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## Physiologic aspects of lymphatic contractile function: current perspectives.

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The lymphatic system plays an important role in fluid/macromolecular balance, lipid absorption, and immune functions, and is involved in many different pathologic conditions, like inflammation, spread of cancer cells, and lymphedema. There are several forces that drive lymph centripetally. Extrinsic driving forces, or the passive lymph pump, include lymph formation, arterial pulsations, skeletal muscles contractions, fluctuations of central venous pressure, gastrointestinal peristalsis, and respiration. Intrinsic forces, or the active lymph pump, are the result of coordinated contractions of lymphangions, the morpho-functional units of the lymphatic vessels, which include the valve and portion of the vessel extending to the next valve. The contractions of the lymphangions are initiated by the pacemaker activity of the smooth muscle cells of lymphangion wall. Transmural pressure is an important hydrodynamic factor that modulates pacemaking. Under conditions of low filling, lymphangions might produce negative intraluminal pressures and a suction effect. Because of the complicated hydrodynamic conditions in lymphatic beds, the passive and active lymph pumps sometimes work together to propel lymph centripetally. In other cases (i.e., under conditions of enhanced lymph flow), flow-mediated inhibition of the active lymph pump could serve to decrease lymphatic outflow resistance and save metabolic energy when the driving force of the passive lymph pump is enough to propel lymph. We have recently found that there are profound differences in the pressure and flow sensitivities of lymphatic vessels derived from different tissues, such as the thoracic duct and mesenteric lymphatics. Such results, when considered in light of the controversy surrounding some studies performed in different animals, lead to the idea that the active lymph pumps in humans may have greater regional differences in contractile function than has been seen in animals, because of the upright posture in bipedal humans. This posture creates an additional outflow resistance for lymphatics of the lower part of the body. Thus, despite the ongoing attempts to determine the mechanisms of lymphatic diseases and useful therapies to treat them, there are many disputable or unknown issues regarding the physiology of lymph transport in humans.

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