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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and carbon labelling demonstrated them to be insufficient. There is intracellular edema of the endothelial cells and of smooth muscle cells of arteries and veins. More marked is the thickening and edema of the subendothelial basement membrane and of the basement membrane of smooth muscle cells. Due to the endothelial damage, fibrin thrombi are encountered frequently in blood and lymph vessels. The interstitial tissue both of the epi- and subfascial space of the extremity is massively edematous, multiple lymphocytes and phagocytes are present. Similar, but less pronounced transitory changes of blood and lymph vessels are found in acute lymphedema[12–15], but they regress almost completely, following subsidence of the edema. In our experimental, manifest chronic lymphostatic lymphedemas of 2 and more years duration, the tissue changes were found to be irreversible. The lymphatics of the epi- and subfascial space become enormously dilated. They are massively increased in number, as observed in lymphangioma-like alterations. The walls of lymph collectors and precollectors are thickened and sclerosed, and these structures are difficult to differentiate from veins without carbon labelling. The basement membranes of the lymph capillaries are continuous and thickened, the anchoring filaments are increased in number. The thrombi within the lymph vessels, found during the latent phase, become organized and recanalized. Also, the walls of the arteries and veins are affected by marked localized arteriosclerosis, consisting in connective tissue sclerosis of all tissue layers, predominantly involving the adventitia. The blood vessel sclerosis leads in many arteries and veins to thrombus formation. The connective tissue of cutis and subcutis as well as of the subfascial space is increased, heavily sclerozed and contains infiltrates of chronic inflammation. The deep fascia, anatomically dividing the epi- from the subfascial space, is thickened, but is found to be traversed by many ectatic lymph vessels. This leads to a free functional communication between the two compartments and is especially important if the lymphatic system of only one compartment is obstructed. The structures of the nerves and muscles were not found to be altered by chronic lymphostasis[16].

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Pathology of Lymphoedema

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The histological equivalent of the macroscopic appearance in acute and chronical lymphoedema is not very easy to recognize. Lymphoedema cannot be distinguished from other oedema rich in protein with morphological methods. Lymphostasis induces dilation of lymph vessels, but, lymphangiectasia can also be observed under increased load of the lymph vascular system. For instance, dilated lymphatics can be observed accompanying ovarial cysts, lung oedema, and within almost every inflammatous tissue, although there is no blockage of lymph outflow. In spite of these difficulties in interpretation of dilated lymph vessels, it is of great importance from the clinical and morphological point of view to get more information about the appearance of lymphoedema caused by blockage of lymph vessels.

For this reason, experiments have been performed with ligation of lymph collecting vessels and of lymph trunks to induce renal lymphostasis, lymphostasis of the liver, and cardiac lymphostasis. Interruption of renal lymph outflow induces nephrotic changes with disturbances of renal concentration. Blockage of lymphatic outflow from the liver aggravates considerably the effects of other loads, as for instance that of cholostasis. Cardiac lymphostasis causes myocardial oedema and oedema of the cardiac valves leading to rather severe fibrosis of the valve leaflets. The experimental lymphostasis, as mentioned above, cannot be maintained for longer than 1 week since regeneration of newly formed lymph vessels and opening of anastomoses will soon permit a sufficient outflow of lymph. First experiments with 'malignant' complete and continuous lymphostasis by encapsulating the liver or other organs with plastic material seem to induce severe degenerative effects within the enclosed organs. In addition, complete lymphostasis of organs can be controlled by non-morphological investigation methods, as for instance cardiac lymphostasis leads to electrocardiographical disturbances like ST-depression. Lymphostatic liver damage increases SGPT and alkaline phosphatase during the first 2 weeks after blockage of hepatic lymph flow.

Signs of lymphostatic organ diseases in man are rare and hard to prove. Classical lymphostasis of extremities and of organs can be observed in cases with malformations, hypoplasia or aplasia of the lymph vascular system. In addition, blockage of lymphatic outflow can be caused by tumorogenic lymphangiosis, inflammatous lymphangiosclerosis, and sclerotic vascular obliter-