length up to 0.5 to 1 cm in length and were located at the adventitial-medial junction as well as superficially (Figure 6).

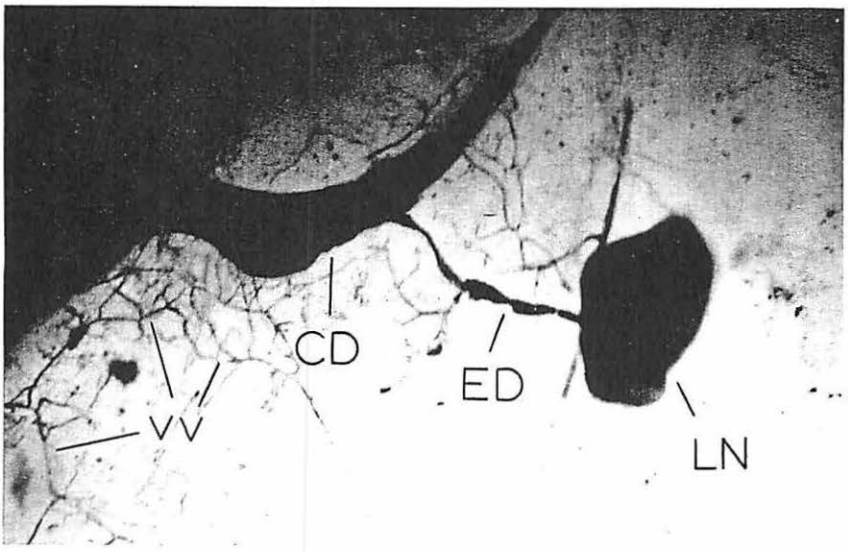

Fig. 3 Small lymph node (LN) 5 mm. in length in the deep adventitia overlying the media of aorta from a pig. An efferent duct (ED) from the node joins a lymphatic collecting duct (CD) 2–3 mm. in width at the adventitial-medial junction. The collecting duct (CD) continued for several more centimeters along the aorta and joined the thoracic duct beyond the left lower portion of the photograph and is not included in the illustration (see text). Small blood vessels (vv-vasa vasorum) are noted at the adventitial-medial junction of the aorta. Magnification x10.

In none of the specimens could lymph channels be seen penetrating into the media of the aorta or into areas of atheromata, intramural hemorrhage, calcification, or aneurysmal dilatation.

Anastomoses between blood vessels and lymphatics were not observed on the wall of the human aorta.

Lymphatics of Veins. Lymphatic channels (20–50 microns in width) were demonstrated in the media and adventitia of veins in all three species (Figure 7). The depth of penetration within the media was not determined due to limitations of the techniques applied. Specimens of superior and inferior vena cava and pulmonary vein were studied. Small lymph nodes were not seen in the adventitia of veins as they were in the adventitia of the aorta. The lymph channels in the media of the vena cava joined superficial adventitial vessels. In those specimens of vena cava in which the paravascular tissues were left intact at the time of removal of the specimens, lymphatic collecting ducts led to large lymph nodes situated between the aorta and vena cava. The denseness of the lymphatic capillary bed of the venous system was similar in the three species. Relation of lymphatic channels of the superior vena cava and pulmonary vein to regional lymph nodes was not determined since the paravascular tissues beyond the adventitia were not obtained when the specimens were collected.

Lymphatics of Coronary Arteries. Lymphatics of the heart have been described elsewhere (13, 14, 15, 16); in general they form a fine network in the subendocardium and subepicardium with collecting ducts and transmyocardial connecting channels.

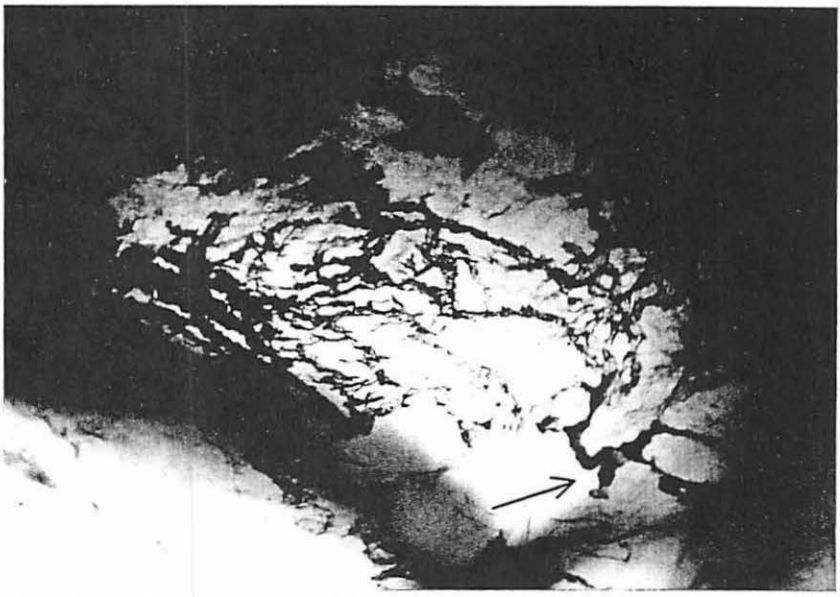

Fig. 4 Lymphatic plexus at the adventitial-media junction of the pulmonary artery from a pig. These channels measure between 75 and 300 microns in width. The prominent channels in the right lower corner of the photograph (arrow) are extending over the right ventricular myocardium. Magnification x10.

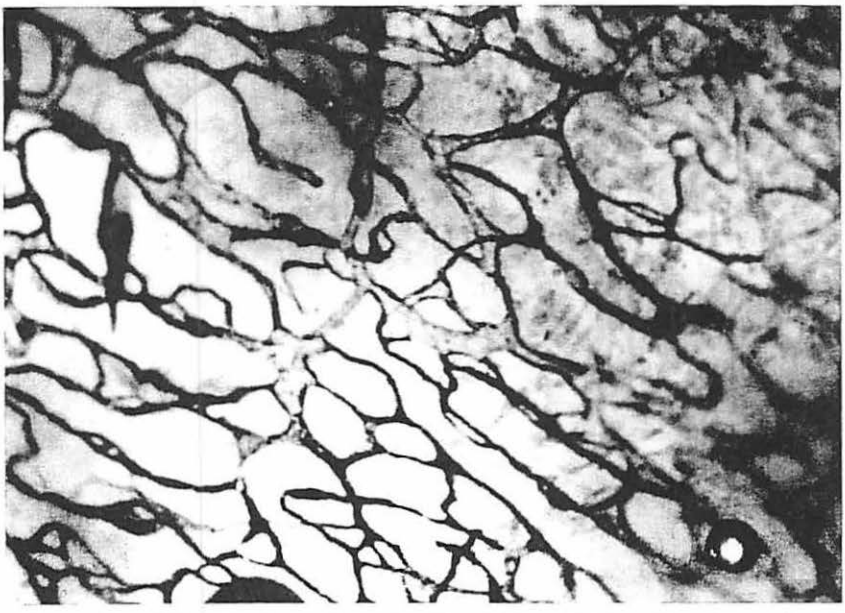

Fig. 5 Plexus of small lymphatic vessels at the adventitial-medial junction of aorta from human with severe atherosclerosis magnified 20 times for detail. The vessels measure between 15 and 50 microns in width.

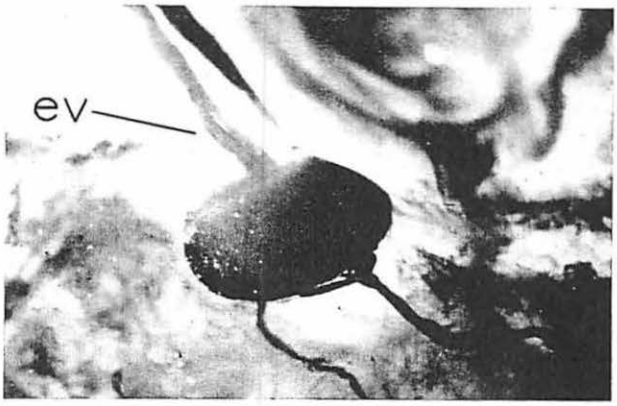

Fig. 6 Small lymph node 5 mm. in length in the deep adventitia near the medial junction of aorta from a human. Efferent (ev) and afferent vessels are shown (250–350 microns in width). Magnification x10.

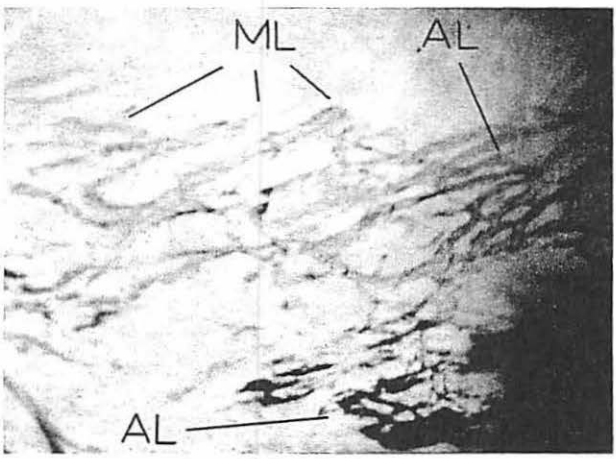

Fig. 7 Lymphatics of vena cava from a pig. Lymphatic channels in the deep adventitia (AL) are seen to the rigth of the photograph continous with lymphatic channels to the left (ML) that are intramural. These vessels range between 50 and 75 microns in width and penetrate to a depth of about one half the thickness of the media. Not seen on the illustration are smaller channels (15–20 microns in width) emanating from those shown toward the luminal aspect of the vein wall. Magnification x15.

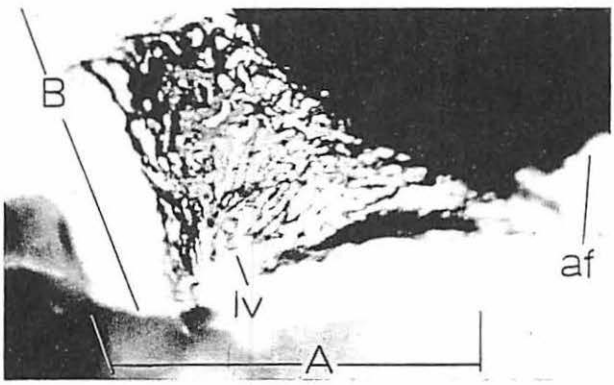

Fig. 8 Lymphatic plexus at the adventitial-medial junction of the proximal portion of the left anterior descending coronary artery from a human. The vessel has been sectioned and the width is approximately 6 mm. (A). The course of the longitudinal axis of the coronary artery is denoted by (B). The lymphatic vessels (lv) overlie the media and are between 30 and 150 microns in width. Ink injection artifact (af) is noted in the adjacent epicardium. Magnification x15.

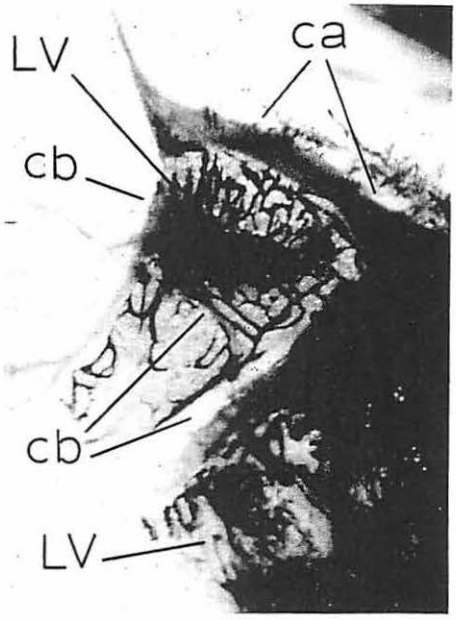

Fig. 9 Subepicardial lymphatic channels and their relationship to secondary and smaller branches of the coronary arteries in man. The background of the illustration is myocardium. (Ca-distal portion of left anterior descending coronary artery; cb-denotes smaller branches from the artery; LV-lymphatic vessels 15–75 microns in width in the subepicardium.) Magnification x7.

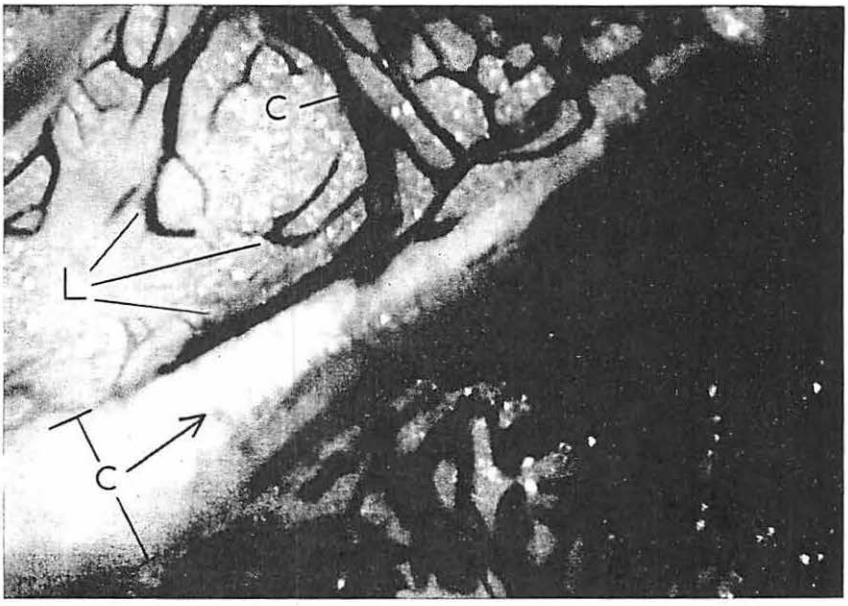

Fig. 10 The same illustration as fig. 11 magnified thirty times for detail of the relationship of lymphatic capillaries (L) to the small arterial branches (c). See text.

In dogs and pigs no direct anatomical relationship was observed between cardiac lymphatics and the coronary arteries. Lymphatic capillaries in the subepicardium overlie the coronary arteries and are in the superficial adventitia but do not penetrate to the adventitial-medial junction.

In humans, subepicardial lymphatics overlying the main coronary arteries penetrate the adventitia as deep as the medial junction where dense networks of lymphatic capillaries are formed similar to those seen about the aorta (Figure 8). The penetration of lymphatics into the media of coronary arteries was not observed. In relation to the secondary and smaller branches of coronary arteries in humans, lymph channels in the adventitia course along the longitudinal axis of the vessel wall and enter regional lymphatic plexuses of the subepicardium (Figures 9 and 10).

In some specimens, anastomoses between lymphatics (100–200 microns in width) and small branches of the coronary venous system (1–2 mm in width) were observed in all three species. In none of the specimens was blood observed in the lymphatic channels. Lymph nodes have not been observed in any of the hearts.

Discussion

The concept that walls of blood vessels are functioning organs and that metabolic processes occur within them was emphasized in recent years by *Kellner* (17) and *Holman* and associates (18). The means by which blood vessel walls are nourished are not understood completely, however, it is surmised that vasa vasorum and lymphatics must of necessity be present to supplement nutrition of the vessel wall and return to the general circulation certain interstitial fluids and constituent substances obtained from plasma or resulting from inherent metabolism. Although the methods for studying the morphology of vasa vasorum and lymphatics are rather crude and not physiological, observations in dogs, pigs, and humans have indicated that there is an abundant supply of vasa vasorum and lymphatics in the adventitia of blood vessels. We have observed also that vasa vasorum and lymphatics are present normally in the muscularis of veins; and in relation to arteries, intramural vasa occur only in diseased vessels (4), but lymphatics remain in the adventitia. The general arrangement of perivascular lymphatics is much the same in the three species studied with the exceptions that in some atherosclerotic humans lymphatic capillaries at the adventitial-medial junction of main coronary arteries and aorta form plexuses much denser than observed in healthy dogs and pigs.

Perivascular lymphatic drainage pathways have not been investigated specifically, but the presence of small lymph nodes in the adventitia of the aorta, particularly prominent in humans, suggests that adventitial lymphatics are afferent to the minute regional nodes. Presumably, efferent collecting ducts from them transport lymph via other larger regional systems which eventually reache the major lymph ducts. In dogs and pigs small collecting channels were observed which joined directly the thoracic duct or its larger tributaries. Since small lymph nodes were not observed in the adventitia of veins lymph drainage apparently progresses directly toward the major regional node systems. The aorta and vena cava are related closely anatomically and the major regional nodes appear to be common to both. Because of the continuity of the sub-

epicardial lymphatic channels about the base of the heart with those of ascending portions of the aorta and major pulmonary vessels, it is difficult to ascertain which course lymph drainage may take. In several specimens lymphatic channels interpreted as collecting ducts were directed toward the subepicardial lymphatic system which suggests that some lymph drainage of the proximal portions of the aorta and pulmonary vessels are handled by the cardiac lymphatic drainage system.

The significance of the functions of perivascular lymphatics related to primary disease states of blood vessels has never been assessed adequately. One aspect of the function of lymphatics about blood vessel walls that needs further study is their relationship to atherogenesis. Much work has been done to evaluate the physiological characteristics of lymphatics and to determine biochemical and biophysical properties and other characteristics of substances for which lymphatics are best suited to reabsorb. In general, there is an overlap in the resorptive abilities of blood capillaries and lymphatics. But substances that are not capable of re-entering blood capillaries because of their molecular weight, size, and structure, and perhaps electrical charge, are returned to the general circulation by the lymphatic system (11, 12, 19). Some of these substances are proteins, lipids, lipoproteins, cholesterol, carbohydrates, and enzymes. In relating the functions of perivascular lymphatics to blood vascular diseases not only must the biochemical and biophysical properties of metabolic products concerned be taken into consideration but also, as suggested by *Holman* (18), the significance of the pulsatile characteristics of the blood vessels themselves must be clarified.

Perhaps, the inner wall of arteries does not need lymphatic capillaries since the relatively forceful pulsatile action may serve to push the interstitial fluid substances through intercellular cleavage planes toward the adventitia where they are resorbed normally by the lymphatics there.

One aspect of the many theories of atherogenesis is related to the hypothesis that there may be a defect in removal from the blood vessel wall of certain substances obtained from plasma and resulting from inherent metabolism. In 1955, *Kellner* (17) pointed out that the arterial wall is an organ which is bathed in plasma constituents constantly and that metabolic processes may occur intramurally. Also he believed that an impediment to the flow and absorption by lymphatics of these plasma constituents (phosolipids, beta-lipoproteins) may lead to deposition with "mischievous side effects" resulting in atherosclerosis. This concept relative to atherogenesis also was emphasized more recently by *Holman* and his associates (18).

Presumably when the arterial wall reaches a critical thickness (20) intramural vasa vasorum develop to help support the metabolic demands of its constituent cells. In the process of thickening of its wall an artery may lose its ability to push interstitial fluids and constituent metabolic by-products effectively toward the adventitia. In addition, if lymphatics do not accompany intramural vasa for the purpose of assisting in maintaining homeostasis of the arterial wall, then a situation may exist which satisfies metabolic demands but also favors storage or deposition of atherogenic substances and in effect enhances atherosclerosis.

Although atherosclerosis with its complications is a universal and serious disease that has been studied extensively for many years, diseases of veins are serious also with their complications, in particular thromboses and fatal embolic phenomena which

in recent years are believed to be more prevalent than suspected previously. Veins, in contrast to arteries, are exposed to lower intravascular pressures, contain poorly oxygenated blood and numerous waste products and are physically less active. Yet veins remain relatively free of atherosclerosis. The ample supply of intramural vasa vasorum and lymphatics normally in veins may indicate that they are more capable than arteries in maintaining homeostasis of their walls which serves to „protect" veins from atherosclerosis. Also this arrangement of vasa and lymphatics in veins may indicate that imbibition is less significant in supporting metabolic demands of the vein wall than it is in arterial wall.

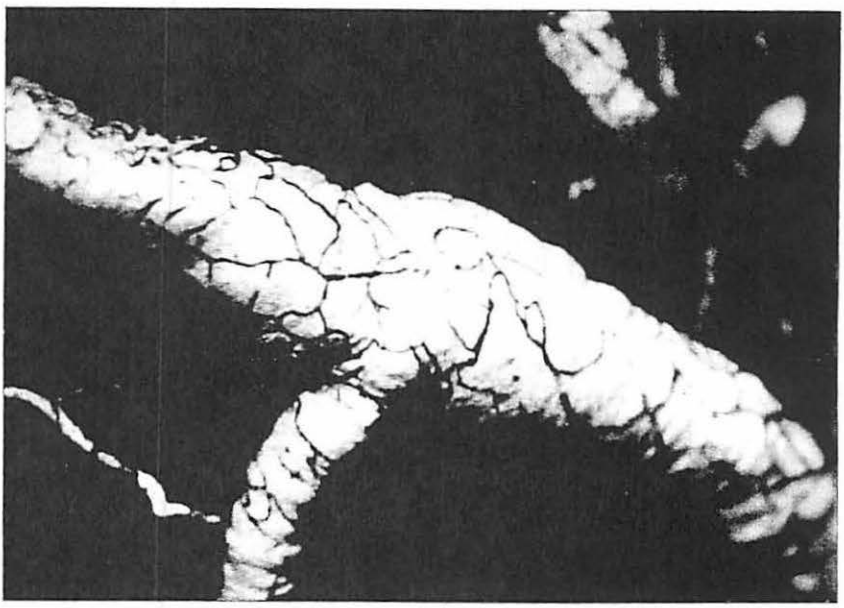

Fig. 11 Paracoronary lymphatic duct from a pig with concomitant vasa lymphorum. The lymphatic duct is approximately 2 mm. in diameter and has been injected with a room temperature vulcanizing silicone rubber compound (see reference 4). The vasa contain India ink and measure approximately 10–20 microns in width. Magnification x15.

Conceivably phlebothrombosis and thrombophlebitis may be related to a breakdown in the vein's ability to maintain homeostasis of its wall. The classical example of trauma to a leg vein resulting in thrombophlebitis and thrombosis may be illustrative of a situation in which lymphatics and vasa vasorum of the vein have been injured also. This situation may produce accumulation of interstitial products (lipids, lipoproteins, fibrin, blood and blood products) and result in intravascular thrombosis much the same as might occur in the arterial system as a complication of atherosclerosis. Experimental studies (21) have shown that autogenous venous grafts transplanted into the arterial system do develop atherosclerotic changes. Here the vein is being bathed in arterial blood, exposed to the higher pressures of the arterial system, and also has had interference with its vasa vasorum and lymphatics. This situation might indicate

that the metabolic demands of the vein wall have become supported more by imbibition than normally and removal of by-products and plasma constituents has been impaired.

The observations of small lymphaticovenous communications on the aorta and in the coronary system are interesting but their physiological significance is unknown. The anastomoses in the coronary system may explain the appearance in lymphatics of injection mass introduced into the coronary arteries and veins observed in our laboratory during previous investigations of the vasa vasorum (4).

It may be appropos to include a comment on the vasa vasorum of lymphatic vessels themselves. During a previous investigation of the microcirculation of the heart (4), blood capillaries were frequently observed about the wall of paracoronary lymphatic collecting ducts (Figure 11). In the current study capillaries were seen on the thoracic duct wall. There was no evidence that these capillaries communicated with the lumen of the lymphatic ducts. These vasa probably have a role in the nutrition of the constituent cells of the lymphatic vessel wall and it is conceivable that if the lymphatic vessel wall were denied its nutritional support, the lymphatic vessel could no longer function normally which may have implications in such disease processes as pericardial effusion, ascites, and edema. Lymphatic capillaries on the walls of lymphatic ducts were not observed.

In conclusion, the perivascular lymphatic system should be considered as a component part of the vasa vasorum of blood vessels. Further studies are needed in humans and experimental animals to correlate the anatomical relationships between these two vascular systems and the modifications that may occur in non-diseased and diseased blood vessels. In addition, it is quite apparent that in living animals and humans the physiology of blood vessel walls and their nutrient vasculature (including lymphatics) needs further elaboration.

Summary

The anatomy of lymphatics of blood vessel walls in dogs, pigs, and humans has been described. In general, the arrangement of perivascular lymphatics in the three species is similar. In diseased and non-diseased arteries, lymphatics did not enter the media, whereas in veins intramural lymphatics appear to be a normal occurrence. No clinical correlations are presented, but some features of lymphatics of atherosclerotic arteries in humans are described and the possible significance of perivascular lymphatics in atherogenesis is discussed.

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"Communicating Lymphatics" and Lympho-Venous Communications in Relation to Deep Venous Occlusion of the Leg

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Dilatation (ectasia) of the subcutaneous lymphatics and opening up of new lymphatic channels were observed in cases of swollen legs due to deep venous thrombosis of the calf – (Fig. 1) (9, 1, 7). The severer the degree of deep venous occlusion, the more the subcutaneous lymphatics were found to dilate and the more channels to open-up, denoting a direct relationship between the flow of lymph in the subcutaneous lymphatics and the increased venous tension within the musculo-fascial compartment of the leg (3). This points to the existence of some form of mechanism whereby the effects of such an intrafascial deep venous hypertension could be transmitted to the subcutaneous lymphatics across the tough deep fascia of the leg. The following suggestions were put forward for the explanation of such a mechanism:

1. In deep venous hypertension of the calf, the high pressure in the deep veins is "blown-out" into the subcutaneous veins (5). With an increased pressure in the subcutaneous veins, a decreased uptake of normal capillary effusion with an increased tissue pressure would result in the formation of excessive amounts of tissue fluids which, in turn, throws an increased load on the subcutaneous lymphatics.

2. The possible existence in the leg of lymph vessels, which cross the deep fascia, similar to communicating veins. These may help to drain tissue fluids from within the deep fascia outwards into the subcutaneous lymphatics.

3. The possible existence in the leg of functioning lympho-venous communications which could transmit the increased venous tension directly to the subcutaneous lymphatic trunks.