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RESISTANCE IN THE SHEEP'S LYMPHATIC SYSTEM

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ABSTRACT

Saline was infused in a downstream direction into the afferent lymphatics in the metacarpal region of anesthetized sheep. The changes in inflow pressure were measured over 10 min periods with flow rates ranging from 10-2000µl/min. Flow rates in the physiological range generated mean pressures of about 30mmHg and flows of 1ml/min generated mean pressures of about 60mmHg. Resistance was relatively high at flow rates in the range of 10-15µl/min but sharply decreased above that and was relatively constant at flows greater than 500µl/min. Adding isoprenaline (1µg/min) to the infusate reduced spontaneous contractile behavior in the infused system and lowered the resistance at the lower flow rates. It is concluded that the peripheral lymphatic system in the sheep offers substantial resistance to lymph flow and that substantial intralymphatic pressure is needed to return lymph from the periphery especially at higher flow rates.

The resistance offered by the lymphatic system to lymph flow determines the amount of energy required to drive lymph from the periphery to the central circulation. This interrelationship in turn has implications for the mechanisms involved in lymph propulsion. In the present experiments, we attempted to quantitate lymphatic resistance by measuring the pressure head needed to drive fluid at constant rate into an afferent lymphatic in the sheep's foot in a downstream direction.

MATERIALS AND METHODS

Afferent lymphatics were exposed in the metacarpal region of sheep anesthetized with pentobarbitone 20-30mg/kg IV and halothane (2-3% in O_2). These were cannulated in a downstream direction with PVC tubing (internal diameter 0.4mm), 6-8cm in length and connected to a syringe pump. The inflow pressure was measured by a pressure transducer connected to a side arm of the infusion catheter. Normal saline was infused via the catheter at rates varying from 10 to 2000µl/min for 10 min periods. Saline introduced in this way has to traverse the afferent lymphatics, the lymph nodes en route and the efferent lymphatics before entering the thoracic veins *(Fig. 1)*. Resistance in the system undergoing perfusion was calculated from the flow through the system (taken as the pump infusion rate) and the pressure drop across the system. The inflow pressure to the lymphatic system was determined from the side arm pressure minus the pressure drop due to the resistance of the infusion tubing which was measured separately at the end of each experiment. The outflow pressure was considered to equal that in the thoracic veins and assumed to be zero. The sheep lay on its side during the experiments, and the cannulated lymphatic was kept at heart level. The increase in pressure at each flow rate was taken as the difference

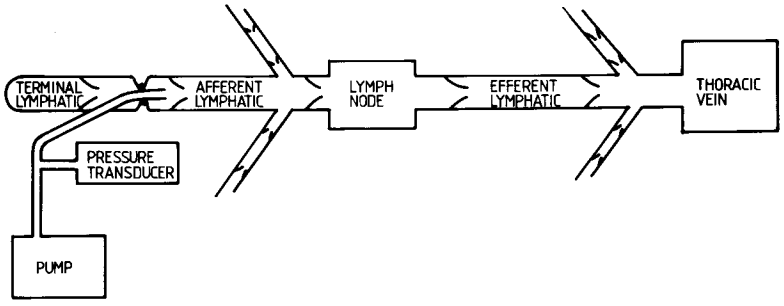

Fig. 1. Schematic representation of the experimental set-up.

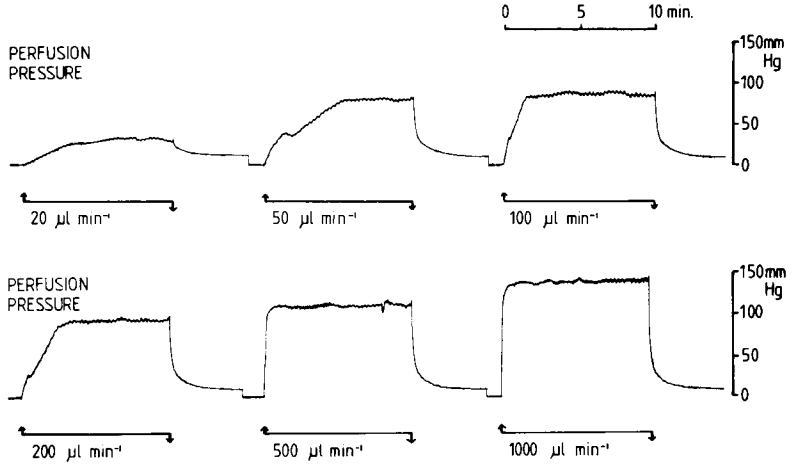

Fig. 2. Inflow pressure traces when saline was infused at increasing rates into an afferent lymphatic in the sheep's leg. Very low flow rates caused substantial rises in inflow pressure but the increase in pressure with flow rate was not linear.

between the mean pressure in the final minute of each infusion and the pressure 5 min after the infusion was stopped. In some experiments isoprenaline was added to the perfusate at a rate of 1µg/min to determine the possible role of lymphatic contractility in the flow-pressure interrelationship.

RESULTS

Fig. 2 depicts examples of inflow pressure tracings obtained when saline was infused for 10 min periods at increasing rates. Incremental increases in flow were associated with progressive increases in lymphatic pressure. Even low flow rates (e.g., 50µl/min which is equivalent to about one drop every 25 sec) induced a substantial rise in pressure. The pressure changes during infusion were complex and showed fluctuations superimposed on the rise in pressure due to the infusion especially at the lower flow rates. The pressure increments with increasing flow rate were not linear, e.g., the pressure increment when flow was increased from 20-50µl/min was greater than that seen when flow was increased from 200-500µl/min.

Fig. 3 shows the overall relationship of infusion rate to intraluminal lymphatic pressure and represents the averaged results of twin experiments of the type shown in *Fig. 2*. The rise in pressure as flow increased was curvilinear and convex to the flow axis. The rate of increase of pressure with flow was greatest

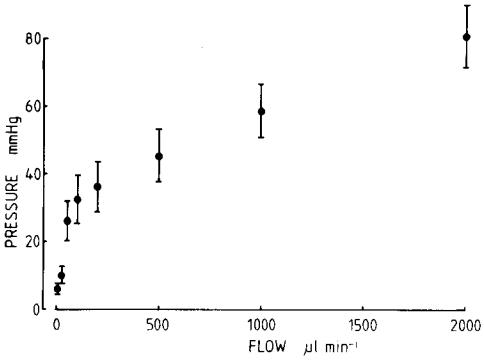

Fig. 3. The inflow pressure changes with increasing lymphatic flow rates (means ± SEM from experiments of the type shown in Fig. 2*).*

at low flow states. Thus a flow rate of 50µl/min yielded a mean pressure increase of about 30mmHg suggesting that flow rates of about 2 drops/min required intralymphatic pressures of this magnitude to overcome lymphatic resistance. Although higher flow rates generated proportionately much smaller increases in pressure, the absolute lymphatic pressure was comparatively high. Thus at a flow rate of 1ml/min (1000µl/min), the mean pressure rise was 60mmHg. *Fig. 4* shows the data contained in *Fig. 3* plotted as lymphatic resistance against flow rate.

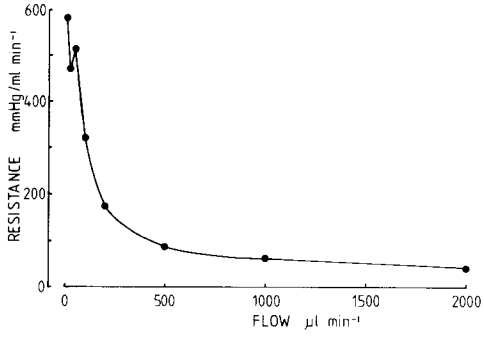

Fig. 4. The data in Fig. 3 *plotted as lymphatic vascular resistance against flow rate. Resistance was much higher at the lower flow rates. It was particularly high in the 10-50µl/min range. Above that range it fell off rapidly and was relatively constant at the higher rates.*

Whereas lymphatic vascular resistance was notably high in the flow range 10-50µl/ml (the physiological range for flow in these vessels in anesthetized sheep), above that, vascular resistance fell off rapidly and was relatively constant at flow rates greater than 500µl/min.

Fig. 5 demonstrates the effect of saline perfusion at low flow (50µl/min over a 10 min period). Inflow pressure

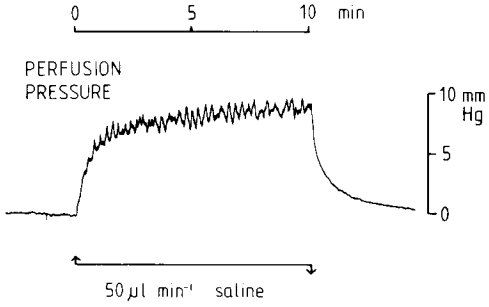

Fig. 5. The inflow pressure changes when saline was infused for 10 min in a downstream direction into an afferent lymphatic in the sheep limb.

rose about 10mmHg but superimposed on the pressure rise were spontaneous fluctuations of about 2mmHg with a frequency of 2-4/min. This frequency is in the range of the "normal beat" frequency of these peripheral lymphatics. *Fig. 6* shows the effect of isoprenaline. When a peripheral lymphatic was perfused in a downstream direction for a 50 min period at 50µl/min with saline (the 1st, 3rd, and 5th 10-min period), a similar response as depicted in *Fig. 5* was seen. During the 2nd and 4th 10-min periods, however, the perfusate contained isoprenaline in a concentration calculated to deliver 1µg/min to the lymphatic, and the spontaneous rhythmic activity of lymphatic contractions was greatly reduced (1) and the intralymphatic pressure rise compared to saline infusion was considerably lower.

DISCUSSION

Because of the general similarity of their structures there is a tendency to consider peripheral lymphatics and veins as conduits of relatively low resistance. The small pressure gradients observed between that in peripheral lymphatics and in the thoracic duct have been taken as evidence of low lymphatic resistance on the assumption that these gradients are

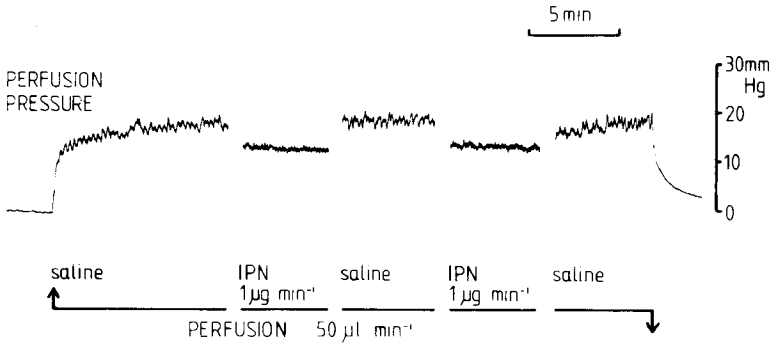

Fig. 6. The effect of isoprenaline on lymphatic vascular resistance. The addition of isoprenaline to the perfusate decreased the inflow pressure and the degree of spontaneous activity in the system.

responsible for lymph flow (2). However, other evidence suggests that peripheral lymphatics offer considerable resistance. First, individual lymphatic contractions can generate substantial intralymphatic pulse pressure. In the sheep, levels up to 25mmHg have been recorded in a peripheral lymphatic, and in afferent lymphatics draining the human foot, Olszewski and Engeset (4) have found pulse pressures up to 35mmHg. With the relatively low lymph flow rates in these vessels, such pulse pressures could not occur if the lymphatic system offered a very low resistance. Second, when high lymph flow rates are generated in the afferent lymphatics of the sheep leg by maneuvers such as compression of the foot (5) or by injection of saline into the interdigital cleft (6) intralymphatic pressure can rise to over 40mmHg. Again, such high pressures would not be generated in a very low resistance system. Third, the smooth muscle of afferent lymphatics can, by its intrinsic contractions, overcome outflow pressures of over 70mmHg (7). Hall *et al.* (3) found that when an afferent popliteal lymphatic in the sheep was obstructed, the strength and frequency of lymphatic contractions were increased, and pressures up to 100mmHg were generated. In the present experiments, too, although the fall in intraluminal resistance with increased flow rate was due in part to the increasing distension of the system by the higher pressures generated by the higher flow rates, *Figs. 5 and 6* demonstrate that some of the resistance, especially at the lower flow rates, was also generated by spontaneous contractile activity in the lymphatics. Indeed, inhibition of lymphatic contraction by administration of isoprenaline blunted the rise in both intralymphatic pressure and resistance during saline infusion.

It seems unlikely that normal peripheral lymphatics would be capable of generating pressures as great as those seen in the arterial system if they had only to drive fluid through a low resistance circuit. On the other hand, if lymphatics offer substantial resistance to lymph flow, the peripheral lymphatics are capable of generating intraluminal pressures necessary to overcome such resistance.

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