

The Permeability of the Lymphatic Wall.

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The permeability of the walls of lymph channels can be studied with the aid of innocuous vital dye solutions isotonic with blood. When such solutions are injected with a micro pipette into the tissue near the edge of the upper surface of the ear of the mouse, the dye rapidly finds its way into the lymphatics draining the region, rendering them clearly visible. When one of the vessels carrying the colored fluid empties this latter into a larger channel draining a normal part of the ear, one sees the color swept away and diluted by a stream that is itself unseen. Lymph formation and flow are thus shown to be active processes in the ear, even in the absence of hyperemia.

Poorly diffusible dyes (Pontamine blue,¹ Chicago blue 6B, vital red, and Congo red), which pass with difficulty out of the blood vessels into the tissues, tend to be retained by the lymphatic wall as well, whereas more highly diffusible ones (trypan red, brom phenol blue) pass out with ease.

According to the accepted view, lymphatics are everywhere separated from tissue spaces by a continuous endothelial wall. Our observations support this view. When lymph carrying the dye that is retained by the lymphatic walls is put under pressure, it passes out into the tissues only when frank ecchymosis of it takes place. No sign is to be found of pre-existing lacunae in the wall.

Lymph flow is stopped by a pressure of 2 to 4 cm. of water exerted by way of a sausage-shaped, collodion bag laid across the lymphatics. The pressure obstacle causes the dye to escape in greater abundance than ordinarily. It does not interfere in the least with the venous channels but so effectively blocks the lymphatics that mild edema develops within the hour. The phenomenon is further proof that lymph formation is an active process in the ear.

Isotonic sodium chloride solution appears to exert an injurious effect upon the lymphatic endothelium, to judge from the rate of escape of dye dissolved in it. Tyrode's solution is much more tolerable as judged by this criterion, and so too with amniotic fluid of the mouse. Dye introduced in homologous serum diluted with 3

¹ Rous, Peyton, and Smith, F., *J. Exp. Med.*, 1931, **53**, 219.

parts of Tyrode solution to reduce the protein percentage approximately to that of lymph from an extremity escapes relatively slowly. When in undiluted serum, it is long retained, as would follow from the influence of the serum proteins.

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The Breakdown of Lymph Transport.

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The method described in a preceding paper to render visible the lymphatics coursing through normal tissue has provided us with the opportunity to study the permeability of the lymphatic wall under pathological conditions. Lymphatic permeability is greatly altered by slight causes, as can be shown by following the escape into the tissue of vital dyes ordinarily retained within the lymph channels.

When Pontamine blue or Chicago blue 6B, dyes having the requisite character, are introduced into the lymph, one sees the lymphatics of the ear as dark blue channels much broader in general than the blood vessels, and having the alternation of pear-shaped dilatations and constrictions seen in specimens injected after death. Their outlines are sharp because the dye does not pass from them into the tissue that they traverse. But a mere gentle stroke across their course, with a blunt instrument, at this time or just prior to the dye injection, results in an immediate escape of color into the region directly affected. This escape is closely localized to the line of the stroke and it endures for some minutes.

Greater degrees of disturbance of the lymphatics have proportional results. When unfiltered light from an arc is allowed to fall for a fraction of a minute upon a small area of the ear, there results an immediate and abundant escape into the tissue of the colored lymph. A similar phenomenon is to be seen when local inflammation has been produced with xylol.

These observations prove that the lymphatic wall becomes more permeable upon relatively slight stimulus, letting substances through into the tissues, which ordinarily it would retain. That the small blood vessels do this upon occasion is well known; and the process is held to be mainly responsible for urticaria, especially factitious urticaria. Incompetence of the lymphatics of urticarial regions may