# THE EFFECTS OF VENOUS OBSTRUCTION UPON INTERSTITIAL PRESSURE IN ANIMAL AND HUMAN SKIN

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It has long been known that fluid collects in human limbs subjected to partial or complete venous obstruction. As the fluid accumulates it exerts a pressure upon the outer walls of the blood and lymphatic vessels which hinders the further escape of fluid from the blood and favors the formation of lymph. Pressure and volume changes taking place in the limb as a whole under these conditions have been investigated by plethysmographic methods (1–5) or by other indirect techniques (6–12), and workers have been able to estimate by direct means the pressure changes in subcutaneous tissues (13–18), or muscles (19). Little is known on the other hand about the changes of intracutaneous pressure or the flow of cutaneous lymph. No such studies have been made upon animals and there are only three clinical reports available (14, 18, 20), these latter presenting discordant or contradictory findings. Clearly an investigation of the subject by accurate methods is called for.

Techniques developed recently in this laboratory (21–24), have opened the way for such a study. For example, it was shown that during venous obstruction, enough freely movable fluid escapes into the cutaneous tissues to permit one to measure its pressure manometrically. The finding indicated that during periods of venous obstruction, as in states of edema, accurate determination can be made of the interstitial pressure changes taking place in the skin of living animals and men. A complete study of these changes requires a comparison with the pressures occurring in normal skin but unfortunately the interstitial pressure within normal cutaneous tissue cannot as yet be measured directly because of a lack of enough freely movable extravascular fluid to make manometric determinations. Through work reported in an accompanying paper (21) this difficulty has been circumvented for practical purposes by the measurement of the least pressure necessary to introduce minute amounts of a relatively unabsorbable test fluid into normal skin at a very slow rate. The pressure found has been termed the interstitial resistance, and it closely approximates the true interstitial pressure.

With the techniques just mentioned pressure changes during and following periods of venous obstruction in men and animals have been studied anew. The data will be presented in the present paper and following their presentation the discordant findings of earlier workers will be discussed.

## *Methods*

Most of our previous work upon the pressures within tissues has been carried out on the white mouse and the animal was used for the present study. It seemed best to produce venous obstruction by means of a pressure cuff at the level of the thigh and to measure the intracutaneous pressure in regions near the feet.

Before beginning the experiments, it was necessary to learn what pressure to apply to the cuff to produce venous obstruction without arterial occlusion. Since little was known about the peripheral arterial blood pressure in the legs of mice, a method was devised (25) to furnish the needed information. A special sphygmomanometer, adjustable about the animals' thighs, was inflated and deflated while the arterial and venous blood flow in the transilluminated claws of the same legs was observed under the microscope. The peripheral arterial pressure readings corresponded closely with direct readings taken from the carotid arteries. It was found (25) that a pressure cuff about the upper leg of a mouse deeply anesthetized with luminal or nembutal should not be inflated to pressures higher than 65 mm. of mercury if arterial occlusion is to be avoided with certainty. In lightly anesthetized animals somewhat higher pressures can be used. A marked venous obstruction can be obtained by a pressure of about 40 mm. of mercury.

Having determined these facts we next studied intradermal pressure conditions during venous obstruction in the following way:—Young mice, 26 to 30 gm. in body weight, were anesthetized by intraperitoneal injections of nembutal, 0.5 cc. of a 1 per cent solution of the latter for each 25 gm. of body weight. One shaved leg of the anesthetized animal was placed in the apparatus for determining blood pressure in the mouse (25),—a device which incidentally retained the small sphygmomanometer cuff around the animal's thigh and also immobilized the leg so that the interstitial resistance or extravascular fluid pressure could be easily measured.

The needle of the injecting device (21, 22) for measuring interstitial resistance, or interstitial pressure was inserted into the skin of either the dorsum of the ankle or the distal portion of the lower leg and an initial measurement was made in the usual manner (21). For the purpose a test fluid described in a preceding paper (21), a 1/2 per cent solution of a vital dye, pontamine sky blue in Locke's solution, was brought at atmospheric pressure into contact with the tissues, with care that there was no direct penetration of either the blood vessels or the lymphatics.

In our earlier work the interstitial resistance was determined in the loose skin of the ears, backs, and thighs. In the tense skin of the dorsum of the foot and the lower third of the leg, which were employed in the present work, it was found slightly higher, varying between 2.6 and 4.6 cm. of water as compared with an average of 1.7 cm. in the earlier work. Further, the reaction of the ankle skin to the presence of the needle was more pronounced than that of the skin of the ears, backs, and thighs, hyperemia occurring, followed within a few minutes by the development of mild edema. The edema fluid tended to flow into the injecting apparatus and, by exerting enough pressure there to prevent its entrance, the pressure of the edema fluid, and hence the existing interstitial pressure, could be determined. Since the edema developed very slowly and never became severe, the pressure of the fluid can have been only very slightly higher than the initial interstitial resistance. The phenomenon served to great advantage in the present work for, owing to the presence of free fluid in the tissues both before and after venous obstruction, one could follow the true interstitial pressure directly during the entire experiment.

Having made the initial measurements of interstitial resistance and of the edema fluid

pressure as just described, the pressure of the test fluid in the injecting apparatus was kept equal to that of the edema fluid while the sphygmomanometer cuff was inflated to pressures between 40 and 47 mm. of mercury. Usually within 2 to 4 minutes fluid began to flow from the tissues into the apparatus. At once, to check this backflow, the pressure in the injecting apparatus was raised by several centimeters. At times no further fluid movement occurred to the apparatus, at times backflow continued, at times there was inflow into the tissues. When no flow was observed the pressure on the test fluid equalled that of the extravascular fluid pressure and it was recorded as the interstitial pressure prevailing at that moment. If backflow continued the pressure in the apparatus was rapidly raised until flow ceased. If inflow occurred upon first selecting a new pressure in the apparatus, the pressure was reduced until the inflow ceased. In this way the interstitial pressure was repeatedly determined during various periods of venous obstruction.

Next, with the limb still immovable, the cuff pressure was released and pressure determinations continued. Within less than a minute after release of the cuff, the test fluid began to enter the tissues rapidly, which indicated that the interstitial pressure, or tissue fluid pressure, was falling swiftly. The pressure in the apparatus was immediately lowered until slow backflow appeared and was left at this level until, in a few minutes or seconds, the backflow ceased. The pressure was recorded as the interstitial pressure at that moment. This procedure was continued for varying periods after the release of obstruction or until the pressure had fallen to levels approximating the original ones;

### *Pressure Conditions in the Skin during and after Venous Obstruction*

Twelve experiments were made in all. For the sake of brevity the findings from a typical one have been summarized below and plotted in Chart 1. The pressure changes found in three other typical experiments appear in Charts 2 to 4. In each chart the black dots indicate pressure readings which yielded neither inflow nor backflow in the apparatus, that is to say they indicate the times at which the pressure of the extravascular fluid was accurately balanced. Plus signs (+) indicate pressure readings which led to fluid movement into the tissues, the pressure in the apparatus being higher than the interstitial pressure. Minus signs (−) show that backflow occurred into the apparatus and that the plotted pressure was lower than that of the extravascular fluid. The initial interstitial resistance is shown at the beginning of each chart by six-pointed stars.

*Summary of the Data from a Typical Experiment (Chart 1).*—The intradermal interstitial resistance in the dorsum of the ankle of a 28 gm. mouse, under nembutal anesthesia, was measured several times and found to average 3.8 cm. of water. While taking these measurements, over a period of about 15 minutes, a mild edema appeared. By the 15th minute the edema fluid pressure (the interstitial pressure) equalled 4.5 cm. of water and the interstitial resistance had risen to 5.0 cm. of water. The latter readings are indicated at the beginning of Chart 1, by the symbols mentioned above.

While the pressure in the apparatus was maintained at 4.5 cm. of water the cuff about the upper leg was inflated to a pressure of 42 mm. of mercury. By the 3rd minute of venous obstruction backflow had become marked. This is indicated in the chart by a minus sign at the 3rd minute along the abscissa and at the 4.5 cm. pressure level along the ordinate. At the end of the 4th minute the pressure in the apparatus was raised to 10.0 cm. which, by chance, not only stopped the flow but just balanced the pressure of the fluid within the tissues.

This is indicated in the chart by a black dot placed along the abscissa at the end of the 4th minute and on the ordinate at the 10.0 cm. level. This state of affairs endured but a few seconds and during the 5th minute fluid began to flow backwards into the apparatus, showing that the pressure of 10.0 cm. of water therein had now become lower than the extravascular fluid pressure. The fact is indicated in the chart by the minus sign at the 5th minute. At

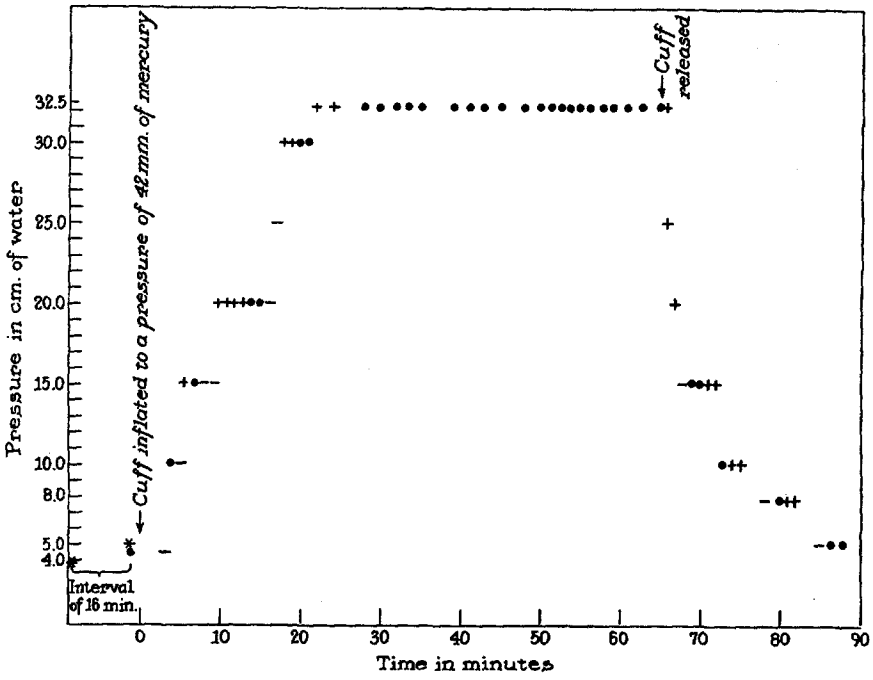


CHART 1

CHARTS 1 to 4. Changes of interstitial pressure in the skin of the lower legs and ankles of mice during and after venous obstruction. In all the charts the black dots indicate pressure readings which yielded neither inflow into the skin nor backflow into the apparatus. They indicate the times at which the pressure of the extravascular fluid was accurately balanced. Plus signs (+) indicate pressure readings which led to fluid movement into the tissues, the pressure in the apparatus being higher than the interstitial pressure. Minus signs (−) show that backflow occurred into the apparatus and that the plotted pressure was lower than that of the extravascular fluid. The interstitial resistance at the beginning of each test is shown in the charts by six-pointed stars.

the 6th minute the pressure in the apparatus was raised to 15.0 cm. of water and slow inflow resulted for about 1 minute. This ceased at the 7th minute, indicating that the extravascular fluid pressure had been balanced. A plus sign and a dot on the chart at the appropriate times and levels indicate these findings. Between the 8th to the 10th minutes the pressure of 15.0 cm. of water in the apparatus became too low to match the interstitial pressure as the latter rose and backflow occurred again into the apparatus, as indicated by the two minus signs on the chart at the same pressure level and at the 8th and 9th minutes respectively. At the 10th minute pressure within the apparatus was raised to 20.0 cm. of water but the

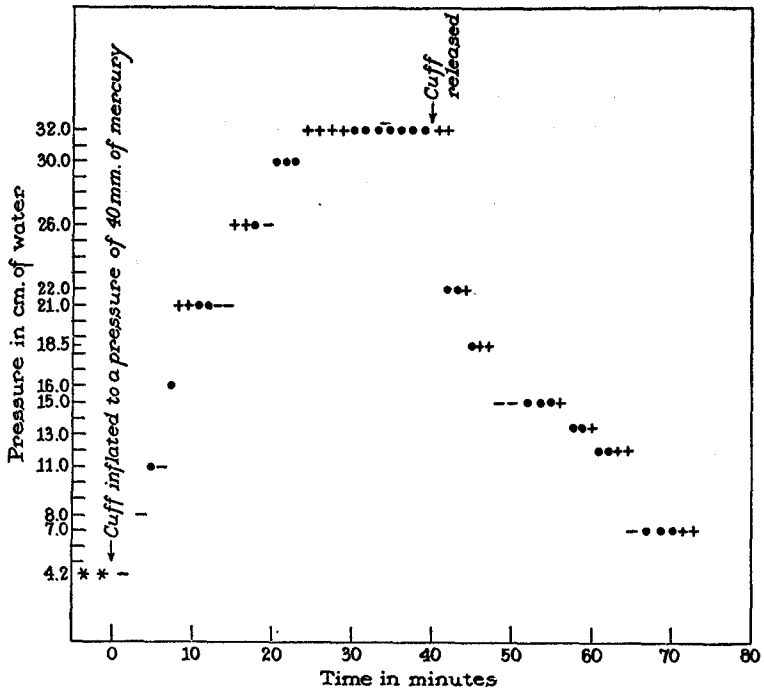


CHART 2

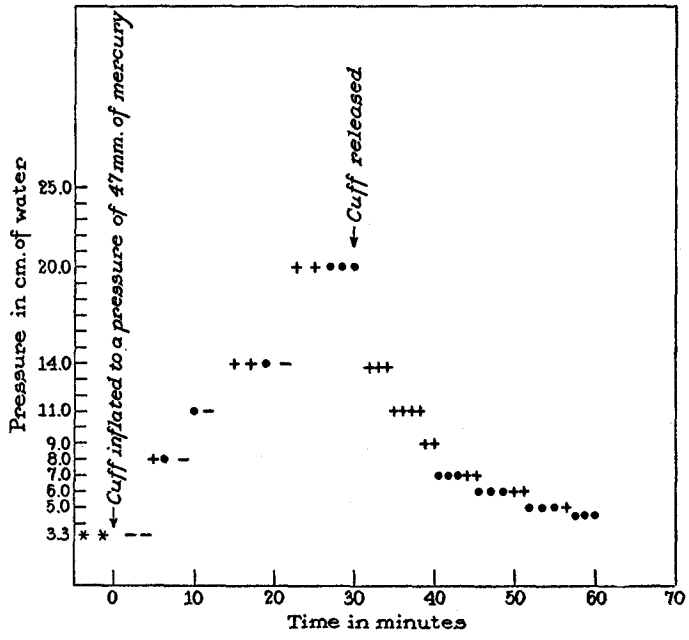


CHART 3

interstitial pressure had not yet reached this level, and consequently until the end of the 13th minute, flow into the tissues occurred, as indicated on the chart by a row of four plus signs. By the 14th minute, however, this flow ceased; the pressure in the apparatus now balanced of the fluid within the tissues. This state of affairs, shown on the chart by two black dots, endured for 2 minutes. Then, as the interstitial pressure rose still higher, backflow into the apparatus began at the 16th minute, as shown by a minus sign on the chart.

Further details need not be given but, as the chart shows, the interstitial pressure rose to the level of 30.0 cm. of water by the 20th minute and to 32.5 cm. of water by the 28th minute and failed to rise higher by the 50th minute. At this time, to determine whether or not an

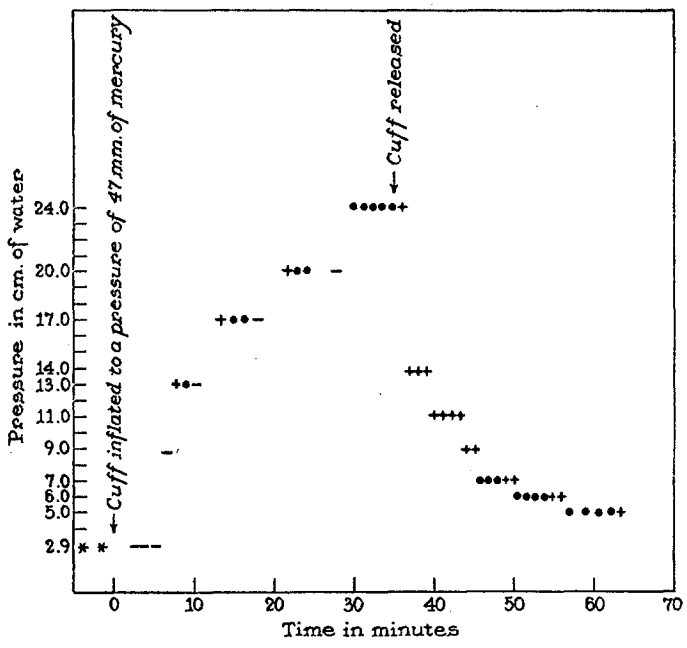


CHART 4

increase of the pressure of the cuff on the upper part of the leg would squeeze fluid from the lower, edematous portion of the leg into the apparatus, the cuff was inflated to a pressure of 100 mm. of mercury. For the next 5 minutes there was no flow to or from the injecting apparatus, showing that the increase of pressure in the cuff had no effect. Other control tests bearing upon this point will be detailed below.

Observations were continued for another 10 minutes, during which a pressure of 32.5 cm. of water continued to balance the tissue fluid pressure.

At the 65th minute, all pressure in the cuff was released. For the first half minute no movement of fluid occurred, then flow into the tissues began suddenly, as shown by the plus sign on the chart near the 65th minute. Obviously the interstitial pressure had fallen rapidly. Half a minute later, that is 1 minute after release of the cuff, the pressure in the apparatus was lowered to 25.0 cm. of water, and at the end of the 2nd minute to 20.0. In spite of the lowered pressure fluid continued to run into the tissues, showing that the extravascular fluid pressure had fallen faster than we had reduced the pressure in the apparatus. The finding is repre-

sented by two plus signs at the 66th and 67th minutes. At the 3rd minute after the release of the cuff, the pressure in the apparatus was lowered to 15 cm. of water and fluid flowed backwards into it. The interstitial pressure had not yet fallen to 15.0 cm. of water· accordingly a minus sign appears on the chart at the 68th minute. One minute later backflow ceased, as shown by a dot on the chart; the extravascular fluid pressure now equaled 15.0 cm. of water. Two minutes later, at the 71st minute, as the interstitial pressure fell below that level flow took place toward the tissues. At the 73rd minute the pressure in the apparatus, lowered to 10.0 cm. of water, balanced the extravascular fluid pressure. As the chart shows the pressure continued to fall until it reached its initial level of 5.0 cm. of water by the 87th minute, 22 minutes after the release of the cuff.

In eight of the twelve experiments cuff pressures of 40 to 47 mm. of mercury were used. In four, (see Charts 1 and 2 for the plotted findings from two of these), the interstitial pressure rose to levels between 30.0 and 32.5 cm. of water. In the other four, (Charts 3 and 4 give the findings from two of these), the interstitial pressure reached 20.0 to 24.0 cm. of water. In the remaining four experiments, cuff pressures of 25 to 30 mm. of mercury were used, inducing only partial venous obstruction for periods of 15 to 25 minutes. The interstitial pressures ranged from 5.0 to 20.0 cm. of water.

The experiments show that the interference to blood flow resulting from a pressure of about 40 mm. of mercury resulted in immediate and profound changes in the interstitial pressure in the skin of the lower portions of the leg. As already mentioned the skin in this region is not loose and pressure changes may be greater than those which occur elsewhere in the body following venous obstruction.

*Control Experiments.*—In all the experiments the interstitial pressure in the skin of the lower leg rose after inflation of the pressure cuff and fell after its release. It seemed important to learn whether or not the pressure put upon the upper leg by the cuff could be transmitted directly to the extravascular fluid in the skin of the lower leg or ankle and produce a rise of interstitial pressure there.

To test the point, five control experiments were carried out upon mice. In three the needle was placed in the skin of the dorsum of the ankle; while in the other two it entered the skin of the distal third of the lower leg. In each the procedure led to the appearance of a little free interstitial fluid, the pressures of which ranged from 3.0 to 5.0 cm. of water. Venous obstruction, produced in the usual way for half hour periods, increased the pressures to 22 to 30 cm. of water. After release of the cuff, the interstitial pressure in all instances fell to levels between 5.0 and 7.0 cm. of water. In all, during the obstruction, some additional edema developed in the skin near the needle's tip. The animals were then killed with chloroform, the pressure cuff was inflated to the same pressure that had been used before death, and the interstitial pressure was determined. In no instance was there a rise of interstitial pressure during or after inflation of the cuff. In all the experiments the pressure cuff was again released; there occurred no appreciable change of interstitial pressure. In two other control experiments the lower left leg and feet of two mice were rendered markedly edematous by rapidly and repeatedly inflating and deflating the pressure cuff (25). After edema had developed, the animals were killed with chloroform and, while the cuff was uninflated, the edema fluid pressure in the skin of the ankles

was determined. The cuff was then inflated again, to bring pressure upon the thigh, but no changes occurred in the edema fluid pressure in the ankle.

The application and release of pressure in the cuff about the upper portion of the leg of these recently killed animals did not directly transmit changes in pressure to the skin of the lower leg even when the skin was edematous. There seems to be no reason why there should have been any transmission of pressure during life.

*Changes in Interstitial Pressure in Human Skin during Venous Obstruction*

The increase in interstitial pressure in the skin of the mouse's leg during venous obstruction was rapid and striking in every instance. However, the findings obtained by previous clinical workers in the skin of human beings under these circumstances are contradictory and some are not in agreement with those now obtained in the mouse. Consequently, intracutaneous pressure changes were measured in the arms and legs of normal human subjects before, during, and after various periods of venous obstruction with certain minor modifications of method already described in the accompanying paper (21). The tests required up to an hour of enforced immobility of the limbs and many of them were vitiated by movement. Hence we can present only seven which, in our opinion, measure up to the observational needs.

The tests were made upon three men using in each the volar surface of the forearm and the anterior surface of the ankle. One additional test was carried out upon the dorsal surface of the forearm of one of the men. When readings were made in the skin of the arm, the subject sat in a comfortable chair with the arm flexed so that the surface of the forearm lay at the level of the apex beat of the heart. The forearm was raised from the table by padded blocks placed at the elbow and wrist, to avoid direct pressure effects. When readings were made in the skin of the ankle the subject lay upon a table, in a comfortable position with the legs slightly flexed. Before commencing the readings the sphygmomanometer cuff was adjusted about the upper arm or the thigh and an initial measurement of the interstitial resistance was made. Unlike the skin of the lower leg of the mouse, human skin did not readily become edematous and no reading of extravascular fluid pressure could be made prior to the obstruction of venous blood flow. Consequently while the pressure in the injecting apparatus was maintained at the pressure equal to the interstitial resistance, the cuff was slowly inflated to a pressure of approximately 100 cm. of water. Thereafter, the procedure was like that already described in the tests upon mice.

Usually within 2 to 4 minutes after inflation of the cuff backflow began to occur from the tissues into the injecting apparatus, showing that freely movable extravascular fluid was collecting in the skin. From that time on we were able to abandon determinations of the interstitial resistance and measure instead the extravascular fluid pressure, the true interstitial pressure, as it increased during venous obstruction or fell afterwards. Accordingly, after observing the backflow for several minutes, the pressure in the injecting apparatus was increased arbitrarily as in the experiments on mice, and inflow to the tissues, backflow to the apparatus, or stasis was looked for.

In two of the seven tests the cuff pressure was released after only 15 minutes because of the discomfort of the subjects. In the remainder, the effects of venous obstruction were measured

for periods varying from 17 to 45 minutes; then, with the limb still immobile, the cuff pressure was released and pressure determinations continued for 15 to 25 minutes. The release of pressure in the cuff was followed shortly by the flow of test fluid into the tissues indicating a rapid fall of interstitial pressure. The fall of interstitial pressure was studied by lowering the pressure in the apparatus until backflow appeared and maintaining the pressure at this level until backflow ceased.

Table I summarizes the results of the seven tests and the findings from three, made on the volar surface of the forearm, on its dorsal surface, and on the dorsal surface of the ankle respectively, are plotted in Charts 5 to 7. It is obvious that in all instances venous obstruction produced by a cuff led to a rapid increase in the intracutaneous pressure in man. The rise was not significantly different in the skin of the arms and legs. In all a prompt rise to

TABLE I

| No. | Initial interstitial resistance | Interstitial fluid pressure at the 15th minute of venous obstruction | Maximal interstitial pressure | Time at which maximum pressure was attained | Time of release of cuff |
|---|---|---|---|---|---|
| | *cm. of water* | *cm. of water* | *cm. of water* | *min.* | *min.* |
| 1 | 2.6 | 15.0 (approximate) | 23.0 | 26th | 30th |
| 2 | 3.0 | 13.0 | 18.0 | 20th | 45th |
| 3 | 2.8 | 15.0 (approximate) | 20.0 | 22nd | 38th |
| 4 | 2.5 | 13.0 | 19.0 | 22nd | 27th |
| 5 | 3.0 | 15.0 | 15.0 | 23rd | 37th |
| 6 | 2.9 | 15.0 | 15.0 | 18th | 18th |
| 7 | 3.3 | 12.0 | 16.0 | 17th | 17th |

about 15 cm. of water occurred within as many minutes after the onset of venous obstruction. Thereafter, in some cases, the rapid rise continued to levels of 20.0 to 23.0 cm. of water. In others the further rise, if it took place at all, was slower. No doubt as the interstitial fluid pressure increased it acted to prevent the escape of fluid from the blood, as Landis and Gibbon have pointed out in their plethysmographic studies (3) of whole limbs during venous obstruction. In all the tests a rapid fall of interstitial pressure followed the release of pressure in the cuff.

There were some variations in the findings which are of much interest. In some of the tests the cessation of increase of interstitial pressure was abrupt, and in two tests, as shown in Charts 6 and 7, there actually occurred a decrease after it had risen to levels of 18.0 and 20.0 cm. of water respectively.

For example, in one test, as Chart 6 shows, the interstitial pressure in the dorsal skin of the ankle had risen to 18.0 cm. of water by the 20th minute of venous obstruction. No movement of the test fluid occurred for 5 minutes when suddenly there took place an abrupt inflow of fluid into the skin. A minute or two prior to this the subject experienced a sensation of strong congestion in the leg followed by a feeling of sudden relief of the congestion just at the time

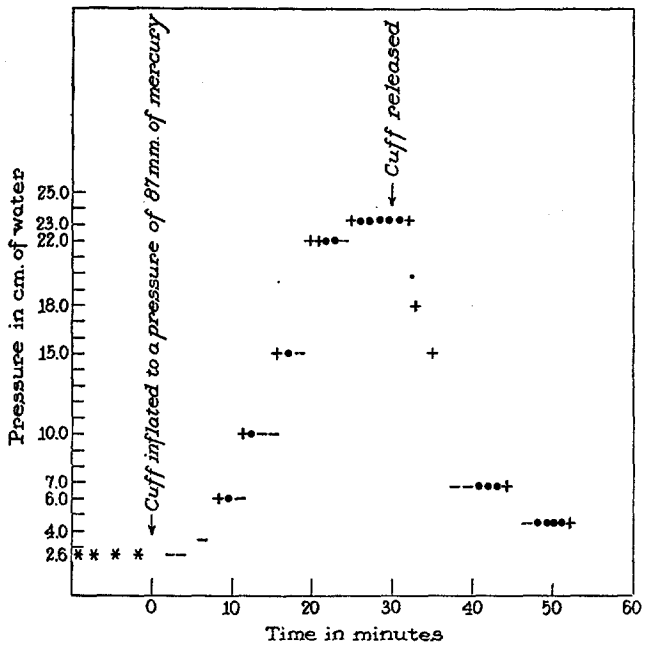


CHART 5. Changes of interstitial pressure in the skin of the volar surface of the forearm of a normal human subject during and after venous obstruction.

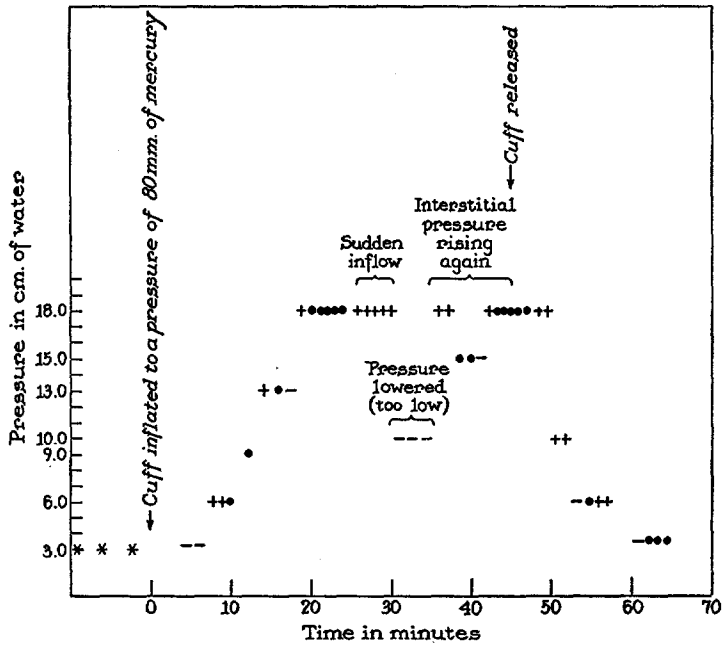


CHART 6. Changes of interstitial pressure in the skin of the dorsal surface of the forearm of a normal human subject during and after venous obstruction.

that the test fluid began to flow from the injecting apparatus to the skin. During this inflow the manometer attached to the pressure cuff showed no change in the pressure exerted by the latter. There had also been no visible movement of the leg. The inflow was allowed to continue for 5 minutes, to be sure that it was not caused by some movement. The pressure in the injecting apparatus was then lowered in an attempt to measure the new interstitial pressure. A pressure of 10.0 cm. of water was found too low and backflow occurred from the 31st to 35th minutes. A trial pressure of 18.0 cm. of water exerted by the injecting apparatus was found too high during the 36th and 37th minutes. By further trials between the 38th and 40th minutes the interstitial pressure was found to be 15.0 cm. of water. Two minutes later the

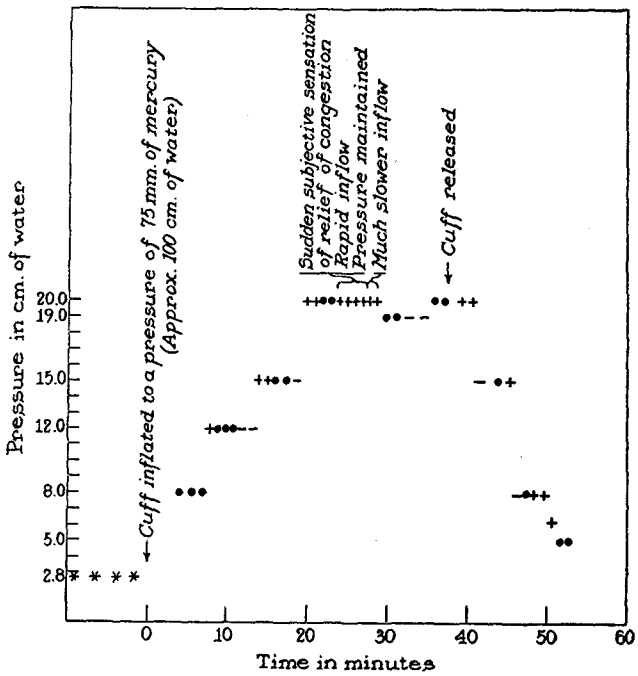


CHART 7. Changes of interstitial pressure in the skin of the dorsal surface of the ankle of a normal human subject during and after venous obstruction.

pressure in the skin had risen to its former level of 18.0 cm. of water. At this point it became necessary to release the cuff because of the subject's discomfort, whereupon the interstitial pressure fell promptly in the usual manner.

A similar phenomenon appeared in another test carried out on the volar surface of the forearm of a different subject (Chart 7). In this test the interstitial pressure was found to be 15.0 cm. of water between the 16th and 18th minutes of venous congestion. It rose by the 22nd minute to 20.0 cm. of water. During the 23rd minute the subject experienced a sudden feeling of congestion followed by relief, although no change in the pressure of the cuff occurred and no movement of the arm was seen. The arm which had been purplish and blotched became paler. A sudden decrease of the interstitial pressure occurred, as evidenced by a great inrush of the test fluid from the apparatus to the skin for a period of 4 minutes. For the next 2 minutes the inflow almost ceased and then, between the 31st and 32nd minutes, a measurement of the inter-

stitial pressure was obtained at the level of 19.0 cm. of water. By the 33rd minute the interstitial pressure had apparently begun to rise once more, for backflow of fluid occurred into the injecting apparatus. From the 36th to 38th minutes the pressure stood again at 20.0 cm. of water. The cuff pressure was then released and the interstitial pressure fell as usual.

The findings just described might be attributed to errors of the method were it not for the strong subjective sensations of congestion followed by relief experienced by both of the subjects. The phenomenon suggests some tissue or vascular readjustment which prevented further increase in the interstitial pressure, or perhaps a sudden opening of some venous by-passes in the marrow which relieved the venous obstruction.

## DISCUSSION

In the present work only intradermal pressure changes have been studied. The state of affairs in subcutaneous or other tissues of the limbs has not been investigated.

The interstitial pressure in the skin of the legs of mice rose during venous obstruction to levels of 32.0 to 33.0 cm. of water but no further. This finding approximates that obtained by the indirect estimates of tissue pressure during venous obstruction in human limbs by the plethysmographic method of Landis and Gibbon (3). These authors showed that during venous obstruction the filtration rate from the blood to the tissues was cut down to the same extent that it would have been by a counter force of 35.0 cm. of water outside of the vessels.

One cannot tell from our data whether or not an equally great change of intracutaneous pressure would occur, under like circumstances, in the looser skin of other parts of the body of the mouse and there are no measurements recorded by others which enable such a comparison to be made. There is only a report by Landerer (13) that subcutaneous pressures of 2.5 to 3.0 cm. of water in the leg of a normal dog rose to 10.0 to 11.0 cm. during venous obstruction.

In the skin of man the intracutaneous pressure did not reach the high levels obtained in the skin of the mouse, perhaps because the skin of the arm and lower leg of man is looser than that of the ankle of the mouse. It fell short by a good deal of the figure Landis and Gibbon obtained by their indirect method. But it may be pointed out that the pressure change they noted stood for the limb as a whole and not for the skin itself. In relation to our findings it is of interest that Krogh, Landis, and Turner (2) have shown that the increase in volume of a limb resulting from the collection of extravascular fluid, brought about by partial venous obstruction from external pressures of 15.0 to 20.0 cm. of water, ceased after a time, as if the pressure within the distended tissue became great enough to equal the pressure responsible for the filtration of fluid.

The reports by previous workers upon the pressure changes taking place in human skin during venous obstruction can now be profitably discussed. Wells, Youmans,

and Miller (18) found pressures of 5 to 9 cm. of water, in the normal skin of the lower legs of men, increased by only 2 or 3 cm. when a cuff was placed about the thigh at a pressure of about 100 cm. of water. They did not give details of the length of time that obstruction occurred in these intradermal tests but in studies made in subcutaneous tissues obstruction endured for 80 minutes as will be seen below.

Our findings are in complete disagreement with the report of Hajen (20) to the effect that tissue resistance and tissue pressure in the skin fall during venous obstruction. In his studies Hajen injected relatively large amounts of saline solution, 0.01 to 0.02 cc., into human skin with sufficient force to disrupt it and raise visible wheals. The pressures required to bring this about in normal skin were exceedingly high, 125 to 175 mm. of mercury. In states of edema, and during venous obstruction, lower pressures of 70 to 50 mm. of mercury sufficed to raise wheals. These pressures were compared and taken as a measure of the change in the pressure within the tissues. As fully discussed in preceding papers (21–24) from this laboratory, when such large amounts of fluid are forced into the skin, the high artificial pressure causes disruption of the cutaneous structures. It has been shown (21) that the passage of fluid through skin, in amounts greater than that taking place naturally, is resisted more strongly by normal skin than by that which contains freely movable fluid. From this it is apparent that Hajen measured in normal skin high artificial pressures created by the forceful introduction of enough fluid to distort it and form a wheal, and then, assuming these pressures to be normal, he found that less force was required to disrupt the tissues when they were edematous or when they already contained large amounts of extravascular fluid in consequence of venous congestion.

Meyer and Holland (14) found no change of pressure in human skin during venous obstruction. The error in their method responsible for the finding has been fully discussed in a preceding paper (21) and need not be detailed again. Suffice it to say here that these authors, like Hajen, forced such large amounts of fluid into the tissues at such high pressures that disruption occurred. It is significant that these authors, like Hajen, reported a decrease in pressure in edematous skin.

The changes of intracutaneous pressure recorded in the present work during venous obstruction in human skin seem to be far greater than the changes found by others (13–17, 19) under the same conditions in subcutaneous tissue. Wells, Youmans, and Miller (18) reported pressures of 6.0 cm. of water, rising from 2.0 to 4.0 cm. during 80 minutes of obstruction by a pressure cuff inflated to a pressure of 40 mm. of mercury. In other experiments increases of only 1.0 to 3.0 cm. of water were found, on the average, although in two instances pressure levels of 11.0 and 15.0 cm. were attained. Using a pressure cuff about the upper arm, Burch and Sodeman (17) investigated the immediate effects of venous congestion upon the pressures in the loose subcutaneous tissue in the back of the hand. After 10 to 12 minutes values of only 2.4 to 2.6 cm. of water were found. Longer periods with the pressure cuff were not tried nor were the conditions in the skin itself studied. Meyer and Holland (14, 15) found no increases during venous congestion; their lack of positive findings has already been explained.

The difference in the behavior of intracutaneous and subcutaneous pressure during venous obstruction is no doubt explainable by the difference in the structure of the two tissues. In the loose subcutaneous tissue collections of fluid have more room to spread. This supposition is supported by the observa-

tion in the present work that during venous obstruction the intradermal pressure changed even more in the tense skin of the ankle of the mouse than in the looser skin of man.


## SUMMARY

The changes of intracutaneous pressure in the limbs of mice and human beings have been followed during and after periods of venous obstruction with almost unhindered arterial flow. During the first 30 minutes of obstruction the interstitial pressure in the tense skin of the lower legs of mice, a pressure which is slightly higher than that in the loose skin of the ears, backs, and thighs (21), rose from 2.6 to 4.6 cm. of water to about 32 cm., thereafter remaining constant. It would appear that the escape of fluid from the capillaries is checked at this pressure. In the skin of the arm and leg of man the interstitial pressure rose from 2.5-3.7 cm. of water to 15.0-23.0, within 15 to 27 minutes after venous obstruction had been produced, mounting no higher during the period of observation. When venous obstruction had existed for about 20 minutes or more the subjects sometimes experienced sensations of relief from congestion as if some tissue adjustment or the opening of some venous by-pass in the marrow had occurred, preventing a further rise of pressure. However this may be, the pressures still appeared to be great enough to prevent further escape of fluid from the capillaries, at least for the time being.


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