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Comments

by A. Silberberg

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Transport of macromolecules across the microvessel wall and their return to the blood stream via the lymph is by now a generally accepted mechanism. In fact, the question has been posed by Zweifach, whether or not under physiological conditions the lymph represents the major return path, not only for protein, but also for water. This flux, water and protein, which will eventually become the lymph, has to cross the extravascular space and the possibility that, in this process, a system of low resistance channels is used is a most intriguing idea.

Two apparently independent candidate systems of pathways have here been described: a pathway along the tissue fibers and a pathway along the conducting channels. It would be interesting if a relationship between these two, the fiber network path and the conducting channel system path, existed. Such a correlation would go a long way towards 'explaining' the origin of the heterogeneity in proteoglycan distribution which creates the channels.

We know that hyaluronic acid and the associated proteoglycans are in principle free to diffuse through the tissue space even though they are severely constrained. Unless, therefore, the heterogeneity which is seen is a (perhaps a very slowly relaxing) transient one, the phase separation, i.e. the concentration distribution which is found, must have arisen voluntarily either due to incompatibility of the macromolecular components or because of a pre-existing, pre-imposed heterogeneity formed by the fibrous network system in the tissue space. It would, indeed, be considerably easier to account for the occurrence and stability of the conducting channel system if it were correlated to the fiber system. Two points should be checked however: are the channels really seen under physiological, i.e. non-edematous conditions? are the channel contents of a higher protein concentration than the surrounding gel?

An important point to note is that drainage of the channel contents into the lymphatic system will be down a pressure gradient, even though this can be extremely slight. It would be hard to imagine that the pressure in the channel is lower than that at the mouth of a terminal lymphatic.

On the semantic score, I think that the use of the terms 'bound' and 'free' water is much more misleading and reprehensible than 'prelymphatic'. The water in the gel is as free, on the molecular level, as the water in the sol. There are stronger frictional constraints on convected transport, but this is all. Diffusional freedom is hardly impaired. I do agree, however, that the term 'prelymphatic' is better used only where the channels are essentially unique extensions of the terminal lymphatic vessels. In instances where the channels merely represent connected regions of lower proteoglycan content they are better attributed, also by name, to the connective tissue space.

Final remarks

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Critical remarks center essentially on two areas: the terminology employed and experimental interpretation and conditions. The term 'prelymphatic tissue channels' was not created by us and first used by Casley-Smith. We prefer also the term 'low resistance pathway' (see also Clough and Smaje, J. Physiol. (283 (1978)). But the topographical term 'prelymphatic channels' does not anticipate anything and is open from a morphological view. The term can always be specified. Important seems the fact that new findings obtained by different methods in different tissue and animals suggest the existence of preformed structures in the extravascular space which are not identical with the true lymphatic system. However, identification of the electronmicroscopical and vitalmicroscopical findings is yet to be made. The vitalmicroscopic studies show the direct connection of the channel-like structures with the true lymphatics. This cannot be the effect of an edematous swelling or damage of the tissue. Consequently, the interpretation must be, that the beginning of the fluid drainage system is more peripheral than with the true lymphatics. The beginning would be localized in the surroundings of groups of tissue cells, defined as drainage unit. The investigations were carefully performed and the tissue was protected against unphysiological conditions as far as possible.