

LYMPH PRESSURES IN STERILE INFLAMMATION

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The literature contains but few reports on the normal pressure in peripheral lymphatics. In 1850, Noll (1), working in Ludwig's laboratory, found that the lateral pressure in the cervical lymph trunk of the dog, measured in terms of centimeters of a soda solution, varied between 8 and 18 mm. of soda solution, reaching in one experiment a height of 26 mm. The lymph pressure rose during expiration and fell during inspiration, and was readily increased by any peripheral pressure such as stroking. In 1861, Weiss (2) made some measurements on the lymph pressure in the cervical lymphatics of dogs and colts, and found that in the case of the dog, the pressure varied between 5 and 20 mm. of a soda solution having a specific gravity of 1.080.

Measurements of the lymph pressure in the thoracic duct, of which there are several, have no bearing on our immediate problem, and those on the cervical lymphatics are so complicated by the depth and type of anesthesia and by respiratory changes that they cannot be considered typical of all peripheral lymphatics.

Starling (3), in 1894, remarked that if the foot of a dog was kept in water at 60°C. for 5 minutes, the lymph flow was increased and the lymph became much richer in protein. About a year ago two of the present authors (4) followed the changes in lymph protein and measured the amount of lymph produced under conditions of sterile inflammation. The extraordinarily large production of lymph invariably observed has led us to determine what pressures are reached in the lymphatics of the leg inflamed in a sterile manner.

Technique

Dogs anesthetized intraperitoneally with nembutal (sodium-ethyl barbiturate) were used. The two main lymphatics at the ankle of the hind leg were isolated.

When size permitted, both vessels were cannulated and attached *via* a Y-tube to a vertical manometer. If one of the lymphatics was too small to cannulate, it was tied off. All other lymphatic paths were open. Injections of trypan blue into the legs of dogs confirm Baum (5) in showing two large lymphatics on the dorsal surface of the foot, in the region of the ankle, with a number of interconnections at different levels. There are also connections with smaller lymphatics draining the posterolateral side of the leg, so that in tying off these two lymphatics the drainage of lymph is diverted into collateral paths and is not materially obstructed. The pressure of lymph in the lymphatic was determined by allowing the lymph to flow directly into a calibrated vertical manometer.

In several of the experiments venous pressure measurements were taken at the same time. A cannula was tied into a small venous branch at the ankle in the same region which was exposed through the same incision as that in which the lymphatics were picked up. The venous cannula was attached to a citrate wash-out system and the pressure was recorded in terms of centimeters of water.

TABLE I

Maximum Lymph Pressures in Sterile Inflammation

No. of dog	Date	Weight	Treatment	Maximum lymph pressure
		<i>kg.</i>	<i>min. at 100°C.</i>	<i>cm. of lymph</i>
1	Dec. 8, 1931	23.0	2	106.4
2	Feb. 24, 1932	19.5	2	118.2
3	Feb. 26, 1932	20.0	2	78.0*
4	Mar. 2, 1932	22.0	2	118.8
5	Mar. 4, 1932	20.0	2	120.0

* Graphite previously injected plugged cannula at one time.

After a series of normal readings had been taken, the whole paw up to the ankle was immersed either in water at 100°C. for a period of 2 minutes or in water at lower temperatures for varying lengths of time. Lymph pressure and venous pressure were recorded during the immersion and at intervals thereafter until the lymph pressure reached a maximum.

The rate and amount of lymph produced were determined in some experiments by the use of calibrated cannulas in the opposite leg which was treated in the same manner. Protein determinations were made refractometrically.

RESULTS

In an anesthetized dog, the pressure in the lymphatics of the quiescent leg is not measurable. It has been our experience and the experience of others (Paschutin (6), Emminghaus (7) and Starling (3))

that no lymph is obtained from a cannulated leg lymphatic unless massage or passive motion is employed.

Leg Lymph Pressure in Sterile Inflammation.—Table I summarizes a series of experiments in which inflammation was produced by immersing the foot in water at 100°C. for 2 minutes. The maximum pressure obtained from a leg lymphatic was found to be 120 cm. of lymph and the range was from 78 to 120 cm. The lymph pressure rises immediately after the immersion and usually reaches a maximum in the course of 3 to 4 hours.

Since the lymphatics are well provided with valves, a possible fall in pressure after the maximum had been attained and held for some

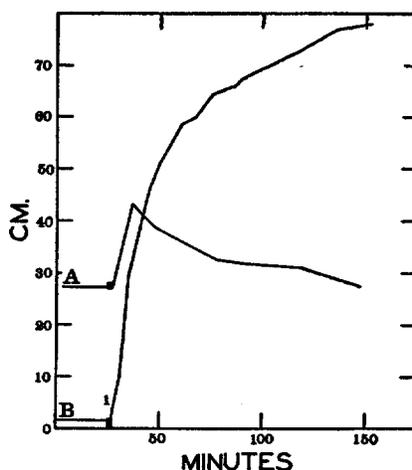


FIG. 1. Lymph and venous pressure in sterile inflammation. *Ordinates*, centimeters of water or lymph; *abscissae*, time in minutes. *A*, venous pressure; *B*, lymph pressure. At mark 1, foot immersed in water at 100°C. for 2 minutes.

time would not be recorded by the type of manometer used. To determine whether this was the case, in one experiment in which the maximum pressure had remained constant for over 1½ hours the manometer was disconnected and a second one was attached. In 20 minutes the pressure had risen 75 cm., and in 1 hour it had attained its previous maximum. In another experiment, after connecting with the second manometer the maximum pressure then attained was 20 cm. less, showing that in this case there had been a fall in the pressure.

Fig. 1 illustrates a typical experiment in which both lymph and

venous pressure were recorded simultaneously. The venous pressure rises as soon as the water at 100°C. touches the foot and reaches a maximum about 16 cm. above normal in from 10 to 15 minutes. The lymph pressure rises rapidly, though always lagging a few minutes behind the rise in venous pressure. Shortly after the venous pressure begins to rise arterial pulsations are visible in the venous pressure manometer, indicating the direct transmission of arterial pressure through the dilated capillary bed to the venous side.

The protein content of normal leg lymph, which may vary from 0.5 to 1.5 per cent, was usually found to be around 4 per cent after a sterile inflammation had been produced. Under such conditions the capillaries become injured and extremely permeable to the blood proteins. After such an experience blisters were commonly found between the toes. In one experiment it was possible to measure the protein content of the lymph, of the blister fluid and of the tissue fluid obtained by inserting a needle into the subcutaneous tissue. Both the lymph and the tissue fluid had an average protein content of 3.5 per cent (three determinations, 15 minutes apart) while the blister fluid contained 2.5 per cent of protein.

Marked swelling of the leg occurs in from 7 to 45 minutes after the inflammation has been produced. No measurements were made of the amount of the swelling and its initial appearance was recorded in the gross. The increase in lymph production and the other lymph changes always occurred some time before swelling was noticed.

Since immersion of the foot in water at 100°C. produces a severe inflammation, it seemed worth while to see what effect simple hyperemia induced by water at lower temperatures would have on lymph pressure and to determine if possible at just what temperature changes in the lymph flow begin.

Fig. 2 illustrates a typical and complete experiment in which lymph pressure and venous pressure were recorded simultaneously in one leg, and in which the protein content and the amount of lymph produced were measured in the other leg which was treated in exactly the same manner. After a series of normal control determinations had been made, the two feet arranged side by side in identical positions were placed in a water bath in which the temperature could be raised to any desired degree. Control readings were also taken in water at

40°C. When the temperature was raised to 50°C., there was an average rise in venous pressure of 15 cm. of water but the effect on the lymph pressure and on the amount of lymph produced was extremely slight. Between 50° and 60°C., however, marked changes were pro-

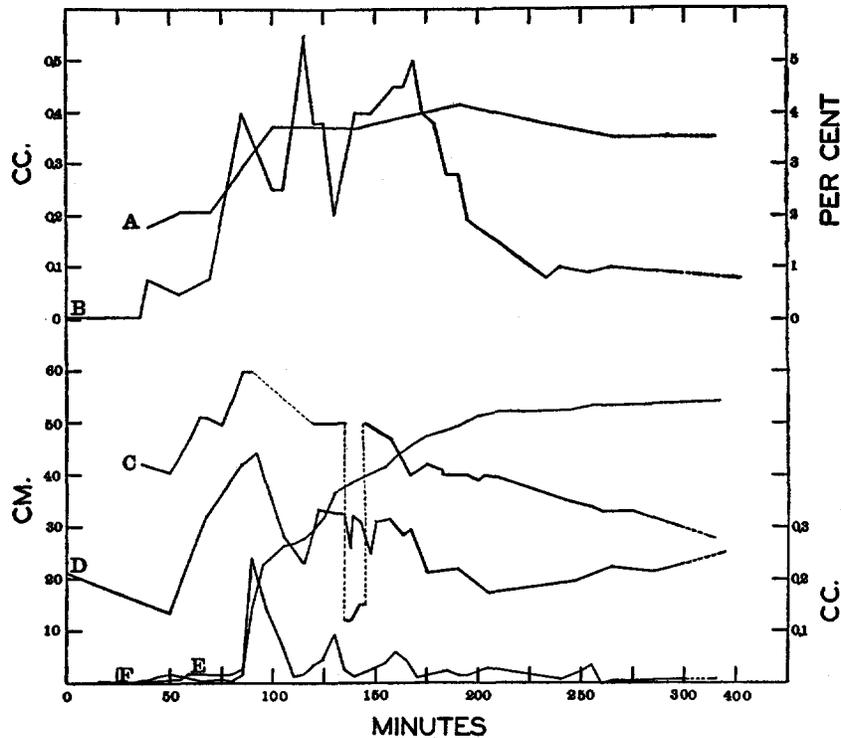


FIG. 2. The effect of water of varying temperatures on the lymph pressure, venous pressure and rate and amount of lymph produced. *Ordinates*, per cent of protein, cubic centimeters of lymph, degrees C. and centimeters of water or lymph; *abscissae*, time in minutes. A, per cent of protein in left leg lymph; B, amount and rate of lymph collected from left leg; C, temperature of water bath; D, venous pressure of right leg; E, lymph pressure of right leg; F, rate of lymph production in right leg.

duced. The venous pressure then rose 27 cm. above the normal average to a height of 44 cm. At this point also the lymph pressure began to rise and continued to rise thereafter. The amount of lymph pro-

duced by the opposite leg became very abundant and this lymph was more highly proteinized. The rate of lymph production of one leg plotted from the lymph pressure changes and measured directly on the opposite leg is seen to follow rather closely the changes in venous pressure produced by the water of varying temperatures, though there is always a slight lag.

In order to determine whether or not lymph obtained from legs inflamed in a sterile manner contains any toxic or depressor substance, intravenous injections into rabbits and cats whose arterial blood pressure was being recorded were tried. Normal lymph was used as a control. It was found that the inflammatory lymph contained no depressor substance and was as innocuous as normal lymph.

DISCUSSION

Under conditions of sterile inflammation such as have been produced here, there can be no question of generalized lymphatic thrombosis during the periods of observation, which were often 8 hours in length. The lymph flow is enormously increased and the ease with which the lymphatics may be entered can be demonstrated by injecting graphite into the subcutaneous tissue. Very often the injecting needle will enter a distended lymphatic directly and graphite will appear in the cannulated ankle lymphatic in less than a second after pressure has been applied to the plunger of the syringe. This is not the case with injections in the normal leg. One observation was made on the inflamed leg 24 hours after the onset of inflammation. In this case the lymph was still flowing though not as abundantly as it had been 12 hours previously.

The greatly increased extravascular fluid must cause the lymphatics to become dilated since the foot is able to swell freely in all directions. If the lymphatics were attached on their outsides to surrounding tissue, as Heimberger (8) has observed in the case of the capillaries at the base of the nail, then swelling would cause them to be pulled apart rather than to collapse, as the pathologists would have us believe, when fluid gathers in the extracellular spaces (Adami (9)). Our experience is quite in accord with some observations of the Clarks (10) on edematous tadpoles and chicks in which they found that in cases of generalized edema the lymphatics invariably enlarged and

that the delicate lymph capillaries did not collapse with the increased pressure outside the vessels, but on the contrary continued to absorb fluid until they became very much distended.

Menkin (11) has shown that trypan blue injected directly into the site of inflammation in the subcutaneous tissues is fixed in the inflamed area and fails to reach the regional lymph nodes. He has explained this failure of penetration by the occlusion of the lymphatic vessels and by the presence of a fine network of fibrin in the tissue spaces of the inflamed area. Because of the large amounts of free flowing lymph which we have always obtained up to 8 hours and in one case 24 hours after the onset of the inflammation, it is difficult to see how there could be any generalized thrombosis of the lymphatics in the region drained, yet trypan blue is fixed under such conditions. Examination of the subcutaneous tissues in such an inflamed leg shows that the tissue is extremely gelatinous in appearance. It would seem more likely, in the type of inflammation dealt with here, to explain the failure of trypan blue to reach the lymphatics on the basis of its inability to diffuse through such a mass, rather than by actual lymphatic blockage. In the dog in which the inflammation was of 24 hours duration and in which trypan blue had been fixed, mere handling of the leg caused the trypan blue to appear in the lymph in a very short time. In this case there could have been no lymphatic blockage.

SUMMARY

1. The normal lymph pressure in the legs of anesthetized dogs is not measurable.
2. The maximum pressure of lymph in the quiescent leg under conditions of sterile inflammation is around 120 cm. of lymph.
3. Venous pressure rises immediately in a region subjected to sterile inflammation and then slowly returns to normal. The rise in lymph pressure follows the rise in venous pressure.
4. Changes in lymph flow, lymph pressure, and protein concentration of the lymph occur when the part producing lymph is subjected to external temperatures between 50° and 60°C.

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