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Effect of the Pulse on Lymph Formation and Interstitial Movement of Substances.

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The results of recent investigations suggest that connective tissue fibers serve as pathways for the extravascular transport of vital dyes escaping from lymphatics.[1] In unpublished studies on the ear of the mouse, gentle, alternating, external pressures (0 to 2 cm. or 8 cm. of water) caused squeezing of the tissues and bending of these fibers and at the same time the rapidity of spread of vital dyes through the interstitial tissues was increased. That gentle massage increases the lymph flow from a part is well known.[2] The work to be reported now deals with the effect of pulsation of the blood vessels both upon lymph flow and upon the movement of substances through the interstitial tissues.

Warmed, defibrinated, aerated rabbit's blood was perfused for periods of 1 to 1½ hours, through freshly cannulated rabbit's ears, with the use of an apparatus providing pulsatile and non-pulsatile pressures. "Systolic" and "diastolic" pressures of 141/60 mm. of mercury were used in the case of the pulsatile pressure at about 100 "beats" per minute, while for the constant pressure the equivalent of 141 mm. of mercury was employed. It will be seen that a somewhat higher mean pressure was used in the latter instances. Lymph formation and flow were estimated by filling a few peripheral lymphatics near the tip of the ear with a vital dye and noting the movement of the dye colored lymph toward the base of the ear. The method has been previously used in human skin.[2] To study the rate of spread of substances through the tissues, minute amounts (0.01 to 0.02 cu. mm.) of a vital dye (pontamine sky blue) were introduced through micropipettes into the subepidermal connective tissue of the ear by capillarity without utilization of pressure. Camera lucida drawings of the outline of the dye spots were made immediately after placing the dye in the tissues and again half an hour and 1 hour later. To express the rate of interstitial spread of dye, the area of each spot as determined after one hour was divided by

1 McMaster, P. D., and Parsons, R. J., PROC. SOC. EXP. BIOL. AND MED., 1938, **37**, 707.

2 McMaster, P. D., *J. Exp. Med.*, 1937, **65**, 347.

its initial area. For comparative data, only dye spots of approximately the same initial area were used.

Lymph flow was 15 to 20 times more rapid in the ears perfused with pulsatile pressure, despite less blood flow per gram of ear per minute in most instances. In the pulsatile perfusion experiments, the lymph channels transported the blue dye from near the tip to the base of the ear in 7 to 12 minutes and the color began to pale in the channels in 12 to 20 minutes as the result of dilution by newformed lymph. In many instances segments of the channels had become colorless after 20 minutes. In the constant pressure perfusions, the dye reached the base of the ear in only one of 13 instances and then after 46 minutes had elapsed. Clearance of color in the channels was never observed in these.

Edema sometimes developed during the course of a pulsatile perfusion and as it did so lymph flow increased enormously even when the volume of blood perfused was relatively small. Very little lymph flow attended the edema that occurred in the constant pressure perfusions.

Perfusion with pulsatile pressure greatly increased the rate of spread of dye through the tissues. One group of data will serve to illustrate the results. The camera lucida drawings of the dye spots used had initial areas of between 100 and 125 planimetric units and no edema occurred around any of them. See Table I.

TABLE I.
Spread of Dye Spots in Interstitial Tissue.
Initial Area—100 to 125 Planimetric Units.

Ears perfused with	No. of Dye Spots	Aver. Initial Area, P.U.	Increase in Size of Dye Spots final area ÷ initial area	
			Extremes	Average
Pulsatile pressure	6	112	4.5 to 8.7	5.4
Constant pressure	7	112	3.2 to 5.0	3.8

Pulsation of the blood vessels seems to provide the motive force for lymph flow through the resting, unmoved tissue. It seems probable that much of its effect is exerted through the connective tissue fibers associated with the walls of the blood vessels and lymphatics. The extent to which other factors are responsible is now under investigation.

Physiologists have long known that perfusions at pulsatile pressure are more efficient than those at constant pressure. The more rapid movement of substances through the tissues and the more rapid formation and removal of lymph, as demonstrated in the present work, will largely explain this fact.