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STUDIES ON HUMAN CAPILLARIES: *II. Observations on the Capillary Circulation in Normal Subjects*

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STUDIES ON HUMAN CAPILLARIES

II. Observations on the Capillary Circulation in Normal Subjects

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Until the later years of the nineteenth century the current view of the capillary circulation was that the capillaries were passive and that the rate of blood flow through them was determined by the state of the arteriole supplying them. Since then many researches have been carried out which show changes in the capillaries which the observers were unable to explain on the basis of arteriolar changes. The discovery by Rouget (1) of cells on the walls of the capillaries which he believed to be of a contractile nature lent strong support to the view that there is independent contractility of the capillaries. Of late years most observers agree that the capillaries both in man and in animals have the power of independent contractility. Whether they can do this normally without the application of a stimulus to them is disputed and there is also considerable doubt as to the mechanism which is involved in this action.

The literature on the subject of capillary physiology has been so admirably reviewed by Krogh (2) that only some important points in the literature of more recent date will be referred to. There seems to be no doubt that the capillaries in both man and in animals can be made to contract by the application of suitable mechanical or chemical stimuli. It has also been definitely shown in animals that electrical stimulation of nerves can cause changes in the caliber of the capillary loops independent of the changes which take place in the arterioles. The work of Krogh (2) on the muscle capillaries has demonstrated that the number of capillaries in which blood is flowing is constantly changing and that the vascular supply is adjusted to the needs of the muscle by continuous alterations in the capillary flow. Carrier (3) made observations of the skin of the forearm under the microscope and found in this situation that the capillaries were constantly changing—individual capillaries could be seen to disappear and to reappear while others appeared in new situations. In their studies of the glomeruli of the frog's kidney Richards and Schmidt (4) observed that in only part of the glomeruli was blood flowing at any one time and that the capillary pathways in a single glomerulus varied. No observations have been recorded in which the capillaries at the nail fold in man have been seen to appear and disappear as described by Carrier in the corresponding vessels of the forearm but changes in the flow in these vessels have been frequently described.

A question which has interested many observers is whether under normal conditions independent contractility is displayed by the capillaries and whether the nature of this contraction is a peristaltic wave which would tend to propel the blood forward. Variations in the flow undoubtedly take place but whether these are due to contraction in the capillaries themselves is uncertain. Krogh (2) brings forward evidence in favor of the view that the changes which take place in muscle are of this nature. But Richards (4) in his work on the frog's kidney has been unable to find any evidence in support of the idea that independent contractility takes place under normal conditions. Many observers have stated that they have seen changes in the capillaries of the nail fold in man under the microscope which they interpret as showing evidence of capillary contractility. Thaller and Draga (5) described alterations which they think to be of the nature of peristaltic contractions of the capillaries. This view has been strongly upheld by Kylin (6). Krogh (2) on the other hand has seen no evidence in favor of the occurrence of this mechanism in his observations in human subjects and thinks the conception is probably incorrect. Müller (7) as the result of extensive studies in the Tübigen school agrees with Krogh and does not think that the changes can be due to peristalsis. Many observers have brought forward evidence both for and against this view.

Although the conclusion that capillaries can contract independently has been generally accepted, two views are held as to the cells which are responsible for this behavior. Some believe that it is caused by changes in the endothelial cells as first suggested by Stricker (8) and others that it is due to cells outside the endothelium of the capillary wall. In 1873 Rouget (1) described cells in this position which he thought to be of the nature of smooth muscle and to possess a contractile function. The existence of these cells has been amply confirmed. Under Krogh's direction Vimtrup (9) has carried out an extensive study of their nature chiefly by histological means. In his report of these studies Vimtrup gives a full review of the literature of this phase of the subject. He confirms Rouget's results and says that he has been able to trace the transition from the smooth muscle of the smallest arteries to the Rouget cells. He also studied the changes which take place in the capillary wall in the living animal and states that the contraction which follows nerve stimulation always starts at one of these cells. Clark and Clark (10) have studied the problem from a different angle. They found it possible to observe the development of the capillaries in the tail of living amphibian larvae and to make camera lucida drawings of the selected area under observation at frequent intervals for eight days. They found that the Rouget cells were not contractile elements but developed from stellate connective tissue cells. In their opinion two types of contraction occur in the capillaries; an active one which may occur spontaneously, and a passive one which is caused by temporary disturbance of the circulation. Both types of contraction were independent of the pressence of adventitial cells. Contraction was indeed often to be seen before the development of these cells. After they were developed contraction began frequently at places at a distance from them. During active contraction or passive narrowing of the vessel, the capillary might be seen to draw away from the Rouget cells and to leave a space between cell and wall when viewed from a suitable angle. They came to the conclusion that both the power of contractility and tonicity are independent of any form of adventitial cell.

The present observations were undertaken in order to study the nature of the changes which take place in the capillaries by means of cinematographic records. Exposures were taken at intervals of $\frac{1}{16}$ second. It was possible therefore to measure the diameter of the capillary walls throughout a long series of consecutive photographs with the hope of throwing light on certain of the problems which have been discussed above. The technique of making the photographs has been described in another paper (11). The results reported are based on a study of the capillaries at the nail fold in 8 normal individuals (4 men and 4 women) between the ages of 25 and 35. Observations on all cases were made on 4 consecutive days at the same hour. In every instance the temperature of the room showed practically no change from day to day.

METHOD OF STUDYING THE FILMS

Projection. In the film the individual capillaries were magnified 14.4 times. With this magnification it would be impossible to estimate any but gross changes with any degree of certainty as the error in measurement would be so great. The greater the magnification at which the contour of the capillary was sharp the less the error in measurement. A special projectoscope which enlarged the capillary 350 times was constructed thus considerably reducing the possibility of error. At this magnification a sharp picture of the capillary was obtained. The contour of the individual capillaries in a large series of consecutive pictures was traced on paper and these tracings were used for measurement.

Measurement. The point at which measurement is made is of paramount importance. The most satisfactory arrangement would be to provide a base line in the tissues and to measure the diameters of the arterial and venous limbs at a constant distance from this line. It was not however practicable to do this. A marker placed on the finger might also have been tried but its position was liable to be fallacious as it might not follow accurately any movement of the finger itself which took place. An indicator close to the film might lead to inferences even more fallacious. In place of methods of this sort we have selected a point on the magnified image 2 cm. from the tip of the capillary loop (0.06 mm. from the tip of the actual capillary) as the point at which to measure the diameters of the arterial and venous limbs. The tip of the loop is taken as the point of reference, for, barring one reservation, movement here is accompanied by movement of other points in the loop. Between the tip and any other nearby point on the loop, the distance may be regarded as remaining constant. The reservation which was mentioned concerns the possibility of lengthening of the loop for any reason, notably that which may occur at the time of cardiac systole. The method of measuring was as follows: A line was drawn through the center of the long axis of the capillary loop roughly parallel with the two limbs and at right angles to this a second line which touched the tip of the loop. A third line was drawn parallel to the second at a distance of 2 cm. which cut the arterial and venous limbs (fig. 1). Changes in the diameters of these limbs at this level have been taken to indicate changes in behavior of the capillaries. Curves were prepared in which the values so obtained were charted, the abscissa representing the time and the ordinate the diameter of the limb. These have been used for comparison of the changes in the various observations. In other observations of the same subject other methods of measurement were used and the several curves compared to those obtained by the method just described. The opportunity for comparison occurred in certain capillaries in which owing to their peculiar shape two or more characteristic points could be selected as reference points (fig. 1). In such cases parallel lines were drawn through the points selected and at right angles to the long axis of the loop. The distance between these was measured.

Obviously several interpretations may be drawn of the behavior of the capillaries, depending on changes which are disclosed when the measurements are taken. 1. If the distance (*a–b*) remains uniform and the measurements of the diameter (*c*) at a point 2.0 cm. from the tip of the loop show no significant variations, it is unlikely that an important change in the state of the capillary has taken place. 2. If the distance (*a–b*) increases, and the measurements of the diameter (*c*) decrease, the inference may be drawn that stretching of the capillaries has taken place. If on the other hand the measurements of the diameter (*c*) increase or remain unchanged, an effect on the vessels by stretching may be excluded. The change in measurement is then the result of another function. 3. If the distance (*a–b*) decreases, and the measurements of the diameter (*c*) increase, the inference may be drawn that this result depends on the decreased length of the tube. But if the diameters (*c*) decrease or remain unchanged an effect on the vessels as a result of this action may be excluded and must depend then on another function. In point of fact, behavior of all these types was observed. It was impossible to infer that uniform changes in the diameters took place. From these observations one cannot draw a conclusion on the events which take place in the capillaries during the heart beat. They permit the statement to be made how-

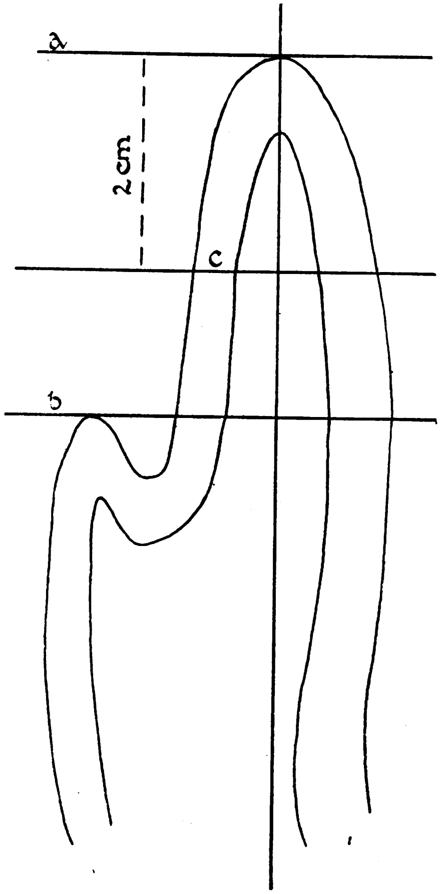

FIG. 1. SCHEMATIC DRAWING OF A CAPILLARY TO ILLUSTRATE THE METHODS WHICH WERE EMPLOYED IN THE MEASUREMENT OF THE DIAMETERS OF THE LIMBS OF THE CAPILLARY LOOPS

(For description, see text)

ever that changes in the diameter, should they be found to occur, do not depend on this factor. They do moreover show that to measure the diameters 2.0 cm. from the tip exposes the measurements to no systematic distortion. To obtain this measurement was our purpose. Curves drawn from observations of capillaries which afforded this opportunity did not differ in form from those obtained when it was impossible to utilize this check.

In many of the films photographs have been obtained of 4 or more capillaries all of which were in sufficiently sharp focus to allow accurate measurements. The positions of the tips of all these loops have been compared with respect to one another in a large series of exposures over a long period of time. It was found that these remained constant. But the objection may be made that the tips of all these changed at an equal rate, and that therefore no relative changes could be observed. When adjacent loops were compared by measurement of the diameter it was found that the various loops showed changes which were quite dissimilar. In other words, no relative movement of the tips takes place or should there be movement, this is congruous whereas the measurements of the diameters are incongruous. The total area of the loop distal to the line drawn 2 cm. from the tip through the arterial and venous limbs has also been measured by means of the planimeter and it was found that this area remained practically constant. As a result of a comparison of these measurements the method first described appears to be subject to slight error only and provides a useful way of estimating the changes which take place in the loops.

OBSERVATIONS

The size of the loops. As is well known there is great variation in the size of the capillary loops at the nail fold both in the same subject and in different subjects. It seems almost useless to state the size of the normal capillary as the variations between capillaries in the same subject and in different subjects is so great. A review of the literature shows that it is not possible to compare the values given by different authors unless these are measured at the same point on the loop. The measurement of the arterial limb in most of the present observations at the selected point has varied from 0.014 to 0.016 mm. while that of the venous has usually been slightly larger, 0.015 to 0.017 mm. In many instances, however, smaller and larger capillaries have been measured but similar variations have taken place in all.

Variations in diameter. Both the arterial and venous limbs of the same capillary varied in diameter from moment to moment and from day to day in the same subject (fig. 2). Although these changes take place they are relatively small compared to the breadth of the limbs

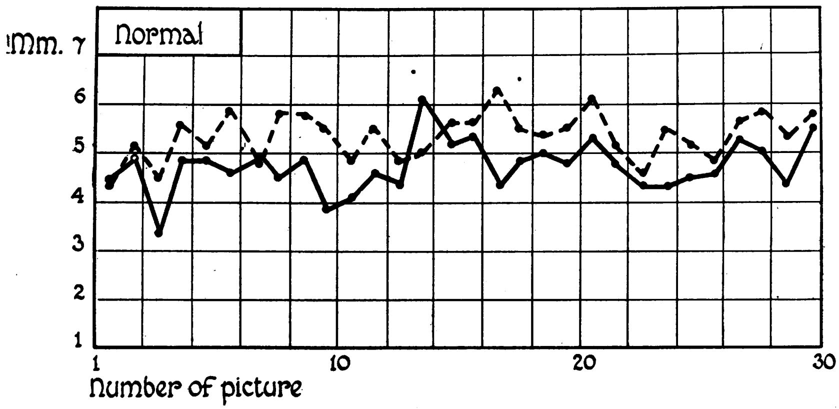

FIG. 2. CHANGES IN CONSECUTIVE PICTURES IN THE DIAMETERS OF THE ARTERIAL AND VENOUS LIMBS OF A CAPILLARY IN A NORMAL SUBJECT

Abscissa = number of the picture. There were 10 exposures per second. Ordinate = diameter in millimeters at a point 2 cm. from the tip after magnification of the capillary 350 times. •———• arterial. •– – –• venous.

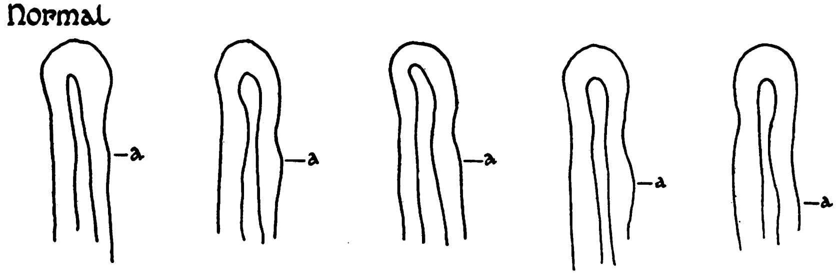

FIG. 3. TRACINGS OF FIVE CONSECUTIVE PICTURES OF A CAPILLARY LOOP IN A NORMAL SUBJECT. × 350

which remains approximately the same from day to day. These changes are very noticeable on observation of successive magnified pictures (fig. 3). The daily changes were of a similar nature to those taking place from moment to moment while the extent of the variations was usually about the same in the two limbs. The magnitude of the changes also varied from capillary to capillary and from subject to subject. In some it was small while in others it was much more marked.

Evidence of a peristaltic wave of contraction. If the mechanism which is responsible for the changes which take place were peristaltic in nature recurrent alterations in form ought to occur with approximate regularity as regards both time and magnitude. We have studied all our curves from this point of view but have been unable to find any evidence for the presence of this mechanism (fig. 4). In a few in-

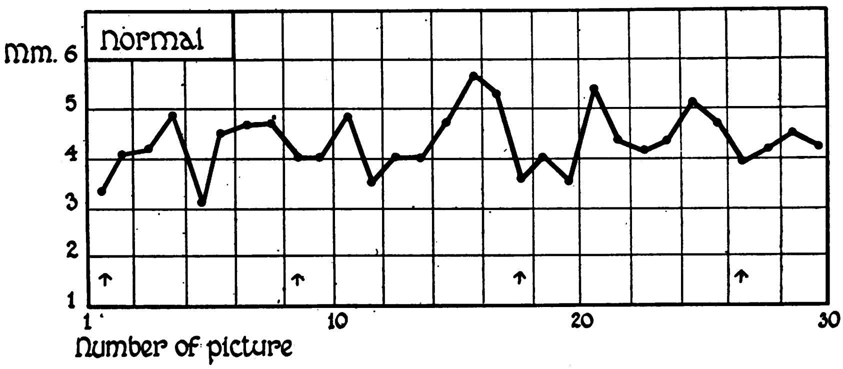

FIG. 4. CHANGES IN THE DIAMETER OF THE ARTERIAL LIMB OF A CAPILLARY IN A NORMAL SUBJECT. × 350

↑——↑ = one complete cardiac cycle

stances a small part of the tracing suggested this possibility but the subsequent changes through a long period of observation show that this occurrence was merely accidental. One of these rare instances is illustrated (fig. 3). A hump (*a*) can be seen on the loop and this can be followed throughout the series of pictures. If this hump were due to a peristaltic wave it might be expected to proceed in the same direction at a constant speed. The most prominent point on the hump has been measured with reference to a line drawn through the tip of the capillary and it was found that both the direction and speed varied. In the second picture it was slightly lower, in the third it had returned to practically its original level while in the fourth and fifth it became progressively lower. A large number of consecutive pictures studied later in the series showed no evidence of a hump in this situation.

Evidence of rhythmical contraction of the capillaries. A second type of motion of the capillaries is possible, namely, rhythmical contraction. Observations on this question have been made by extended inspection of the capillaries themselves and the curves of the measurements have also been studied. In neither method has any evidence in favor of this mechanism been seen.

Evidence of changes of a pulsatory nature. In the examination which was next undertaken it was the object to discover whether the changes that have been described depend on the cardiac pulse. In this case again, the phenomenon should be recurrent. Knowing the heart rate and the number of exposures per second, photographs corresponding to the same phase of the cardiac cycle can be measured and compared. If the behavior of the capillary were congruent with the pulse, the measurements of corresponding photographs should be similar and should form a characteristic curve. It has been impossible in any of our tracings to relate the changes to a mechanism of this nature (fig. 4). In some cases the diameter of the capillary remained approximately the same for the duration of a heart beat while in the following heart beat for the same period it was either considerably larger or smaller. In most cases however the changes were totally irregular.

Blood flow. The blood flow was observed by simple inspection of the capillaries with the microscope but no measurements of this phenomenon were made. The blood flow varied in the different capillaries in the same subject and also in the same capillary from moment to moment. At one time the flow might be very rapid while a little later the stream might become very sluggish and indeed might stop momentarily. All gradations between these two extremes were to be observed but in this situation capillaries have not been seen to disappear and others appear, as has been described in other situations. A considerable difference could also be observed in the capillary circulation of the different subjects studied.

DISCUSSION

The observations which have been made show that the diameter of the capillaries at the nail fold in man is constantly changing. Although individual capillaries do not appear and disappear as they do in certain other tissues nevertheless definite variations occur in this situation. They also show that the reactions which take place are of a similar nature over a period of several days and that different subjects exhibit individual peculiarities in the changes seen. These have been described by other observers but we have now been able to measure them and to record the rapidity with which they can take place. These are discussed later in detail.

In these observations as in all similar studies in man the diameter of a capillary limb has been inferred from the breadth of the stream of blood flowing in it as the wall of the vessel cannot be identified. In order to make accurate statements one ought to be able to photograph the actual wall of the capillary which is impossible. The width of the blood stream has been used as a criterion because the capillaries remain continuously full of blood except for the occurrence occasionally of small gaps in the stream whose significance is discussed below. A diligent search has been made by inspection to discover whether there is evidence of an axial stream of corpuscles and a peripheral zone of pure plasma in the capillaries. If this arrangement were found the corpuscular stream would not be an accurate representation of the changes in the capillary wall. Observations made on this point have confirmed those of Krogh (2) that this zone of pure plasma is practically non-existent. We have concluded therefore that the breadth of the corpuscular stream offers a basis for measuring the diameter of the capillary loop in this stituation and can be used as such.

It is particularly important in a study of the circulation to know whether under normal circumstances the capillaries play an active part in the forward propulsion of the blood. Changes have been seen which have been taken to be movements in the walls of the capillaries and an endeavor has been made to relate this to the occurrence of certain possible rhythmical mechanisms. There are two types of motion of which the capillaries might, as has been said, be capable. The first is peristaltic contraction and the second local rhythmical contraction. It has been impossible to correlate either of these mechanisms with the changes observed. The former has received considerable support based principally on the fact that gaps in the stream of corpuscles have been observed. These gaps are not often seen in normal subjects and usually take place when the stream is slow. Krogh (2) discussed the significance of these gaps and did not consider that they were due to peristaltic contraction of the capillary wall. One can watch many capillaries for a long time without these gaps appearing and in those in which they are seen they appear so irregularly and unless the stream is very slow so infrequently that they do not appear to be due to a peristaltic wave. The rate of progress of the gaps is very variable and often very rapid and the whole appearance suggests a gap in the corpuscular stream rather than a contraction of the wall. The mechanism involved is probably an agglutination of corpuscles which causes a momentary stoppage of blood flow and thus allows a gap to be formed.

The cause of the variations which were found is in doubt. They may be due to local contraction of the capillary wall occurring in an irregular manner. Or they may be due to alterations in the tonicity of the arterioles. It has been definitely established that the latter possess tone (12) and frequent spontaneous changes in their tonicity, controlled in great part by the central nervous system, have been shown to take place by Langley (13). There is however an objection in relating what has been seen in the capillaries to the contraction of the arteriole as a whole, for if this were the responsible agent all the capillaries supplied by an arteriole should be similarly affected. But as has been shown, similarity of action on the part of the capillaries in the same field is not the case. Tarchanoff (14) has found however that on applying an electrical stimulus to the capillaries of a frog's nictating membrane contraction appeared much sooner at the junction of the arteriole and capillary than in the rest of the capillary. Richards (4) states that experiments in his laboratory on arterioles and capillaries in the muscle of the frog showed that the action of adrenalin is more marked at the branching of the vessels than along their course. He thinks that this may be the explanation of the variations in flow which are observed in the frog's kidney. The changes seen in the present studies might thus be related to variations in the tonicity of the arteriole at its junction with the capillary. Which of the possible explanations, capillary contraction or changes in arteriolar tone, is correct, remains unsolved by these investigations.

It appears then that the capillaries in the nail fold behave differently from those located in other tissues of the body, at least in other species than man. For in man the capillaries of the skin and visible mucous membranes only seem to have been examined; in animals there is, of course, information of their motions also in certain viscera. It is of some importance to keep in mind this phase of the state of knowledge of this subject. In this study there has been added a precise description of what was observed in a single portion of the skin. To remember this has its importance in view of the difference in action which Carrier has seen in the capillaries of the skin of the forearm. It may be said in a general way then that a single capillary area does not supply the criteria which may serve as a basis for making statements of the mechanism of the capillaries in the whole body. It is necessary apparently in making calculations of the circulation and in dealing with other physiological processes such as respiration and edema to allow for this matter of diversity of function.

CONCLUSIONS

1. The caliber of the arterial and venous limbs of the capillaries at the nail fold has been studied by means of cinematography over a period of days in 8 normal individuals.

2. Changes took place from moment to moment and from day to day. These changes were relatively small compared to the total breadth of the limbs which remained approximately the same from day to day.

3. The extent of the changes in the arterial and venous limbs of the same capillary was about the same, but the various capillaries in the same subject different from one another. Marked variations were also seen between the different subjects. There was no evidence that these changes were due to a peristaltic wave of contraction, a contractile motion of the capillary like that of the heart, or a pulsatile motion conveyed to the blood stream by the heart beat. The mechanism of their production is uncertain.

4. The blood flow in these capillaries has been studied by inspection and was seen to vary continuously.

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