spasms of moderate violence come on, and after these have lasted a few seconds he usually puts his hands to his head and complains in a confused voice of pain in the head before all the spasm has passed off."

FIG. 20.

The tracing shown in Fig. 20 was taken during one of these attacks. The increase in the auricular rate during

Feb 24. Pulse rate, as calculated from eight traces. 9. per minute

FIG. 21.

the period of asystole is well seen, and is doubtless the expression of the fall in arterial pressure. The duration of

FIG. 22.

asystole is twenty-one seconds; the point of time at which consciousness was completely lost is indicated, and it will be seen that the tonic spasm interfered with the record from the venous pulse.

His pulse, which as I have said was about 22 on ad-

mission, tended to become less frequent, and Fig. 21 was taken at a time when the pulse rate had fallen to 9 per minute. Sometimes long pauses of ten or eleven seconds

occurred, and towards the end of these pallor, without unconsciousness, prevailed.

Apparently in connexion with the long periods of asystole—and here I refer to those which were not associated with convulsion or with loss of consciousness—Cheyne-Stokes respiration was present. The relation was constant and peculiar, and it is shown in Fig. 22; the period of apnoea does not begin until after that of asystole has passed off; there is sometimes an interval of a few seconds between the two phenomena; they never coincide in time. I am not aware that this relationship has been formerly noted. In this tracing the return of the pulse is of the staircase variety. I have looked through my many

tracings, but find, as I have already mentioned, that as a rule the pulse returns with a full beat.

REFERENCES.

¹Heart, vol. iii, No. 2. ²Quarterly Journal of Medicine, vol. iii No. 10.

A Lecture

ON

CAPILLARY PRESSURE AND OEDEMA.*

BY

LEONARD HILL, M.B., F.R.S.

It is generally held, both in physiological and pathological teaching, that the transudation of fluid through the wall of the capillaries is due to the pressure of the blood within these vessels—that is to say, to the force of the heart beat. The average capillary pressure is taken as something between 20 and 30 millimetres of mercury, and it is suggested that this pressure is sufficient to overcome the osmotic force which is found to be exerted through gelatine membranes by the proteins of the blood and separate the water and crystalline substances which pass out from the capillaries into the tissues. According to the modern theory of the secretion of urine, it is assumed that such filtration takes place through the Malpighian capsules, and it is supposed that to maintain this filtration and to overcome the osmotic pressure of the colloids the pressure within the glomerular capillaries is about 20 per cent. less than that in the aorta. The assumption that there is any such high pressure within the capillaries I believe to be erroneous.

My attention was first drawn to capillary pressure some twenty-five years ago when I was inquiring into the principles of the cerebral circulation. I measured the pressure of the brain against the skull wall by means of a tube filled with water and closed by a thin rubber membrane, which was so screwed into a trephine hole that the rubber membrane came into contact with the bulging brain; the tube was connected with a glass tube

containing an air-bubble index, and this by a T-piece with a pressure bottle and a manometer. When the tube was screwed in and the rubber membrane came in contact with the brain, the air-bubble index was pushed out from the zero pressure position. On raising the pressure bottle, so as to restore the air bubble to the zero position, the manometer recorded the pressure required to push in the bulging brain, and restore it to its natural position within the closed skull cavity. The pressure of the brain against the skull wall is due to the distension of the cerebral arterioles and capillaries by the heart, and my method, I believe, gave me a measure of the pressure in these vessels.

In the anaesthetized animal lying in the horizontal position this pressure was about 5–10 mm. Hg, and was the same as the pressure measured in the torcular Herophili; in the dog this was a bony cavity, and therefore suitable for the insertion of a tube and the measurement of the cerebral venous pressure. Trephining the lamina of the atlas and screwing in a tube there, I obtained the pressure of the cerebro-spinal fluid. I found the pressure of the cerebro-spinal fluid, cerebral venous pressure, and the pressure of the brain against the skull wall were the same and varied together, and I concluded that the cerebral capillary pressure is only some 5–10 mm. Hg, and is practically the same as the pressure in the cerebral veins; only the least difference is required to maintain the flow. I may point out here that whether blood is extravasated within the skull or we are dealing with a depressed fracture, either the blood clot or the depressed bone expresses blood out of the brain contiguous to it, and occupies the room of this blood, and so raises the circulatory pressure up to arterial pressure in adjoining parts. The clot or the bone do not continue to press, but occupy room. The increased brain pressure is due to the shutting up of the capillary-sized vessels.

The brain is enclosed within a rigid case—the skull—and the total content cannot vary, but there may be more blood in the brain and less tissue substance and cerebro-spinal fluid on the one hand, while on the other hand

* Given at St. Mary's Hospital in the Institute of Pathology and Research during the course on Pathological Research in its Relation to Medicine.

there may be less blood, and more fluid or tissue substance. The arteries may dilate and the tissue cells may swell, and these together may confine the size of the veins and raise the pressure in the capillaries, so that there is a relatively rapid flow through a more rigid set of vessels, or the arteries and the tissue cells may shrink and the veins dilate, so that there is congestion of these and a sluggish flow. In a healthy state of activity the cerebral arteries are moderately expanded; the tissue cells in a normal state of turgescence, the veins narrow, and the flow of blood and oxygenation good. In a state of collapse the opposite conditions hold: arterial pressure is low, veins congested, or there is more fluid in the spaces, and blood flow is slow and oxygenation poor.

It has commonly been taught that in the eye the aqueous fluid, which is at a pressure of some 25 mm. Hg, is filtered through the walls of the capillaries, the blood within those vessels being supposed to be at a pressure of 20 to 30 mm. Hg higher. That the pressure of the aqueous balances the capillary pressure in the iris is shown by the fact that on letting this fluid escape the iris bulges forward, and may touch the cornea, and on compressing the abdomen the vessels burst, and the blood comes into the anterior chamber. No such bulging or haemorrhage can be brought about by squeezing the belly when the eye is intact.

Martin Flack and I also showed that when one of the venae vorticae was opened, and the venous outflow from it was observed, while the pressure in the eyeball was raised by forcing normal saline into the aqueous chamber, the outflow of venous blood did not cease until the pressure in the carotid artery was just overtopped; this indicated that the capillary and venous pressures rise together and equally with the fluid pressure within the eyeball just as they do within the cerebro-spinal cavity. The contents of the eyeball are confined by unyielding membranes, and the intraocular pressure is ruled by the secretory action of the cells of the ciliary processes. Just as in the case of the brain if the cells secrete more fluid, there is less room for blood, the veins narrow and the capillary venous pressure rises. Suppose the pressure within the blood vessels rises, this increase of pressure is instantly transmitted to and balanced by the aqueous; both in the brain and the eye the pulse helps to keep up the outflow of venous blood and fluid, cerebro-spinal or aqueous.

Abrading the skin, no less than opening the eyeball or skull cavity, removes the balancing counter-pressure of the tissue fluid enclosed by resistant membranes, and allows plasma to escape through the capillaries, which are no longer supported. The tissue cells and capillary walls, too, are damaged by exposure, and the transudation of fluid thus enhanced.

While in the living kidney, confined by its capsule, the pressure of the tissue fluid and secretion balances the capillary pressure; in the dead kidney, on the other hand, water driven through the renal vessels may filter out into the pelvis of the kidney.

A sharp distinction must be drawn between the living conditions and those in a wound or in an organ of a dead animal.

In the case of a salivary gland, it is known that on stimulating the chorda tympani nerve the pressure of the saliva, when its escape is obstructed, rises greatly above that in the carotid artery. Flack and I found that the outflow from the salivary vein was not obstructed under these conditions; in fact the outflow might be rapid, while the gland became tense and swollen. There is a strong membrana propria which confines the secretory cells of each alveolus and limits its expansion, acting like the leather case of a football or the pericardium of the heart. Each lobule and lobe and the whole gland is surrounded with membranes limiting expansion. When the secretion is obstructed the alveoli swell, the lobules and lobes swell, and the whole gland swells until limited by the membranes, and the veins within the gland are narrowed while the arteries dilate owing to the influence of the vasodilator nerves, and the circulatory pressure is thus raised until arterioles, capillaries and veins approximate towards a rigid system at arterial pressure with a fast rate of flow.

In the sweat glands the structure is similar; the same high secretory pressure can be produced. In the kidney there are figured membranae propriae enclosing secretory cells of both renal capsules and tubules, but they are less well defined. The secretory pressure does not rise up to the arterial pressure.

Direct Measurement of Capillary Pressure.

Now let us turn to direct measurement of capillary pressure. Roy and Graham Brown used a small brass cylinder closed at one end by glass and at the other by a cup-shaped piece of transparent peritoneal membrane. A tube entered this little chamber, by means of which the pressure could be raised within it, a manometer being attached to indicate the pressure. With the peritoneal membrane in the domed-up position, the web of a frog's foot or other transparent tissues can be brought in contact so as to flatten down the dome somewhat. The web is then covered by a thick glass cover-slip attached to a holder. The chamber is placed beneath the low power objective of a microscope, and the capillary circulation observed. The pressure is then raised in the chamber so that the web is compressed between the membrane and the glass cover-slip, and the pressure is found which just obstructs the flow. In the case of man a similar apparatus inverted has been applied to the skin just behind the finger nail, and strong direct illumination used. A drop of castor oil is placed upon the finger before the application of the membrane, and the capillaries can then be seen in the papillae of the skin. Measurements of this kind have been made by a considerable number of observers, and give high values such as 20 to 40 mm. Hg.

Instead of microscopically observing the capillaries of man in the way just described, another method has been used—namely, that of finding out the pressure which just suffices to blanch a small area of the skin, as seen by the naked eye. To blanch the skin, 55 to 75 mm. Hg are required according to some observers, but the average generally given is 35 to 45 mm. Hg.

Basler has compared the colour of the compressed finger with another placed beside it, and taking the least change of colour as the index has found a much lower pressure than other observers—namely, 5 to 8 mm. Hg. He has also used a very ingenious method of making a small cut in the finger and inserting the finger in a tube connected with a manometer and finding to what pressure the escape of blood raised the manometer. Here again he finds the same low pressure. Now it is quite clear that in cutting the finger one probably would not only cut capillaries but might wound an arteriole, and the pressure might, therefore, indicate not capillary pressure, but that of the arteriole.

The arterioles in their end branches consist of endothelial cells and circularly arranged muscle cells. As they branch into capillaries the muscle cells cease, and the capillaries have an endothelial lining only. When the capillaries join together to form the venules, the endothelial lining first becomes coated with connective tissue fibrils, and then further on muscle cells are added. It seems very unlikely that there should be any great difference of pressure between the venous end and the arterial end of the capillaries. We know that the venous pressure is very small—for example, in a number of observations made by Bayliss and Starling on anaesthetized dogs while the pressure in the aorta was 81 to 125 mm. Hg, that in the vena cava was from 2 to 5 mm. Hg, and the pressure in the portal vein 5 to 8 mm. Hg. If in the upper arm the pressure is measured which just hinders the outflow from the lower, the arm being placed horizontally at heart level, it is found to be from 1 to 5 mm. Hg (L. Franks, Elpers).

The method used by Roy and Brown, and the method of blanching the skin first used by v. Kries, are methods which stop the flow of blood in the capillaries and arterioles, but obviously, if the flow of blood is stopped, the pressure rises to that within the arteries which feed these vessels. What has been measured then has not been capillary pressure but the pressure in the small arteries.

Krogh, who has made a great many observations of interest recently on the contractility of capillaries, says that mechanical excitation causes a contracted and closed capillary in the frog's tongue to dilate at the venous end first and the blood to advance from the venous end until finally the capillary dilates up to its connexion with the arteriole, when the current is suddenly reversed. Krogh finds then that the venous pressure is enough to fill the capillary, and overcome the resistance to flow within it, and the venous pressure is agreed to be only a very few millimetres of mercury.

I have examined the capillary pressure, using a modified

form of the Roy and Brown apparatus, kindly made for me by Dr. E. Schuster—

1. In the tadpole's tail.
2. In the toad's lung, tongue, mesentery, and bladder.
3. In the frog's lung, tongue, mesentery, web, bladder, and kidney.
4. In the newt's lung and mesentery.
5. In the grass snake's lung, mesentery, and kidney.
6. In the mouse's ear, mesentery, and abdominal muscular wall.
7. In the cat's mesentery and muscle.

To determine the pressure correctly the transparent membrane covering the compression chamber must be tied on loosely, as Roy and Brown direct, so that when blown up it forms a dome over which the web or other organ is spread; the threads attached to the toes in the case of the web, for example, are carried to pins, and the leg arranged so that the flow of blood is free and unobstructed. The glass against which the web is compressed is lowered until it touches the web, the top of the dome being thereby slightly flattened. The web is compressed between the flattened part of the membrane and the glass. Care must be taken to secure that the toes are not pressed by the glass cover against the metal rim of the pressure chamber, and that pressure is not spent in merely expanding the membrane.

Capillary pressure I take to be that pressure which just begins to lessen the velocity of flow in those capillaries wherein the flow is slowest. These naturally first undergo compression, the blood taking the pathway of least resistance through other capillaries. If the compression be gradually increased the flow is slowed, then stopped in more and more of the capillaries until it continues only through the most direct pathways connecting the arterioles with the venules wherein the velocity was greatest to start with. With further increased compression the flow of blood becomes pulsatile not only in the arterioles but in these capillaries and even in the venules, the compression being sufficient to stop the flow in diastole, but not in systole. Finally the blood is expressed out of the capillaries and veins, and the pulse is seen swinging the corpuscles to and fro in the arterioles, but not translating them onwards. The pressure required just to produce this effect is the systolic pressure in the arterioles supplying the compressed part.

All those phenomena which take place on the application of pressure to the arm by means of the cuff of the sphygmomanometer can thus be observed and taught to the student. The diastolic pressure can be measured in the frog's web just as well as the systolic pressure. Diastolic pressure is that which just arrests the onward flow of the corpuscles in diastole; to give an example, in a frog's web diastolic pressure was 17 mm. Hg and systolic pressure 26 mm. Hg.

The pressure required just to modify the capillary flow in the outer part of the tadpole's tail or at the edge of a frog's web is from 1 to 3 mm. Hg. There are some capillaries which require a higher pressure than this—for example, 5 to 8 mm. Hg—such as the capillaries in the papillae of the frog's tongue, or in the glomeruli of the kidney of the frog. Glomeruli may be observed with the blood corpuscles running through the afferent vessel, spinning round the network of capillaries and out by the efferent vessel—the whole giving a most striking picture. The following is the technique which was briefly described in the BRITISH MEDICAL JOURNAL of April 9th, 1921, p. 526:

The frog is put under urethane, an injection under the skin of the back of about 0.3 c.cm. of a 20 per cent. solution being given. The animal chosen is a rather small active one, not a female full of spawn. It is fixed on its side by pins through lip and ankle-joints; a lumbar incision is made through the skin and abdominal wall and the ileum on that side is removed. All haemorrhage is stopped by means of a cautery heated to a dull heat. The external edge of the kidney on which runs the renal portal vein is picked up in the forceps about the middle of the kidney and a ligature tied on at this point. The animal is then arranged belly upwards at the side of the Roy and Brown apparatus, and by a very gentle traction on the thread the kidney is drawn over the peritoneal membrane and the glass cover brought down upon it. The manipulation of the body and the traction on the thread must be so carried out as to expose the outer edge of the kidney to the light, when brought under the microscope, without stopping the circulation in the renal arteries. It is along this edge that the glomeruli may be found.

On examining the preparation the whole surface of the kidney is seen pervaded with wide venules and their capillary branches coming from the renal portal vein, through which the blood is flowing in slow and most ample streams. On putting on a pressure of 2 to 3 mm. Hg the blood is squeezed out of these veins, and glomeruli may then come clearly into view and exhibit the arterial blood coursing through them. I found a pressure of some 4 to 8 mm. Hg definitely slowed the flow in the glomeruli, while it took some 25 mm. Hg to stop the flow in the renal arteries. There is nothing extraordinary about the behaviour of the glomerular capillary network; it resembles that of other capillaries; the flow in the afferent and efferent vessels is stopped by the same pressure. I found it took very little pressure to drive the corpuscles out of the glomerulus when the circulation had stopped. I have seen the flow reverse under pressure before the glomeruli empty.

I find that a pressure of 2 to 5 mm. Hg momentarily applied checks the flow of corpuscles in the arterioles of the frog's web, etc., while it takes some 25 mm. Hg to stop the flow altogether. In the chief capillary branches, where the velocity of flow is rapid, the same pressure momentarily checks the flow, and at the same time as in the arteriole, but in the case of the venules the flow may be accelerated during and retarded momentarily after such an application of compression. The acceleration is due to the expression of blood from the capillaries, the retardation to the capillaries filling again. The pressure which momentarily checks the flow in the arteriole is, I take it, a measure of the pressure of the blood against the wall of the vessels. It closely approximates to that pressure which, when continuously applied, retards the flow in those capillaries with the slowest rate of flow. If the compression is maintained the pressure, of course, banks up behind it to that of the artery which feeds the obstructed arteriole. As the water manometer, owing to its inertia, does not fully record the value of the momentary compression, I have also used an air manometer with a xylol index, graduating this against the water manometer.

The conclusion then is reached that the pressure in the arteriole with unobstructed rapid flow is 2 to 5 mm. Hg, and that the fall of pressure from arteriole to venule is a very slight one. The flow in the venules is affected by a pressure of 1-2 mm. Hg.

The observations I have made on the mouse and cat show that the pressure in the capillaries and arterioles is no higher in the warm than in the cold-blooded animal. The assumption which has been made that the capillary pressure is some 30 mm. Hg, and the hypotheses as to the transudation of lymph, urine, etc., based on that assumption, appear then to be untenable.

Proof that the resistance in the capillaries is very slight is afforded by the following experiments: If the flow in the frog's web or tongue is stopped by a ligature placed round the thigh, we find, on exploring the field, one or more of the vessels, an arteriole, say, connecting some capillary with a venule, in which the flow continues for some minutes at a speed which is scarcely less than the normal speed in the capillaries. I have seen such a flow in the capillaries of the frog's web on placing it under the microscope forty minutes after cutting off the leg. The application of warm water to the web may restart such a flow when arrested. The flow may reverse, and this is against its being caused by contraction of the arteries. Again, when the web of the excised leg is compressed in the Roy and Brown apparatus a momentary pressure of 2 mm. Hg will cause the corpuscles to rush along the capillaries and venules no less rapidly than in the normal flow.

To try and arrive at a juster measure of the pressure in the capillaries in man my co-worker, Dr. James McQueen, designed the following method:

Warm water from a jet fed from a reservoir kept at constant pressure-head is played on the skin below the nail or on the skin covering the distal end of the metacarpal bone of the thumb, the jet having a 2 to 2.5 mm. bore diameter. If the pressure be sufficiently high, the area impinged on is rendered white, and when the jet is moved a red blush of returning blood can be seen. To determine the pressure which just suffices to produce blanching, the jet is now turned so as to throw its column of fluid into the air alongside a meter scale; the distance of the upward throw of water is obviously the pressure of impact on the thumb in centimetres of water.

When readings of pressure are taken by this method with the arm held at heart level they do not materially

differ from the readings of pressure obtained by v. Kries and others. But, be it noted, as the flow is stopped in the blanched part the readings are of arteriole not capillary pressure. Moreover, there remains to be considered the considerable resistance of the convex horny layer of skin to compression. There are also the resistance of the vascular wall to compression, the friction of the blood as it is expelled from the compressed area, the resistance of the lymph or tissue fluid surrounding the capillaries. These resistances are very small, as is shown by the fact that a pressure of 1 cm. of water applied to the membrane of the Roy and Graham Brown apparatus is sufficient to drive the corpuscles quickly along the vessels of the web wherein the circulation has been arrested. Their sum can be accurately estimated provided the blood pressure in the compressed area can be reduced to zero. Then the pressure taken to blanch the area is a measure of the resistance factors. To effect this the hand is raised above the heart level, at a certain point the veins collapse, because the venous pressure has been overtopped by gravity, and is, in the hand, zero. If the brachial artery is now occluded, the arterial pressure entering the hand is, in its turn, reduced to zero. Accordingly the capillary pressure becomes zero. A tourniquet of rubber tubing can be used, or the cuff of the sphygmomanometer connected with a compressed air cylinder so as to secure a rapid application of pressure to the artery.

In order to keep enough blood in the capillaries to give a clear index, it is advisable to put a rubber band round the wrist before elevating the arm and compressing the artery, and then to remove this band. If the jet be projected on the thumb when the area has thus been brought to zero pressure, a measure of the pressure in centimetres of water required to blanch the area is now obtained. This pressure measurement—the measurement of resistance factors—has to be subtracted from the original measurement obtained when the normal conditions of pressure pertained in the arterioles. The diminished reading is now the actual arteriole pressure. To cite an example:

Subject E.—Hand at heart level. Pressure to blanch 2.5 mm. area = 35 cm. water. Resistance measurement (after vascular area reduced to zero pressure) = 24 cm. water. Difference = arteriole pressure = 11 cm. water. This method gave us an arteriole pressure of about 10 mm. Hg.

In the case of the bat's wing I found the main arterial branch in the second segment measured about 0.08 mm. in diameter, and the main arterioles about 0.015 mm., these coming off at right angles. When the bats are hibernating the pressure in the main branch is low, rising from some 20 mm. Hg to 50 mm. Hg as the bat becomes warm. When the systolic pressure in the main arterial branch is 50 mm. Hg that in the main arterioles is about 15 to 20 mm. Hg.

There is then a great drop of pressure on passing from the main arterial branch to the main arterioles. It is in these vessels that the great fall of arterial pressure takes place through resistance to rapid flow.

I now pass to the consideration of the contractility of the capillaries.

Effects of Arterial Contractility.

According to the general view the contractility of the arteries regulated by vasomotor nerves controls the flow of blood to each part, diverting greater streams to parts in action. But the contractility of the capillaries and venules is now an established fact, and the evidence seems to show that it has an important share in the local and general control of blood flow. Stricker (1865) noted on appropriate stimulation the constriction of the capillaries in the nictitating membrane of the frog, and ascribed it to turgescence of the endothelial cells, which form the capillaries. His observations have been confirmed by several, but no one has proved how the constriction is brought about.

The capillaries of the web dilate after the momentary touch of a brush dipped in chloroform, stasis being prevented by well washing with water. Inhibition of the heart had no effect on this dilatation, it was not brought about by blood pressure (Roy and Brown). A small drop of nicotine applied locally to the area vasculosa of the chick on the fourth day of incubation produced such dilatation that the rest of the area was almost emptied (Vulpia). Lewis and his co-workers found that in the arm, with the artery blocked by the cuff of the sphygmo-

manometer, a scratch on the skin with a blunt instrument produced the well-known white and red lines. In such case they must be ascribed to capillary contraction and dilatation. Local injection of adrenin also blanched the skin when the arterial flow had been stopped.

Temporary anaemia produced by ligation or compression of an artery dilates the capillaries. Almroth Wright attributes this to the production of acid through anaemia. We know that oxygen want leads to the appearance of lactic acid in muscles, and a drop of acid dilates the capillaries. On the other hand, Krogh attributes the dilatation to some unknown property of the blood, for he finds it takes place when the frog's tongue is exposed to oxygen. The capillaries are conceived by him as spontaneously contracting and dilating, and thus alternating the blood supply to the tissues, dilatation following on the anaemia produced by contraction.

Krogh finds that local mechanical, or thermal, stimulation, or the application of minute drops of weak acid, cocaine, and adrenaline produce local dilatation of both arterioles and capillaries. The effect spreads to a wider area than that stimulated. A drop of urethane (20 per cent.) dilates the capillaries and not the arterioles. The spread of the reaction due to stimulation is abolished by cocaine, and not affected by mere section of the nerves, but disappears when the nerves have degenerated, being then sharply limited to the point excited. The reactions are considered to be due to a spread of excitation along sensory nerve fibres to that antidromic vaso-dilator effect discovered by Bayliss in the posterior root axons. The contraction of capillaries may reduce their diameter by more than half and their sectional area fivefold. Dilatation occupies several seconds, contraction one to three seconds. A single stimulus is ineffectual; the galvanic current is better, and mechanical stimulus most effectual. A vast number of capillaries are at any one time not open, as may be seen by the growing flush and swelling of the hand on occluding the veins of the arm. The aching sensation which arises from congestion keeps one naturally restless, and every movement helps onward the flow.

Krogh finds an enormous increase in the number of open capillaries in muscle during activity. In the mammal he used intravenous injections of Indian ink to render the capillaries visible. He estimated that in the guinea-pig the total surface area of the capillaries per cubic centimetre of muscle was 3 to 32 sq. cm. at rest and 360 to 750 in activity; in the frog 1 to 12 sq. cm. at rest and 70 when active. The oxygen supply to the active muscle is thus kept ample.

I find a very instructive preparation of the abdominal muscular wall of the mouse (under urethane) can be made by an incision through the median line of the lower half of the abdomen and another carried laterally outwards from the mid-point, the skin being reflected, the triangular flap of muscles with the blood vessels entering from below is brought on to the membrane of the Roy and Brown apparatus. In such preparations all the capillaries appear filled, perhaps owing to exposure or to the fact that the muscle is always in respiratory action.

Venous Contractility.

In the hibernating bat's wing most of the capillaries are empty, and the veins contract in such period as to help the feeble flow. There may be, and probably are, contractions of all veins which further flow. We know that muscular contractions and change of posture greatly contribute to return of the venous blood to the heart. Thus Burton Opitz on stimulation of the sciatic nerve found the outflow from the femoral increased three to four times above the resting value during the shortening of the muscles, but it was diminished to about a third during the height of tetanus.

Hooker isolated the sigmoidal area of the large gut of the dog, and leaving the artery open connected the vein with a manometer. Excitation of the nerve supply from the inferior mesenteric ganglia increased the venous pressure by 5 mm. Hg, asphyxia increased it by 3½ mm. Hg. Although the lumen of the gut did not show this rise of pressure when closed and connected to a manometer, I believe that the contraction of the tissues caused the rise.

Hooker also finds that after death from ether, the capillaries first contract and empty, then dilate and fill, and finally contract and empty when rigor comes on. This does not happen in the cat in a state of shock—for example, in one poisoned by histamine.

The arteries of the ear in such a cat contract on stimulation of the nerves or on injecting adrenin, but not the dilated veins and capillaries.

Shock.

The work of Dale and his co-workers indicates that shock produced by histamine has its origin in primary failure of the peripheral circulation. All the capillaries open and venules dilate at once, and there is increased passage of fluid from the blood into the tissues, and so the circulation fails while the heart is beating efficiently. While Dale injected histamine, I watched the venules dilate in the mesentery and the flow slow down and almost become arrested in these and in the capillaries, but have not so far been able to see the opening up of closed capillaries, probably because the capillaries are already dilated by exposure. Histamine is formed by decarboxylation of the amino-acid histidine, which is derived from proteins, and it is conceivable that such substances are produced in trauma. Herein we have an explanation of shock differing from that of acid causation put forward by Almroth Wright.

Be it noted, histamine acts in the cat anaesthetized by ether, but not in the normal cat or one anaesthetized by nitrous oxide and oxygen. The last is by far the best anaesthetic for preventing shock, and as P. Bert proved forty years ago, and Dale and I have confirmed recently, may be given with ease and safety and efficiency of depth in a pressure chamber at + 7 lb. pressure. An operating chamber can easily be constructed so that the patient, surgeon, and anaesthetist are all within the chamber at slightly increased atmospheric pressure. The effect of inhaling gas and oxygen, given in the usual way from a bag in such a chamber, is an increase of partial pressure, or concentration, of both in the blood, and deep anaesthesia with no want of oxygen.

Effects of Oxygen Inhalation.

The beneficial action of oxygen inhalation in relieving oedema and chronic ulcers has recently been made evident to me by the use of an oxygen tent bed, constructed for me by Messrs. Siebe, Gorman, Ltd. This tent bed allows 30 to 40 per cent. oxygen to be breathed in comfort for days, with intermissions for meals. The oedema disappears, the part becomes warm and of good colour, the granulations healthy, the edges of the ulcer flatten, and the skin hastens to spread over the ulcer.

The question arises as to how the capillaries contract and dilate. It is generally assumed, but unproven, that it is due to changes in the swelling of the endothelial cells of the capillary wall. I suggest that it is due to the tissue cells outside the capillaries; these, by swelling or shrinking, control their own blood supply. By increase of waste products with higher osmotic pressure they take up fluid from the blood in the capillaries and swell, and so contract the capillaries. By chemical-physical changes resulting from the taking up of fluid from the blood the osmotic pressure falls, and the fluid passes back into the blood or lymphatic channels.

I have pointed out what happens in the salivary gland on excitation of the chorda tympani, and how the membranae propriae and other membranes confine tissue expansion so that the capillaries and veins may be narrowed but not occluded. I do not believe fluid is transuded out by the force of the heart producing a filtering pressure, but that the heart just succeeds in maintaining a flow in the capillaries with no excess of pressure for other purposes, and the tissues by inhibition swell or shrink, taking or giving up fluid.

Charles Bolton, narrowing the inferior vena cava to one-third by a rubber ring, has shown that oedema results in dogs, not when the temporary small rise of venous pressure occurs at first, but later, when the venous pressure has returned to normal. Oedema is due to ill nutrition of the tissues, not to increased vascular pressure and filtration, whether it arise from poor flow and want of oxygen in heart disease or from a chemical poison in kidney disease, or from a bacterial toxin.

The swelling of the tissues in oedema, by pressing upon the venules, raises the capillary pressure.

I have measured the pressure in a case of hydrocephalus with the infant lying horizontal. It was nearly 15 mm. Hg. On raising the head from the pillow the pressure

rose owing to my hands squeezing the head which was a bag of fluid. The capillary venous pressure in the pial vessels must have risen *pari passu*, there is no mechanism for shielding them from the pressure of the fluid. I moreover found, on drawing off the fluid, that the pressure sank to 0—that is, to atmospheric pressure—and the soft wall of the skull by its weight sagged in. So it remained for hours, until the fluid was re-secreted.

In a case of oedema of the leg, with the patient sitting propped up, the pressure of the fluid equalled about 40 mm. Hg; here again the pressure rose on lifting the leg up, owing to squeezing by the hands, and the capillary venous pressure must have risen *pari passu*, and kept as it is normally, the least bit above the tissue fluid pressure, so as to maintain the venous outflow.

In inflammation the products of tissues damaged by bacterial toxins cause dilatation of arteries and swelling of tissues. The swollen tissues, confined by the membranes, press upon and narrow the veins and capillaries. The blood pressure rises, and we have a more rigid system with fast flow, redness, swelling, and a throbbing pulse in the part. The tissues may swell so that stasis is produced; the surgeon's knife then relieves the swollen, tense condition, and allows lymph with its immunizing powers to escape. Bier's bandages obstructing venous flow may cause increased outflow of lymph, not by transudation under pressure, for capillary pressure is balanced by tissue fluid pressure, but by increased imbibition of tissue cells due to oxygen want. The salt solution treatment of wounds devised by Almroth Wright pulls fluid out in increased amount, and washes the wounds just as the breathing of cool air, with its low water vapour content, by evaporating moisture from the respiratory membrane, draws abundant lymph from the blood and keeps this clean and healthy.

Krogh finds that, after putting in a drop of 20 per cent. urethane on the capillary field and injecting neutral red intravenously, the dye passes through the dilated capillaries and stains the bordering tissue, the stain fading away from the capillary. This he ascribes to increased permeability. It may equally well be due to increased force of inhibition exerted by the damaged tissue cells. The escape of white blood cells during stasis and of red cells on severe injury shows a pathological permeation of the capillary wall; but normally the tissue cell, not the capillary pressure, governs the passage of fluid.

References to literature are fully given by Tigerstedt, *Ergebnisse der Physiol.*, 1920, 18, and Hooker, *Amer. Physiol. Review*, 1921, 1, Part I. See also Krogh, *Journ. Physiol.*, 1920, 53, 26; Leonard Hill, *Proc. Physiol. Soc., Journ. Physiol.*, 1920-21, 54; Leonard Hill and J. McQueen, *Brit. Journ. Exper. Pathol.*, 1921, 2, 1.

DUAL RADIOTHERAPY IN MALIGNANT DISEASE.

BY

S. GILBERT SCOTT, M.R.C.S., L.R.C.P.,

DIRECTOR OF THE RADIOLOGICAL DEPARTMENT, LONDON HOSPITAL.

X RAYS and radium are undoubtedly powerful therapeutic agents. But, since the technique required to obtain their complete beneficial results has not as yet been mastered, we are at present unable to make full use of them. Consequently most of our failures must be attributed to the uncertainty of our technique rather than to the agents themselves.

Physicists have given us much help in solving some of the problems connected with x rays and radium. But until they can give us not only an accurate means of measuring dosage to pathological cells lying below the surface of the skin, but also indications of the conditions and dose required to produce a full lethal effect on these cells, our results are bound to be erratic. At present results depend partly on luck—that is to say, on whether the particular dose administered happens to be the most effective one—and partly on the practical experience of the radiologist, which enables him to gauge this with a certain amount of accuracy. It should, indeed, be possible to administer x rays and radium radiations as accurately as drugs. It should equally be possible to have some idea of the prescription required for the case in hand.

There are, perhaps, no therapeutic agents affecting such a variety of diseases, or from which more remarkable