THE STATE OF THE VESSELS OF THE MESENTERY IN SHOCK PRODUCED BY CONSTRICTING THE LIMBS AND THE BEHAVIOR OF THE VESSELS FOLLOWING HEMORRHAGE

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Plates 8 and 9

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Contemporary evidence has left unanswered the question as to whether or not during shock the small vessels are constricted or dilated. That is not to say that the subject has not been extensively investigated. But it has remained a vexed problem, perhaps because the methods employed for demonstrating caliber changes in vessels have usually been indirect ones and often highly unphysiological.

Not only is there disagreement as to whether arteriolar constriction occurs in shock, but also as to whether such constriction, if it does occur, is of sufficient intensity to play an important part in the mechanism of shock.

The clinical observation that during shock patients exhibit extreme pallor has usually been cited as evidence indicating vasoconstriction. Not only is the skin pale and cold but incision into it is almost bloodless. We have inspected the eyegrounds of such patients and found the arterioles markedly constricted. This is at least suggestive that arteriolar constriction is generalized if the analogy holds for shock as it does in hypertension. Both in animals (1, 2) and man (3) blood flow to the periphery decreases conspicuously during shock. This has been demonstrated by the finding of decreased cutaneous venous oxygen and increased arterio-venous oxygen difference (4–6), as well as by other methods.

According to the work of Seelig and Lyon (7) vascular tone in shock seems to be maintained to some degree by nervous impulses, for severance of the sciatic nerve, *when* shock had occurred, resulted in marked increase in venous blood flow. Proportionately there was a greater increase in flow in shocked than in normal animals, suggesting vasoconstriction in the former. These measurements were only approximate, however, and Bartlett (8) believed he could show from calculation that if vasomotor tone had been markedly increased the change in outflow after section of the sciatic nerve should have been greater than it was. He injected salt solution under constant pressure into medium sized arteries partially isolated temporarily from the circulation and studied the rate of its inflow as the arterial pressure fell in consequence of induction of shock. The method is an artificial one whose results

appear difficult to interpret. Nevertheless, he found the rate of inflow faster in shock than normal and concluded that decreased vasomotor tone accompanied it.

Erlanger, Gesell, and Gasser (9) slightly modified the method of Bartlett for determination of peripheral resistance and produced shock by intestinal manipulation. They found that at about the time arterial pressure began to fall and portal pressure rose, peripheral resistance began to fall and by the time arterial pressure was about 50 mm. Hg resistance was practically always below normal. The vessels preserved some residual tone to the time of death.

Cattell (10) using Bartlett's method while inducing shock by crushing the leg found that gradually increasing vasoconstriction occurred, reaching a maximum in 2 to 4 hours. At this time the blood pressure had long since fallen to about 65 mm. Hg. After this, dilatation occurred which continued until death.

Mann's (11) results are more convincing. He observed that the larger vessels in the rabbit's ear, and in the paws of kittens and puppies, all constricted when shock was produced. Femoral vein pressure fell *before* arterial blood pressure had fallen, suggesting constriction of the arterial tree. Furthermore, stimulation in dogs of the lingual nerve, which contains most of the vasodilator fibers, caused marked vasodilatation in animals in shock. Section of the hypoglossal nerve, which contains most of the constrictor fibers, caused noticeable dilatation of the tongue vessels. Thus, according to this work also, there appears to be some vasomotor tone in the vessels of animals in shock.

Reduction of peripheral arterial resistance initiates the fall in arterial pressure according to the results of Wiggers (12), drawn from study of the configuration of the central arterial and intraventricular pressure curves. Baldes, Herrick, Essex, and Mann (13) found a progressive decrease in blood flow in the femoral artery following manipulation of the intestines. Flow was measured by the thermostromuhr. It is of interest that reduction in blood flow occurred before the arterial pressure had been significantly reduced.

The evidence regarding the state of the blood vessels after severe hemorrhage is also confusing. Most authors seem to agree that the total area of the vascular bed is reduced but are uncertain as to precisely where the reduction occurs.

Meek and Eyster (14) observed constriction of the capillaries and venules in the ears of dogs after bleeding the animals about 2 per cent of their body weight. It is difficult to determine from their photographs just what vessels are involved. They believe the constriction is an attempt on the part of the body to increase the effective blood volume by adding blood from vessels in which the blood has been more or less stagnant. Cope (15) used in principle the method of Marey to measure peripheral resistance and found it increased in dogs exhibiting post-hemorrhagic recovery of arterial pressure. Since the viscosity of the blood and the venous pressure both decreased, thus reducing resistance, the increase in total resistance observed must have resulted from peripheral vasoconstriction. These experiments also do not disclose the site of vasoconstriction.

Gesell (16) suggests that vasoconstriction after hemorrhage is to be attributed to reaction to decreased blood volume. Using the method of Cattell for measuring the tone of large arteries, Burch and Harrison (17) found that normotensive animals

under barbital anesthesia responded to hemorrhage by initial vasoconstriction. After the arterial pressure had fallen below 40 mm. Hg, vasodilatation occurred and death soon followed. The constrictor response to hemorrhage was abolished by spinal anesthesia, suggesting that it is mediated entirely by the nervous system.

The confusion in the literature is evident. Direct microscopic observations of the vessels seemed the method of choice for further studies of this problem; hence we have employed it in the study of shock produced by constriction of the blood supply to the limbs, and in a study of the behavior of the vessels following the removal of large amounts of blood.

Method

Cats were used, and the vessels studied were those of portions of the mesentery enclosed and exteriorized within transparent celluloid chambers. Such chambers were described by Zintel (18) in 1936. When the chamber is to be inserted, a midline incision is made in the body wall and a portion of the intestine and its attached mesentery gently drawn from the peritoneal cavity and placed between the two pieces of the chamber, which are then bolted together. Except for the space through which the intestine and mesentery pass into the chamber, the hole made in the body wall is completely filled by the chamber, which is anchored in position by being sewed to the cut edges of the body wall. The sides of the chamber are kept from pressing against the mesentery by buffers cut from paraffin-impregnated blotters.

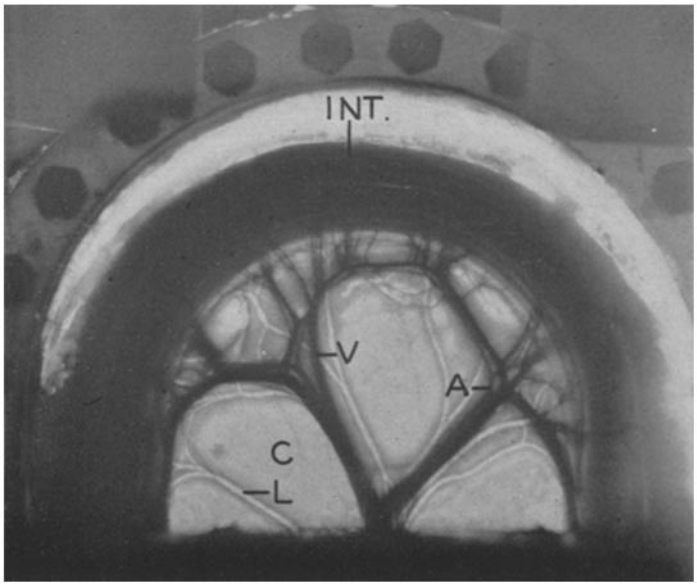
In such a chamber (*cf.* Text-fig. 1) the blood vessels and lymphatics of the mesentery are clearly visible. In the present experiments they were studied at magnifications of from 16 to 200 diameters before and after the production of shock. At the higher magnifications even the endothelial nuclei in the walls of the capillaries could be distinctly seen and so could the blood cells within the vessels. The portion of intestine visualized was always the jejunum or ileum. The response of the vessels proved to be the same in both.

Shock was elicited by tying cords tightly around each leg as close to the body as possible, leaving them on for approximately 3 hours, and then cutting them. In most instances the cats died in shock within 3 to 6 hours after the cords were cut.

Before the cords were tied on the legs, control ocular micrometric measurements were made of the diameters of from 4 to 8 arteries and veins in each chamber. The control sizes of the vessels in the different chambers varied only slightly, the different arteries studied having diameters of from 0.10 mm. to 0.75 mm. The veins studied were of many different sizes, starting with small venules having diameters of only about 0.02 mm. and going up to the larger veins of the mesentery, which were approximately 1.2 mm. in diameter.

Thus the arteries studied were arterioles and arteries having slightly larger diameters than arterioles. No differences were observed between the reactions of such arterioles and the other arteries studied. When only the term "artery" is used in the subsequent portions of this paper, it applies to arteries of all of the sizes studied, including the arterioles.

Photographs of the vessels were taken with a Leica camera at regular intervals before and after tying of the cords and also after cutting them. In the experiments in which the effect of hemorrhage upon the vessels was tested, photographs were taken before and after removal of blood.



TEXT-FIG. 1. Photograph of an intestinal-mesentery chamber in a normal, anesthetized cat (cat 6) showing arteries (*A*), veins (*V*), and lymphatics (*L*) of the mesentery, and the loop of intestine (*INT.*) exteriorized in the chamber. The lighter areas of the mesentery (*C*) contain blood capillaries and venules. The magnification is too low for them to be distinguished clearly in this photograph, but in the living animal they can be distinctly seen when studied at higher magnifications. The nuts and bolts which fasten the two halves of the chamber together are visible, and in the upper corners of the photograph the edges of the clamps which hold the chamber upright can be seen. The dark region at the bottom of the photograph is the surface of the cat's abdomen. The arteries, veins, and lymphatics of the mesentery pass through the abdominal wall and into the chamber at this point, as shown in the photograph. × 1.6.

The chambers were inserted in the morning and shock induced in the afternoon. The cats were anesthetized by intraperitoneal injections of 30 mg. of sodium pentobarbital (Lilly) per kilo. Following the insertion of the chamber one carotid artery was cannulated and the pressure recorded on a kymograph by a mercury manometer. The cats were then allowed to remain on their backs for from 1 to 3 hours in order to establish constant control conditions.

In two instances (cats 1 and 4) from 3 to 5 cc. of blood were drawn at various times from the femoral vein for hematocrit determinations. This was not done in further cases, since it was felt that the withdrawal of even such small amounts of blood might affect the behavior of the vessels.

In order to ascertain whether the kidneys, the suprarenals, and the pancreas played any part in the behavior of the vessels in shock, intestinal-mesentery chambers were inserted into cats with the kidneys, suprarenal glands or pancreas removed under surgical conditions, and the vessels in these chambers studied before and after the production of shock, as described above.

The intestine as well as the mesentery can be seen in intestinal-mesentery chambers, so that in these experiments it was possible to tell something about the amount of blood being supplied to both of these structures by their color, blanching indicating a decreased supply and flushing the opposite.

In order to see whether any of the reactions of the vessels observed in shock occurred in unshocked cats when treated in the same way as the other cats except for not eliciting shock, an intestinal-mesentery chamber was inserted into a normal cat and the vessels studied for an even longer period of time than in the shocked cats. Autopsies of all cats were made within half an hour after death.

In the experiments in which the effect of hemorrhage upon the blood vessels was observed, the blood was always drawn from the femoral vein. The amounts of blood removed, and the times of such removal are given subsequently.

Nineteen cats were used in these experiments, ocular micrometric measurements of approximately 100 arteries and veins made, and 750 photographs taken.

OBSERVATIONS

Behavior of the Vessels of the Mesentery of Normal Cats in Shock.—Three cats (Nos. 1, 2, and 4) were used in these experiments. Marked constriction of the arteries of the mesentery occurred following application of cords to the limbs. It persisted for several hours and was accompanied by blanching of the mesentery and intestine and narrowing of the mesenteric veins. Arterial constriction finally gave way to relaxation, and two of the cats died shortly thereafter.

Arterial constriction was observed within 1 hour following the tying of the cords. It persisted for $1\frac{1}{2}$ hours after the cords were cut in chambers 2 and 4. The arteries of the mesentery at the time of greatest narrowing constricted to 0.4 their control diameters in chamber 2, to from 0.5 to 0.7 in chamber 4, and to from 0.6 to 0.8 in chamber 1. The subsequent relaxation was to from 0.9 to 1.1 the control diameters.

Blanching of the mesentery and intestine occurred when the arteries constricted. A typical example is that of cat 4, in which blanching was so marked 1 hour and 10 minutes after the cords were tied that it could be clearly observed from across the room when compared with the pink color of the mesentery in a control chamber in a normal cat.

Although the blood supply to the mesentery and intestine was evidently reduced when the arteries constricted, as shown by blanching, the degree of constriction was not sufficiently great to interrupt the flow of blood through any of the vessels studied.

Following relaxation of the arteries, the mesentery and intestine once again became pink, but so far as could be ascertained, not appreciably more so than in normal cats. No pooling or stagnation of blood was seen in the vessels of the mesentery, although in each experiment the vessels were watched continuously until death of the cats in shock. The blood corpuscles within the capillaries and venules could be clearly seen, yet no crowding together of the corpuscles was observed as when increase in permeability with extensive loss of plasma occurs.

The veins of the mesentery also became narrower following the tying on of the cords. Measurements showed that narrowing was from 0.4 to 0.7 of their control diameters. Thus the narrowing of the veins was of about the same degree, compared to their original diameters, as that of the arteries. In one instance the veins returned approximately to their control diameters following relaxation of the arteries, while in the other two they did not.

Figs. 1 to 4 show the vessels in chamber 4 before the cords were tied on, after the cords were tied on, and after the cords were cut. Figs. 5 to 7 show a portion of these vessels at higher magnification.

In cats 2 and 4 the blood pressure rose above the control level directly following tying of the cords (from 150 mm. Hg to 200 mm. Hg in the case of cat 2, and from 120 mm. Hg to 150 mm. Hg in the case of cat 4). During this period of elevated pressure the arteries of the mesenteries in both cats were constricted and the veins narrowed. In the case of cat 2, the arteries relaxed within approximately 3½ hours after the onset of their constriction, and the blood pressure gradually fell until it reached 88 mm. Hg, 2 hours and 30 minutes after the cords were cut. The cat died 15 minutes later. Autopsy showed hemorrhages in the liver, lungs, and left ventricle. In cat 4, the arteries began to relax after a period of constriction of similar length, and the pressure gradually fell until it reached 20 mm. Hg, 7 hours and 27 minutes after the cords were cut. The cat died 1 minute after this low pressure was reached. Autopsy showed marked hemorrhages in the left ventricle, a few small ones in the right ventricle, and a splotched and hemorrhagic spleen.

In cat 1, the pressure began to fall as soon as the cords were tied on, and during the period of arterial constriction. 5 hours after they were cut it had fallen to 93 mm. Hg from a control level of 120 mm. Hg, and the arteries had relaxed. At this time blood was removed from the femoral vein until the pressure fell to 56 mm. Hg. After this the arteries constricted again, following which they relaxed somewhat, and the pressure fell gradually until it reached 20 mm. Hg, 2 hours later. The cat died 10 minutes after this low pressure had been reached. Autopsy showed hemorrhage in the liver and hemorrhages in both chambers of the heart.

The hematocrit determinations made in the case of cats 1 and 4 indicated progressive hemoconcentration. In cat 4, the control hematocrit reading showed the erythrocyte volume to be 41 per cent; this increased to 45 per cent 2 minutes before the cords were cut, and 47.5 per cent 6 hours and 35 minutes later, 50 minutes before the death of the cat. In cat 1 the erythrocyte volume increased from a control level of 36 per cent to 45 per cent 5 hours and 26 minutes after the cords were cut.

A slight narrowing of the lymphatics of the mesentery was observed in chambers 1 and 2 during the late stages of shock.

The data secured with cat 4 are typical, and a protocol of this experiment follows:—

Cat 4. Female, weight 9 pounds.

9:00 a.m. 30 mg. per pound pentobarbital injected intraperitoneally. 9:30–10:30 a.m. Intestinal-mesentery chamber inserted. 2:15 p.m. Carotid cannulated. 2:45 p.m. 3 cc. blood drawn from femoral vein for hematocrit determination. 3:00–3:30 p.m. Control photographs showing all of the vessels in this chamber. 3:30–3:45 p.m. Control ocular micrometric measurements of 8 arteries and 4 veins. 3:45 p.m. Control pressure, 120 mm. Hg.

3:46–4:00 p.m. Cords tied on all 4 legs.

4:15–4:30 p.m. Ocular micrometric measurements of the diameters of arteries and veins showed arterial constriction and venous narrowing. 4:48–4:54 p.m. Photographs of constricted arteries and narrowed veins. The mesentery and intestine were seen macroscopically to be blanched.

4:55 p.m. Pressure 150 mm. Hg. 5:27–5:35 p.m. Photographs of constricted arteries and narrowed veins.

5:35–5:58 p.m. Comparison of chamber 4 with a control chamber, No. 5. Mesentery and intestine of chamber 4 markedly blanched; no blanching of mesentery and intestine in control chamber.

5:59–6:48 p.m. Photographs. 6:20 p.m. Pressure 140 mm. Hg. 7:20 p.m. Pressure 116 mm. Hg.

7:21 p.m. Ocular micrometric measurements showed some arterial relaxation in 6 out of 7 arteries, but continued narrowing of all but 1 of the 4 veins measured.

7:35–7:41 p.m. Photographs. 7:50 p.m. Pressure 88 mm. Hg. 7:51 p.m. 3 cc. blood drawn from femoral artery for hematocrit determination.

7:53 p.m. Cords cut.

7:56 p.m. Pressure 100 mm. Hg.

8:00 p.m. Ocular micrometric measurements showed that 3 of the 7 arteries measured are still constricted, and that the other 4 have returned to their control diameters. All veins are still narrower than their control diameters.

8:10–8:12 p.m. Photographs. 8:14 p.m. Pressure 88 mm. Hg. 8:19 p.m. Pressure 90 mm. Hg. 8:47 p.m. Pressure 72 mm. Hg. 8:55 p.m. Photographs. 9:30 p.m. Photographs. 10:00 p.m. Photographs. 10:05 p.m. Pressure 80 mm. Hg.

10:12 p.m. Control chamber examined. Vessels of mesentery normal; no blanching of mesentery or intestine.

10:15 p.m. Ocular micrometric measurements, chamber 4. Two arteries still

constricted; 4 arteries have returned to their control diameters. All veins still narrowed, but not quite as much as earlier.

11:05 p.m. Photographs; pressure 80 mm. Hg. 1:40 a.m. Pressure 68 mm. Hg. 1:52 a.m. Photographs. 2:20 a.m. 3.0 cc. blood drawn for hematocrit determination. 2:25 a.m. Photograph. 2:45 a.m. Pressure 60 mm. Hg. 2:55 a.m. Pressure 46 mm. Hg. 2:58 a.m. Photographs. 3:03 a.m. Photographs. 3:05 a.m. Pressure 50 mm. Hg.

3:07 a.m. Ocular micrometric measurements of blood vessels; all arteries have returned approximately to their control diameters, and so has one of the veins; the other 3 are still narrowed.

3:10 a.m. 2 samples of blood (each 3 cc.) drawn for hematocrit determinations; the blood seemed thick and viscous and was secured with difficulty. 3:30 a.m. Pressure 36 mm. Hg. 3:32–3:34 a.m. Photographs. 3:34 a.m. Pressure 20 mm. Hg. 3:36 a.m. Flow has stopped through vessels in chamber.

3:38–4:35 a.m. Photographs. Cat dead. No appreciable hemorrhages in mesentery or intestine; no evidence of pooling of blood or concentration of erythrocytes in the vessels.

4:05 a.m. Photographs of control chamber 5. Cat 5 alive and in good condition. Vessels and blood flow in mesentery appear normal.

4:20 a.m. Control cat 5 killed by intravenous injection of 2.75 mg. histamine. Marked arterial constriction and sudden fall in arterial pressure occurred.

4:25 a.m. Autopsy of cat 4; spleen splotched and hemorrhagic; hemorrhages in endocardium of left ventricle, and a few small ones in the right.

4:40 a.m. Autopsy of cat 5 (control); no hemorrhages or abnormalities observed.

Behavior of the Vessels of the Mesentery of Nephrectomized Cats in Shock.— Four cats (Nos. 9, 10, 12, and 15) were used in these experiments. In each case both kidneys were removed on the day preceding the introduction of the intestinal-mesentery chambers and production of shock.

In 3 of the cats (Nos. 9, 10, and 12) death from shock occurred within from 2 to $5\frac{1}{2}$ hours after the cords were cut; in the fourth case (No. 15) the cat recovered, after having shown many of the typical signs of shock.

The behavior of the vessels in the mesenteries of these nephrectomized cats was similar to that in normal cats put into shock. As in the normal cats, arterial constriction and narrowing of the veins occurred following application of the cords (*cf.* Figs. 10 and 11). In three cases (Nos. 9, 10, and 15) the pressure rose above the control level after the cords were tied on; the arteries constricted, and the veins became narrowed during the period of elevated pressure. The pressure subsequently fell in all instances and the cats died in shock. In the fourth case (No. 12) the pressure fell progressively following tying on of the cords, even during the period of arterial constriction and narrowing of veins.

When the arteries of the mesentery constricted, the mesentery and intestine

were seen to become markedly blanched, as in normal cats following tying on of the cords. Arterial constriction persisted for 4 hours in cats 10 and 12 and for from 4 to 6 hours in cat 15. Constriction was followed by relaxation to approximately the control diameters. When the arteries relaxed, blanching of the mesentery and intestine disappeared. Arterial constriction and venous narrowing was observed for 3½ hours in cat 9 following tying on of the cords.

In cat 15 although the pressure gradually fell to 78 mm. Hg and arterial relaxation occurred, the animal survived. The following morning it was still alive and at this time the arteries had the same diameters as when control measurements were made 16 hours previously. The pressure was 80 mm. Hg as compared to the control pressure of 122 mm. Hg. The arteries remained unchanged in diameter until 3:45 p.m. at which time 20 cc. of blood were drawn. The arteries then constricted, the pressure fell from 80 to 54 mm. Hg, and the cat died 7 minutes later.

Narrowing of the lymphatics in the chambers was observed during shock in the nephrectomized cats (*cf.* Figs. 10 and 11).

Autopsies of the nephrectomized cats showed the following:—

(1) *In cat 9*, small hemorrhages in the spleen, large hemorrhages in one lobe of the liver, large hemorrhages in one lobe of the lung; small hemorrhages in the right ventricle, and large and numerous hemorrhages in the left ventricle; (2) *in cat 10*, hemorrhages in the spleen, liver, lungs, and left ventricle; (3) *in cat 12*, hemorrhages in the liver, spleen, lungs, and both ventricles; (4) *in cat 15*, hemorrhages in the liver and in the heart at the origin of the aorta.

No evidence of stagnation or pooling of blood in the mesentery was observed at any time, even following relaxation of the arteries or shortly before death. In cat 12 the flow of blood through the capillaries and venules of the mesentery was watched continuously during the terminal stages of shock. The corpuscles could be clearly seen moving through the vessels. The flow stopped when the pressure fell to 20 mm. Hg and at this time the corpuscles were seen to be floating in what seemed to be the normal amount of plasma. Death was not preceded by crowding together of corpuscles in any of the capillaries studied and cessation of flow was presumably due to failure of the heart.

During the terminal stage of shock, the movement of leukocytes along the walls of the capillaries and venules of the mesentery was studied. The leukocytes rolled along without change of shape at phase 1 of the Clark and Clark (19) scale. There was no evidence of increased sticking of leukocytes to the walls of the capillaries or venules.

Behavior of the Vessels of the Mesentery of Suprarenalectomized Cats in Shock.— In one cat the suprarenal glands were removed the day before introduction of

the mesenteric chamber and in two others they were removed on the same day as the chamber was inserted and shock elicited.

Following tying on of the cords, arteries of the mesenteries of the suprarenalectomized cats constricted, just as did those of normal cats and nephrectomized cats. A similar narrowing of the veins also occurred. (*cf.* Figs. 8 and 9.)

The response in cat 11 was typical. In this cat the suprarenal glands were removed between 11:15 and 11:30 a.m. and the intestinal-mesentery chamber inserted between 11:40 a.m. and 12:40 p.m. A carotid artery was cannulated at 2:15 p.m., at which time the pressure was 136 mm. Hg. The cords were tied on at 3:12 p.m. By 3:28 the arteries had constricted to 0.7 their original diameters, and the veins to 0.8. The pressure had by this time fallen to 70 mm. Hg. The arteries relaxed 3 hours later, shortly before the cords were cut. The cat died approximately 3 hours after the cords were cut, and after the pressure had gradually fallen to 34 mm. Hg. In this case the arterial pressure fell even during the period of arterial constriction. Autopsy showed hemorrhages in the spleen, liver, lungs, and kidneys. Narrowing of the lymphatics was also observed in these adrenalectomized cats during shock (*cf.* Figs. 8 and 9).

The capillaries and venules of the mesentery were watched carefully to see whether any concentration of corpuscles, with stasis, occurred in them. None was observed. Nor was any pooling of blood in the mesentery, or increased sticking of leukocytes to the walls of the vessels seen.

The experiment with cat 13 resembled that of cat 11, with the exception that in this case the cat died before the cords were cut, 2 hours and 55 minutes after the cords were tied on the legs. Autopsy showed marked hemorrhages in the left ventricle; small hemorrhages in the right ventricle, and hemorrhages in the liver and spleen.

In cat 14, both suprarenals were removed the day before insertion of the intestinal-mesentery chamber, and after removal of the suprarenals the cat was given ½ cc. of Wilson's suprarenal cortical extract. The results secured with this cat were similar to those secured with cat 13. Autopsy showed massive hemorrhages in the liver; hemorrhages in the lung; and hemorrhages in the spleen.

Behavior of the Vessels of the Mesentery of Pancreatectomized Cats in Shock.— Two cats, (Nos. 16 and 17) were used in these experiments. In both cases the pancreas was removed the day before the insertion of the intestinal-mesentery chambers. Arterial constriction, narrowing of veins, and blanching of the mesentery and intestine occurred in the cats.

In cat 16 no arterial constriction was observed until 1 hour and 23 minutes after the cords were tied. At this time constriction was from 0.7 to 0.9 the original size

of the arteries (7 were measured). 2 hours and 33 minutes after the cords were tied all of the arteries had relaxed to their control diameters or slightly more. They remained relaxed until half an hour after the cords were cut, when they all constricted again, this time to a slightly greater degree than before (from 0.6 to 0.9 their original diameters). This second constriction was followed by a gradual fall of arterial pressure until the cat died in shock, 6 minutes after the pressure had reached 36 mm. Hg. For 1 hour preceding death the pressure had been 52 mm. Hg or below, but the arteries did not relax.

During the final 18 minutes before the cat's death, the vessels of the mesentery were continuously watched. The endothelium of the vessels could be clearly seen, and so could the erythrocytes and leukocytes within the capillaries and venules. The flow of blood through the capillaries and venules gradually became slower and slower with the progressive fall in blood pressure. When the pressure had reached 39 mm. of mercury the flow stopped in many of the capillaries, but still persisted in those which formed the most direct passages from the arterioles to the venules. It finally stopped in these also when the pressure fell below 25 mm. Hg. No crowding together of erythrocytes was observed, the flow evidently stopping because of failure of the heart. Even after death, the corpuscles could still be seen floating in plasma. Death was not preceded by pooling of blood in the mesentery, nor by any increase in sticking of leukocytes to the walls of the blood vessels.

Autopsy showed large hemorrhages in the lungs, spleen, and liver. The heart seemed unusually flabby and soft, but no hemorrhages were seen in it. There were small hemorrhages in the mesentery and intestine.

The results in cat 17 were similar, but death followed arterial relaxation without the intervention of a second phase of constriction. The degree of arterial constriction was somewhat greater, being from 0.46 to 0.53 the control diameters. Autopsy showed massive hemorrhages in the spleen, and hemorrhages in the liver and lungs.

Behavior of the Vessels of the Mesentery Following Removal of Blood from the Femoral Vein.—Three cats (Nos. 6, 7, 8) were used in these experiments. Removal of blood was followed in all cases by constriction of the arteries of the mesentery. The veins also became narrower and so did the lymphatics. (*cf.* Figs. 12 and 13.)

The removal of blood caused in all cases an initial fall in pressure. This, however, was followed in two cases by a rise in pressure to a level above the control pressure. The arteries remained constricted during this period of elevated pressure. In cat 6 death occurred suddenly during the period of elevated pressure. In cat 7 the pressure fell progressively until the cat died; in cat 8 the pressure fell following removal of blood, then rose above the control level, where it remained for a short time, and then fell progressively until the cat died shortly after the pressure had reached 30 mm. Hg. In cat 7 death was preceded by arterial relaxation.

The data for cat 7 are summarized below:—

Female, weight 6 pounds.

Chamber inserted 9:45–10:45 a.m.

1:00 *p.m.* Pressure 90 mm. Hg. 1:18 p.m. Control measurements of arteries. 1:27 p.m. Control photographs.

1:45 p.m. 20 cc. blood drawn.

2:13 p.m. Photographs show marked constriction of arteries and narrowing of veins. In this cat no lymphatics were present in the portion of the mesentery in the chamber.

2:15 p.m. Ocular micrometric measurements showed that the arteries constricted to approximately 0.65 of their control diameters.

2:19 p.m. 20 cc. of blood drawn. Total = 40 cc.

2:22 p.m. Photographs; arteries markedly constricted and veins narrowed. 2:26 p.m. Pressure 52 mm. Hg. 3:00 p.m. Pressure 68 mm. Hg.

3:15 p.m. 10 cc. blood drawn. Total = 50 cc. 3:16 p.m. Pressure 54 mm. Hg. 3:25 p.m. Photographs. Arteries constricted and veins narrowed.

3:30 p.m. 10 cc. blood drawn. Total = 60 cc. 3:37 p.m. Pressure 24 mm. Hg; photographs; arteries relaxed. 3:40 p.m. Pressure 12 mm. Hg. Arteries relaxed. 3:42 p.m. Photographs. 3:45 p.m. Blood flow stopped; cat dying.

Autopsy.—Spleen splotched and hemorrhagic; hemorrhages in valves of heart; hemorrhages in the mesentery.

Behavior of the Vessels of the Mesentery in the Pithed Cat.—One cat (No. 3) was pithed and kept alive by artificial respiration through a cannula inserted into the trachea. The pressure fell immediately after pithing to 58 mm. Hg from a control pressure of 156 mm. Hg. No change in diameter of the arteries, veins, or lymphatics occurred, nor was any blanching of the mesentery or intestine seen. The cat was kept alive for 6 hours and 7 minutes after pithing, and was then killed by intravenous injection of 2.75 mg. of histamine, which caused sudden and marked arterial constriction and an abrupt and fatal fall in blood pressure. The cat died within about 6 minutes after injection.

Behavior of the Vessels of the Mesentery in a Normal Anesthetized Cat (Control Chamber).—An intestinal-mesentery chamber was inserted in cat 5 between 10:30 and 11:30 a.m. It was observed until 4:20 a.m. the following morning. No constriction of the arteries or veins occurred during this time, nor did the mesentery become blanched. At 4:20 a.m., 2.75 mg. histamine was injected intravenously. The arteries of the mesentery constricted almost at once and the mesentery and intestine became blanched. The cat died 6 minutes and 30 seconds after the injection.

DISCUSSION

The present experiments show by direct observation that marked and prolonged constriction of the arteries, arterioles, and veins of the mesentery occurs following incomplete occlusion of limb circulation, and also after hemorrhage.

The length of time that such constriction persisted varied in different cats, but it usually lasted for from 3 to 4 hours. The final stages of shock were characterized in most instances by arterial and arteriolar relaxation.

Narrowing of the arteries and arterioles was not passive, but was due to muscular constriction, since in many cases it occurred when the arterial pressure was above the control level. Furthermore, relaxation occurred late in shock when hemoconcentration was greatest and the blood volume is known to be smallest. Also the walls of these vessels were seen to be thickened during the period of constriction. That such thickening occurs when arterioles constrict has been shown previously by Clark, Clark, and Williams (20), by Clark and Clark (21, 22), and by Abell and Page (23).

It would be of interest to know whether constriction such as observed in the mesentery in the present experiments also occurred in the case of the superficial vessels. In this connection certain unpublished observations by the present authors might be mentioned:—

When arterioles in a transparent moat chamber (Abell and Clark (24); Abell (25)) in a rabbit's ear were studied at magnifications of 400 diameters during shock produced by incomplete occlusion of the circulation to the limbs, they were observed to constrict markedly. They remained intensely constricted for 3 hours and 40 minutes, after which they relaxed. The rabbit died in shock, about 2 hours later. Observations of the vessels in an intestinal-mesentery chamber were made simultaneously with those upon the ear, and showed that during the period of constriction of the arterioles in the ear, similar constriction was also present in the mesentery.

The constriction observed in the cats, and also in the rabbit noted above, caused a decrease in the amount of blood being supplied to the mesentery and intestine, as shown by the blanching of these structures. That it also caused a decrease in venous return from them could be seen by direct observations of the blood flow in the mesenteric veins.

Burton-Opitz (26) has shown that even a moderate constriction of the splanchnic blood vessels, produced by stimulation of the splanchnic nerve, reduces the venous supply to the heart. The degree of such reduction was shown to depend upon whether or not the superficial vessels also constricted, the reduction being greatest when they did constrict.

If constriction such as that observed in the mesentery in the present experiments occurs generally throughout the splanchnic region during shock, as is suggested by the experiments of Mann (11), and if the superficial arterioles also constrict, as is indicated by the behavior of the vessels in the rabbit's ear noted above, then it would seem that in shock such constriction might play a not unimportant part in helping to bring about the decrease in venous return to the heart. Wiggers (27) has recently reviewed the literature dealing with

such decrease in venous return to the heart during shock, and has pointed out its significance.

That loss of fluid at the site of injury is of fundamental importance in decreasing the venous return to the heart during shock has been shown convincingly in recent reviews of the literature by Blalock (28) and Harkins (29). The present observations suggest that constriction of the small arteries and of the arterioles may also be an important factor in decreasing the venous supply to the heart during shock, especially during the primary stages.

The site of injury in the present experiments was the legs, and that loss of fluid occurred in them was shown by the marked swelling always observed following tying on of the cords, and the hemorrhages in them, distal to the point of application of the cords, seen at autopsy.

Veins the size of the ones studied in these experiments have muscle in their walls and are able to constrict in response to a variety of pressor substances injected intravenously. Constriction of veins of comparable size was observed by Wilson (30) in preformed tissue chambers in rabbits' ears, and of veins of even smaller diameter by Abell and Page (23) in transparent moat chambers in rabbits' ears. It is thus possible that the narrowing of the veins in the present experiments may have been due to active muscular contraction. Since in the pithed cat the arterial pressure fell to 58 mm. Hg and remained there for many hours without constriction of the arteries and arterioles, or narrowing of the veins of the mesentery, it is clear that such changes in animals put into shock were not due simply to fall in pressure.

If the narrowing of the veins observed in the mesentery in the present experiments occurred generally, then, in these experiments at least, relaxation of veins did not play a part in causing decrease in venous return to the heart. This is in accord with the conclusion by Wiggers (27) that there is no good evidence that in shock the peripheral circulatory failure is caused to any appreciable degree by failure of a venopressor mechanism.

In view of the many reports in the literature suggesting pooling of blood in the splanchnic area and loss of fluid in this region during shock, it was a surprise to us not to find in these experiments stasis of blood in the capillaries and venules of the mesentery, and crowding together of the erythrocytes. It is, of course, quite possible that some increase in permeability may have occurred short of that necessary to cause crowding together of erythrocytes, but no evidence either for or against this possibility was secured.

In these experiments with cats marked hemorrhages, such as those found at autopsy in the viscera by Moon and his associates (31) were usually not observed during shock. In this connection it may perhaps be mentioned that in experiments with dogs, we observed quite large hemorrhages in the mesen-

teries during shock, when the vessels were examined in intestinal-mesentery chambers.

That arterioles respond by dilatation to local injury or trauma has been observed repeatedly by Clark and Clark (personal communication) in transparent chambers in rabbits' ears. When shock is caused by exposing and manipulating the intestine and mesentery, such arteriolar dilatation with increased blood flow, congestion, and even hemorrhages would be expected to occur in these structures. It is well known that this does take place. This cannot be taken as evidence, however, that such reactions occur generally throughout the body during shock caused in this way. That they do not is indicated by the report of Mann (11) that in shock produced by traumatizing the intestines, the peripheral untraumatized visceral arteries constrict, as shown by shrinkage in volume of the kidney. The present experiments show by direct observation that when the site of injury is in the legs, and also when large amounts of blood are withdrawn from the femoral vein, the vessels of the mesentery constrict. This is in accord with the view expressed by Wiggers (27) that the conception of primary arteriolar dilatation as an initiating agent in shock should be abandoned.

That the kidneys, suprarenal glands, and pancreas are not essential for the production of shock in cats and that arterial and arteriolar constriction following injury to the limbs occurs in the absence of these structures, is shown by the experiments with nephrectomized, suprarenalectomized, and pancreatectomized cats. The behavior of the vessels and the shock that occurred seemed to be comparable in every way to that observed in cats with these organs intact.

SUMMARY

1. Direct observations of the arteries, arterioles, capillaries, veins, and lymphatics in the mesentery of anesthetized cats put into shock by incomplete occlusion of the circulation of the limbs showed that:

(*a*) Marked constriction of the arteries and arterioles, produced by muscular contraction, occurred usually within an hour after incomplete occlusion of the limbs, lasted several hours, and finally gave way in most instances to relaxation an hour or more before death. The constriction reduced the blood supply to the mesentery and intestine and the venous return from them. It did not, however, interrupt the blood flow. No pooling or stagnation of blood was seen even as a terminal phenomenon.

(*b*) The veins of the mesentery also became constricted but showed less tendency to dilate as death approached. The lymphatics likewise became somewhat narrowed. Even during the terminal stage the leukocytes moved along without change in shape or sticking to the walls of the capillaries or venules.

(*c*) Hematocrit determinations showed progressive hemoconcentration of moderate degree.

(*d*) Autopsy usually showed the presence of small hemorrhages in many parts of the body, especially the heart, liver, spleen, and lungs.

(*e*) Bilateral nephrectomy, suprarenalectomy, and pancreatectomy did not significantly alter the morphological picture elicited by shock induced by restriction of the circulation to the limbs.

2. Removal of large amounts of blood was always followed within a short time by constriction of arteries, arterioles, veins, and lymphatics of the mesentery.

3. Fall in arterial pressure produced by pithing was not accompanied by change in diameter of the arteries, arterioles, veins, or lymphatics, or by blanching of the mesentery or gut.

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EXPLANATION OF PLATES

PLATE 8

Photographs of blood and lymphatic vessels in an intestinal-mesentery chamber in an anesthetized cat (cat 4), showing the appearance of the vessels of the mesentery before shock and after the production of shock.

FIG. 1. Control photograph, taken at 3:14 p.m. The blood pressure at this time was 136 mm. Hg. *A*, artery; *V*, vein; *L*, lymphatic; *C*, region of capillaries and venules. × 2.5.

FIG. 2. Photograph of the same vessels as shown in Fig. 1, taken at 4:48 p.m. Pressure 145 mm. Hg. The cords were tied on the legs at 4:00 p.m. The arteries are constricted and the veins narrowed. × 2.5.

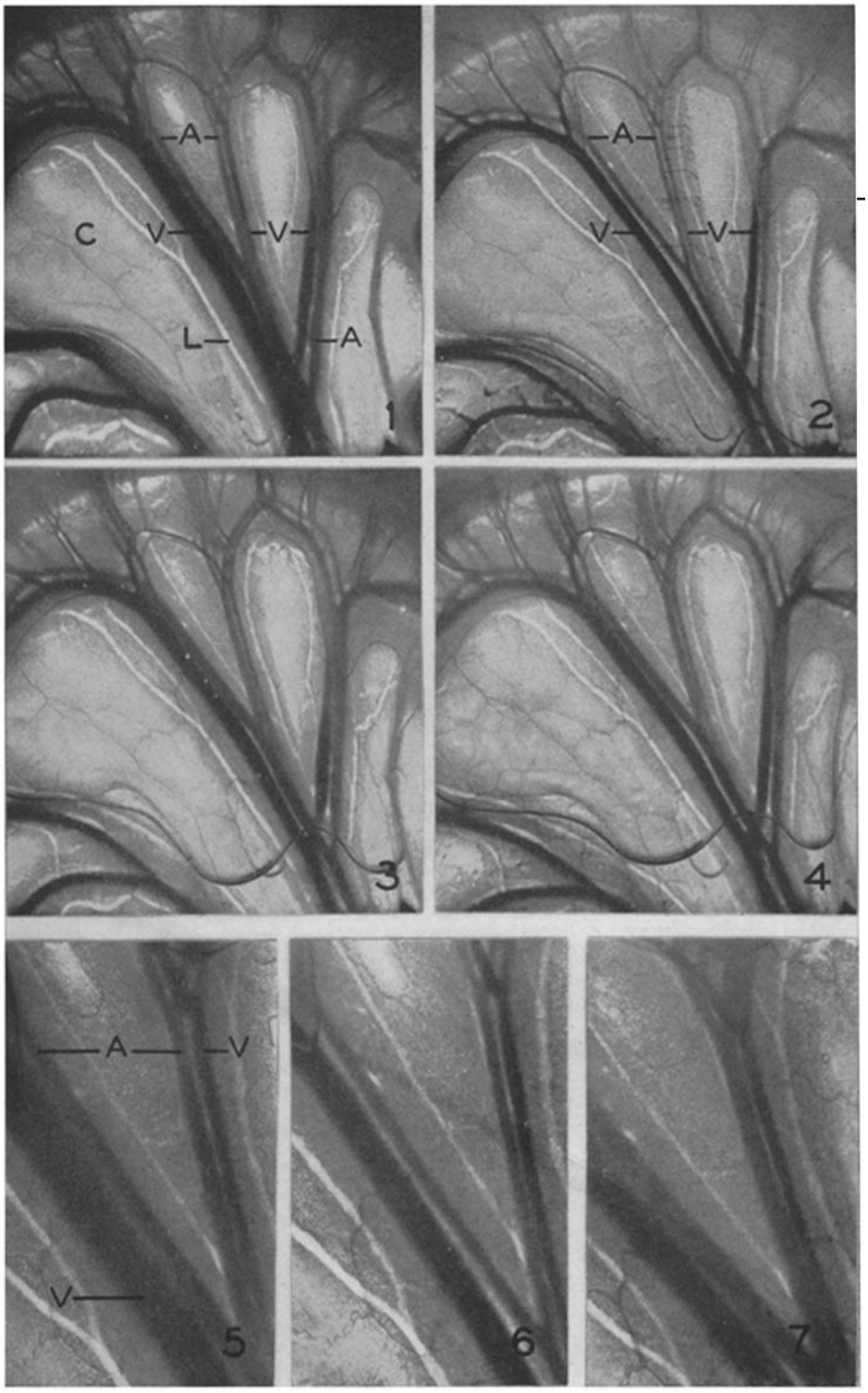
FIG. 3. The same vessels at 11:05 p.m. Pressure 80 mm. Hg. The arteries have relaxed to approximately their control diameters, but the veins are still somewhat narrowed. The cords were cut at 7:53 p.m. × 2.5.

FIG. 4. The same vessels at 3:03 a.m. Pressure 46 mm. Hg. The arteries are still relaxed and the veins still somewhat narrowed. This photograph was taken during the terminal stage in shock. The cat died at 3:35 a.m., without further changes in the appearance of the vessels. × 2.5.

FIG. 5. Photograph at higher magnification of a portion of the vessels shown in Figs. 1–4. *A* of this photograph indicates the same position on the branches of the artery as does *A* of Fig. 1. This photograph was taken at 2:30 p.m., and shows the control diameters of the vessels. Pressure 136 mm. Hg. *A*, artery; *V*, vein. × 6.3.

FIG. 6. The same vessels at 4:51 p.m. Pressure 145 mm. Hg. The cords were tied on the legs at 4:00 p.m. The arteries are constricted and the veins narrowed. × 6.3.

FIG. 7. The same vessels at 2:55 a.m. Pressure 46 mm. Hg. The arteries have relaxed and are now slightly larger in diameter than during the control period (compare with Fig. 5). The cat died in shock 40 minutes after this photograph was taken. × 6.3.



(Page and Abell: Vessels of mesentery in shock)

PLATE 9

Photographs of blood and lymphatic vessels in intestinal-mesentery chambers in anesthetized cats.

FIG. 8. Control photograph of vessels in a portion of the mesentery of an adrenalectomized cat (cat 11). Both adrenal glands were removed 3 hours and 20 minutes previously. This photograph was taken at 2:20 p.m. The pressure at this time was 136 mm. Hg. × 3.6.

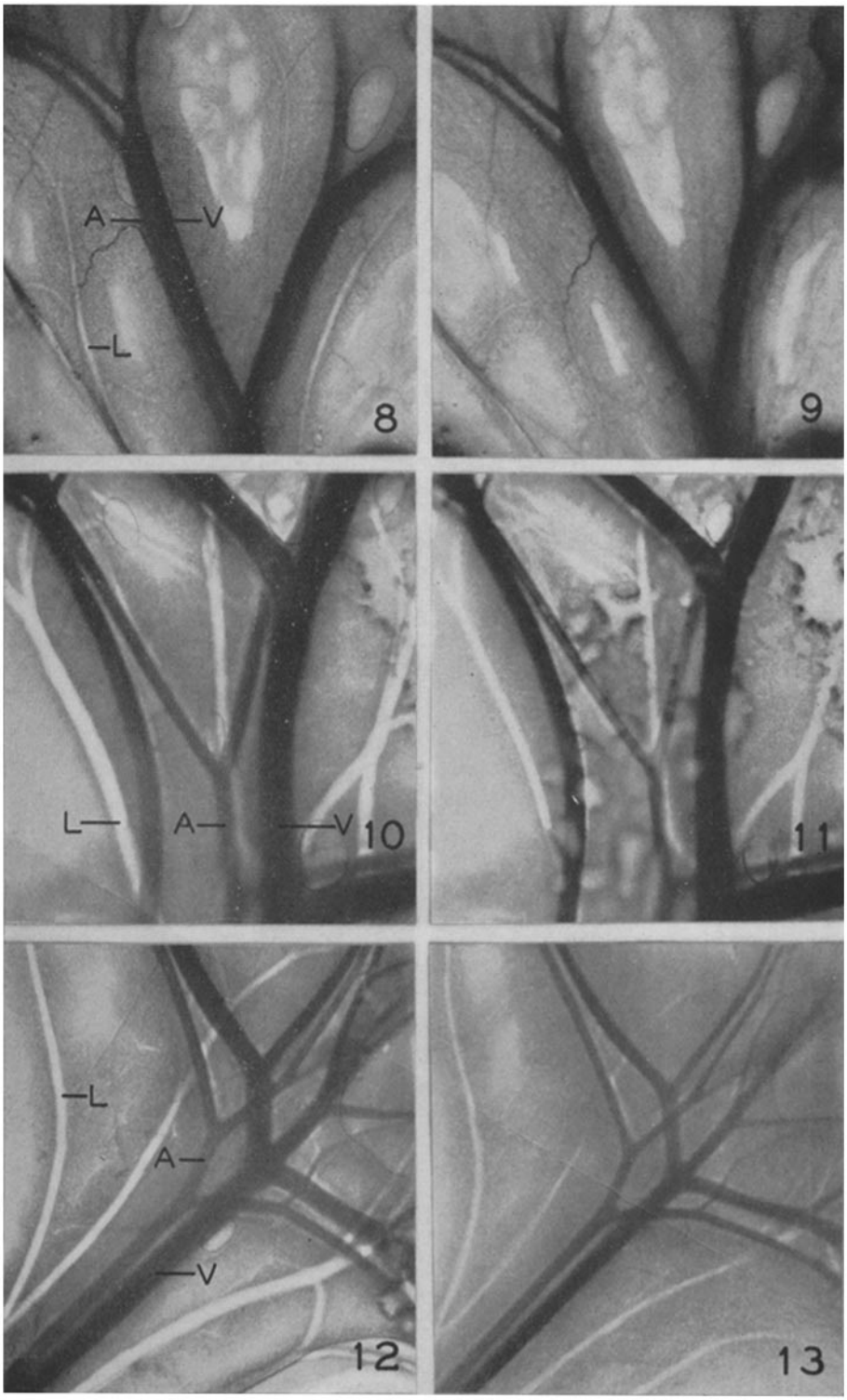
FIG. 9. The same vessels as shown in Fig. 8, at 3:37 p.m. Pressure 70 mm. Hg. The cords were tied on the legs at 3:12 p.m. The arteries are constricted and the veins and lymphatics narrowed. The cat died in shock at 9:15 p.m. × 3.6.

FIG. 10. Control photograph of vessels in a portion of the mesentery of a nephrectomized cat (cat 9), taken at 11:29 a.m. Pressure 120 mm. Hg. The kidneys were removed the day before this photograph was taken. *A*, artery; *V*, vein; *L*, lymphatic. × 6.3.

FIG. 11. The same vessels as shown in Fig. 10, at 3:37 p.m. Pressure 70 mm. Hg. The cords were tied on the legs at 11:52 a.m. and were cut at 3:19 p.m. The arteries are constricted and the veins and lymphatics narrowed. The cat died in shock at 5:10 p.m. × 6.3.

FIG. 12. Control photograph of blood vessels in a portion of the chamber shown in Text-fig. 1. The region of the artery indicated by *A* in this photograph is also indicated by *A* in the text-figure. This photograph was taken at 1:07 p.m. Pressure 84 mm. Hg. × 6.3.

FIG. 13. The same vessels as in Fig. 12, after 32 cc. of blood had been drawn from the femoral vein. This photograph was taken at 3:42 p.m., and the pressure at this time was 110 mm. Hg. The blood was drawn as follows: 10 cc. at 1:38 p.m.; 10 cc. at 2:15 p.m.; 12 cc. at 3:40 p.m. The arteries are constricted and the veins and lymphatics narrowed. × 6.3.



(Page and Abell: Vessels of mesentery in shock)