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LETTER TO THE EDITOR

MEASURING LYMPHATIC LEUKOCYTES IN INFLAMMATION

Shield's article entitled "High Points in the History of Lymphology: 1602-2001" was exceptionally well done, but the article did not address events that occurred after the 1960's in which the lymphatic system was used to evaluate the permeability of the microvascular membrane to macromolecules in almost every organ in the body. See reference 18 for a review of permeability measurements using various lymphatic models developed by the real "movers and shakers" of lymphology, i.e., Yoffey and Courtice (1); Ruszynak, Földi and Szabo (2); Mayerson (3); Warren and Drinker (4) and Marlys and Charles Witte (5).

Since lymph provides the only means of assessing all the macromolecules in fluid draining tissues of an organ, DN Granger and I (6) rearranged an equation derived by Patlak et al (7) that could be used to predict pore sizes in microvessels of the GI tract, lungs and skeletal muscle by measuring the concentrations of different proteins in plasma and lymph. Staub (8) was also a very important innovator in this regard since he used lymphatic models developed by Yoffey and Courtice (1) and Strang (9) to evaluate microvascular permeability in lungs of awake sheep by measuring protein fluxes (10).

Also, it is important to recognize Guyton's (11) influence on understanding the importance of the lymphatic system, since he defined an "edema safety factor" which Landis had termed a "margin of safety" against edema formation, which was the sum of the decrease in tissue protein osmotic pressure, the tissue pressure increase and the lymph flow increase that occurs when capillary pressure is elevated (12).

Importantly, Starling in a classical paper also defined the lymphatic's ability to remove "capillary filtrate" from the tissues (13). Since Starling knew that lymph flow increased following capillary pressure elevations in organs, he defined a lymphatic safety factor that opposed edema formation which is a function of the filtration characteristics of the microcirculation and the total lymph flow of an organ. This safety factor was re-defined by Guyton as the total steady state lymph flow draining an organ divided by the capillary filtration coefficient (K_{fc}), i.e., the following equation describes the pressure drop across the capillary wall (ΔP) that produces the observed lymph flow.

$$\Delta P = \frac{\text{Total Lymph Flow}}{K_{fc}}$$

This is an important relationship because it defines the pressure drop acting across the microvascular bed when an organ is neither gaining nor losing weight that produces a given steady-state lymph flow. If lymph flow is large relative to K_{fc}, then a large ΔP is dissipated across the microvascular walls to produce lymph. Guyton and his students popularized this concept that was first defined by Starling (14,15). Many other scientists also used lymph protein concentrations and flow to determine permeability in organs subjected to numerous interventions. However, in our zeal to determine

"capillary permeability" and "edema safety factors," we perhaps too often have overlooked the most important feature of the lymphatic system, i.e., to remove leukocytes, tissue cells, and factors released into the tissues during inflammation. The early pioneers such as Courtice and Földi were well aware of this process, but collection of lymph during inflammation has not been used to its maximum in our discipline!

I have written this Letter to re-emphasize the importance of lymph as a useful research tool for both practicing and future lymphologists. The types of leukocytes, their numbers, as well as the concentrations of different cytokines and chemokines in lymph can easily be measured today using lymphatic collection models in inflammation that have been developed to measure microvascular permeability. I can only wish that all the lymph we collected over the years was now available for analysis! What I am trying to emphasize in this letter is: lymph obtained from an organ subjected to the inflammatory response provides a valuable resource to study the response of the various inflammatory cells released during inflammation by the organ, their degree of activation and their roles in the inflammatory responses. The first place to begin would be to study the inflammatory response using lymph collection methods developed by Courtice and Yoffey and Földi, et al. in order to study the most basic phenomenon in our bodies, i.e., how organs react to inflammation which, after all, is the basis of our existence on the surface of this world (16,17).

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Editor's Note:

Perhaps a good start along these lines can be found in the monograph authored by Olszewski, W – "Peripheral Lymph: Formation and Immune Function," CRC Press, 1985. Also see the pertinent next Letter to the Editor and Reply.