The Anatomy of Lymph Vessels in Relation to Function

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The essential functions of the lymphatic system are to pick up large molecules, particles and excess fluid and to transport them from the peripheral connective tissue to the venous system. Within normal tissue most of the lymphatics are collapsed, (Fig. 1a). They can, therefore, hardly be differentiated light microscopically from blood capillaries or from septal connective tissue. Various techniques have been used to visualize the lymph vessels within organs and extremities. Retrograde injection of air, indian ink, lymphangiography of an injection of hydrogen peroxide to lymph drainage of tissue or vessels below mesothelial surfaces; total vascular branches but never the complete to be falsely interpreted as lymphatics (Wutzer 1834, Most 1908, Bartels 1909, Baum 1928, Grau 1943, Jancso et al. 1952, Mori 1963, Mori et al. 1964, Leak and Burke 1966, Viragh et al. 1966, Bergström and Werner 1966, Kuprianov 1969, Casley-Smith 1969, Gerteis 1972). Injection of lymph-specific dyes such as patent blue as well as different tracer techniques demonstrate sectoral lymph vascular branches but never the complete lymph drainage of tissue or organs. Application of hydrogen peroxide demonstrates the lymph vessels below mesothelial surfaces; total lymphangiography of an organ was not possible with this method (Magnus 1922, 1923, Hass 1936, Johnson and Blake 1966; Johnson 1969).

In 1939 Kaiserling and Soostmeyer found a way out of this methodological problem by blocking the lymph flow of an organ like the kidney. This procedure leads to a lymphostasis with dilatation of the lymph vascular branches (Fig. 1b) up to their capillary endings which thus can be seen light microscopically. Other investigators used this method with success in various organs (Romualdi et al. 1946, 1947; Natucci and Zaccharini 1949; Rusznyak, Földi and Szabo 1957; Hankiss 1959; Aiello et al. 1960; Tormene et al. 1965; Csilik and Földi 1967; Huth et al. 1970; Földi 1971; Stroobandt et al. 1976; Lie et al. 1976; Huth et al. 1974, 1976). Cremer et al. (1972) modified the method of blocking the lymph outflow by interrupting the thoracic duct. The possibility of huge dilation of the lymphatics is different from the limited dilatation rate of the blood capillaries (Fig. 2a). Electron microscopy demonstrates that additional properties of lymph capillaries exist in contrast to blood capillaries (Casley-Smith 1965, 1967, 1970; Burke and Leak 1965, 1970; Huth 1967, 1968; Huth et al. 1970). The thickness of the lymphatic endothelium can vary from 0.1 µ to several micra. In contrast to blood capillaries, the lymphatic endothelium is not enveloped in a continuous basal lamina or pericytes (Figs. 1, 2a, b, c, d). Similar to blood vascular endothelium, it contains mitochondria, lysosomes, free ribosomes, a scant endoplasmic reticulum, fine intracytoplasmic muscular filaments, and sometimes numerous microvesicles. The endothelial processes link to each other multiformally: Apposed membranes can be held together by maculae occludentes or adherentes (Fig. 3b). Sometimes the cellular margins are connected by interdigitations (Fig. 3a); in other areas, a close apposition without special cellular protrusions dominates. A specific structure of lymph capillaries is represented by the overlap of endothelial cell processes. The gaps between the overlapping cell processes can separate up to several micra so that complete cells from the interstitium can readily pass the patent junction (Fig. 2b). The patency of the junctions is influenced by another specific structure: Leak and Burke (1968) were able to demonstrate fine anchoring filaments.
emanating from the outer surface of the lymphatic endothelium and extending into the interstitium with its thicker collagen fibrils (Fig. 3b). The overlap of endothelial cells with the possibility of extensive patency and the anchoring filaments maintain the removal of interstitial fluids and corpuscular substances and/or large molecules. Increased interstitial hydrostatic pressure will expand the interstitial space, hereby drawing the collagen fibrils. In this way the intercellular clefts are opened by pulling the filaments attached to the endothelial wall. This adaptive mechanism of lymphatics in response to altered hydrostatic and osmotic interstitial pressure has been proven not only in subcutaneous connective tissue (Casley-Smith 1967, Leak 1972) but also in other organs such as the kidney, the liver, and the heart (Huth 1968; Huth et al. 1970, 1976; Lie et al. 1976; Stroobandt et al. 1976). Kalima and Kalima (1975) demonstrated different gaps between the overlapping endothelial processes of mesenteric lymphatics. They referred to them as perilymphatic channels. They thought the channels played a significant role in the uptake of liquids or substances into the lymphatics. We saw comparable structures in organ lymphatics (Fig. 2d). Casley-Smith used the term prelymphatic for all interstitial spaces which are finally drained by lymphatic vessels. The tremendous dilatation rate of the lymphatics cannot be completely explained by the special connections of the endothelial cellular processes. A further extending capacity such as an intensive folding of the lymphatic endothelium within non-altered organs or tissues exists (Fig. 2f). In addition, the numerous cellular protrusions of lymphatic endothelial cells (Fig. 1a) must be regarded as a structural reserve for dilation since they disappear during dilation. It was Casley-Smith (1967), Földi (1972), and Leak (1972) who differentiated between the special manner of transporting fluids, proteins, and lipids via draining lymph vessels and the characteristic submicroscopical structures. Increased interstitial pressure leads to opening of the endothelial junctions while higher pressure inside the vascular lumen presses the overlapping cell processes together thus closing the junctions. At this point one could speculate that the peripheral lymph drainage system functions adequately until the endothelial junctions are pulled too far apart and lymph fluid can again escape.

Uptake of particles and fluids into lymphatics from the interstitium can also occur across the endothelium within multiple vesicles (Fig. 3b). The transcellular passage has been elucidated by experiments with different parti-
Fig. 2a Dilated lymph capillary between blood capillaries of myocardium. x 3.750
2b Open junction between two endothelial processes of a lymph capillary. x 13.800
2c Dilated lymph capillaries with endothelial siderosomes, following venous congestion. x 4 000
2d Dilated lymph capillary with splitting of an endothelial cell, forming a perilymphatic channel (above). x 3.675
2e "Confluence" of several lymphatics at the inner surface of the chylous cisterna. x 230
2f Top view of lymph vascular endothelium with intensive folding of the endothelial cells. x 600
Fig. 3a Interdigitation of two endothelial processes in the lymph capillary wall. x 29,500
3b Partly transversally, partly tangentially sectioned lymph capillary with intensive microvesiculation of the endothelium beside the adjacent collagen fibrils and finer filaments. Zonula occludens formed by two endothelial cell processes at the right below. 44.250 x
3c Parasitic lymphangiosis (onchocercosis). HE, 60 x

cles and substances (Casley-Smith 1964, 1965, 1968; Leak and Burke 1966, 1968). The further transport of lymph following its resorption is maintained by valves which can already be observed in smaller lymph-collecting vessels like those of the epicardium or the hilar lymph vessels of different organs (Fig. 1b). Lymph vascular valves differ in size and shape. With the aid of stereomicroscopy and scanning electron microscopy, it has been proven that funnel-like valvular structures dominate (Lauweryns 1971). Blood vessels, i.e. veins of comparable size, do not contain valves. The existence of valves, therefore, support the identification of medium-sized lymph vessels. Within the lymph-collecting vessels, not only the valves but also a special wall structure helps to propel the
lymph centripetally. Lymph propulsion by rhythmic contractions has been demonstrated experimentally in vivo and in vitro by Florey (1927), Smith (1949), Horstmann (1951, 1959), Webb and Starzl (1953), Mistlin (1961, 1963, 1976), Kimmonth et al. (1963), Schipp and Schäfer (1969), Yoffey and Courtice (1970). The contractability of a lymph vascular segment between two valves with autonomous nervous stimulation enables functional adaptation to the amount of lymph by the number of contractions. Another control mechanism for lymph transport is provided by the wall structure of the cisterna. The lymph vessels running into the chylous cisterna take a helical course within the cisternal wall. This structural property makes it possible to compress the entering lymph vessels during the filling phase of the cisterna. In addition the cisternal lymph vessels have valvular folds at their orifices which can block the afferent vessels during the filling phase (Fig. 2e) (Lenz and Huth 1976).

Transport of lymph within the lymph trunks, especially in the thoracic duct, is facilitated by the elastic and muscular wall components, by their well-developed valvular apparatus, and probably by the pulsation of the adjacent aorta. Adrenergic nerves have been demonstrated in close contact to muscle cells of the thoracic duct wall (Wenzel 1972). A final regulative mechanism for the lymph flow to the venous system is represented by the ductal orifice at the venous angle with its individual variability and its special ductal branching at the venous angle as well as by its special valvular apparatus. The importance of these structures has been emphasized by endoscopic findings (Seeliger 1973, 1974). The lymphatic vascular wall structures and their alterations considerably influence the pathological changes in the interstitium of almost every organ. Only a few examples are mentioned in the context of this article. Brain tissue which does not have its own lymphatic vascular system, can be split by lymphostatic oedema as has been shown experimentally and after human pharyngitis, sinusitis, neck dissection, etc. (Földi et al. 1962, 1967). Interstitial cardiac fibrosis and sclerosis of the heart valves in cases without carditis have been correlated with lymphostatic conditions (Kline 1964, Miller et al. 1960-70, Goldberg 1968, Bullon and Huth 1972). Pulmonary lymphostasis with interstitial fibrosis has been demonstrated after obliteration of lymph vessels in pneumoconiosis as well as primary fibrosis of the lung (Meessen 1949, Vanek 1954, Szabo 1960).

Lymphostatic alterations with lymphangiectasia and enteral protein loss are increasingly being detected with the aid of modern methods of investigation. The importance of lymphatic vascular drainage of the cirrhotic liver and consequently, the dynamic insufficiency of the great lymph trunks in liver cirrhosis with ascites as well as their interdependence have been clarified in the past ten years (Baggenstoss and Cain 1957; Baggenstoss 1960; Dumont et al. 1960–1969; De Benedetti et al. 1965; Ludwig et al. 1968; C.L. and M.H. Witte et al. 1968, 1969, Beltz et al. 1969; Borchard et al. 1972).

The special architecture of the peripheral lymphatics in lymph nodes and spleen as well as their role in the spread of blastoma cells has been elucidated by combined scanning and transmission electron microscopy. For the urinary tract, chyluria, for instance following filariasis impressively illustrates the possible importance of this drainage system (Fig. 3c).

A connection between general diseases such as widespread tumorous processes and the lymphostatic symptoms caused by them often remains occult. The lymphovenous pressure gradient and/or the shunt of the fluid into the venous system can be influenced by generalized factors such as venous congestion in heart failure or venous thrombosis. An oedema resulting from such factors can just barely be correlated with lymphostasis.

The sequence of organic diseases involving specific lymph vascular structures ought to be researched further. Finally, attention should be drawn to the fact that the diagnosis of lymphangiomata over against hemangiomata often depends on the evidence of specific lymphvascular features such as valves within smaller vascular lumina.
In summary, the morphology of the lymph vessels not only determines the function of this drainage system but also influences its pathologic reactions.

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