stention of the lymphangion wall just before the onset of the contraction, findings which are consistent with Starling's law of the heart.

With [1] REDDY observed that a rise in the interstitial fluid pressure causes the intraluminal pressure of the terminal lymphatics to increase. Therefore, if the pressure in the terminal lymphatics is larger than the pressure in the lymphangion adjacent to the terminal lymphatics, then fluid flows from the terminal lymphatics into the lymphangion adjacent to the terminal lymphatics. From [2] it can be seen that the lymphangion pressure increases with the inflow due to the contribution of the hoop stress in this terms. If, now, the dilation of the lymphangion wall reaches its threshold, an active contraction in the lymphangion is initiated so as to propel the lymph into the lymphangion in front of it. It is clear that the outflow from the lymphangion causes the lumen size to decrease. During the recovery phase of the active contraction, the contribution of active contractility stress terms is zero. In their note on the mechanisms of lymph flow through the terminal lymphatics, REDDY, KROUSKOP and NELL JR.[13] offer an explicit explanation of these mechanisms: 'The negative pressure is responsible for the lymph absorption by the terminal lymphatics. If the threshold strain required to initiate an active contraction in the lymphangion adjacent to the initial lymphatics is zero or just above zero, then this lymphangion acts as a pump regulated by the tissue pressure'. This suction effect of the terminal lymphatics is very unlikely, as is shown by actual measurements of intralymphatic pressure given by ZWEIFACH and explained by CASLEY-SMITH[14], who proposes an alternative explanation for terminal lymphatic filling. However, even with this, variations in tissue pressure will affect the filling of the terminal lymphatics. Thus, the rest of the explanation of REDDY et al. will hold.

The duration of a contraction and the duration of the refractory period can be altered by several pharmacological agents: MISLIN[15], TIRONE et al.[16].

This theory suggests that the lymph absorption is dependent on the pressure gradient between the interstitial pressure and the pressure in the lymphangion adjacent to the initial lymphatics and can be in agreement with the conception of CASLEY-SMITH.

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Diseases of Lymphostasis

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Definition

Lymphoedema of the extremities is the only sequela of chronic stagnation of lymph on which interest is focused. It is, however, a well established fact that lymphostasis will induce not only extracellular oedema, but an intracellular too, i.e. it causes parenchymal cell lesions. A whole series of lymphostatic syndromes; 'diseases of lymphostasis' have been identified.

'Diseases of lymphostasis' may appear in any organ drained by lymphatics, independently of whether the lymph capillaries lie inside the parenchyma organs with short prelymphatics (e.g. dermis, gut) or outside (organs with long or very long prelymphatics, e.g. liver). They are characterized by typical functional and pathological alterations. 'Diseases of lymphostasis' form a new chapter in medicine. Although most of them are described up to now as experimental syndromes and still await clinical application, it is possible to outline our knowledge of this new field.

Experimental lymphostatic syndromes

Experimental 'diseases of lymphostasis' are induced surgically. The usual methods are: a) By ligating or resecting all lymph vessels and lymph nodes found, or by an intralymphatic injection of phlogogenic substances, thus provoking lymphangitis and lymph-vessel thrombosis, an acute or subacute lymphatic disease may be induced which will be terminated by lymphatico-lymphatic and/or lymphatico-venous anastomoses. b) To induce chronic forms of lymphostatic diseases, not only lymphatics must be resected but also a strip of connective tissue, even the adventitia of blood vessels, too. Such techniques have been devized, by CLODIUS (extremities) and LIE (liver), in order to delay regenerative processes. Repeated intralymphatic injections of sclerosing substances may be helpful too.

Pathomechanism

As a result of lymphostasis, the plasma proteins accumulate in the interstitium; this leads to an increase in interstitial colloid-osmotic pressure and to lymphoedema. Intracellular oedema and cell damage will soon follow due to the increase of interstitial pressure, disturbed cell nutrition and transport of metabolites. Stagnation impairs the 'vehicle function' of proteins; hormones and vitamins bound to plasma proteins participate in their extravascular circulation as well as

lipids and a large number of other endogenous and exogenous compounds.

Lymphostatic haemangiopathy – lymphoedema of the wall of blood vessels accompanied by a reduction of the activities of enzymes localized there – due to a mechanical insufficiency of the lymph drainage of blood vessel walls associated with most lymphostatic syndromes causes additional disturbances. Water, plasma proteins and lipids penetrate the walls of the blood vessels from two directions: a) from the lumen, directly from the blood, through the endothelial lining; b) from the blood capillaries of the vasa vasorum. Plasmatic perfusion ot the vascular wall is, on the other hand, maintained by lymphatic transport by vasa lymphatica vasorum.

Experimental lymphostatic diseases have hitherto been described in the brain, heart, lung, liver, gut, and kidney[1–4]. In every case, the function of the organ is disturbed; intracellular enzymes are released into the blood and pathological alterations occur both in the morphological and the histological (light and electron microscopical) level.

In man, lymphostatic diseases may appear as a result of: a) surgical intervention ('block dissection'): removal of lymph nodes in the treatment of malignancies, combined with X-ray irradiation. b) Any pathological change of the lymph vessels and/or nodes with blockage of flow; aplasia; lymphangiectasia, lymphangiopathia obliterans; lymph-vessel thrombosis; malignancies.

Safety-valve insufficiency of lymph flow

Pure lymphostatic diseases are supposedly rare. *Lymphostatic enteropathy*, causing hypoproteinaemia in consequence of protein excretion via the intestine and *lymphostatic encephalopathy*, causing central nervous signs and symptoms are examples of such syndromes. On the other hand, a *'safety-value insufficiency'* of lymph flow – lymphatic stasis in some conditions (inflammation; increased venous pressure, etc.) which normally evokes compensatory augmented lymph flow – is very common. Severe oedema, hemorrhage and diffuse necrosis are the characteristic features.

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Chronic Experimental Lymphedema of the Extremities Pathological Changes

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The basic physiological and pathophysiological knowledge on formation, composition and transport of lymph has been obtained from experimentally produced acute lymphedema. The influence of acute lymphstasis upon morphology and function of various organs has been published[1–8]. Little, however, is known about experimental chronic lymphstasis, because the regenerative capacity of the lymphatic system is difficult to overcome in the experimental animal[9–15].

Most frequently, the clinician is confronted with secondary lymphedema of extremities, subsequent to the removal of lymphatics at the root of the extremity. We have been able to produce in dogs a secondary chronic obstructive lymphedema[9,10] which can be compared, concerning its pathophysiology and clinical picture, with the secondary obstructive lymphedema of the human. Using the light and electron microscope, our findings in these experimental animals are as follows: During the latent, non manifest phase of lymphostatic lymphedema (1–6 months following institution of the lymph block), the lymph vessels are massively dilated. The smooth muscle and endothelial cells of lymphatic precollectors and collectors reveal intracellular edema, the cyternes of the endoplasmatic reticulum are dilated, the cytoplasma becomes vacuolized and the number of osmophilic microbodies is increased. The interendothelial junctions are wide open

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