CHANGES IN THE CUTANEOUS LYMPHATICS OF HUMAN BEINGS AND IN THE LYMPH FLOW UNDER NORMAL AND PATHOLOGICAL CONDITIONS

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Earlier work (1) has shown that intradermal injections of vital dyes are to a large extent intralymphatic, for dye enters the lymphatics where they are torn or ruptured by the injecting needle. It renders the rich superficial plexus visible and within a few minutes some of it passes into the larger, subcutaneous, draining lymphatics and these appear now through the skin like colored streamers. The existence of a significant cutaneous lymph flow as thus evidenced has suggested the present study of the variations in flow under physiological and pathological conditions.

It was necessary to ascertain first of all whether intradermal injections of dye would yield evidence of changes occurring in the character of the lymph flow. A series of tests directed to this end showed the method to be adequate to demonstrate those variations in lymph flow which are known to occur. Long and intensely colored streamers appeared in the skin of limbs heated or actively moved and short, lightly colored streamers in limbs at rest, conditions known to increase or decrease the flow of lymph respectively (2–4). The technique was next employed to detect changes in the character of the lymph flow under conditions having an unpredictable influence upon it.

Method

In the previous work (1), demonstrating lymphatic capillaries in human skin, 0.05 to 0.1 cc. of an 11 per cent aqueous isotonic solution of a vital dye, patent blue V,[1] was injected intradermally in the forearms of healthy volunteers. These

[1] General Dyestuffs Corporation, New York.

relatively large injections led to the formation of colored streamers in normal arms, which extended so rapidly to the axilla that one could hardly employ the rate at which they formed to detect increases in lymph flow. In the present work, desiring to distinguish between increase and decrease in streamer formation under differing physiological conditions, we have resorted to much smaller injections of diluted isotonic dye solution which produced short, pale streamers in normal skin, that increased or decreased in length or intensity when conditions were varied. A mixture of equal parts of Locke's solution and the aqueous isotonic 11 per cent solution of patent blue V was employed in all the work and the resulting 5.5 per cent solution, autoclaved, was injected intradermally during a period of 45 seconds to 1 minute in amounts ranging from 0.01 to 0.04 cc. Thus the concentration of the dye was but half of that used in the previous work and the amount of pigment introduced but 1/10 to 2/10 the previous quantity.

Luer tipped, glass and metal 1 cc. record tuberculin syringes served for all the injections. They were graduated upon the handle of the plunger so that accurate measurements could be made, because the intensity of the color of the dye in the barrel obscured the markings there. To obtain exceedingly superficial blebs of dye, thus insuring injection of the superficial plexus of lymphatic capillaries, No. 30 gauge platinum iridium needles were used. Unless otherwise stated injections into the forearm were made while the subjects sat with it horizontal, comfortably supported upon a table at the level of the apex beat of the heart. Injections into the skin of the ankle were made while the subjects sat or reclined with both legs supported horizontally. Before each test the subject remained at rest 30 minutes or longer. Similar injections were then symmetrically placed in both limbs, one of which remained at rest while the other was subjected to the test procedure. When this was not practicable, the control injection was first made, and its effects observed for half an hour, after which the test injection was given.

For the photographs a steel gallows was used with an extensible horizontal arm 40 cm. in length supporting at its outer end a universal joint carrying a standard leica camera (f. 3.5 lens) and lighting apparatus. A binocular microscope was similarly arranged on a long metal arm. Both camera and microscope could be tilted at any angle and extended over a hospital bed when studies were to be made upon patients, and the results of the injections were simultaneously observed and photographed. The camera carried on its face a 1 to 1 reproduction device for taking pictures at natural size, and the device and frame were of such length that when the instrument was placed a millimeter or two above the skin surface the focal point of the lens was situated a millimeter or more deep in the skin. A photoflood bulb and a series of 8 inch condensing lenses throwing a beam of light 2.0 inches in diameter at the focal point of the camera gave a brilliant and constant illumination. The natural size photographs were taken at exposures of 1/20 of a second, and at intervals of 5 seconds when desired, using supersensitive panchromatic film and a red gelatine filter,[2] to bring out the blue color of the dye. To record

[2] An Eastman Kodak Co. No. 25 gelatine film light filter.

streamers following the injection photographs were taken at regular intervals during 20 minutes at a distance of 40 cm. A single photoflood bulb and reflector afforded sufficient light for 1/10 second exposures. Tracings of the dye streamers on a piece of curved celluloid held over the limb, were made with patent blue V instead of ink, the dye giving far better results than the latter when used with the finest drawing pens.

As a matter of routine the appearance of the dye in the lymphatics and the behavior of their colored contents was noted, as was too the state of dilatation or contraction of the channels, the ease or difficulty with which dye entered them, the distance it extended in them when first injected, and the extent to which the superficial plexus was filled at that time. For example, only part of the dye injected into normal skin finds its way into the lymphatics directly, much remaining as an interstitial bleb at the point of injection. In other circumstances, as will be seen in the following paper, almost all the dye enters the channels directly and is carried farther in them. We observed also the rate of dye escape from the lymphatics, as evidencing changes in their permeability, and further, the extent of interstitial spread of color and the rapidity of its disappearance. The speed and intensity of streamer formation was watched for a period of half an hour, as evidence of the rate of lymph flow. At hourly intervals or oftener, for 5 hours, observations were made of the increase or decrease in the intensity of the streamers with their final disappearance perhaps, together with the rate of paling of the dye bleb, or its interstitial spread.

The Behavior of Dye Solutions in Lymphatic Capillaries of Normal Skin

The events which follow an injection of dye on the volar surface of the forearm have been described in an earlier paper (1). In the present work, as mentioned above, much smaller amounts of dye were used in order to produce short streamers which varied in length or intensity according to the local conditions. Natural size photographs of typical injections in the skin of the volar surface of the normal forearm are shown in Figs. 1 and 2 as a standard wherewith later findings are to be compared. In each figure the first four exposures were taken at intervals of 15 seconds after beginning an injection of approximately 0.02 cc. of dye solution, the fifth and sixth at intervals of 30 seconds, the seventh and eighth after 3 and 4 minutes and the last at the 20th minute.

The figures show dye directly entering the network of superficial lymphatics (through channels torn by the needle) and spreading out within them. At the point of the injecting needle much dye remains as an interstitial bleb. In all instances, during the injection and for

some time thereafter, the colored fluid continues to spread through the superficial lymphatics, increasing the area of the injected region. Diffusion occurs, blurring the borders of these channels, where before the outlines had been distinct (Figs. 1 *e* to *h*; Figs. 2 *d* to *h*). In a few minutes the injected region may show one or more pseudopods of color, extensions of dye in subcutaneous lymphatics. As the lymph flow carries the dye further from the injection site, they become visible through the skin as colored streamers, which, even in a resting arm, may extend 10 or 15 cm. in 20 minutes.

In the skin of the ankle the lymphatic plexus seems less rich, the channels smaller and lymph flow slower. In the following paper, photographs of the results of a dye injection in the normal ankle are compared with those of similar injections in the skin of edematous ankles.

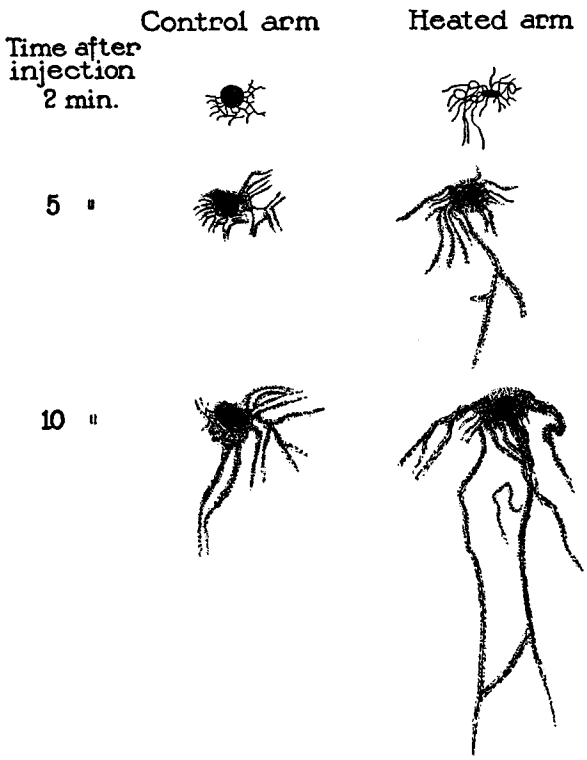
The Effect of Agents Known to Stimulate Lymph Flow

It is common knowledge that lymph flow is increased by applications of heat (2, 4–6), by massage (4, 7–9), by activity (3, 7, 10–13) or by hyperemia (5, 6), and that it is diminished in limbs that are at rest (4, 7, 9, 14).

The Influence of Heat.—We injected patent blue V into the skin of the volar surface of both arms of 8 normal individuals, subjecting one arm to the influence of heat while the other remained at room temperature.

During a 45 minute rest period prior to the test the subjects sat with both forearms lying on the table, as already described. One arm was then gently submerged in a large cauldron filled with water maintained at 46–47°C. while the control arm rested, in the same relative position, either upon the table, supported at wrist and elbow by wooden blocks, or submerged in a large basin of water at room temperature. After variable periods of immersion, 5 to 15 minutes, 0.02 to 0.03 cc. of the dye mixture was injected into the volar surface of the control forearm about one-third of the way from the wrist to the elbow. As soon as possible thereafter, a similar injection was placed in the submerged arm while it was still under water. In a few instances the arm was lifted out, injected and at once resubmerged. In alternate tests the warmed arm was injected first. In all of them the arm remained just covered by the hot water where the effect of the injections could be observed through the binocular microscope and tracings made on celluloid. Photography was not attempted in these instances.

In every case hyperemia developed in the immersed arm. The lymphatic capillaries disclosed by injection seemed slightly wider than in the control arm.



TEXT-FIG. 1. The effect of warmth on lymph flow. Tracings of 2 similar intradermal injections of dye in the forearm, 2, 5 and 10 minutes after injecting. Dye escape from the lymphatics is indicated by the stippling. Column 1 shows the result in the normal resting arm, column 2 in an arm resting in warm water at 46–47°C. In the latter the streamers developed more rapidly, the interstitial bleb of dye was smaller. 1/2 natural size.

Dye entered them much more readily than was the case in normal skin and seemed to be distributed farther in them. As a result, the area of lymphatic capillaries injected occupied a wider circumference, the network seemed more richly injected, and the amount of dye remaining as an interstitial bleb was far less. Dye escape from such capillaries was rapid too and colored streamers, more intense than in the control arms, appeared earlier and became longer. Text-fig. 1, a 1/2 natural size reproduction of the celluloid tracings of a typical test, shows the behavior of the colored streamers. As indicated, the tracings were made 2, 5 and 10 minutes after the beginning of the injections in the two arms. Each injection required about 1 minute.

The findings show clearly that the application of heat increases the size and intensity of the colored streamers of dye flowing away in the subcutaneous lymphatics from a localized region of injection. The changes are such as one would expect with increased lymph flow.

The Effect of Muscular Movement.—In 8 tests on 4 normal persons approximately 0.02 cc. of patent blue solution was injected intradermally on the volar surface of both forearms, following the rest period as usual. For 20 minutes thereafter the muscles of one arm were contracted and relaxed by clenching the fist at intervals of 3 to 5 seconds and making punching movements every 10th second, drawing the exercised arm back to the chest at the same level as the control arm. Occasional pauses were allowed for the inspection of the injected area under the binocular microscope and to make tracings.

In all the tests dye escaped more rapidly from the lymphatic capillaries of the exercised arms and diffusion of dye into the tissues was also greater. Dye streamers developed sooner, were broader, longer, more numerous and more deeply colored. In some instances streamers only twice as long as those in the resting arm developed in the 20 minute period, that is to say streamers about 25 cm. long. In other instances deeply colored bands reached the axilla with excessive speed, in 3 or 4 minutes. The results were too irregular to show in a single typical tracing or photograph, yet always the streamers were greater in the exercised limb.

Similar injections were made in the skin of both ankles of the same 4 volunteers, first in one leg which was allowed to rest horizontally for 20 minutes and then in the other, after which the subjects walked shoeless about the laboratory. The activity brought about changes in the dye movement, long streamers often reaching above the knee in 5 to 10 minutes, when walking was permitted, whereas they had extended only 3 to 7 cm. after 20 minutes in the limbs at rest. Once again a procedure increasing lymph flow brought about enhancement of the movement within lymphatics.

Effects of Massage.—In 7 tests the limb was massaged after an intradermal dye injection in either the ankle or forearm. When the area injected was massaged immediately, the colored fluid extended 1 or 3 cm. farther into the superficial lymphatic capillaries than in the skin on the control side, and longer and more brilliant streamers appeared earlier. These streamers were much darker than in

our previous instances. Although it is well known that massage produces an increase in lymph flow from cannulated lymphatics (4, 7, 9), the rapid appearance of colored streamers can be taken only as evidence of a movement of the dye within the channels, not of a flow of lymph. Manipulation of the limb may have squeezed dye into the opened lymphatics and forced it along them. The intensity of the color of the streamers showed that the dye had been diluted less than usual. It is of interest to note, in connection with other tests reported in the accompanying paper, that retrograde movement of colored fluid within the lymphatics did not occur, save for a distance of 1 or 2 cm. and then only within the superficial lymphatic capillaries.

In 6 other tests dye injections were made 5 cm. below the antecubital fossae of both arms, and the lower arm, wrist and hand were massaged carefully, avoiding manipulation or pressure upon the injected area. In all these instances too, dye streamers extending from the sites of injection in the massaged limbs were longer and more deeply colored than was the case in the controls. The differences were like those shown in Text-fig. 1, but varied much from instance to instance. In these tests as in those just described, much pressure must have been transmitted to the injected area.

The Effects of Passive Movement, Suction and Posture

The findings reported to this point have all shown that procedures which are known to increase lymph flow caused an enhancement in the size, number and intensity of the colored streamers developing after injection of small amounts of dye in the skin. In resting limbs, in which presumably lymph flow was least, that is to say in the control arms, streamer formation was least. With this much ascertained, we next studied the movement of dye in the skin lymphatics of limbs subjected to passive movement, to suction and to changes in posture, all of which must influence lymph flow in the intact limb in ways which though not definitely known are reasonably predictable.

The effects of passive movement were found to be far less pronounced than those of active movement. 4 tests were carried out, on 2 normal individuals. A brief summary of one will suffice.

Both arms were allowed to lie at rest on the desk for half an hour, after which 0.02 to 0.03 cc. of dye was injected, either on both forearms as usual or, in 2 tests, over the biceps muscle. At once one wrist was placed in a sling attached to the rim of a wooden wheel a foot and a half in diameter, placed at the subject's side, a little in advance of him and with its hub at the level of the control arm. A motor revolved the wheel once each second for a period of 20 minutes. With the wrist resting in the sling in mid-pronation and supination a movement was imparted to

the arm not unlike the punching motions used in studying the effects of active movement. During the movement every attempt was made to keep the muscles as relaxed as possible. Movement was stopped at the end of the 3rd, 7th, 10th, 15th and 20th minutes to make rapid tracings of the dye streamers.

The tests gave evidence of definite differences in the spread of dye in the two arms but these were relatively slight. In each instance the streamers in the test arm were less than twice as long as those on the control side, which averaged 10 cm. after 20 minutes.

Suction Increases the Lymphatic Drainage of Dye Injected into Living Skin.—Earlier work (1) has shown that dyes and other foreign substances gain entrance into the skin lymphatics surrounding a cut or scratch. Immediate pressure or massage over an injected area of skin drives colored fluid into the lymphatics. The time honored custom of sucking a cut or scratch presents a question: What happens under these circumstances to the foreign material which has entered the superficial lymphatics? A few injections were done to test the point.

Small injections of dye were made in the usual way in both arms of normal subjects, one to serve as a control, the other to be sucked as would be done by an individual pricked or cut in every day life. Under the binocular the spread of dye in the lymphatics was observed and subsequent streamer formation followed as usual.

The act of sucking not only failed to remove all the dye but forced it into the lymphatic capillaries draining the injected area. In 3 to 5 minutes streamers 4 to 6 cm. long appeared while in the control arms no streamers developed in so short a time. Dye escaped into the tissues in larger amounts, judging from the intensity of the secondary diffuse staining about the injected lymphatics, and subsequent lymphatic drainage was also greater, for streamers appeared earlier and were longer and more intensely colored than in the control arm. 15 or 20 minutes later dye could be seen 20 cm. or more above the site of injection as in arms which had been massaged. In the control arms the dye had moved but 8 or 10 cm.

The test was repeated three times with similar results.

The Effects of Posture on Lymph Flow.—Changes in posture brought about great variations in the movement of dye in the lymphatics, as judged by the character of streamer formation.

In 12 trials a subject was seated with one arm resting as usual on a desk, the forearm in supination and one leg propped horizontally on a chair of the height of the one in which the individual sat. Limbs placed in this way served as controls.

The subject's other arm hung downward and the other foot rested on the floor. After a preliminary period of half an hour 0.02 to 0.03 cc. of dye solution was injected intradermally on the anterior surface of each ankle at the level of the malleoli of the tibia and on the volar surface of each forearm about 1/3 the way between the wrist and elbow, keeping the relative positions of the limbs constant for 20 minutes thereafter. At the end of this period each dependent limb was raised to a level far above that of its fellow, the test arm being raised vertically from the shoulder and the test leg propped on the desk at the level of the lower ribs or by means of blocks at a level well above the shoulder.

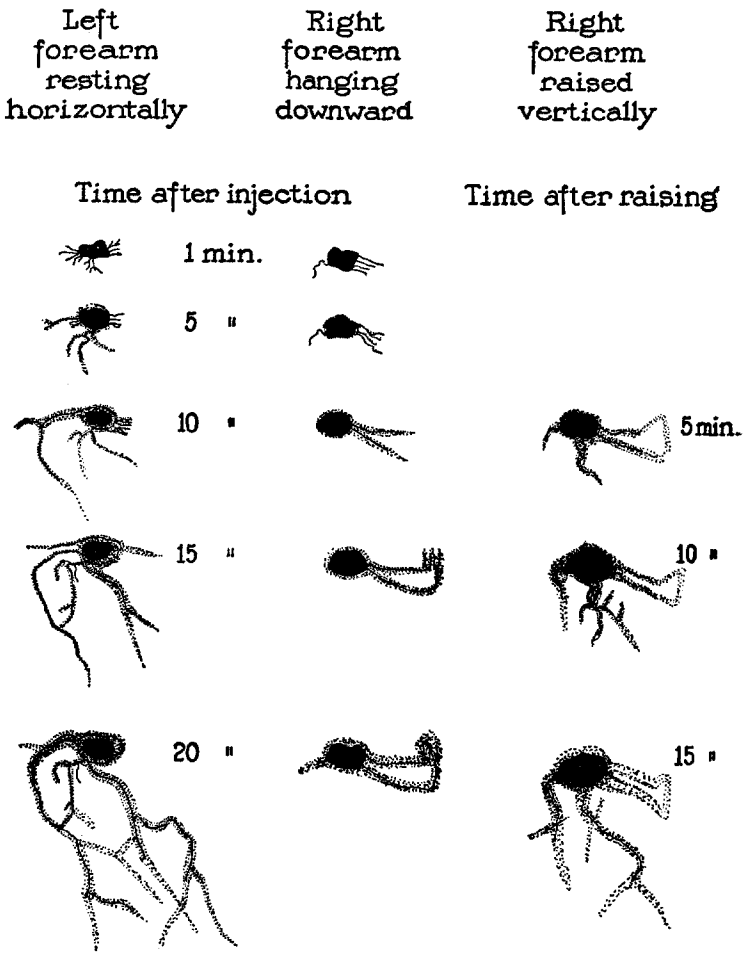
In another 8 instances one leg or arm, after both had remained horizontal or hanging directly downward for 20 minutes, was raised and at once injected, leaving the control limb, also injected at nearly the same time, in the original position. The new posture was maintained for another 20 minutes during which streamer formation was noted. Finally the control limb was also raised and observed for any further extension of its dye streamers.

In Text-fig. 2, tracings are reproduced from a test of the first type. In column 1 the dye spread in the control arm is depicted, in tracings taken as soon as possible after making the injection and at 5 minute intervals thereafter. In column 2 the condition in the dependently hanging arm is shown at the same time intervals. It will be seen that only a few channels running transversely were filled with dye. After 20 minutes this arm was raised vertically over the head, and column 3 shows the tracings of streamers from the same untouched injection site at intervals of 5 minutes thereafter.

Invariably elevation of a dependently hanging limb to a horizontal position, or better to a vertical position, led to extension of dye streamers and frequently to a formation of new ones. Their formation was greatest when a limb which had been hanging downward was raised and then injected immediately. They were less prominent when the limb previously held in a horizontal position was raised vertically and injected, and least marked when a dependently hanging limb was injected and 20 minutes later raised and no further injection made, as in Text-fig. 2. Presumably in such instances much of the dye had already escaped from the lymphatics into the interstitial tissues and hence was no longer carried along rapidly.

The Movement of Lymph Following Release of Lymphatic and Venous Obstruction

The changes in lymph flow in a limb just raised from a dependent position may be regarded as the result of a release of partial lymphatic and venous obstruction. Fluid accumulates in a dependent limb



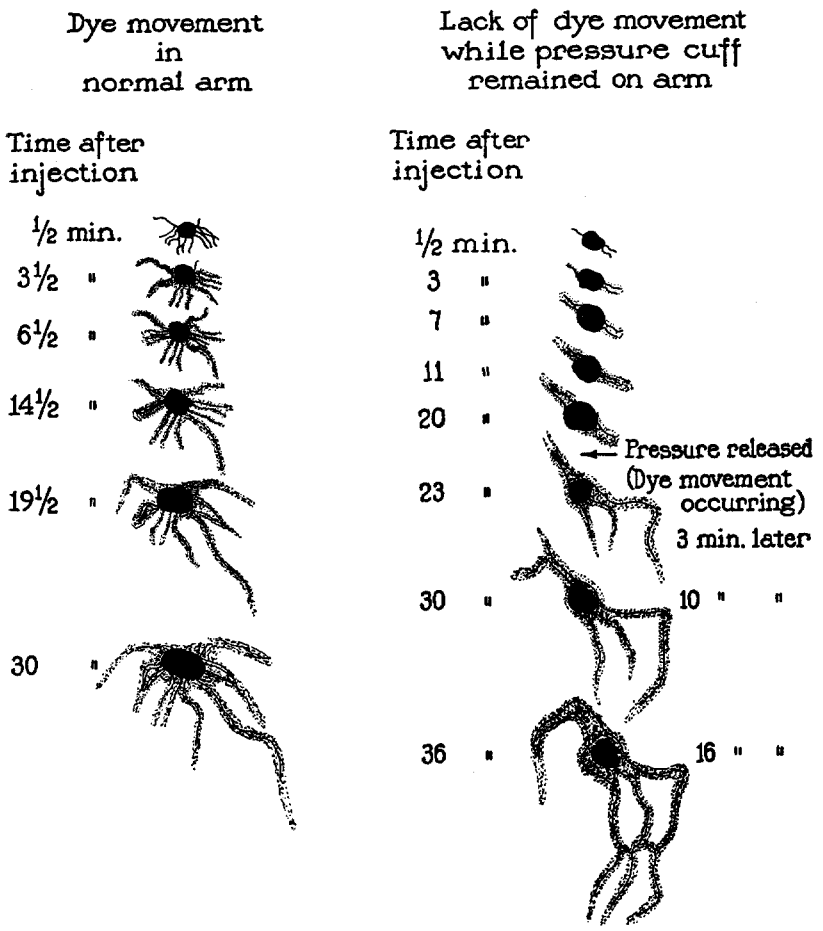
TEXT-FIG. 2. The effect of posture upon lymph flow. Tracings of 2 similar intradermal injections of dye in the skin of the volar surface of normal forearms, drawn as soon as possible after the injections and at 5 minute intervals thereafter. The subject sat with one arm resting on a desk, the forearm in supination and the other arm hanging downward. The left column shows the spread of dye in the skin of the forearm resting horizontally, the center column the behavior of the dye in the dependently hanging arm. After the fifth tracing this arm was raised vertically above the subject's head. Three more tracings at 5 minute intervals show the influence of change in posture upon the dye movement. 1/2 natural size.

(15–19), and in this posture lymph flows more freely than usual from a lymphatic cannulated in the dependent region (7). Starling first showed an increased production of thoracic duct lymph during a rise in abdominal venous pressure (2, 14), and White, Field and Drinker (7) have reported similar effects of peripheral venous obstruction upon subcutaneous lymph. More will be said of this below, but in all the experiments mentioned lymph flow has been measured from opened cannulated lymphatics no longer subjected to the hydrostatic pressure of the column of lymph above the point of cannulation. In the intact resting dependent limb lymph does *not* flow, as our tests have just shown.

What can be said of the movement of fluid in the closed lymphatic system during and after periods of lymphatic obstruction and of partial and complete venous obstruction? Upon release of a temporary venous or arterial occlusion there follows an intense reactive hyperemia. What effect does this have upon lymph flow? An attempt was made to answer these questions.

With the subject seated in the usual posture a sphygmomanometer cuff was placed over the right upper arm and inflated to a pressure of 20 to 25 mm. of mercury, the left arm resting free in a similar position. After an interval of 15 minutes both forearms were injected with dye in the usual way and watched for 20 minutes, after which the pressure previously maintained on the right side was suddenly released and the progress of the dye observed for another 20 minutes. In these tests and in all to follow, when pressure was released the entire cuff was removed as rapidly as possible to avoid any obstruction whatever to lymphatic drainage. Text-fig. 3 shows the tracings from a trial typical of 5 that were made. But little of the dye entered the lymphatics of the obstructed side, as the tracings show, only a few small twigs filling upon injection. On the control side the usual network of capillaries appeared, and streamers began to form in the usual time. This might be regarded as a chance difference, since the findings after intradermal injections vary not inconsiderably from time to time and from individual to individual, were it not for the fact that it was noted quite regularly in every case in which the pressures employed were low, that is to say 15 to 40 mm. of mercury, and the venous circulation not severely hampered. On release of pressure streamer formation was so rapid that soon the dye distribution equalled that in the other arm.

In 10 other tests pressures of 30 to 40 mm. of mercury were employed for periods varying from 5 to 15 minutes. In these instances as in those just described, no lymphatic streamers were noted during the period of obstruction, but upon release dye streamers promptly appeared.



TEXT-FIG. 3. The effect of pressure on lymph flow in the arm. Tracings of the spread of intradermal dye in a normal forearm (left column) compared with that from a similar injection in the other forearm (right column). A pressure cuff inflated to a pressure of 20 to 25 mm. of mercury had been placed about the upper arm 15 minutes previously. The pressure was released 20 minutes after injecting this arm. The last three tracings in the right column show the effect of the release of this slight pressure after 3, 10 and 16 minutes respectively, as detailed in the text. 1/2 natural size.

An abnormally rapid movement of lymph in the skin follows the release of lymphatic obstruction even when accompanied by only a slight impediment to the venous circulation. The findings, which were to have been expected, are preliminary to those which now

follow. They are an additional illustration of the fact that the results of dye injection serve as an indicator of even small differences in peripheral lymph flow, and that the failure of colored streamers to develop indicates the existence of lymphatic obstruction.

Still greater changes in pressure yielded significant differences.

In a series of 7 tests total venous obstruction, and hence lymphatic occlusion too, were effected for periods of 15 minutes to 1/2 hour, by throwing into the cuff pressures of 90 mm. of mercury. The arm became deeply suffused with blood. The lymphatic capillaries were far more easily injected than in the tests in which weaker pressures were used. (Compare the diagram in Text-fig. 3 with the photographs in Fig. 3.) The lymphatic capillaries were wider on the side where stasis existed and, during the injection, dye spread through them as far or even farther than in the normal arm, though it failed to proceed any further in the channels thereafter. While stasis was maintained no deep dye streamers appeared, indicating that there was no lymph flow.

Figs. 3 *a* to *h* show the results of an intradermal injection of 0.02 to 0.03 cc. of dye into a forearm 20 minutes after a pressure of 90 mm. of mercury had been thrown into a pressure cuff placed over the biceps. The photographs were taken 15, 30, 45 seconds, 1 minute and 2 seconds, 1 minute and 30 seconds, 2, 2½ and 3 minutes respectively after beginning the injection, which took 47 seconds. The first three photographs of the series, taken before much dye had escaped from the channels, show their actual size. Dye escape blurs their outlines in the later ones. 5 minutes after making the injection and 25 minutes after pressure was first begun, the cuff was released and removed as rapidly as possible. Immediately intense reactive hyperemia occurred during which a streamer began to form in less than a minute, with a suddenness and intensity of color never seen before. In all these tests the same phenomena occurred. The photograph, Fig. 3 *i*, which is typical, was taken but 2 minutes after the release of pressure, and it shows part of the deeply colored streamer formed in that brief period. This extended along the upper arm too, half way to the shoulder, and was longer and more brilliantly colored than the longest streamers arising from similar injections in normal arms even after half an hour. In most control tests such brilliant streamers are never seen at any time.

Peripheral Lymph Flow after Periods of Total Circulatory Obstruction

The findings suggest that some of the fluid accumulating in the tissues during and after complete venous or lymphatic obstruction, is rapidly removed by way of the lymphatics after the release of pressure. How much of the lymph flow results from this excess of fluid and how much is consequent upon reactive hyperemia cannot be said. The matter will be discussed below.

What are the effects on the lymphatics of complete cessation of the

circulation, either by sudden constriction of the limb, shutting off arteries and veins instantly, or by slow pressure occluding just the veins and somewhat later the arteries?

In 12 tests on 8 normal individuals, both types of obstruction were tried. In half, a sudden injection of air under 215 mm. pressure into the pressure cuff arranged on one upper arm induced total circulatory obstruction in a second or two, while in the other arm a period of 5 to 7 minutes of venous engorgement at 85 mm. pressure was allowed to elapse before total circulatory stoppage was brought about by raising the pressure to 215 mm. In the other half of the tests one arm was subjected to one of these procedures while the other, normal one served as a control. At varying periods after the occluding pressure had been put on small amounts of dye were injected in both arms. In some instances 4 or 5 injections were made in each arm with release of pressure immediately after the last injection. The period of total obstruction varied from 8 to 35 minutes, but the varying time interval did not appreciably affect the behavior of the dye.

In the majority of these tests, involving about 35 injections in 8 different subjects, the lymphatic capillaries seemed wider than usual and dye entered them quite as readily as in the normal skin. One did not find the resistance to injection observed in the instances in which partial venous and complete lymphatic obstruction were effected by lesser pressures in the Riva-Rocci cuff,—for example 25 to 35 mm. of mercury. However, many exceptions were noted, and one cannot state that the lymphatics of the skin are always dilated in brief periods of total circulatory obstruction of the limb.

With the release of pressure reactive hyperemia developed at once, and with it, in both types of test, an extraordinarily rapid streamer formation indicative of very active lymph formation and flow. In a few seconds deeply colored streamers suddenly appeared 15 or 20 cm. in length and of an intensity never equalled by such small injections of dye in any of the tests so far described. Even pale streamers of this length require approximately half an hour or more to form under normal circumstances. A brief description of a typical test follows.

As the subject sat with both arms resting on a table before him, a pressure of 215 mm. of mercury was abruptly thrown into the cuff on one upper arm, and maintained for 16 minutes. At intervals of approximately 3 minutes thereafter 4 dye injections were made in the now livid skin of the volar surface of the arm. The spread of the dye at each situation was photographed and traced and observations were also made under the microscope. In these tests it was planned to release pressure in less than a minute after making the last injection, while dye still remained within the lymphatic capillaries and could be observed under the

binocular microscope. 29 minutes after first obstructing the circulation, pressure was suddenly released while the fourth colored area, injected but a minute before, was carefully watched through the microscope. There was no sudden movement of dye within the superficial lymphatic capillaries. After a few seconds reactive hyperemia appeared, and in less than 40 seconds dye was carried up the arm in the subcutaneous lymphatics for a distance of 15 cm. These streamers, 1½ and 3 minutes respectively after the release of pressure, appear in Figs. 4 *a* and *b*. They well show the intensity of the color.

The upper left arm of the same subject was now bound with the pressure cuff and the test repeated save that pressure was first raised to 85 mm. of mercury for 6 minutes to occlude the lymphatics and engorge the arm. At the end of this period pressure was abruptly raised to 215 mm. and at the same intervals as in the preceding test dye was injected. The reactive hyperemia following release of pressure brought about no sudden movement of dye in the lymphatic capillaries, which could be made out under the microscope, but as before several streamers appeared with great speed and became intensely colored. Such streamers, appearing after periods of total circulatory obstruction preceded by venous occlusion, are shown in Figs. 7 and 8. Their significance will be discussed below.

In one trial, upon another subject receiving but a single injection, dye passed in less than a minute into 2 broad lymphatic channels and there developed what resembled beginning streamers but these progressed no further during the remaining 15 minutes of circulatory obstruction. Extensions of dye such as these were observed but rarely and only in arms which had been subjected to total circulatory obstruction for 15 or 20 minutes. When they appeared they extended, not upwards as did the genuine streamers, but transversely across the arm in the direction of the floor as if the dye were moving by gravity in lymphatics already distended by stagnant fluid. 2 minutes after the release of pressure, a long streamer appeared, running from the tip of the dye extensions to the elbow. In this particular instance, the injected area and the region about the extensions of dye whealed at the same time. The skin containing the streamer which had formed during this period also whealed a minute later. A wide hyperemic flare was present about both the streamer and the injected area. Fig. 5, a photograph taken without color screening, 4 minutes after release of the pressure, shows the flare extending up the arm about the dye-containing lymphatic. As can be seen in the photograph, the streamer takes its origin from the 2 laterally directed dye extensions described above.

The findings disclose a very rapid formation and flow of lymph following periods of total circulatory obstruction, equally rapid whether or not the limb has been previously engorged with blood. Reactive hyperemia in an arm deprived of oxygen seems to have been responsible for the results, for no large amount of fluid can have accumulated outside the vessels of the arms in which the circulatory

arrest had been abrupt. Undoubtedly the blood vessels were more permeable, after the period of circulatory arrest, as Lazarus-Barlow (20) and Landis (15) have shown, and, with the advent of reactive hyperemia, they furnished much fluid for lymph.

Retrograde Lymph Flow.—Following the release of pressure in 2 of the 8 subjects and during the subsequent reactive flush, a single streamer of dye appeared, running down the arm toward the wrist for 7 cm. in one instance and 15 in the other. In the latter instance a streamer ran proximally as well, both streamers appearing in a photograph, Fig. 6, taken 2 minutes after the release of pressure. Retrograde flow of dye has never been found save after total circulatory obstruction or in severe cardiac edema, as described in the following paper.

Reactions of Lymphatic Capillaries within Bier's Ischemic Patches

When an arm is engorged by venous obstruction and shortly thereafter all circulation is stopped for several minutes, irregular pale areas,—the ischemic patches of Bier (21),—appear in the skin, interspersed among purple congested regions. The engorged cutaneous vessels contract in local areas and drive blood into adjacent regions which in turn become congested. It seemed a matter of interest to determine whether the activity of the blood vessels responsible for the blanching in Bier's spots is accompanied by corresponding changes in the lymphatics. Intradermal injections of minute amounts of dye were accordingly made into Bier's spots and the flushed areas surrounding them.

In human skin Bier's spots are best elicited by total obstruction of the blood flow in a limb that has previously been overfilled with blood by venous occlusion. We determined the blood pressure of the 8 volunteers employed in the work just described, and after the usual rest period the subject was placed at the low table with the forearm, volar surface up, and propped only at the wrist and elbow. It has been shown by Rous and Gilding (22, 23) that Bier's spots are prone to appear on the upper side of a horizontally propped arm supported in this way. A pressure of 70 to 80 mm. of mercury thrown into a sphygmomanometer cuff adjusted about the upper arm, maintained venous occlusion for 6 or 7 minutes. At the end of this period the pressure was abruptly raised to 200 mm. of mercury to secure complete stasis. When the pale and purple mottling of the Bier's spots and congested areas was well advanced, an intradermal injection of dye solution

was made into the largest Bier's spot available. As usual the progress of dye was watched through the binocular microscope to distinguish the ease or difficulty with which it entered the lymphatics, and to observe their state of dilatation or contraction, the rate of dye escape, the extent to which dye moved within the channels and any evidences of lymphatic drainage. Photographs were taken as usual. 5 to 8 minutes later a similar injection was placed in a highly congested purple area of skin and the fate of the dye compared with that of the first injection. During this period occasional photographs and observations were made of the region first injected. Finally a third injection was made into another Bier's spot. As soon as dye entered the lymphatic channels and before its escape had occurred the pressure was released and the cuff removed as usual. Under the binocular the effect upon the dye movement in the lymphatics was sought while other observers with hand lenses watched the two regions first injected.

For such tests a period of total occlusion of 40 to 45 minutes sufficed. At once upon release of the pressure brilliant reactive hyperemia occurred, with immediate and striking formation of streamers. In alternate instances the order of the injections was reversed, that is to say the first injection was made into a congested area, the second into a Bier's spot, but the last always into another Bier's spot.

It is well known that injury to the skin leads to vasodilatation (24) and it was feared that the prick of the injecting needle might of itself destroy the contraction of blood vessels within Bier's spots. In our work it seemed wise to test the point in each of the 8 subjects before injecting dye. In scores of Bier's spots insertion of the hypodermic needle without expulsion of dye or else with the injection of 0.02 cc. to 0.03 cc. of Tyrode solution has failed to change the blanched appearance. When dye was to be injected, spots previously untouched were employed, of course.

The very marked contrast in the caliber of the blood vessels within Bier's spots and the surrounding congested areas is not duplicated in the lymphatics. Nonetheless there are noticeable differences.

Within the Bier's spots we have found the caliber of the lymphatic capillaries to be variable, much constricted in 4 of 8 individuals and approximately as in normal skin in the others. They were usually definitely narrower than in the congested areas of the same arm but in 2 of the 8 instances the difference was not definite. Less dye appeared to enter the lymphatic capillaries within Bier's spots, that is to say fewer channels became visible than in normal skin, or in the congested areas of the test arm; and during and after the injection the dye passed but a little way from the point of the needle. As result the interstitial bleb was relatively large, the amount of dye within the lymphatics small. Dye escaped from the injected channels within Bier's spots more slowly than from those within the dark congested regions and even more slowly than in normal skin. Secondary diffusion of escaped dye was practically absent.

In the congested skin the lymphatic capillaries were usually dilated as one

would expect from our earlier tests with venous obstruction. In 2 of 8 instances they were found about normal in appearance. Always in these regions dye passed readily from the needle into the lymphatics, the amount of fluid remaining interstitial being small, that within the lymphatics large. Dye was carried farther in the lymphatics of a congested area than in a Bier's spot or in normal skin. As a consequence the area of coloration seemed greater for a given amount of dye. The colored fluid escaped far more rapidly from the lymphatic capillaries in these areas and occasionally one could see slight movement of dye into a drainage trunk for a centimeter or more, as in the previous experiments involving total circulatory obstruction.

In Fig. 7, photographs *a* to *e* were taken at 15, 30, 45, 90 and 107 seconds respectively after beginning the injection into one of the congested areas of the arm of a healthy young man, with blood pressure 118/80. The injection required but 43 seconds. 4 minutes later photographs *a'* to *e'* were taken at similar time intervals during and after a similar injection into a Bier's spot. Owing to the red color filter used the spot cannot be seen. One can note however that the injection into it required more time, 59 seconds, for the needle is seen in one more picture; the spread of dye in the lymphatics is less and dye escape from them much slower. Photographs *f* and *g* will be discussed below. The result is typical of the majority of the experiments.

The apparent resistance to the entrance of injected dye offered by the lymphatic capillaries within Bier's spots is probably due to the narrowing of the channels, for this showed itself in a different way in a test now to be described.

The injecting needle had been inserted in the center of a small Bier's spot and by the 15th second after beginning the injection (Fig. 8 *a'*) the dye had entered scarcely any channels. As pressure was continued (Fig. 8 *b'*) colored fluid suddenly darted into 2 or 3 channels and, in them, passed completely through the blanched area to congested skin beyond. Once in the latter it swept around the pale area, still in the purple skin (Fig. 8 *c'*). The circumference of the Bier's spot, not visible in the photograph because of the screening, lay just within the broken ring formed by dye in the lymphatics. There was no further filling of channels within the Bier's spot itself, and as result there formed only the interstitial bleb shown in the pictures, with later some secondary diffusion of dye therefrom. The injection in the congested area required about 44 seconds, that in the Bier's spot 61. Secondary dye escape from the circumferential channel, lying within the congested skin, was quite marked (Figs. 8 *c'* and *d'*), as also was that within the Bier's spot itself. The photographs were taken at intervals identical with those of Fig. 7, as shown by the legends.

In all these tests no significant widening or constriction of the lymphatic capillaries took place immediately upon release of the pressure, either in the Bier's

spots or in the congested areas. Nor was there any sudden visible extension of dye in the superficial channels, or movement of that which was interstitially placed. With the development of the usual violent reactive hyperemia, intensely colored streamers of dye extended from each of the injection sites even more suddenly and with greater intensity than in the preceding experiments. Within 15 to 20 seconds after release of pressure, in 6 of the trials upon 4 of the 8 subjects, colored streamers of great intensity extended 16 to 20 cm. above the site of injection. In the remainder similar ones invariably developed within 1½ or 2 minutes. Such streamers were always far more intensely colored than those arising from injections in normal skin, even after half an hour or more.

For example in Figs. 7 *f* and *g* the arm is shown 1½ and 3 minutes respectively after the release of pressure. The injected area, shown in detail in the series of photographs *a* to *e*, lies in Figs. *f* and *g* directly above another injected area which is the one shown in photographs *a'* to *e'*. The 3rd injection of the test was made into a Bier's spot immediately before releasing pressure, and consequently no detail photographs were taken of the dye spread. This appears nearest the wrist in photographs *f* and *g*. Figs. 8 *f* and *g* show the formation of dye streamers at similar intervals after release of pressure, as they occurred in the second test. The 2 dark spots from which no streamers appear are dots of dye placed upon the surface of the skin and hence have no significance.

Reverse Flow of Lymph in Certain Instances.—Following the release of pressure, in three of these instances, retrograde colored streamers moved toward the wrist in the subcutaneous lymphatics, as in some of the tests described above in which complete circulatory obstruction had also been induced. Such a streamer is shown in Figs. 8 *f* and *g*, running toward the wrist from the lower injected area. It is well known that the valves of the deeper layer of lymphatics normally resist retrograde flow.

DISCUSSION

In the present work changes in the character of the peripheral lymph flow have been demonstrated by the visible passage of small amounts of intradermally injected dye from the superficial lymphatics to subcutaneous channels in which, as it extended subsequently up the limb, it gave the appearance of colored streamers.

The dye of the streamers was in the lymphatics. This has been shown repeatedly in animal experiments in which after the injection of small quantities of dye into the skin of the lower portions of limbs or ears the pigment has been found in the subcutaneous lymphatics, diluted and pale and draining to the nearest lymph node. Can one

assume that the extension of the colored streamers in the present work is truly indicative of a flow of lymph? The streamers were always short and pale at first. They gradually became longer in 15 or 20 minutes, still pale at the upper end but darker near the site of injection as if the lymph flowing in the subcutaneous channels had been stained by gradually increasing amounts of dye coming to it from the site of injection. The fact should be stressed that this is a very different phenomenon from that obtained when larger amounts of dye are forcibly injected into skin to obtain anatomical preparations of the lymphatics. In such injections, undiluted dye is actually forced into the subcutaneous channels, not transported by the flowing lymph. In the present work the dye solution was injected with as little pressure as possible. This pressure seems to have been of little importance, for when similar amounts of fluid dye were deliberately introduced with great force no streamers appeared until after the usual time. Evidently the small amounts of fluid (0.01 cc. to 0.04 cc.) which were injected, largely into the interstitial tissue and only partly into the lymphatics, were not enough to account for the formation of long streamers of color. Further, great differences in streamer length and intensity occurred corresponding to known changes in lymph flow, although the amount of dye fluid and the pressures at which it was injected remained constant. Attention has already been called to many such instances. For example, in normal, horizontally placed limbs the streamers required some minutes to develop, but during the reactive hyperemia following release of obstruction of the circulation they appeared immediately. Streamers were found short and faint in the resting limb but long and intensely colored in the warmed but also resting limb. Had the streamers been due to pressure alone they would have been approximately uniform in all instances. It is plain that intradermal injections of dye demonstrate changes in the flow of peripheral lymph and that the method can be used clinically.

The superficial lymphatics appear to be about the same in width from day to day in the normal skin of any one individual. Variations in the width of the lymphatic capillaries can be recognized, even though the changes are not great. For example, in the ischemic skin of Bier's spots and in the adjacent, congested areas they are

narrow and wide respectively, but the differences are not as marked as those shown by the blood vessels. Following other changes in the physiological state of the skin the lymphatic capillaries have appeared wider or more narrow, but much stress should not be laid upon these differences save when they are pronounced. For the method is qualitative at best and some individuals vary considerably from the average in the width of their lymphatics. Whether the variations in caliber are passive or are the result of active contraction we are unable to say.

The tests have yielded direct indications of what happens within the skin lymphatics. In the resting limb horizontally placed there is slight continuous lymph formation and flow. Warmth with its accompanying hyperemia produces longer and more brilliant streamers than those appearing in normal skin. Lymph flow is well known to be increased during the hyperemia of heat (4–6). When the arterioles are dilated, capillary pressure is increased, as Landis (15, 25) and others (26–28) have shown, fluid escape from the blood vessels is greater and dyes injected into the blood stream pass more rapidly into the tissues (29). Muscular movement, massage,—even passive movement to a mild degree,—increase lymph flow as already known and as the present experiments attest anew.

The effects of posture are striking. In the arm intradermally injected with dye and held vertically downward at rest, lymph flow is absent, as judged by the lack of streamer formation. When the same arm is raised vertically above the head and then injected, lymph flow is found to be rapid. It is absent in the injected lower legs of normal subjects seated quietly with the feet resting on the floor, but becomes conspicuous in the form of long and highly colored streamers when the injected leg is propped on a table or desk while the subject remains seated. As is well known capillary pressure is high in dependent portions of the body (15). Standing diminishes blood volume (17–19) and the legs increase in size (17). Landis and Gibbon (16) found fluid accumulation in the arm at the rate of 0.2 cc. per minute per 100 cc. of tissue when venous pressure was increased to 80 cm. of water. In an arm or leg hanging vertically downward and at rest, the effect of posture is practically that of an increased lymphatic and venous pressure. The mechanism is charged as it

were for increased lymph formation. But the present experiments prove that there is no lymph flow in the cutaneous lymphatics of the intact, motionless, dependently hanging arm or leg,—no activity on the part of the lymphatic system to relieve its increasing fluid content even though the lymphatics themselves may fill and become distended, as will be demonstrated in the following paper. With muscular activity, though, lymph is forced up the leg against gravity. Changes in the position of the limb in relation to the body, friction, rubbing and intermittent changes in tissue pressure brought about by bodily activity are of great importance for lymph flow, certainly greater under some circumstances than are the physicochemical changes occurring in the limb.

Lymph flow was observed to cease in the subcutaneous channels of the forearm when, by means of a cuff about the upper arm an external pressure was applied which was far less than that required to obstruct venous flow. Upon release of the pressure the lymph flow was greater than in normal skin. The fluid which may have accumulated in the tissues during the period of pressure was apparently removed in part by way of the lymphatics. Lymph flow was still more rapid after the release of greater pressures, sufficient to occlude the veins and engorge the arm with blood. The most active lymph flow we have ever observed under normal or pathological conditions, as judged by streamer formation, has occurred during the reactive hyperemia following upon the relief of total circulatory obstruction. It was equally great whether or not the arm had previously been engorged with blood as described above. Lazarus-Barlow (20) has shown that total occlusion of blood flow leads to little transudation into the tissues but that lymph under these circumstances is rich in protein, presumably the result of increased capillary permeability (15). No doubt the intense lymph flow observed in our experiments during the reactive hyperemia following total circulatory obstruction is to be attributed to a greatly increased circulation through a vascular bed which had previously been deprived of oxygen and had become more permeable than normal (15). The same assumption will explain the streamer formation which arose from injected ischemic Bier's spots and from their neighboring congested areas, following the release of circulatory arrest. In the congested areas local accumu-

lations of fluid must have occurred; in the ischemic areas, no doubt, they were less; but from both streamer formation was equally great. The intense reactive hyperemia coming on at once after release of pressure obliterated the local effects. These experiments show further that, under certain conditions, lymph flow can be great in a resting limb.

Tests to demonstrate the influence of cold upon lymph flow were attempted but the occurrence of hyperemia rendered the results indecisive. Cold lowers capillary pressure for a few minutes (15, 25, 27) but after a variable time reactive hyperemia occurs (25). One would expect lymph flow to be oppositely affected by the two conditions but the dye streamers were not sufficiently different from those appearing in normal skin to warrant any conclusions. Unfortunately too the methods employed did not allow us to demonstrate the effect of rest upon a previously active limb, or of cold upon previously heated skin. Dye draining in subcutaneous lymphatics escapes to some extent into the surrounding tissues. A slight difference in the length or intensity of a colored streamer cannot be appreciated because of the escaped dye. Clearly, however, the dye method brought to light the existence of less lymph flow in the control limbs.

One further point deserves mention. When dye is injected intradermally and the skin immediately sucked, much of the color is driven into the lymphatics draining the injected area. Once within these channels it cannot be recovered by suction but instead is driven farther along in them. By sucking a wound or a cut much material may be removed and its subsequent entrance into blood vessels or lymphatics prevented; but much is also distributed widely in the lymphatics.

SUMMARY

Vital dyes injected intradermally enter lymphatic capillaries directly, rendering them visible, and appear later in the draining lymphatic trunks as colored streamers. The method enables one to perceive the state of the lymphatic channels and the rate of lymph flow within them. It yields consistent results when tested under physiological conditions known to increase or decrease lymph flow.

In the horizontally placed normal limb at rest there is slight lymph flow. In a normal leg or arm hanging downward lymph flow ceases although fluid in the limb increases. When a previously dependent arm is raised above the head, or when the foot of a seated subject

is propped on a table, lymph flow in the raised limb becomes active. It ceases in the skin of an arm subjected to partial obstruction of the veins by pressure from without, but very active lymph flow appears during the reactive hyperemia which follows upon the release of venous obstruction. It is still greater following release of total circulatory obstruction, and seems to be the same whether or not the limb has previously been engorged with blood. In the ischemic patches which appear in the skin of a limb during total circulatory obstruction (Bier's spots) the lymphatic capillaries are definitely and considerably constricted, whereas they are slightly dilated in the purple, congested regions of the skin round about. On release of obstruction there occurs a strikingly rapid, equal lymphatic drainage from both regions.

The significance of all the findings is discussed.

When dye is injected intradermally and the skin sucked, much of the foreign material is driven into the lymphatics draining the injected area.

BIBLIOGRAPHY

1. Hudack, S. S., and McMaster, P. D., *J. Exp. Med.*, 1933, **57**, 751.
2. Starling, E. H., *J. Physiol.*, 1894, **16**, 224.
3. Asher, L., *Z. Biol.*, 1898, **36**, 154.
4. Drinker, C. K., and Field, M. E., Lymphatics, lymph and tissue fluid, Baltimore, Williams & Wilkins Co., 1933.
5. Field, M. E., and Drinker, C. K., *Am. J. Physiol.*, **98**, 378.
6. Field, M. E., Drinker, C. K., and White, J. C., *J. Exp. Med.*, 1932, **56**, 363.
7. White, J. C., Field, M. E., and Drinker, C. K., *Am. J. Physiol.*, 1933, **103**, 34.
8. Drinker, C. K., and Field, M. E., *Am. J. Physiol.*, 1931, **97**, 32.
9. Weech, A. A., Goettsch, E., and Reeves, E. B., *J. Exp. Med.*, 1934, **60**, 63.
10. Bainbridge, F. A., *J. Physiol.*, 1900, **26**, 79.
11. Carlson, A. J., Grier, J. R., and Becht, F. C., *Am. J. Physiol.*, 1907, **19**, 360.
12. Asher, L., *Z. Biol.*, 1899, **37**, 261.
13. Schmidt, C. F., and Hayman, J. F., Jr., *Am. J. Physiol.*, 1929–30, **91**, 157.
14. Starling, E. H., The fluids of the body, Chicago, Keener, 1908.
15. Landis, E. M., *Physiol. Rev.*, 1934, **14**, 404.
16. Landis, E. M., and Gibbon, J., *J. Clin. Inv.*, 1933, **12**, 105.
17. Waterfield, R. L., *J. Physiol.*, 1931, **73**, 110.
18. Thompson, W. O., Thompson, P. K., and Dailey, M. E., *J. Clin. Inv.*, 1927–28, **5**, 573.
19. Youmans, J. B., Wells, H. F., Donley, B., and Miller, D. G., *J. Clin. Inv.*, 1933, **12**, 965.
20. Lazarus-Barlow, W. S., *Phil. Tr. Roy. Soc. London, Series B*, 1894, **185**, 779.

21. Bier, A., *Virchows Arch. path. Anat.*, 1898, **153**, 306.
22. Rous, Peyton, and Gilding, H. P., *J. Exp. Med.*, 1929, **50**, 489.
23. Rous, Peyton, and Gilding, H. P., *J. Exp. Med.*, 1930, **51**, 27.
24. Lewis, Sir T., The blood vessels of the human skin and their responses, London, Shaw & Sons, 1927.
25. Landis, E. M., *Heart*, 1930, **15**, 209.
26. Goldman, E., *Arch. ges. Physiol.*, 1934, **159**, 51.
27. Danzer, C. S., and Hooker, R., *Am. J. Physiol.*, 1920, **52**, 136.
28. Lewis, Sir T., and Haynal, I., *Heart*, 1928, **14**, 177.
29. Hudack, S. S., and McMaster, P. D., *J. Exp. Med.*, 1932, **55**, 431.

EXPLANATION OF PLATES

PLATE 11

FIGS. 1 and 2. Natural size photographs of the distribution of dye on intradermal injection into the skin of the volar surface of the normal arm. The photographs were taken at intervals of 15, 30, 45 seconds; 1, 1½, 2, 3, 4 and 20 minutes after beginning the injections which lasted 52 and 48 seconds respectively. Fig. *i* is reduced to 1/7 natural size.

Note the size of the interstitial bleb of dye at the needle point in proportion to the amount within the lymphatic capillaries. Dye escape soon caused blurring of their outlines. The last photograph of each figure taken after 20 minutes at a distance of 40 cm. shows a pale blue streamer extending up the arm from the injected area.

PLATE 12

FIG. 3. Results of an intradermal injection of dye in the skin of the volar surface of an arm during a period of venous obstruction caused by inflation of a Riva-Rocci cuff to a pressure of 90 mm. of mercury. The injection, which required 47 seconds, was made after pressure had endured for 20 minutes. The natural size photographs *a* to *h* were taken at intervals of 15, 30, 45 seconds, 1, 1½, 2, 2½ and 3 minutes respectively after beginning the injection. Fig. *i* is reduced to 1/7 natural size.

The lymphatic capillaries are slightly dilated. The final photograph shows only part of an intense blue streamer which formed in the 2 minute period after release of the pressure and extended along the upper arm half way to the shoulder. Prior to release of the pressure no streamer existed.

FIG. 4. Streamers developing in 1½ and 3 minutes following the release of total circulatory obstruction as described in the text. Their intensity should be noted. × 1/7.

FIG. 5. Skin injected with dye during a period of total circulatory obstruction occasionally whealed upon release of pressure, and showed an hyperemic flare about both the injection and the resulting streamers. Total circulatory obstruction of an arm was maintained for 15 minutes, and then the usual dye injection

was made in less than 1 minute. No streamers developed during another 15 minute period of obstruction. 2 minutes after release of pressure a streamer formed extending almost to the axilla. At this time the injected area, and a minute later the skin adjacent to the streamer whealed. The photograph was taken without a color screen at the 4th minute after the release of pressure. It shows the extensive hyperemic flare about the injection and accompanying the streamer as far as the elbow. × 1/2.

FIG. 6. The appearance of retrograde streamers. The usual intradermal injection of dye was placed in the forearm 26 minutes after total circulatory obstruction was effected. No streamers developed during the period of obstruction. The photograph shows 2 streamers as they appeared 2 minutes after release of the pressure. One of them is a retrograde streamer extending to the wrist. × 1/7.

PLATE 13

FIG. 7. A comparison of the characteristics of the lymphatic capillaries in deeply congested skin (*a* to *e*) surrounding a Bier's spot, and within the Bier's spot itself (*a'* to *e'*). The photographs were taken at the same time intervals after dye injection (see text). Figs. *f* and *g* show that streamers of equal length and intensity had developed 1½ and 3 minutes after release of the total circulatory occlusion. This had endured for about 40 minutes and had produced the Bier's spots. The injected areas shown in the detail photographs (*a* to *e* and *a'* to *e'*) lie in a nearly vertical line in Figs. *f* and *g*. The lower is where the Bier's spot was. The third spot shows the injection which was made into another Bier's spot just before release of pressure, and no detail photographs were taken. A streamer is beginning to form from it. The detailed photographs are natural size. Figs. *f* and *g* are reduced to 1/7 natural size.

FIG. 8. Photographs taken in a test similar to that which furnished Fig. 7. They are described in detail in the text. Magnifications as in Fig. 7.

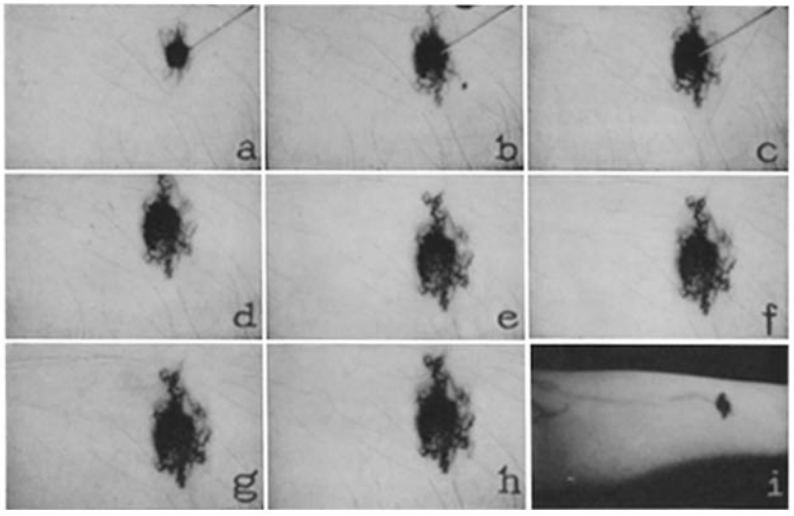


FIG. 1

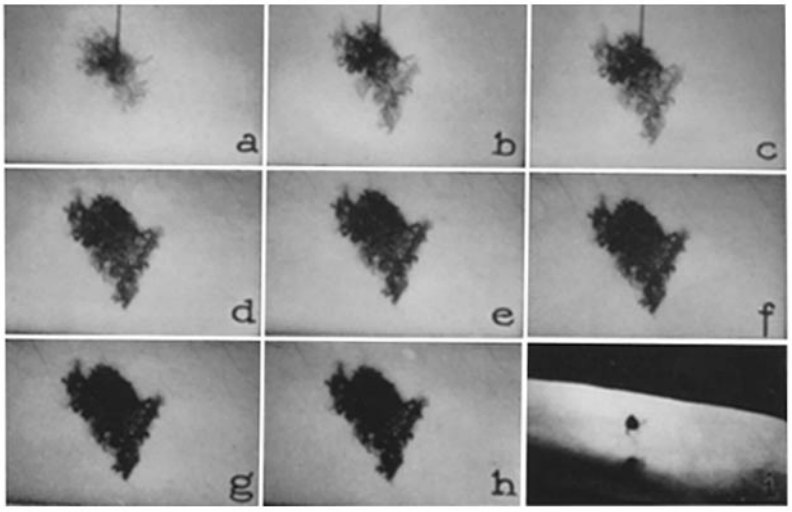


FIG. 2

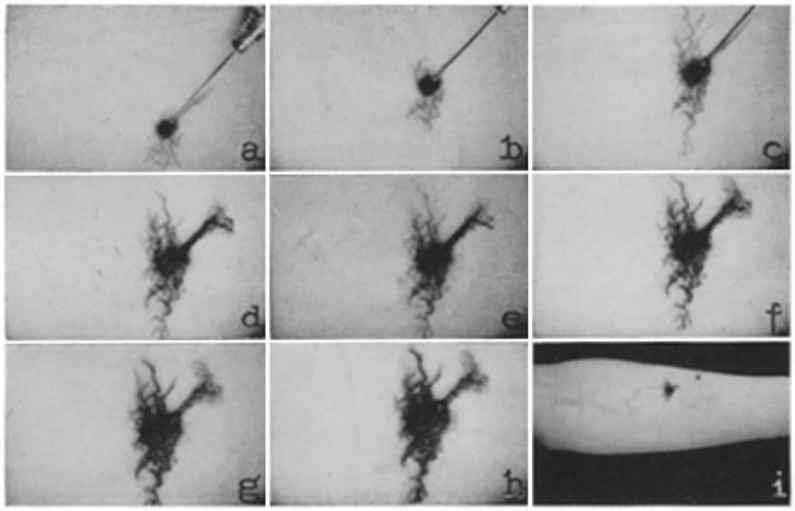


FIG. 3

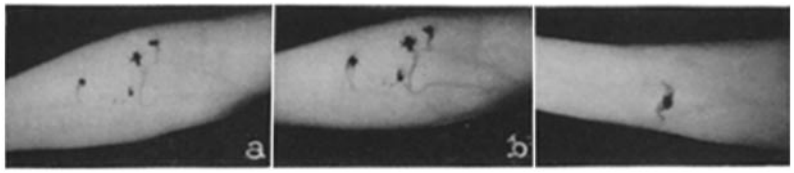


FIG. 4

FIG. 6

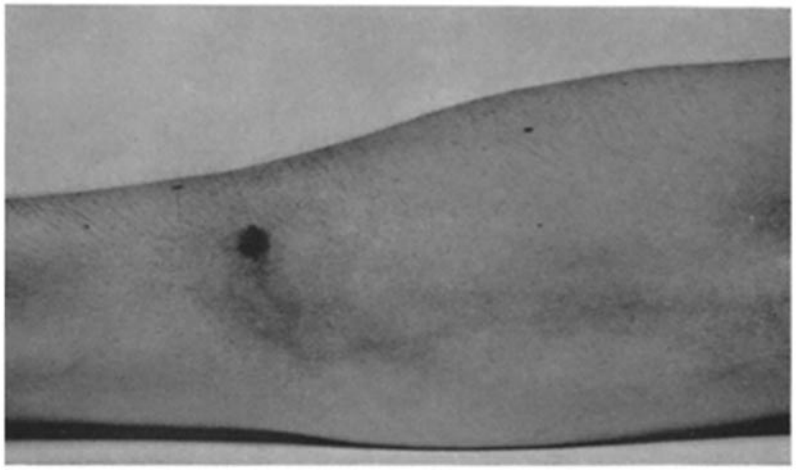


FIG. 5

(McMaster: Cutaneous lymphatics and lymph flow)

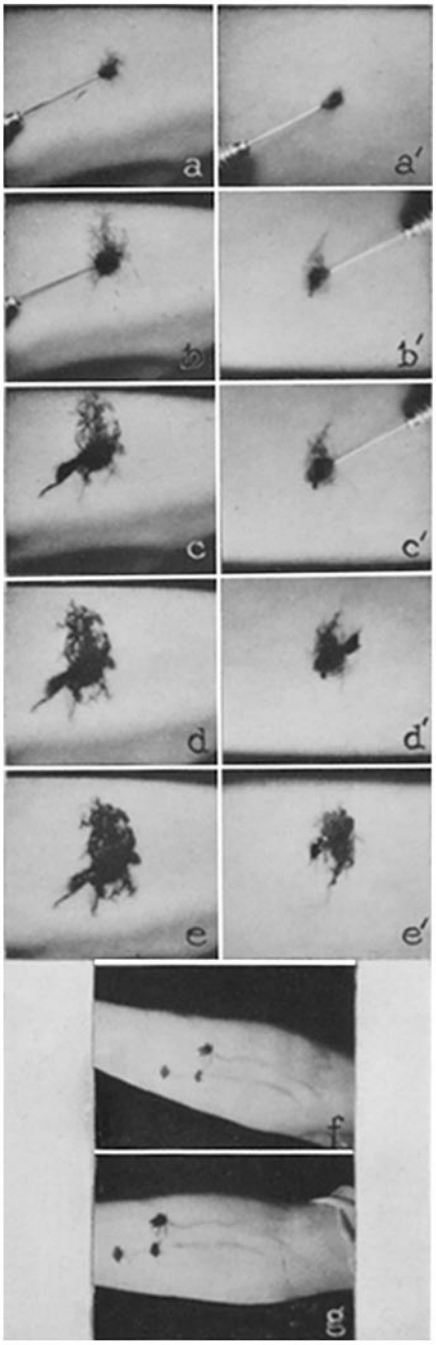


FIG. 7

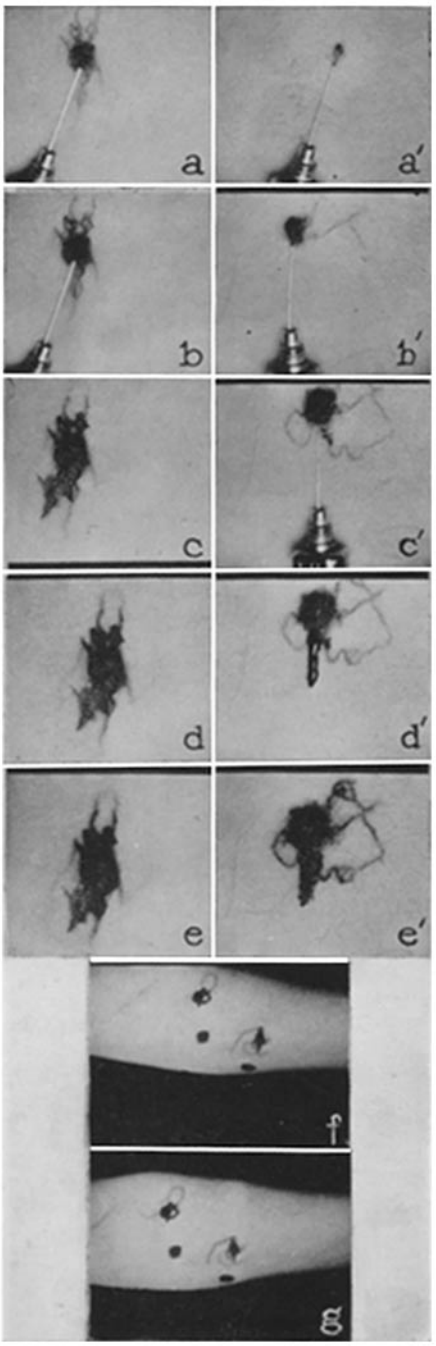


FIG. 8

(McMaster: Cutaneous lymphatics and lymph flow)