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LETTER TO THE EDITOR

I read with great interest the article "Regulation of water balance between blood and lymph in the frog, Rana Pipiens" by A.L. Baldwin et al., which appeared in the March 1993 issue of Lymphology. The experimental model used by the authors, in which lymph hearts are totally inactivated, can be, to a large extent, considered an analogue to lymph stasis in humans. Of course, stoppage of lymph heart contractions is an acute event whereas in humans lymph stasis develops over some time period after excision of lymphatics and nodes. Nevertheless, Starling's microvascular forces are operative in both situations. The data obtained from Baldwin's model are consistent with what we have seen in human lymphedema, namely that lymph protein concentrations remain within normal limits after lymph flow interruption (1,2). Moreover, the observations on lymph hearts adapting their activity to the changes in the interstitial fluid volume can be extrapolated to the reaction of contracting human leg lymphatics (3). Thus, the paper provides data useful for analysis to what happens with lymph dynamics in human limbs after groin or iliac radical nodal dissection.

I would direct the attention of clinical lymphologists specifically to Baldwin's findings of unchanged lymph protein concentrations. In many lymphological papers on human lymphedema a term "protein-rich edema" is used, suggesting that there is a high tissue fluid and lymph protein concentration in lymph stasis (i.e. higher than in normal subjects), although no references to the original sources of this information are given. We have so far not been able to confirm such data, either in patients with obstructive or filarial lymphedema. Tissue fluid and lymph protein levels were consistently within normal limits (1,2). According to Starling's hypothesis an increase in tissue fluid proteins (in our patients after interruption of lymphatic transport) raises tissue oncotic pressure, and attracts water from the blood vessel compartment. In other words, a transient rise in tissue fluid protein concentration should promote a prompt increase in convective flow and water diffusion into the interstitium (à la the Kedem-Katchalsky equation) with restoration of tissue protein concentration back toward normal levels. The overall consequence is clinical edema but with a rise in tissue fluid protein *volume* and not tissue protein *concentration.* The tissue pressure safety factor as well as skin and subcutaneous tissue compliance readily accommodates this increased volume.

From the data presented in Baldwin's paper it can be readily deduced that during stoppage of the frog lymph hearts, lymph volume increases whereas lymph protein concentration remains unchanged. Lack of changes in plasma protein level in this model could be explained by a large plasma volume compared with lymph volume. After a longer observation period a drop in plasma proteins would be anticipated.

In chronic lymph stasis in humans, lymph protein concentration also remains within normal range (1). Peripheral capillary filtration and protein reflection coefficients do not appreciably change (personal observations). A decrease but not increase of these values can only be expected after formation of basement membrane-like structures around blood capillaries (4) hindering transcapillary

protein transport. The lymph space steadily expands not only because of the increase in volume of tissue fluid and lymph proteins and stretching of tissue structures, but also from the "overgrowth" of skin and subcutaneous tissue affected by lymph stasis allowing more room for gradually accumulating lymph. The latter phenomenon is most easily observed in young patients with congenital and filarial lymphedema. Here, an increase in limb volume is accompanied by greater total mass of skin and subcutaneous tissue. On histologic section, however, the skin has normal thickness.

In conclusion, Baldwin's observations on unchanging (i.e. normal) lymph protein concentration after interrupted lymphatic flow are consistent with both our findings in human obstructive lymphedema, and with protein and fluid kinetics according to the Starling hypothesis.

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Editor Comment:

Professor Olszewski questions the designation of lymphedema fluid as high-protein and wonders where this concept arose. In experimental lymphedema (Am. J. Physiol. 108:509, 1934) and human lymphedema (Am. J. Physiol. 109:572, 1934; Brit. J. Surg. 41:31, 1953; Lancet II:1179, 1956; Brit. Med. J. 1:1159, 1958), Drinker, Crockett, Watson, Taylor, and colleagues determined that the protein content of lymphedema fluid varied from 1.5-5.5g/dl (mean 3.0g/dl) which is in sharp contrast to the protein content of venous edema fluid (<1.0g/dl). [CLW]