THE BLOOD-PRESSURE AND ITS VARIATIONS IN THE ARTERIOLES, CAPILLARIES AND SMALLER VEINS.

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IN experimental work of this kind much depends upon the reliability of the method of investigation employed, and we consider it necessary, on that account, to describe somewhat minutely the different apparatus which we made use of in the course of our observations. We believe that with the various arrangements we employed for measuring the height of the blood-pressure in the peripheral vessels, numerical data of very considerable accuracy may be obtained. The more important conclusions, however, which may be drawn from the results of our experiments, are of a kind which would not be directly affected even by a much wider margin of error than that which it is believed may reasonably be ascribed to the method of enquiry.

N. v. Kries[1] is apparently the only observer who has attempted to measure, more or less directly, the pressure of the blood in the capillaries. His measurements were made on the vessels of the human skin, that portion on the back of the distal phalanx of one of the fingers immediately behind the nail being found most convenient for his purpose. The method he employed consisted in pressing, by means of weights, a small glass plate of known area upon the portion of skin selected, and finding the weight required to produce a distinct whitening

[1] N. v. Kries. "Ueber den Druck in den Blutcapillaren der menschlichen Haut." *Ber. d. sächs. Ges. d. Wissensch.* 1875, and Ludwig's *Arbeiten.*

of the compressed, as compared with the surrounding skin. The plates he used were of various sizes, varying from 2·56 to 4·56 sq. mm. Given the area of the plate made use of and the weight employed to press it against the skin, it is of course easy to calculate the equivalent water or mercury pressure. In making his experiments he assumed that the pressure which sufficed to cause an evident change in the colour of the small area of skin lying under the glass plate, was equal to the pressure of the blood in the capillaries lying nearest the surface, being led to suppose from theoretical considerations that the more superficially situated vessels would be fully exposed to the influence of pressure, such as he used, applied to the surface of the skin, while the more deeply seated capillaries would be protected in some measure by the elasticity of the tissues; and taking it further for granted, that the first distinct change in colour, produced by gradually increasing the pressure on the spot of skin, was to be looked upon as indicating a collapse of the upper layer of capillaries. That, with small plates such as those employed by v. Kries, the deeper lying capillaries would be less pressed upon than those lying under the epidermis, is probable enough. At the same time, the degree to which the elastic resilience of the tissue lying between the plate and the bone would lessen the true extravascular pressure as compared with that applied, must necessarily vary greatly with the area of the glass plate employed. We cannot assume, moreover, that the elasticity of the compressed tissue would not also protect to some extent the superficial capillaries from pressure applied to the surface of the skin. How far this would be the case, could not, of course, be learned for any given measurement. That the first distinct whitening of the skin, produced on gradually increasing the weights used to press the glass plate on the portion of skin, could be taken as evidence of collapse of the upper layer of capillaries, is, we believe, only permissible on the assumption, firstly, that the walls of these capillaries, as well as of those lying deeper, and which assist in giving a reddish colour to the skin, are practically inelastic, and secondly, that the extra-capillary pressure which will cause collapse of the capillaries of a given plexus, will be the same for all of its component vessels. According to our own observations neither of these suppositions is correct, as we hope to shew further on. It would be unfair, however, to criticize v. Kries' method as one which was supposed to give absolute values; it was only upon the relative values obtained under varied conditions that weight was laid by the author referred to, and against these there cannot be much objection.

Methods employed.

Our observations were confined to tissues, the capillary circulation of which could be watched through the microscope. Of these, the web of the frog was preferred, as a rule, since it possesses the great advantage of permitting a study of the phenomena of the blood-flow through the minute vessels without interfering to any important extent with either the general or local circulation. To control the data obtained, however, most of our experiments were repeated on the tongue and mesentery of the frog and on the tails of newts and small fishes. As might have been expected, the principal facts learned are of such a nature as to leave little doubt of their general applicability to the peripheral circulation of warm-blooded animals.

In Fig. 1, Pl. x., is represented (somewhat diagrammatically for clearness sake, and enlarged to about twice the natural size) one of the arrangements which was employed, and which was finally found the most convenient[1]. In the centre of the brass plate *f*, measuring 10 cm. long by 4·5 broad, is screwed the small cylinder *a* which is closed below by the little glass plate *b*, the junction of which latter with the brass is made air-tight. The upper outlet of the cylinder is closed by the delicate transparent membrane *d*, which presses upon the web, tongue, or other part examined, when the pressure of the air within the cylinder is raised. Counter-pressure is exerted by the thin glass plate *h*, which is so arranged that it can be fixed at any desired height above the cylinder *a*. The part to be examined is placed between the cylinder and the glass plate *h*, which is lowered as far as is possible without causing compression of the tissue between it and the edge of the cylinder. The arrangement is shewn in the figure, *g* being intended to represent the web seen in section.

It need scarcely be said, that the membrane which closes the little cylinder must possess certain qualities without which but little accuracy could be claimed for the method. (*a*) It must be sufficiently transparent to allow of the capillary circulation being seen clearly even with high power objectives. (*b*) It must be flexible enough to transmit equally to the tissue examined the pressure of the air contained within the cylinder. (*c*) It must be as inelastic as possible, or, at all events, its elasticity coefficient (to use a convenient but scarcely accurate term) must be considerably greater than that of the web or other tissue

[1] The instrument can be supplied by Robert Fulcher, 18, Panton Street, Cambridge.

against which it presses, so that the latter may not be stretched to any important extent when the pressure in the cylinder is raised. (*d*) The manner in which it is fastened on the cylinder must be such, that the pressure acting on that part of the web, tongue, &c. which lies within the field of the microscope, *i.e.* the part lying in the centre of the area of contact between the web and membrane, will, when the instrument is arranged as in Fig. 1, be exactly equal to the pressure of the air within the chamber or cylinder *a*.

The first three of these conditions are fulfilled to perfection by the membrane which we used, and which one of us[1] has elsewhere referred to in connection with other apparatus for physiological work. It is an exceedingly delicate, and when moistened with water, almost perfectly transparent membrane of excessive flexibility, while it is, at the same time, more than sufficiently inelastic to fulfil the part required of it here. It is prepared, we understand, from the peritoneum of the calf, and may be obtained from many druggists who employ it for fastening the stoppers of perfume bottles. It must not be confounded with the much thicker membrane which is also used for the same purpose.

The fourth requirement mentioned above, regarding the manner in which it must be fastened on the cylinder *a*, is illustrated by the diagram—Fig. 2. The way we managed is as follows. A piece of the membrane, having been moistened with water, is placed over the little cylinder *a*, into which it is then pushed with the rounded end of a glass rod or other suitable object, so that it takes up the position represented in section by the dotted line *a*. It is then securely tied by a thread resting in the groove cut for the purpose at the upper edge of the cylinder. On now raising the pressure within the chamber *a*, by introducing air through the tube *c*, the membrane bulges out in the manner indicated by the interrupted line *x*. When, however, it is prevented from taking this position by the presence of the glass plate *h*, or rather by the web, or other part, which is placed below the latter, it applies itself to this tissue in the way represented by the line *d*.

That, in the middle of the area of contact, the presence of the membrane will not in any way interfere with the conveyance of the pressure of the air within the cylinder to the web, might, we believe, be safely taken for granted. In order, however, that there may be

[1] Roy. "On the influences which modify the work of the heart." This *Journal*, Vol. I. p. 452, and "The form of the pulse-wave." *Do. Do.* Vol. II. p. 67.

no room for doubt on this point we have made a number of control experiments, which will be referred to further on.

The pressure of the air within the cylinder—that pressure to which the tissue lying within the field of the microscope is subjected—is regulated by an arrangement which is illustrated by Fig. 4. The caoutchouc bag *a*, containing air, can be compressed between the brass plates *b*, hinged together at one end, and which can be approximated by means of a screw. A T tube connects the caoutchouc bag on the one hand with a water manometer, and on the other with the cylinder *a* (in Figs. 1 and 2). In this way the pressure within the chamber *a* can be regulated with the greatest nicety.

As will have been seen from the figures on Pl. X., the brass plate *f* rests on the stage of a microscope, the optical axis of which passes vertically through the cylinder *a*[1].

In the case of the web, care was at first taken that no part of any of the toes was included within the area to be compressed. It was afterwards found, however, that this precaution was unnecessary, the result of raising the pressure applied being the same so long as the part lying in the microscope field was not too near one of the toes.

In our earlier observations one or two methods, differing from the above described in detail, but similar in principle, were employed. One of these consisted in placing the cylinder to which the membrane is tied, above the web, the little cylinder being screwed to the objective of the microscope, and being closed above by it. In this case the cylinder was made of such a length that when the tissue was in focus the end of the little brass tube was almost in contact with the part examined. Here, the air cushion pressed the tissue against a glass plate placed on the stage of the microscope. In other respects the arrangement was the same as that first described. This method was very handy, but as it did not permit of high-power objectives being used, it was abandoned.

The modification, illustrated by Fig. 3, may be referred to here. We employed it to convince ourselves that the pressure applied to the tissue in the centre of the compressed area is really that which is signified by the manometer. The little round chamber *a*, closed above by the glass plate *b*, and on the under end of which a membrane is fastened, is held by an appropriate holder immediately above the

[1] The internal diameter of the cylinder in the instrument which has been chiefly used is 2·8 mm., and the height of its upper edge above the surface of the brass plate in which it is screwed is 6 mm.

web, but not in contact with it. The ordinary glass slide *e*, upon which the web *g* rests, serves to exert a counter pressure. In order to prevent the membrane bulging out laterally, there is placed round the lower part of the little cylinder, but not connected with it in any way, a light ring of waxed paper, seen in section as *d*. The paper ring rests upon the web, and is so light that its presence has no appreciable influence on the circulation of the part.

In so far as the pressure is concerned, we have, with this arrangement, included a portion of web within a rigid box, closed below by the glass slide lying on the microscope stage, above by the little glass plate *b*, and limited laterally by the cylinder and the ring of waxed paper and the membrane. There is, at the same time, no interference with the entrance and exit of blood to and from the part of the web to be examined, other than that intentionally produced by raising the pressure within the chamber.

We have made a number of careful experiments with this little apparatus, comparing the results obtained by its help, with those given by the simpler arrangement illustrated by Fig. 1, and have thoroughly convinced ourselves that, for any individual case, *caeteris paribus*, the arterioles and capillaries of a given part are made to collapse at the same pressure with both methods. We do not pretend, of course, that, with the arrangement represented in Fig. 1, the pressure on the web is equal over the whole area of contact between it and the membrane. Doubtless, at the edge of this area, the pressure applied will be somewhat less than it is at the centre. It is only the central part, however, which can come within the microscope field, and for this part, as already mentioned, the pressure which acts upon the tissue is correctly indicated by the manometer.

Before describing the results arrived at, it may be advisable to consider briefly, what relation the pressure applied to a portion of tissue such as the web bears to the pressure which acts on the outside of the vessels of the part. The first point to be considered in a question of this kind naturally is, whether the normal extravascular pressure be higher or if it be equal to that of the atmosphere. It is not uncommon to encounter, scattered through medical literature, references to an imagined support which the capillaries receive from the tissue in which they are imbedded. There do not appear to be any facts in support of such a view, and against it there is the fact, that the pressure of the lymph (which has free access to the interstices between the tissue elements) is but very slightly, and sometimes not at all, above that of the atmosphere. In cases of oedema it is another matter; in them the pressure of the exuded lymph, as need scarcely be remarked, may reach a very considerable height. The simple experiment, of cutting off a frog's foot and watching the result on the contents of the vessels of the web, suffices, we believe, to shew that the extravascular pressure is in normal circumstances practically that of the atmosphere. On the leg or foot of the frog being amputated, the current of blood through the vessels of the web gradually ceases, but the capillaries rarely become empty, a certain quantity of fluid blood remaining stationary in their interior. As both arteries and veins are open, if the extravascular pressure were but a little higher than that of the atmosphere this would not occur. If we place the web of such an amputated leg between the cushion and the glass plate of the little apparatus which has been above described, and raise the pressure a few millimeters of water, the blood immediately begins to stream out of the vessels of the compressed part, and their walls are collapsed. A pressure equal to half a centimeter of water suffices to produce this result. When so low a pressure applied externally is sufficient to empty the capillaries, we may reasonably assume that the normal extravascular pressure, which was unable to do this, must be so little above that of the atmosphere that its influence may safely be ignored, as unlikely to lead to error with a method such as the one we employed. The little experiment just referred to also shews us that the epithelial layer and the tissues in which the capillaries are imbedded do not protect the latter from the influence of compression applied to the exterior of the part. For the above reasons, we believe that there is no room for doubt that with the instruments we employed the pressure which acts on the outside of the web is practically that to which the exterior of the vessels of the part is subjected.

The frogs used (*R. esc.* as well as *R. temp.*, and the greater number winter frogs) were, for the most part, uncurarized, as we soon learned that the blood-pressure of curarized animals is liable to variations which do not occur in the case of frogs which have not been placed under the influence of this drug. It was found that it is very easy so to fasten a frog upon an appropriate holder that, while the foot and body are kept fixed, the general circulation is little or not at all interfered with. The animal may, as we learned, be kept under observation with the microscope for many hours on end, without the slightest fall in the blood-pressure resulting.

The greatest care in attending to details is, it need scarcely be said, necessary in investigations such as those in question here. For this reason, it may be advisable to refer to the manner employed for fastening the frogs for examination. Through the narrow slip of wood upon which the animal rests are cut, near one of its ends, two large holes to allow the passage of the piece of tape which is used to fix the fore-limbs. The circulation through these is necessarily interfered with to some extent by their being so held, but this it is scarcely possible to avoid without curarizing the animal, and thereby introducing a more serious cause of error. One web having been spread out and fixed by threads to the forked extremity of the holder, the other leg is bent upon itself, as when it is drawn up voluntarily by the animal, in which position it is held by a tape passing loosely round it. It is not difficult so to arrange the tape that it will only press upon the leg when extension is attempted. The leg corresponding to the web which is to be examined is prevented from being drawn up by means of pins stuck into the wood on each side of it. These are placed so that, while they effectually prevent the least flexion, they do not press upon the limb when the latter is at rest. Usually one was placed on the inner side of the ankle, a second on the outer aspect of the knee, and a third on the opposite side of the body close to the pelvis. These are stuck somewhat obliquely into the wood, so that they overhang the part next them, and prevent the leg being raised from the board.

In these circumstances the frogs will often remain quite motionless for many hours on end, in a condition more or less closely resembling the so-called "magnetized" state which can be so readily induced in birds and some other animals.

When the tongue or mesentery was examined the frogs were curarized. For studying the pressure in the vessels of the tail of the fish, a small trough similar in principle to that recommended by Caton was used, and in this case an arrangement such as that illustrated by Fig. 3, but without the paper ring, was employed.

I. Changes in the Circulation which result from increased extravascular pressure.

The effects, on the circulation, of raising the extravascular pressure over a limited area, differ so much in the case of the arterioles, the capillaries, and the rootlets of the veins respectively, that we think it best to take these into consideration separately. The changes so produced are so uniform, whether the web, tongue, mesentery, or other suitable part be the object of study, that the same general description will hold good for all of these.

a. *Changes in the arterial circulation.* In the case of terminal arterioles, which break up into capillaries within the field of the microscope, the phenomena observed, as the extravascular pressure is gradually raised, are not by any means what we should expect *à priori*. As the pressure, to which the portion of tissue examined is subjected, is raised higher and higher above that of the atmosphere, the current of blood through the smaller arterioles loses the equable character which it normally presents. A rhythmic variation in rapidity, each increase corresponding with a heart-beat, becomes more and more marked as the extravascular pressure is gradually raised. In other words, a pulse, which could not be detected in the small arteries while the tissue was uncompressed, becomes more and more evident. As a rule there is no perceptible variation in the diameter of the vessel accompanying the successive pulse-beats, which consist merely in a variation of the rapidity of the blood-current. Between the pulse-beats the current is slowed, and when a certain pressure is reached, the column of blood in the artery stands for an instant at rest at each successive interval between the ventricular contractions.

The pressure required to produce this temporary arrest in the circulation through the terminal arterioles, can always be found, for any given vessel, with the greatest exactness. For this reason we have been in the habit of noting it, as giving a definite value which could serve as a basis for comparison in our observations. We will refer to it as the "minimum arterial pressure," reserving, for the present, the question as to how far it corresponds with the actual minimum blood-pressure within the artery.

The influence of the respiratory movements on the blood-pressure of the frog is excessively slight, and a line connecting, in an ideal pressure-curve, the highest or the lowest parts of the pulse-waves would be practically straight. The term "minimum blood-pressure" applies therefore to the lowest points between the primary or pulse-waves.

Reference will be made further on to secondary waves which not infrequently present themselves in the frog, and which are more or less analogous to the Traube-Hering curves with which we are acquainted in kymographic tracings obtained, under certain conditions, from dogs and rabbits. At present, however, we will only consider the phenomena which are found in the normal condition of the animal.

As the extravascular pressure is raised above the "minimum arterial pressure," it is found that the column of blood in the vessel under observation undergoes a momentary retrograde movement between the pulse-beats. The blood advances rapidly for a moment after each ventricular contraction, this being followed by a backward flow, and so on alternately, the current of blood however on the whole progressing.

The duration of the backward flow becomes longer and longer as the pressure applied to the part is increased, until, at a certain point, the blood simply oscillates backwards and forwards in the vessel without making any progress. The pressure required to produce this oscillation without advance is readily found with accuracy for any given artery, as the individual blood-corpuscles can be easily followed with the eye. With an extravascular pressure a very little higher than this, the backward movement overbalances that of advance, and the column of blood is forced out of the vessel, all movement in the field of the microscope ceasing. For the sake of convenience, we will refer to the pressure required to produce this result as the "maximum arterial pressure."

It is to be understood, of course, that the phenomena which we have attempted to describe above, refer to the case of typically healthy animals, in which the circulation in the web is, to all appearance, perfectly normal. In unhealthy frogs it is not at all uncommon to find a more or less marked "pulsatile" circulation in the capillaries and arteries of the uncompressed web.

b. *Changes in the capillary circulation produced by gradually raising the extravascular pressure.* As the extravascular pressure is raised, the blood-flow through the capillaries becomes more and more pulsatile in character. In this the capillary circulation follows a medium course between what is found to take place in the terminal arterioles on the one hand, and the venous rootlets on the other hand, when the pressure applied to the tissue is gradually raised higher and higher above that of the atmosphere. In that part of the capillary plexus which lies nearest the arteriole from whence the blood comes, a temporary arrest of the circulation is seen to occur when a certain pressure is reached, although, as need scarcely be added, the pressure required to produce this is not the same for different points in the artery and arterial capillaries. In the venous capillaries, *i.e.* in that part of the capillary plexus lying nearer the venous rootlets, the changes in the circulation produced by raising the extravascular pressure resemble more closely those which are found in the smaller veins, and which will presently be referred to.

As the pressure applied to the tissues is gradually raised, it is found that a certain number of the capillaries cease to convey blood earlier than others of their neighbours. With a pressure of, perhaps, half of that required to cause complete arrest of the capillary circulation of the portion of tissue lying in the field of the microscope, one or two capillaries no longer admit blood through them, and the number of impervious capillaries usually increases gradually as the pressure applied is raised, until only one or two channels remain for the circulation through the part, these, of course, becoming also impervious when the pressure is raised above the "maximum arterial pressure." This fact, in itself, is only what might be expected, as we should naturally suppose that the resistance due to friction, &c., would scarcely be exactly the same for all the vessels composing a capillary plexus.

More careful investigation, however, brings to light an interesting fact, viz. that it is not always the same capillary vessels which first cease to convey blood on raising the extravascular pressure to a certain height. If, for example, we take a curarized frog, and, having arranged the compressing apparatus in the manner above described, and having sketched roughly the position and relations of the various capillaries which can be seen in the field of the microscope, we mark on our drawing the order in which the capillaries cease to admit the passage of blood-corpuscles on gradually increasing the extracapillary pressure; —if, having done this, we lower the pressure to which the portion of tissue is subjected to 0°, and, after leaving everything untouched for, say, half an hour, and again investigate the order in which the capillary vessels of the same part become impervious on raising slowly the applied pressure, we usually find that there is a more or less marked difference in this respect between the two observations. Occasionally it is found, that those capillary vessels which closed in the one observation with a relatively low pressure on their exterior, are, in the other observation, those which remain longest pervious to the blood-flow; and this, although every possible precaution has been taken to insure that the conditions should remain unchanged.

It is difficult to explain this fact otherwise than by assuming, that the relative diameters of the capillaries in the field have changed in the interval between two such observations—that some vessels have expanded, and that others have contracted, resulting in a change in the amount of friction offered by some capillary vessels as compared with others. And in fact, in favourable instances such a change in the diameter of the different vessels can be verified with the help of an eye-piece micrometer.

Having had the above facts forced upon us again and again during the course of our experiments on the capillary circulation, we were necessarily led to assume that the walls of the capillaries of adult animals are capable of active contraction, or, if the term be preferred, of active change of their elasticity. In some experiments, however, which will be referred to further on, this contractility of the capillary wall is much more strikingly evidenced, placing the matter, we believe, beyond doubt.

c. *Changes in the circulation through the venous rootlets produced by gradually raising the extravascular pressure.*—The small veins are the first to shew any change in their circulation on applying gradually increased pressure over a circumscribed area of the web. With a pressure as low as 20 mm. of water, a distinct diminution of their calibre with increased rapidity of flow through them may often be observed. This diminution in diameter increases markedly as the pressure is raised, being accompanied by a corresponding increase in the rate of the blood-flow through their interior. Not rarely the diameter of a vein may be seen to diminish to $\frac{1}{3}$ of its original calibre, as the pressure applied to the tissue is increased.

As in the case of the arterioles and capillaries, a pulsatile variation in the rapidity of the circulation becomes also evident in the small veins of the compressed part. In these latter, however, if they receive their blood from capillaries lying in the field of the microscope, and therefore subjected to the pressure indicated by the manometer, a temporary arrest does not take place. With each pulse-wave in the arterioles, the flow of blood in the veins becomes accelerated, while, between each pulse-beat, the current is more or less markedly slowed. Only when the blood no longer advances in the arteriole, does the corresponding vein or veins become empty and collapsed. As might be expected, those veins which receive their blood more or less completely from capillaries outside of the compressed area, become collapsed with a very much lower pressure than is otherwise the case; with such veins, a pressure of 25—40 mm. H_2O will sometimes suffice to prevent the passage of blood through their interior, shewing how slight must be the normal blood-pressure in the venous rootlets, as well as the ease with which the blood from a given part of the capillary plexus can be diverted from its normal course.

The great readiness with which the diameter of the veins is affected by relatively slight extravascular pressures, is presumably due, as need scarcely be remarked, to the extreme distensibility or low elasticity modulus of their walls.

II. Intracapillary pressure and elasticity of capillary walls.

It has been long known that capillary vessels may present considerable variations in their diameter at different times. The application of an appropriate stimulus to the web of the frog will, in many cases, cause a dilation of some of the capillary vessels to more than twice the calibre which they previously presented. As one of the illustrations to his interesting paper on the "early stages of inflammation," Lister[1] gives two drawings, taken with the help of a camera lucida, of a capillary vessel before and after stimulating the web. As is well shewn in these figures, the diameter of the capillary, in that instance, became more than doubled as a result of the application of the stimulus. So great an expansion does not, however, always result on stimulating with chloroform, mustard, or other agent exerting a similar action. An increase by about one-half of the initial calibre is perhaps more often observed. The degree of such a dilation depends, of course, very much upon the condition of the capillaries as regards their diameter before the irritating substance was applied.

Expansions and contractions of the capillaries are referred to by most writers who have treated of the phenomena of the capillary circulation as studied with the microscope. Since, however, the variations in the diameter of these vessels are practically always accompanied by a corresponding expansion or contraction of the arterioles, most physiologists have naturally assumed that they are the result of variation in the intracapillary pressure; that, in other words, they are due to the elasticity of the capillary walls. Vulpian[2], for example, in his remarks on the subject, observes—"Les observations de Stricker sont loin d'avoir convaincu tous les physiologistes: la plupart d'entre eux admettent encore que les vrais capillaires ne sont pas contractiles... On les voit subir les influences de l'état de la circulation artérielle, se dilater quand les artères se dilatent, revenir sur eux-mêmes quand les artères se resserrent: mais ce ne sont évidemment pas là des effets impliquant l'existence d'une véritable contractilité."

That the capillaries are very elastic there cannot be the least doubt;

[1] *Phil. Trans.* 1858.

[2] *Leçons sur l'appareil vaso-moteur.* Paris, 1875, T. I. p. 72.

but, that their elasticity alone will not suffice to explain the changes in calibre of the capillary vessels, becomes at once evident when we proceed to study more closely the relation which exists between the intracapillary pressure and the degree of dilation of these delicate tubes.

In treating of this point we must first consider shortly, to what degree of exactness the pressure within the capillaries can be learned by the method we employed. A little consideration will shew, that with such a method we can, at least, measure with accuracy the pressure of the blood in the arterioles at their point of entrance into the compressed part. We can also learn with approximate accuracy the pressure in the veins, by compressing them at a point as far off as possible from the capillaries from which they receive blood. The pressure, however, which is required to cause collapse of veins will be always higher than that which their contents normally present, since the effect of local collapse would be a rise of pressure behind the obstructed part. As regards any given vein, we can only be certain that its internal pressure is below a certain height.

We may, then, in any given web, learn the maximum and minimum arterial pressures, and, with much less accuracy, the venous pressure. For example, we may find in a particular case that the maximum and minimum pressures in the arterioles are 300 and 220 mm. (water) respectively, while in the veins the pressure is not so high as 30 mm. In such a case, the pressure of the blood falls, in passing through the capillaries, to an extent equal to the difference between these values.

If the capillaries were tubes of equal length and diameter we could, knowing the pressures at their two extremities, say at once what would be the pressure at any point in their course; *e.g.* in these circumstances, the pressure at the middle point would be half way between the pressures at their arterial and venous ends. The capillaries are, however, far from being of equal length and diameter. Their relative and absolute diameters vary, moreover, to all appearance, incessantly, and, if it were possible to learn the pressures at different points of all the capillary vessels of a limited area, it would certainly be found that these pressures undergo a continual relative variation. This assertion we make on the strength of the phenomena observed on raising the extravascular pressure over a given area of the web several times at intervals of half an hour or so, the conditions being kept as nearly as possible unchanged during the observation.

Under these circumstances we find, as already stated, that the order in which the capillary vessels cease to convey blood is not necessarily, or even usually, the same at each successive compression. At one measurement we may find that, of two capillaries lying side by side, one will collapse with a pressure of, let us say, 250 mm. (water), while its neighbour continues to convey blood until a pressure of perhaps 350 mm. is applied; while, on again raising the pressure in an hour afterwards, the order in which they collapse on applying pressure may have become reversed.

We cannot assume, of course, that the actual intravascular pressures in two such capillaries bear exactly the same relation to one another as the pressures required to cause their collapse. We should expect that the difference between the actual pressures would be less than that between the collapsing pressures. We have, in fact, no means of learning with certainty the blood-pressure in a given point of a given capillary. We can readily find the pressure in the terminal arterioles and, approximately, the pressure in the venous rootlets, but the exact distribution of the pressure in the intervening capillaries can only be roughly judged of by noting the order in which these collapse on raising the extravascular pressure. When, therefore, the intracapillary pressure is spoken of in the pages of this communication, it must be understood that we are not referring to any given value which it is possible to measure.

In seeking to find in how far the intracapillary pressure is capable of influencing the diameter of these vessels, we could scarcely wish for a more convenient method of enquiry than that of simply raising the extravascular pressure, and observing the effect on the calibre of the capillaries. An elevation of the extracapillary pressure equal *e.g.* to 100 mm. (water) will, as need scarcely be remarked, diminish the force which distends the wall of the vessel to the same extent as a diminution of the intracapillary pressure by 100 mm. It is found that the effect, on the diameter of the capillaries, of raising the extravascular pressure nearly high enough to cause collapse of these vessels, is usually so slight as to be barely appreciable. In no case have we seen capillary vessels vary in diameter under these circumstances to anything like the extent to which we know they are capable. Whether these vessels be dilated as a result of the application of a stimulus, or whether they present a tolerably normal calibre, they contract but very slightly when the extracapillary pressure is raised.

Their diameter may sometimes under these circumstances diminish by 10 or 15 per cent., but more often the change in calibre is too slight to admit of measurement.

There are other ways, of course, of obtaining information regarding the relation which exists between the capillary pressure and the diameter of these vessels. And the most evident of these is, to lower the intravascular pressure as much as possible, and observe the effect on the degree of dilation of the vessels. An experiment, which we have frequently repeated, is the following. Having spread out the web of a frog under the microscope, and measured the diameters of a number of capillaries at points which will be easily found again, the foot is cut off at the ankle, and the measurements of the capillaries repeated. If care be taken to avoid stretching of the web, it will be found, that the capillaries do not empty themselves completely on amputating the foot, although the severance of the large vessels of the leg must have reduced the capillary pressure to that of the atmosphere, or but very little above it. It is found, moreover, that, as a rule, the capillaries are but very little narrower than they were before the foot was separated from the trunk.

We need not dwell further upon this point; the examples we have given shew clearly enough, that modifications of the intracapillary pressure, much greater than those which can normally occur, influence but slightly the calibre of the capillaries. The walls of these latter, in other words, are elastic, but not sufficiently elastic to explain the great variations in diameter which we know they can present.

III. Contractility of the capillary wall.

The facts noted in the foregoing pages, appear to us incomprehensible, if we go upon the supposition that the capillary walls are elastic but non-contractile. Considering the importance of the subject, however, we did not think it advisable to rest content with the evidence above mentioned in favour of assuming that the capillaries are contractile, and the more so, that, with the method of enquiry which we employed, it was exceedingly easy to make control experiments of various kinds. It is unnecessary to give a detailed account of these, and we need only refer to one experiment, which, we believe, is sufficiently conclusive of itself. The conclusions that can be drawn from it appear so unavoidable, that it would only lengthen this paper unnecessarily to give the details of other experiments the results of which point in the same direction.

In seeking to find whether or not the intracapillary pressure and the diameter of these vessels bear a certain definite relation to one another, it is only necessary to find the means of varying these two factors independently of one another. This, it need scarcely be said, does not present the slightest difficulty. The diameter of the capillaries can be increased by the application of an irritant to the part, and it is easy so to graduate the stimulation, that either only slight dilation, lasting for a short time, or maximal dilation of longer duration can be produced. The intracapillary pressure can also be reduced at will; and the most convenient method of doing this, we found ready to hand in Goltz's "Klopfversuch." On tapping the abdomen with the handle of a scalpel, the blood-pressure rapidly falls, and the extent of the fall in the peripheral arteries can be easily learned by the method employed by us. As a further means of measuring the blood-pressure, we frequently fastened a small mercurial manometer in one aorta of the previously curarized frog. This can be done on the ordinary water or land frog, but we were fortunate enough to be able to make our experiments on this subject on the gigantic *R. esculenta* which are obtained from Hungary, a number of which were kindly placed at our disposal by Prof. Goltz. It is necessary, before fastening in the manometer, to render incompetent the valves situated at the junction of the aorta chosen and the aortic bulb. This can be easily managed by means of a probe, without a drop of blood being lost in the operation. In a frog provided with such a manometer, the effect of tapping the abdomen, on the aortic as well as on the peripheral arterial pressure, can be followed with considerable accuracy. The aortic pressure falls rapidly to a point near zero, and the peripheral pressure sinks hand in hand with it. After tapping for a short time, it is found that an extravascular pressure of 10—15 mm. water suffices to arrest the entrance of blood into the compressed part; while, a few minutes after ceasing to percuss the abdomen, both the central and peripheral blood-pressures rise, until their former values are more or less exactly attained.

To produce dilation of the capillaries we found chloroform the best suited. The application, for an instant, of a camel's hair pencil soaked with chloroform, produces immediately a maximal dilation of the vessels of the part of the web with which it has come in contact. It is necessary to wash the web immediately afterwards with a stream of water, as, otherwise, capillary *stasis* results from too strong irritation. As Lister[1] has remarked, even the vapour of chloroform suffices to cause an evident hyperaemia of the web.

As already mentioned, application of an appropriate irritant will sometimes cause a dilation of the capillaries to fully twice their previous diameter. This is usually accompanied by a temporary rise of the aortic pressure, due to stimulation of the sensory nerves, and which does not appear if the sciatic has been previously severed. Where the nerve has been cut, the pressure within the arteriole or arterioles rises but little (seldom so much as 30—40 mm. water) as a result of their dilation. It cannot, however, be doubted that, in these circumstances, the intracapillary pressure has risen somewhat as a result of the stimulation of the part. That this increased internal pressure, however, is not the cause of the dilation of the capillaries, becomes at once evident when, by tapping the abdomen, we lower the arterial pressure to nearly that of the atmosphere. We find that the capillaries remain dilated, although the aortic pressure has been so greatly reduced that the two columns of mercury in the manometer stand at nearly the same height. That the pressure in the peripheral arterioles has fallen hand in hand with the central blood-pressure, is shewn by the fact that an extravascular pressure of 10 or 15 mm. water suffices to arrest the entrance of blood into the stimulated part, and to cause collapse of most of the capillaries. A few minutes after having ceased the tapping, both central and peripheral blood-pressures rise to their former height, and the experiment can be repeated as often as desired. With these extreme variations of their internal pressures, therefore, we find that the diameters of the capillaries vary but slightly, and that, with an intracapillary pressure scarcely higher than that of the atmosphere, they remain, in some cases, nearly twice as wide as they were before they were dilated by the application of the chloroform[2].

It might, perhaps, be supposed that the chloroform, by chemical action, had changed the physical properties of the capillary walls, this change being accompanied by new elastic properties. The fact, however, that, where the irritation has not been too strong, the hyperaemia and dilation of the vessels soon disappear, shews us that this dilation must be looked upon as an essentially vital reaction. Moreover, in the case of the hyperaemia which follows temporary anaemia, and to

[1] *Loc. cit.*

[2] The diameter of the vessels, it should be added, was not judged of by the eye alone, but with the help of a good eye-piece micrometer.

which we shall have occasion to refer further on, the same want of relation between the degree of dilation of the capillaries and their internal pressure, can also be shewn to exist. In this case, also, the dilated capillaries remain expanded, although by the "Klopfversuch" their internal pressure has been reduced to but little above zero.

It may be as well to remark, in passing, that certain restrictions must be made in applying the term "contractility" to express the nature of these vital changes in the calibre of the capillaries. It is possible that the term "change of elasticity" may in reality be more appropriate. In the case of striped muscle, we cannot speak of a change of elasticity as the cause of the contraction of the fibres, but with smooth muscles, and with the capillary walls, the case is different. With them, for all we know to the contrary, the expansions and contractions of which they are capable, may be the result of a change in the statical relations of the ultimate molecules. Whether this be the case, or whether their contractions and expansions are due to molecular changes similar in principle to those which apparently produce the contractions of striped muscle, can scarcely be decided, we imagine, in the present state of our knowledge of the subject. Under these circumstances, we prefer to keep to the term "contractility," which does not imply any theory as to the intimate nature of the process which causes the changes of form of which the capillary walls are capable.

In the face of the above mentioned facts, we do not see any way of escape from the conclusion that the capillaries are contractile as well as elastic. The question naturally arises, whether this contractility resides in some anatomically differentiated part of the capillary wall, or whether it be a property inherent in the wall as a whole. On this point, as is well known, differences of opinion exist among those physiologists who have ascribed a contractile power to the capillaries.

It may, perhaps, be as well that we should refer to one or two of the chief papers on this subject.

Before Aeby, Auerbach and Eberth, by means of v. Recklinghausen's "silver method," had shewn that the capillaries are made up of endothelial cells, Stricker[1] had been led, from his investigations on the structure of the capillaries in the *membrana nictitans* of the frog, to the conclusion that these vessels are contractile. In

[1] Stricker. "Unters. üb. d. cap. Blutgefässe." *Sitzb. d. Wiener Akad.*, Bd. LI. 1865.

a second paper[1], published in the following year, he described the changes which he had seen take place in the capillaries of the tail of the tadpole, under the influence of various stimuli. Soon after this, Golubew's[2] article on the subject appeared, giving an account of the contractions and expansions of the capillary walls in parts removed from the frog. He ascribed to the contraction and expansion of the nuclei, which can be seen in the wall of the capillaries in fresh specimens in the form of spindle-shaped thickenings, and to which he gave the name of "spindle-elements," those changes in the internal diameter which he found to result on passing induced currents through the piece of tissue examined. These fusiform elements he found to contract on the application of a stimulus, blocking up more or less completely the lumen of the capillary. Golubew's observations were confirmed by v. Tarchanoff[3] in a series of experiments made in v. Recklinghausen's Institute in Strassburg, he, also, ascribing to the fusiform elements alone, the power of contracting, and assuming that the rest of the capillary walls played a purely passive rôle. The facts brought to light by these observers did not, however, suffice to convince physiologists that the contractility of the capillaries plays a part in the regulation of the peripheral circulation, seeing that, to cause an appreciable change in the diameter of these vessels, relatively strong stimuli must be applied, weak electric currents, for example, having little or no effect on the fusiform elements. That spontaneous changes in the diameter of the capillaries in the tadpole's tail may take place, could not, of course, be taken as proof that the capillaries of adult animals are also capable of active changes of calibre, even if it had been shewn that elasticity alone could not account for the phenomena observed.

More recently Severini[4], in his able monograph on the innervation of the blood-vessels, has laid great weight on the contractility of the capillaries. He found that the fusiform elements of Golubew react with great readiness and certainty when a stream of oxygen or of carbonic acid is passed over the portion of tissue examined, and which has previously been placed in an appropriate moist chamber. Oxygen he found to cause "invariably" a swelling of the parietal

[1] "Studien üb. d. Bau u. d. Leben d. Capill." *Sitzb. d. Wiener Akad.*, Bd. LII. 1866.

[2] Golubew. *Arch. f. mikrosk. Anat.*, Bd. V.

[3] "Beobacht. üb. contractile Elemente in den Blut u. Lymphcapillaren." Pflüger's *Archiv*, Bd. IX. 1874.

[4] *Ricerche sulla innervazione dei vasi sanguigni.* Perugia, 1878.

nuclei which reached a maximum in 1—2 minutes, this swelling being accompanied by a shortening of the nuclei, and causing a considerable narrowing, rarely complete closure, of the lumen of the vessel. Occasionally also, but not always, there took place a uniform contraction of the capillary wall at parts where no nuclei were to be seen. The action of carbonic acid, on the other hand, he found to produce an elongation and thinning of the fusiform elements, invariably accompanied by a dilation of the lumen of the vessel.

Severini's results are opposed to those of Tarchanoff[1], who investigated the action of both O and CO_2 on the capillaries, and obtained only negative results[2].

The weight laid by most of the above-mentioned observers on the part played by the fusiform nuclei, led us to watch with care the outline of the capillaries in their contracted and expanded conditions. When much contracted, as is well known, it is not rare to find at some point in the course of one or more of the capillaries in the field of the microscope a bulging inward of the wall of the vessel, the lumen of which is thereby so much narrowed that the individual blood-corpuscles only pass the obstruction with difficulty.

On the other hand, it is certain that capillary vessels may be seen to vary greatly in diameter without any localized contraction or expansion being visible. The capillary tube expands or contracts as a whole, its diameter remaining equal throughout its whole length. We cannot therefore agree with Golubew, Tarchanoff, Severini, &c., in ascribing to the fusiform elements alone the power of active contraction, and believe that, under normal conditions, it is by the contractility of the capillary wall as a whole, that the diameter of these vessels is changed.

[1] *Loc. cit.*

[2] On becoming acquainted with Severini's work I repeated, in conjunction with my friend Dr v. Mering, these experiments on the influence of O and CO_2 on the capillary walls. We employed the *membrana nictitans* and mesentery of the water-frog, and made also a few observations on the same tissues taken from the *Hyla arborea*. The conditions mentioned by Severini were copied with the most scrupulous care. The gases were well washed, and a No. 10 immersion Hartnack was used to watch the capillaries. In no single instance, however, were we able to observe the slightest change in the calibre of these vessels, either with oxygen or with carbonic acid. Our results therefore coincide with those of Tarchanoff. Why they are so strikingly at variance with those of the distinguished Italian Professor, must presumably lie in some difference in the conditions under which the experiments were made, although, as already observed, the directions given by Severini were followed scrupulously by us.—C. S. Roy.

IV. Effects on the capillary circulation of localized temporary anaemia.

If, after having produced anaemia of the portion of web lying in the field of the microscope, by raising the pressure applied sufficiently to overbalance the arterial pressure, and thereby cause cessation of the circulation through the part, we suddenly reduce the pressure again to 0^0, it is invariably found that a more or less marked active hyperaemia of the part results, which, after a few minutes, gradually disappears. If the localized anaemia has been allowed to last for five or ten minutes, the resulting hyperaemia is often very intense—the arteriole or arterioles frequently dilating to more than twice their former diameter; the capillaries also are markedly dilated as well as the veins, and the flow of blood through the part is very greatly increased in rapidity. Anaemia lasting only two or three minutes is usually followed by a distinct hyperaemia differing naturally in degree in different cases, this effect being, however, much more marked when the anaemia has been of longer duration.

That the temporary cessation of circulation is the important if not the only factor in producing this hyperaemia, is shewn by the fact, that its intensity increases with the duration of the preceding anaemia, which would scarcely be the case if the pressure of the cushion acted as a mechanical irritation, thereby producing reflex congestion. Independently of this fact, it would be difficult to believe that the gentle pressure of the delicate, flexible membrane could act as a mechanical stimulus in the ordinary sense of the term. Examination of other parts of the same web shews that this active congestion is strictly localized to the part previously rendered bloodless.

It should be added that the same phenomenon occurs, under similar conditions, in the case of the tongue and mesentery.

Cohnheim[1] appears to have been the first to draw attention to the fact that anaemia of short duration is invariably followed by hyperaemia. This was doubtless known before to many physiologists, but Cohnheim seems to have first clearly stated the facts of the case. He found that, after the circulation of the frog's tongue had been arrested for some time by tying a ligature round the root of the organ (a piece of soft leather being interposed to prevent cutting of the tissue by the thread), the vessels became, on removal of the ligature, greatly dilated, and

[1] Cohnheim, *Untersuchungen üb. d. embolische Processe*, Berlin, 1872.

this, whether, during the time that the tongue was ligatured off, they were filled with blood or not. Cohnheim's experiments, however, seemed to have more of a pathological than a physiological signification, since the anaemia was usually kept up for, at least, a few hours. The same effect of temporary anaemia was also a marked feature in Mosso's[1] experiments. These were made on the excised kidney and liver, an artificial circulation of defibrinated blood being carried on through them by an arrangement which admitted of keeping the arterial pressure constant at any desired height, while, at the same time, any changes in the volume of the organ, and of the rate of outflow from the veins, could be accurately followed. He found that, on interrupting the artificial circulation for a short time, the vessels, on readmitting blood by the artery, became dilated, the outflow from the veins becoming also increased, an effect which gradually disappeared on continuing the injection of the blood.

The same influence of the blood supply of the tissues on the degree of dilation of the vessels is illustrated by the fact, well known to most physiologists, that, on injecting blood into an excised organ or amputated limb, the flow of the blood, which is at first comparatively free, becomes soon more difficult from contraction of the vessels. Even after *rigor mortis* has set in, this result of the injection of blood is found to take place, as was shewn by the experiments of Bernstein[2] and Severini[3] as well as by Mosso, who found that even 48 hours after removal of the kidney these variations in the diameter of its vessels could be observed.

But, in the living healthy body, this hyperaemia following anaemia is, apparently, a phenomenon of very frequent occurrence. Even relative anaemia is followed by a moderate congestion, as is illustrated by the well-known fact that, after having held one hand raised above the head for some minutes, the pallor thus produced is succeeded, on the hand being again lowered, by a more or less well marked redness, contrasting with the paler colour of the hand which has not been raised. The congestion which results on removing an Esmarch bandage from a limb to which it has been applied, is apparently another example of the same phenomenon. If a portion of the skin of the back of the hand be gently pressed with the finger so as to

[1] Mosso, Von einigen neuen Eigenschaften der Gefässwand." Ludwig's *Arbeiten*, 1874.

[2] Bernstein. Pflüger's *Archiv*, Bd. xv.

[3] Severini. *Loc. cit.* p. 141.

cause anaemia, this, if it have been kept up for a few minutes, is followed, on removal of the finger, by an evident hyperaemia, which lasts for a short time, and which is the more easily produced the more active the circulation of the skin is at the time. Numberless examples of the same fact, viz. that anaemia, produced experimentally, is followed by congestion, readily rise to the mind. We have, however, referred to a sufficient number to recall to the reader how constantly it shews itself under suitable conditions.

To return to the frog's web. This secondary hyperaemia we never found wanting in the many hundred observations which we were led to make on the subject. Its intensity and duration are, as already mentioned, in direct proportion, speaking roughly, to duration of the foregoing anaemia.

We considered it worth while to investigate with some care the mechanism by which it is brought about. That it is not due to any reflex action through the cerebro-spinal vasomotor centres, is shewn by the fact that it can be produced with equal certainty after section of the sciatic nerve, and this, moreover, in cases where, by electrical stimulation of the peripheral end of the cut nerve, strong contraction of the arterioles of the web could be produced. In these instances, therefore, a part or the whole of the vasomotor nerves passing from the spinal cord to the web were contained in the sciatic, and yet section of this nerve produced no appreciable influence on the appearance of this localized congestion following temporary anaemia. We may, therefore, exclude reflex dilation through the cerebro-spinal centres in enquiring into the mechanism of this congestion. We must, then, look for its cause in the action of some peripheral vaso-regulating arrangement.

The existence of some such peripheral vasomotor mechanism was first definitely proved, we believe, by Goltz's[1] classical experiment on the rabbit. After having severed, by means of a galvano-cautery, all the tissues of the thigh of a rabbit, with exception of the crural artery and vein, so that these latter formed the only vital communication between the leg and the rest of the animal, Prof. Goltz shewed that localized stimulation of the skin of the leg, such as that produced by the application of oil of mustard over a limited area, still caused a well marked localized congestion. There can be no doubt, therefore, of the existence of some mechanism by which the degree of dilation of the vessels of the skin is capable of being regulated independently

[1] Goltz' *Bericht über die Naturforscher-Versammlung zu Königsberg*, 1860.

of the cerebro-spinal vasomotor centres. The natural conclusion, of course, would be that there must be peripheral vasomotor ganglia capable of producing, by reflex action, modifications in the degree of dilation of the vessels of the skin in answer to stimuli applied to the latter. There are, however, various objections to this theory of peripheral vasomotor ganglia, the most important of which is, that as yet no anatomical evidence of the existence of such structures has been produced, in spite of careful microscopical examination of the web of the frog.

Moreover, as has been pointed out by Severini[1], if we are to accept the existence of these peripheral ganglia, we must ascribe to them rather complicated functional properties, and assume that there pass to them four different kinds of nerves, viz., vaso-constrictor and dilator fibres from the cerebro-spinal centres, and constricting and dilating fibres from the skin, besides those which leave them to supply the vessels.

From the influence of temporary anaemia in producing dilation of the vessels of the skin, we must, if we are to assume the existence of peripheral ganglia, further suppose, that these hypothetical structures are capable of regulating the relation between the nutritional requirements of the part and the degree of dilation of the blood-vessels. Until there is anatomical evidence of the presence of structures which we can suppose capable of performing functions of so complicated a nature, it must be felt that the physiological evidence, which tends to prove the existence of these ganglia, may, perhaps, be capable of another interpretation.

If, from considerations such as those above mentioned, we reject the theory which requires us to assume the existence of peripheral ganglia, the only apparent explanation of the facts of the case is, that those vaso-motor phenomena, which are undoubtedly due to some peripheral vaso-regulating mechanism, are brought about, either by some stimulus acting directly on the walls of the vessels, or indirectly on these through the medium of nutritive changes of the tissue elements. For example, we might suppose that a diminution in the amount of O or other constituent of the blood present in the tissue, such as would be produced by anaemia due to mechanical compression, or an increase of the CO_2, or other product of the chemical changes of living tissue-elements, might lead to dilation of the vessels as a result of chemical action.

[1] *Loc. cit.*

And, in reality, independent of those facts which lead us to hesitate in accepting the theory of peripheral ganglia, there is much that might be advanced in support of this view of the direct action of chemical changes on the walls of the vessels.

That, in the embryo at least, a kind of vaso-motor regulation exists, independent of the nervous system, is shewn by an interesting experiment of Vulpian's[1].

If, about the fourth day of incubation, a small drop of nicotine be applied to a point on the *area vasculosa* of a chick, it is found that, in a short time, a well-marked congestion shews itself at the irritated part. And this congestion may become so great, that the rest of the vascular system is nearly emptied of blood. This experiment shews that dilation of the vessels may result from stimulation in the absence of any vaso-motor nerves, but from it, we cannot, of course, draw definite conclusions as to the mechanism of the peripheral vaso-regulating arrangements in the adult animal.

On the whole, the balance of evidence appears to be opposed to accepting the theory of peripheral vaso-motor ganglia, at least in so far as the frog's web is concerned. Whether these exist or not, this constant occurrence of hyperaemia as a result of anaemia, either complete or incomplete, seems to us to throw much light on the manner in which the local circulation is carried on under normal conditions. It shews us, that there is a local mechanism independent of the centres in the medulla and spinal cord by which the degree of dilation of the vessels is varied in accordance with the requirements of the tissues.

It must not be forgotten, however, that the relation between the blood-supply and the needs of the tissue-elements may be varied in other ways than by varying the quantity of blood which passes through the tissues, as when anaemia is produced experimentally. The possibility, or even probability, naturally forces itself on the mind, that various congestions of undoubted peripheral origin may be caused by the same mechanism which produces the hyperaemia following temporary diminution or arrest of the blood-supply. It is not difficult to imagine, that an increase in the chemico-vital changes of the tissue-elements will have the same influence on the degree of dilation of the vessels as temporary anaemia. In both cases there will be a relative diminution of some of the constituents of the blood and a relative accumulation of the products of tissue change, one or both of which would probably, as in our experiment, stimulate the vessels to dilate.

[1] *Revue des Cours Scientifiques*, Vol. III. p. 744.

The dilation of the vessels in inflammation is very frequently ascribed to paralysis. We must not forget, however, that, in the paralysed condition, smooth muscular fibres need not, as is the case with striped muscles, be fully expanded, but might more reasonably be supposed to assume, when paralysed, a medium position between full expansion and full contraction. Indeed, in the present state of our knowledge of the subject, to speak of paralysis of the vessels seems to us only one way of escaping from a confession of ignorance as to the nature of this inflammatory dilation. That, however, the muscular walls, in the early stages of inflammation at least, are not paralysed, is not difficult to prove. If, after having cut the sciatic of the frog, and placed its peripheral end on electrodes, we apply chloroform to the web, taking care not to stimulate too strongly, it is found that the dilation of the arterioles thus produced can be made not only to disappear, but that the stimulation of the nerve will, in many cases, cause nearly complete closure of the lumen of the arterioles. It is necessary to add, in passing, that considerable differences exist as to the degree to which the walls of the arterioles of the web respond under normal circumstances to stimulation of the sciatic. The above experiment we have repeated successfully some three or four times. Evidently the dilation of the vessels produced by chloroform, and which apparently corresponds with that of the first stage of inflammation, is not due to "paralysis."

The view, however, that this inflammatory hyperaemia, under which head we class that produced by stimuli such as chloroform, croton oil, mustard, &c., may be most simply explained by taking it to be due to the same mechanism as the congestion which follows anaemia, has at least a few facts to support it. In inflammation we know that the rapidity of the chemico-vital tissue changes is increased, and it is very probable, that the application of the irritants above mentioned also stimulates the cells, with which they come in contact, to increased as well as to abnormal vital changes. We have here the same increase in the demand for blood which is produced by temporary anaemia.

In the case of the congestion produced by stimulating vaso-dilator nerves, the possibility certainly deserves consideration, that the hyperaemia so caused is not due to an inhibition of the constricting vasomotor nerves through the medium of peripheral ganglia, but is brought about indirectly by a change in the relation between the tissue-changes and the blood-supply. The fact that vaso-dilating nerves exist in the sciatic was clearly shewn by Goltz[1], whose experiments have since

[1] Goltz. "Ueber die gefässerweiternde Nerven." Pflüger's *Archiv*, Bd. IX. 1874; and Zweite Abhandlung, Pflüger's *Arch.*, 1875.

been repeated and corroborated by various observers and notably by Bernstein. There is still, undoubtedly, much that is obscure in the facts known regarding these vaso-dilator nerves, and Severini[1] appears to hold a perfectly tenable position in claiming that the experiments of Goltz and his followers may be explained if we assume that trophic nerves exist in the sciatic, stimulation of which causes, indirectly, dilation of the vessels in the same way as temporary anaemia produces congestion. To enter upon this question would, however, lead us too far from our subject.

In passing, we may remark that the congestion which follows stimulation of vaso-constrictor nerves, is very probably a result of the anaemia which is produced by contraction of the walls of the arterioles. This congestion can be very well seen in the web after stimulating the sciatic for a few minutes. It has commonly been ascribed to exhaustion of the stimulated vaso-constrictor nerves or muscles. As is known, even during stimulation of vaso-motor nerves, the anaemia thereby produced may diminish considerably and even be replaced by hyperaemia. Since we know that diminution or arrest of the blood-supply produced by other means, causes secondary congestion, it appears to us more reasonable to assume, that anaemia caused by vaso-constriction has the same result, than to fall back upon some theory of exhaustion of vaso-motor nerves, concerning attributes of which we are comparatively ignorant.

The congestion which follows compression of a portion of the web is not due to dilation of the arterioles alone. As we have already mentioned, the dilation of the capillaries is greater than can be explained by the increase of their internal pressure. The calibre of the venous rootlets is also increased, a change which is apparently active, like that of the arterioles and capillaries.

We have already shewn that the capillary vessels are capable of varying their diameter independently of one another. The conclusion, that each capillary is capable of varying its calibre in accordance with the requirements of the tissues which it supplies with blood, appears to us, in the light of the facts considered in the above pages, to be perfectly logical.

V. Capillary Pulse.

As one constant result of raising gradually the extravascular pressure over a limited area of the web or other suitable part, we mentioned the appearance of a pulsatile acceleration and slowing of

[1] *Loc. cit.*

the blood-current in the arterioles, capillaries and veinlets. This capillary pulse can always be produced by pressure such as we employed, and we have found it a convenient means of counting the heart-beats, with which it is synchronous.

As is well known, the flow of the blood through the peripheral vessels is, in normal circumstances, almost perfectly equable, so much so, that it is usually impossible, even with the closest attention, to count the number of heart-beats per minute by noting the slight variations in the rapidity of the blood-flow in the arterioles. On the other hand, when, by application of an irritant such as mustard &c., a condition apparently corresponding with true inflammation is produced, the flow of the blood in the capillaries usually becomes more or less markedly pulsatile. That, in this latter case, the appearance of a capillary pulse cannot be ascribed to the diminution of friction alone, which must result from the dilation of the vessels, is shewn by the fact that the dilation of the vessels of the web which follows temporary anaemia, does not lead to the appearance of a pulsatile blood-flow in the capillaries. The diameter of the arterioles and capillaries may vary, as is well known, within pretty wide limits, but neither with narrow vessels nor with wide vessels is a capillary pulse to be seen under physiological conditions. As soon, however, it would appear, as the vessels are contracted or expanded in a manner, or to an extent, which is not in co-ordination with the mechanism by which narrowing and widening of the peripheral vessels are physiologically brought about, we find a capillary pulse making its appearance: as, for example, when narrowing is produced by raising the pressure outside the elastic walls of the vessels, or when a pathological change in the properties of the latter, accompanied by a maximal dilation, such as occurs in the vessels of inflamed parts, results from the application of an irritant.

In man, the appearance of a peripheral pulse, under conditions analogous to those produced by the pressure of our little air cushion, is well illustrated by the behaviour of the retinal vessels on pressing with the finger the bulb of the eye. As is well known, even slight pressure of the bulb immediately produces a pulsation in the retinal vessels, synchronous with the heart, and usually first noticeable in the veins.

In the capillary pulse which can often be seen in the vessels lying under the finger nails, and to which attention has been called by Quincke, we have another example of the same phenomenon. The whitish area, which can readily be made to appear under the nails by extending the fingers fully, and which is more or less constantly present in some persons and in some diseased conditions, is evidently due to pressure upon the vessels at that part. The pulsatile advance and retirement of the red margin is, therefore, presumably produced in the same way as the retinal pulse or that in the small vessels of the frog's web on the application of pressure.

We have already described the general characters of this peripheral pulse, which is produced by pressure, in the arterioles, capillaries and veinlets of the web, tongue and mesentery of the frog. These characters, however, vary within certain limits in different animals. They also vary more or less markedly at different parts of the same animal, and for any given part when the conditions are modified. For studying these variations, our method of investigation gives us considerable facilities, since it enables us to express several of the phenomena numerically. For example, the height of the pulse, or in other words the difference between the "maximum" and "minimum arterial pressures" in any given vessel of the web may be compared with that in other vessels or with the extent of the oscillations of a mercury manometer tied in one aorta. Experiments of this kind soon shewed that the height of the pulse-wave in the peripheral arterioles, *caeteris paribus*, rises or falls with the rise or fall in the height of the aortic pulse-wave. As might have been expected, we found also, that, while the maximum and minimum aortic pressures remain practically unchanged, the height of the pulse at the periphery may vary within certain limits. It is impossible, however, to draw very absolute conclusions from these experiments, for, in some instances, the aortic bulb appeared to contract so completely after each ventricular systole as to shut off, for an instant, the communication between the manometer and the blood in the uninjured aorta, so that the oscillations of the manometer were smaller than would otherwise have been the case. Besides, as need scarcely be observed, the interruption of the circulation through one aorta, necessarily introduced a cause of error whose value could only be guessed at. We give extracts from the notes of two of these experiments, in order to illustrate the general nature of the results arrived at.

EXP. 1. Large Hungarian frog. Curarized. Pressure in large arteriole of web; minimum 340, maximum 380 mm. water.

Manometer then fastened in left aorta after valves at its root had been rendered incompetent. The "Klopfversuch" reduced pressure in manometer to nearly zero, shewing that valves were sufficiently torn through.

Ten minutes afterwards in the artery of the web which had been chosen the

minimum pressure = 220 mm. water,
maximum pressure = 240 mm. water,
aortic pressure, minimum = 17·5 mm. Hg.[1] (= 235·8 mm. water),
„ „ maximum = 19·5 mm. Hg. (= 265 mm. water).

On repeating the measurement of the pressure of the arteriole immediately afterwards, it was found viz.:

minimum = 215 mm. water,
maximum = 240 mm. water.

In this instance, the maximum and minimum pressures at the periphery corresponded more closely with those indicated by the aortic manometer than was the case in the rest of our experiments made in the same way.

Exp. 2. Large Hungarian frog. Curarized. Section of right sciatic in the thigh. Manometer in left aorta, the valves of which had been torn through.

After an hour, pressure in an arteriole of web of right side,

minimum = 190 mm. water,
maximum = 250 mm. water.

Pressures in mercury manometer,

minimum = 21 mm. Hg. (285 mm. water),
maximum = 22·5 mm. Hg. (304·7 mm. water).

On again measuring, same values found.

Left leg then pencilled with diluted acetic acid, after which the mercury manometer shewed

minimum = 22 mm. Hg. (299 mm. water),
maximum = 26·5 mm. Hg. (360 mm. water).

In artery of right web previously chosen, pressures were

minimum 200 mm. water,
maximum 325 mm. water.

In this experiment we were not able to convince ourselves that the contraction of the aortic bulb did not more or less completely close the passage from the manometer to the right aorta during the interval between the ventricular contractions.

It is needless to give further notes of this kind of experiments. They shew clearly enough, amongst other things, that the height of the pulse in the arterioles is governed *caeteris paribus* by the height of the pulse in the aorta—a fact which one would scarcely think of doubting.

[1] Measured with cathetometer.

The influence of the degree of dilation of the peripheral vessels upon the height of the pulse-wave in them need not detain us long. Wide vessels shew a higher pulse-wave than narrower ones, although, unless the arterioles are much contracted, the influence of their diameter on the height of the pulse is not great. In the different arterioles of both webs the maximum and minimum pressures are nearly of the same height respectively for any given animal. It is unusual, in measuring the maximum pressures in the various arteries of the webs of a given animal, to find that these differ from one another to the extent of more than 15—20 mm. H_2O. Any exceptions to this are apparently due to some rise or fall of the aortic pressure while the measurements are being taken, or else to extreme contraction, due to some local cause, of one or more of the vessels. Where an arteriole becomes so narrow that its diameter approaches that of a capillary, the maximum and minimum pressures are relatively low, the maximum however being relatively lower than the minimum, the pressures in the other vessels being taken as a standard to go by.

When we compare the minimum pressures in different arteries of the same animal, it is found, as a rule, that they vary somewhat more amongst themselves than do the maximal pressures. In measuring the minimum pressure, it is necessary that the blood, which passes the point watched, should enter capillaries which are fully exposed to the pressure indicated by the manometer connected with the instrument. In measuring the maximum pressures, on the other hand, it does not matter much whether the capillaries supplied by the compressed vessel be subjected to pressure or not. On this account, it is possible to measure the maximum pressure in a larger number of arterioles than are fitted for allowing the minimum pressure to be measured. Still, our observations seem to indicate, that the minimum pressures in the various arteries of any given web vary more among themselves than do the maximal pressures—a fact which, we are inclined to think, must be due to a difference in the elasticity of the capillaries supplied by different arteries.

In seeking to find the mechanism which produces this capillary pulse in compressed parts, there are two possibilities which naturally present themselves. Either that, normally, the rise and fall of pressure, which constitute the pulse-wave, are propagated as far as the capillaries, or, that the pressure applied, obstructing to a certain extent the passage of the blood through a circumscribed area, has had the effect of causing the arteries, say of the hind limb, to contract rhythmically behind each pulse-wave, pushing the latter forward by a vermicular contraction of their walls.

The latter explanation of the appearance of a pulse on applying pressure, it is scarcely possible to accept; for, did such vermicular contraction of the arteries take place, we should expect to find some evidence of it on examining the capillary circulation of those parts of the web which lie outside of the compressed area. No capillary pulse, however, shews itself in those portions of the web which are not pressed upon, nor do the arterioles of the compressed part shew, as a rule, any appreciable variation in diameter with each pulse. We are forced, therefore, to assume that normally the blood-pressure in the arterioles rises and falls with each heart-beat.

If we accept this, and it seems impossible to avoid accepting it, the question arises,—why the blood-flow through the capillaries, instead of being equable, is not normally pulsatile, as we should expect. In many cases the height of the pulse-wave in the arterioles is more than 30 per cent. of the maximum arterial pressure, and yet no evident pulse could be seen in these cases on examining the uncompressed tissue. It is not very easy, for example, to explain, at first sight, how, with a maximum and minimum arterial pressure of 300 and 200 mm. water respectively, the flow of blood through the capillaries can be other than pulsatile.

When we recall the peculiar conditions, however, under which the capillary circulation is carried on, an explanation of this apparent anomaly is not very difficult to find. In these narrow elastic tubes the resistance or friction offered to the blood-flow is, as need scarcely be said, very great. For the sake of illustration let us separate the two most striking characteristics of the capillaries, viz. the elasticity of their walls, and the resistance due to their narrow calibre. Let us suppose that instead of a narrow elastic tube of more or less uniform diameter, we have an elastic tube presenting moniliform dilations, these being separated from one another by relatively narrow communications. Let us further suppose that, through such a tube, blood or other liquid is flowing, the pressure at one end being 200 mm. water, and at the other end that of the atmosphere.

If now we imagine that the pressure at the one end is suddenly raised from 200 to 300 mm., we can easily see what will happen. The blood will flow into the first dilation of our tube somewhat more rapidly than before, but, owing to its small size, the pressure within this cavity will rise rapidly on its contents being but slightly increased, and the rapidity with which the blood enters it will, on that account, diminish, since the difference in the pressure on each side of the point of entrance will be lessened. This same process will be repeated in the case of each of the dilated parts of the tube; the small size of the successive cavities, with the friction offered by the comparatively narrow openings between them, preventing the occurrence of any sudden acceleration of the flow through the tube as a result of the rise of pressure at one end. Under these circumstances a rhythmic rise and fall of the pressure at one end of the tube would produce only slight acceleration and slowing of the flow through it.

We can easily imagine that the course of events in the case of the capillaries more or less closely resembles that which we have attempted to illustrate. If such be the case, it must necessarily follow that, to produce the most equable flow possible, the elasticity of the capillary walls must vary definitely with the calibre of these vessels as well as with the mean pressure of their contents; *e.g.* with a narrow calibre the elasticity modulus of the wall must be different from that which would be most suitable with dilated capillaries, the pressures being supposed to remain the same in both cases.

We can easily understand, moreover, that the blood-flow would cease to be equable, in other words, that a pulse would appear, on this co-ordination between the elasticity of the capillary wall, the diameter of these vessels, and the blood-pressure in their interior, being interfered with sufficiently. This would be the case, for example, if the extra-capillary pressure were raised considerably.

In the same way, in the non-physiological maximal dilation of the capillaries in cases of inflammation, we must suppose that the elasticity of their walls has either ceased to be that best fitted to give an equable flow, or else that the pressure of the exuded lymph acts in the same manner as pressure applied to the outside of the tissue.

We have felt it necessary to seek for some explanation of the appearance of a pulse in the capillaries on the application of pressure. That which we have attempted to sketch above is, of course, only a theory, but it is the only one, capable of explaining the facts, which we have been able to find.

VI. Relation between the diameter of the arteries and their internal pressure.

As a rule, the pressures within the different arteries of any given web are not far apart, although the diameters of these vessels may differ considerably. It is a well-known fact that the arterioles of the web of the frog very frequently vary in calibre in an apparently spontaneous manner. And we have more than once had an opportunity of observing the effect, on the arterial pressure, of these changes of diameter in the case of two neighbouring arteries, both of which lay in the same field of the microscope, and both of which ended more or less completely within the compressed area. Such observations shewed us that, to produce any great difference in the pressures within the two vessels, one of them must contract greatly. Of two such vessels the wider may present a slightly higher blood-pressure than its narrower neighbour, but usually the difference is so slight as to be barely appreciable. It is only when one of them contracts strongly, reducing its calibre almost to that of a capillary, that its pressure falls to any marked extent. Indeed, it would seem that the friction offered by the arterioles to the blood-flow through them is comparatively slight. And this, it must be remembered, is only what we should *a priori* expect, for, were the friction within the small arterioles *normally* considerable, a correspondingly large part of the work of the heart would be uselessly expended in overcoming resistance in the arteries. When, however, the arteries contract greatly, the pressure at their capillary extremities falls considerably, and, in accordance with Poisseuille's law, we find that, with very narrow arteries, slight changes of calibre have an incomparably greater influence on their internal pressure than is produced by equal changes of diameter in the case of moderately wide vessels. These extreme contractions appear to be mostly of central origin, local interests being sacrificed, so to speak, to those of the organism as a whole.

In the case of the contraction of the arterioles produced by electric stimulation of the cut sciatic, the pressure in the arteries may sink to nearly zero, the lumen of the vessels being nearly, and indeed in some instances completely, obliterated. But, as we have said, where the diameters of the arteries are not markedly diminished, their internal pressures are practically the same for any given web.

In curarized frogs, and also in one or two instances with unpoisoned animals, we have met with blood-pressure curves resembling closely those described by Traube, Hering, and others. These are apparently of central origin in the frog, as well as in the dog and rabbit, and are seemingly due to a summation of the apparently spontaneous contractions of which we have spoken above. Some writers have contended that these contractions are of local origin, since variations of calibre take place, to all appearance spontaneously, in the arteries of the web after the sciatic has been severed. We are not inclined towards this view, since those changes in diameter which we have observed to occur spontaneously after section of the sciatic, did not cause any great contraction of the vessels, but seemed to us, although we had, of course, no proof of the fact, to resemble more the dilations of the vessels which result from anaemia.

VII. Elasticity of the walls of the arterioles.

As already stated, the walls of the veins are so elastic that they contract very greatly when the force which distends them is diminished by raising the extra-vascular pressure. Under the circumstances, it is not unusual to find that the calibre of the veins diminishes to less than one half of that which they presented before compression was applied.

In the case of the arterioles it is different. Usually, on raising the extravascular pressure, the arterioles contract but slightly—so slightly that the diminution in their calibre is barely appreciable. And, when the extravascular pressure is raised above that in their interior, they collapse like non-elastic, flexible tubes. We have once or twice met with exceptions to this rule, however. Sometimes, on raising the extravascular pressure nearly to the maximum arterial pressure, we have seen an arteriole, between each pulse-wave, contract until its lumen was completely obliterated, expanding again with each pulse-beat.

CONCLUSION.

We have given evidence sufficient, it is believed, to demonstrate clearly that the capillaries are contractile, and also that their contractility is to all appearance in constant action. As has been shewn, the changes in diameter which they so frequently present cannot be explained by assuming, as is usually done, that they are exceedingly elastic.

It would appear that the individual capillaries contract or expand in accordance with the requirements of the tissues through which they pass. The regulation of the vascular blood-flow is thus more complete than is usually imagined.

We have seen that temporary anaemia is followed by a dilation of the arteries, capillaries and veins. And this, as we have shewn, is only one illustration out of several with which we are acquainted, of the action of a mechanism whereby the degree of dilation of the vessels is regulated independently of the cerebro-spinal vasomotor centres.

The relative diminution in the lymph of certain of the constituents of the blood, or the presence in increased amount of certain of the products of tissue change, or both of these combined, must be looked upon as the cause which leads to the dilation of the vessels which results from temporary anaemia. As we have attempted to shew, the same causes are present in the case of various other congestions, which may be most easily explained by assuming that they are thereby produced.

This action on the vessels is possibly brought about through the medium of peripheral vasomotor ganglia, but is more probably produced, independently of such structures, by direct action on the walls of the vessels. To this automatic regulation of the peripheral circulation we are inclined to ascribe a rôle of very great importance, both from a physiological and from a pathological point of view. It would appear that it is principally, if not exclusively, in connection with it, that the contractility of the capillaries comes into play. We do not intend however to give a résumé of the contents of the foregoing pages. In conclusion, we have to record our grateful thanks for the kind aid and advice which we received in connection with this subject from Prof. Goltz, in whose Institute a number of our experiments were made.

Note. Our method of measuring the pressure of the blood in the peripheral vessels was demonstrated by us at the meeting of the Berlin Physiological Society held on the 15th Feb. 1878. On that occasion Prof. H. Kronecker kindly made a few remarks in our name, describing more fully than our knowledge of the language permitted us to do, the details of the method; and it is our pleasant duty to thank Prof. Kronecker in this place for his kind assistance on that occasion. In the report of this communication which appeared in the *Verhandl. d. physiolog. Ges.*, there occur several errors which have crept in owing to our not having explained to Prof. Kronecker with sufficient clearness the facts which we wished brought forward. Unfortunately we had no opportunity of preventing these mistakes being published, since, from an accidental oversight, the proof-sheet of the report was not submitted to us. We feel it necessary to explain here the reason of the discrepancies which exist between the statements contained in our present paper and those in the *Verhandlungen* of the Berlin Society.

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Fig. 1.

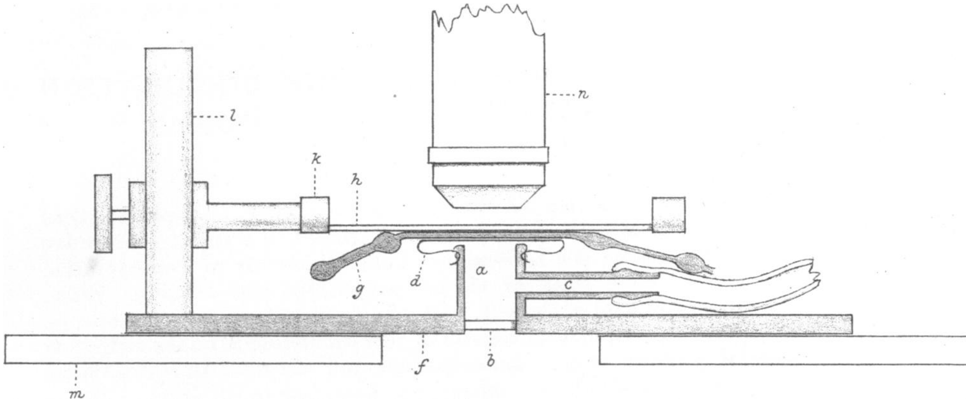
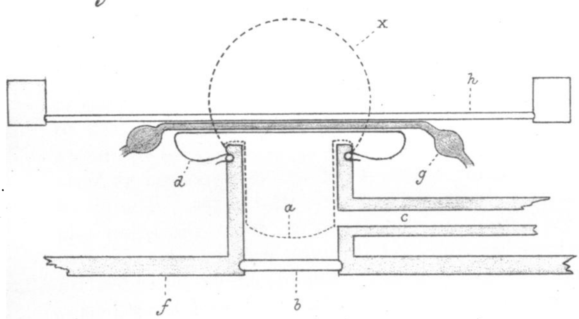


Fig. 2.



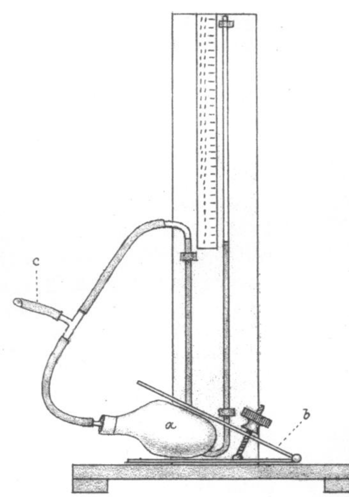


Fig. 4.

Fig. 3.