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SHOCK * †

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FOR an intelligent discussion of the problem of shock it is highly essential that the lecturer and his listeners have the same conception as to what is meant by the term. In order to accomplish this it will be necessary in the course of this discussion to present several definitions of shock including one of my own. For this I ask your indulgence, but, as Meek (1) recently stated, "every worker has given a definition of shock to illustrate his own conception of the condition, and this is, of course, what definitions are for."

In the standard text-books shock is defined as a condition in which the patient is stuporous, with depressed sensation and reflexes, in whom the skin and mucous membranes are cold, pale and often moist, the pulse rapid and thready, the blood pressure low and the pulse pressure small, the superficial veins collapsed and the respiration rapid, irregular and shallow. The term shock is unfortunately applied both to patients with temporarily lowered blood pressure and to patients with profound progressive decline of blood pressure.

SIMPLE HYPOTENSION

Following a sudden acute hemorrhage, immediately after induction of a spinal anesthesia, following painful injuries, during a faint and in other acute conditions the patient may experience low arterial blood pressure and show many of the signs and symptoms enumerated above. This has often led clinicians to consider these patients as being in shock. However, such patients usually recover spontaneously after being placed in the horizontal position, or after brief administration of

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oxygen. This temporary disturbance is called primary shock by many writers, but is probably better designated as simple hypotension.

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Shock, on the other hand, may be defined as a persistent progressive state of hypotension, in which the mean blood pressure may be around 70 mm. Hg or lower, in which the blood pressure tends in the absence of and even despite therapy to decline progressively until death ensues, and in which there is evidence of depression of the functions of most of the body tissues and increased permeability and dilation of the capillaries and venules. In the discussion of shock it will be necessary to consider both the initial stage leading up to shock and the stage of progressive deterioration or true shock.

Shock, as thus defined, is probably never seen immediately following any injury or other assault to the body, but only after the lapse of a half hour to several hours. Immediately following trauma, a patient may exhibit temporary hypotension, but within a few minutes his blood pressure may have returned to normal. On the other hand, during and immediately after the trauma his blood pressure may be elevated. In either case, after a half hour to several hours his blood pressure may begin to decline, and by the time the mean pressure reaches around 70 mm. Hg he may show the symptoms enumerated above and is then said to be in shock. Persistence of low blood pressure from the time of the injury until shock develops, as defined in this paper, will usually be seen only when there is accompanying hemorrhage. Following injuries to a hollow viscus a few patients may, however, even in the absence of hemorrhage, develop an initial hypotension which persists following the initial trauma until shock is fully established.

Shock may appear also at various intervals after burns of large areas of the body, after severe operations and prolonged anesthesia, and in clinical conditions such as cholera, diabetic coma, coronary occlusion and intestinal obstruction. The initial period of low blood pressure following a sudden hemorrhage is not shock as defined in this paper. However, prolongation of the period of hypotension such as that caused by continuous or repeated hemorrhage may induce the stage of progressive deterioration of the circulation which we call shock.

Studies of the shock problem both in the clinic and the laboratory may be divided into three main categories: (1) studies of the various phenomena which may be observed in the initial stage and in shock; (2) studies of the procedures which initiate shock; and (3) evaluation of the various therapeutic procedures and deductions from them regarding the nature of the fundamental disturbance in shock.

PHENOMENA OBSERVED DURING THE COURSE OF SHOCK

As implied above, the course of development of shock can be divided into an initial or prodromal stage in which the blood pressure may be

normal or depressed, and the stage of severe hypotension and progressive deterioration which is called true shock. Usually there is a smooth blending between the end of the initial stage and the beginning of shock, so that it may be difficult to determine whether a given patient or experimental animal is in the initial or the progressive stage.

A. The Initial Stage Leading to Shock.—In the initial stage certain factors, to be discussed below, operate apparently to produce an eventual acute but persistent decrease of cardiac output (see figs. 1 to 4). In most instances, this is due to the production of a discrepancy between the blood volume and the vascular capacity wherein the volume of circulating blood is inadequate to fill the circulatory system. Whether this is due to a relaxation of some part of the vascular system, to an absolute reduction of the circulating blood volume or to both remains a moot question and may in fact depend in any given case on the type of initiating factor. The net result is a tendency for venous pressure to decline, for decreased filling of the heart in diastole, for reduced cardiac output, for decline in arterial blood pressure and for diminished volume of circulation to all parts of the body. The body attempts to compensate for the diminished effective blood volume (*a*) by reduction of the volume of the blood reservoirs such as the spleen and probably also the liver; and (*b*) by speeding of the heart which lowers central venous pressure, and thereby improves the return of blood from the periphery to the heart. If these are inadequate and arterial pressure starts to decline, then some degree of compensatory vasoconstriction may occur in less essential parts of the body, such as skin, connective tissue, abdominal viscera and, under certain conditions, muscle, thus shunting the available circulation to the heart and brain.

If the initial factor continues to operate, the blood pressure may continue to fall despite the compensatory mechanisms and may cause death sooner or later. Whether or not the initial factor continues to operate indefinitely, death may supervene due to the patient entering what may be called the progressive or true stage of shock.

B. The Progressive Stage of Shock begins (see figs. 1 to 4) when the compensatory mechanism fails to maintain the blood pressure, and when diminished circulation begins to appear throughout the body. In the resulting ischemic areas an increase in the permeability and dilation of the capillaries and venules occurs with the result that both the fluids and proteins of the plasma begin to be lost into the extravascular tissues and the red cells begin to be accumulated in the dilated capillaries and venules. The ischemia also results in a depression of the functions and a decrease of the metabolism of the tissues and organs throughout the body. If by some means the circulation is at this time restored to normal the capillaries and body tissues may rapidly regain their normal activity. If on the other hand the diminution be severe or if it persists for a matter of from a half to a few hours, then the depression is less easily reversed and, in fact, recovery may become impossible.

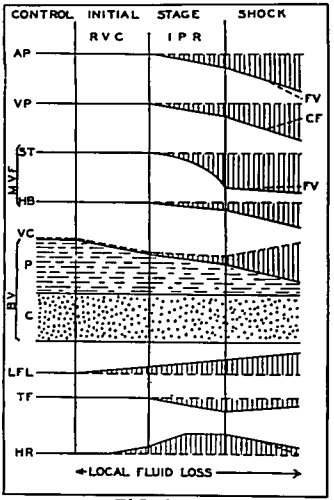

FIG. 1

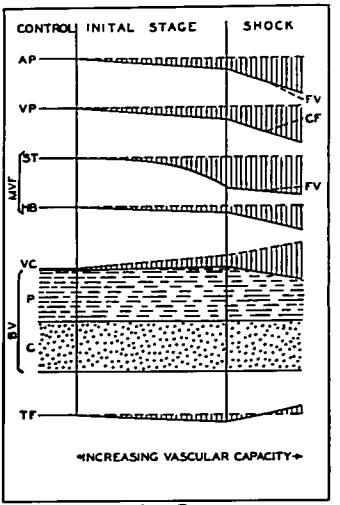

FIG. 2

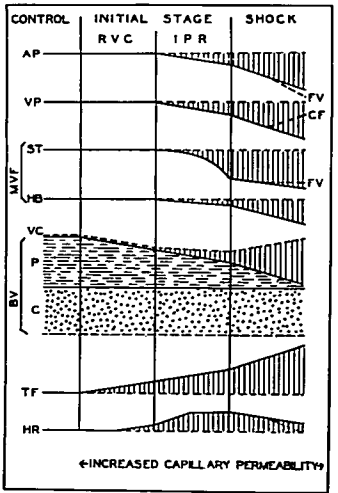

FIG. 3

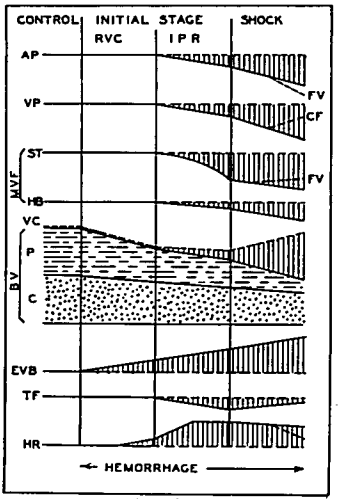

FIG. 4

This depression of capillary and tissue functions serves to accentuate the already existing discrepancy between blood volume and vascular volume by causing an absolute decrease in the circulating blood volume, an absolute increase in the vascular capacity due to the relaxation of the capillaries and of the extravascular support for the blood vessels, and, according to the recent studies of Wiggers, Werle and Cosby (2, 3), in the case of the heart a diminution in the effectiveness of cardiac emptying. As a result, return of blood to the heart, cardiac output, arterial blood pressure and minute volume of circulation to the tissues are further reduced, thus resulting in turn in further depression of capillary and tissue functions. This cyclic activity, spoken of as the vicious cycle, is illustrated in the diagram in figure 5, modified slightly from diagrams recently published by Wiggers (2, 4) and others (5, 6, 7).

Obviously, if this vicious cycle continues unchecked the minute volume of circulation and the arterial pressure will be reduced progressively to zero. However, before this occurs the patient or experimental animal usually dies of sudden failure of the heart, of ventricular fibrillation, of failure of the respiration or, occasionally, of failure to maintain the vasoconstrictor tone due to the impaired circulation to the heart, respiratory and vasomotor centers.

C. Experimental Observations.—It would seem evident that reduction of cardiac output and of blood volume must be present during the initial stage of shock, and during slow continued hemorrhage, even before aortic pressure has appreciably declined. It must be admitted, however, that neither cardiac output nor blood volume studies have demonstrated conclusively such early reduction. Wiggers and Werle (2) have shown with cardiometer records, however, that the cardiac output is decreased considerably when aortic pressure starts to fall.

FIGS. 1–4. Diagrams illustrating possible steps in the development of shock. Fig. 1. Shock due to local fluid loss such as that which occurs at the site of certain types of crushing trauma to muscle and viscera and in fluid loss due to diarrhea and vomiting. Fig. 2. Shock due to generalized increase of vascular capacity such as may possibly be seen as a result of reflex action or release of chemical substances due to trauma to tissues. Fig. 3. Shock due to generalized increase of capillary permeability such as is thought to occur after certain types of trauma to tissues. Fig. 4. Shock developing as a result of continuous slow hemorrhage. These diagrams represent an attempt to separate for analysis certain causative mechanisms; they represent directional trends only—upward movement indicating increase and downward movement decrease of the quantity—and no attempt has been made to make them quantitative. In many clinical cases two or more of these mechanisms will be operating simultaneously.

AP—mean arterial pressure, *VP*—venous pressure, *MVF*—minute volume of blood flow, *ST*—in supporting tissues, *HB*—in heart and brain, *VC*—[dashed line] vascular capacity, *BV*—blood volume, *P*—plasma volume, *C*—red cell volume, *LFL*—volume of fluid lost [at the site of the trauma or by vomiting, etc.], *TF*—volume of fluid in tissues, *HR*—heart rate, *RVC*—interval during which reduction of vascular capacity is occurring, *IPR*—interval during which increase of peripheral resistance is occurring, *EVB*—volume of blood lost by hemorrhage, *FV*—failure of vasoconstriction, *CF*—cardiac failure.

It is a common observation, which we have confirmed (8), that with slow bleeding extending over two-three hours, as much as 2–2.5 per cent of the body weight may be removed before aortic pressure begins to decline appreciably. If this is the case for hemorrhage, then it is possible that a similar quantity of fluid might be lost from the effective circulation in the initial stage of shock due to other agents.

Meek and Eyster (9) observed diminution of the volume of the capillaries and venules of the ear during the course of progressive hemorrhage, and although they did not observe the reduction until after the

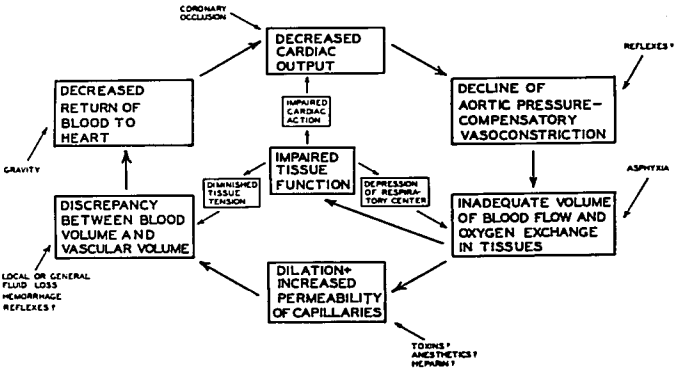

FIG. 5. Vicious cycle in shock.

aortic pressure had begun to decline, they concluded that a similar process must have been operating earlier in the less accessible capillaries and veins.

Gesell (10, 11), studying the blood flow through the salivary glands in response to slow progressive hemorrhage and also traumatic shock, observed that the flow through the gland initially decreased more rapidly than the pressure. He concluded that there was an initial vasoconstriction, but he did not consistently record a diminution of flow preceding the decline of aortic pressure. Seelig and Joseph made similar observations in the innervated as compared with the denervated ear (12).

In our own experiments on the blood flow in muscle, skin, brain and intestine (13), in response to slow bleeding, we have rarely seen much decrease in flow precede a decline of aortic pressure, although the flow in muscle and skin diminishes rapidly after aortic pressure starts to decline (8). Evidently, the first compensatory process in response to diminution of blood volume is a reduction of the capacity of the blood

reservoirs and absorption of fluid from the tissues so as to maintain cardiac output.

During the declining stage of aortic pressure as a result of further bleeding and also in the initial stage of shock developing as the result of operative trauma, we have observed (13), as did Gesell, that the blood flow in skin and muscle is decreased more rapidly than the aortic pressure. While this means that the peripheral resistance was increasing, it does not necessarily mean that vasoconstriction was occurring,

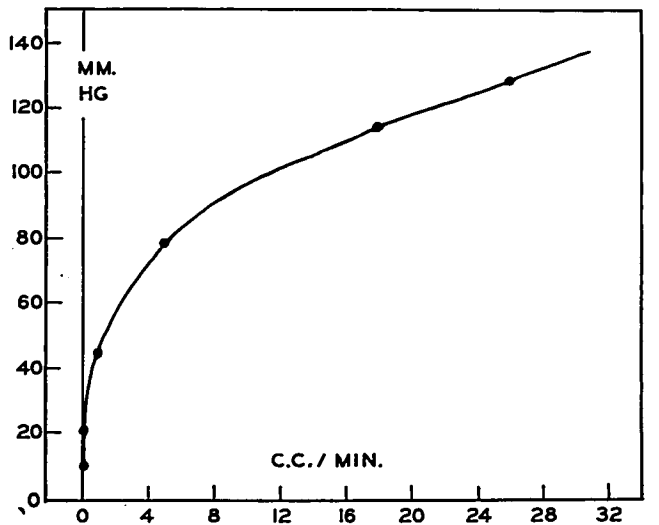

FIG. 6. Relation between arterial pressure and blood flow in an extremity in the absence of vasoconstriction or dilation. Ordinate—mean arterial pressure in mm. Hg. Abscissa—blood flow in cubic centimeters per minute.

since in recent experiments (14) we have shown that without vasoconstriction the flow will normally diminish more rapidly than the head of pressure and may practically cease at mean aortic pressures of 20–50 mm. Hg (see fig. 6). When comparison is made with such control curves relating pressure to flow we find that in skin and in muscle in animals anesthetized with chloralozane the decrease of flow is greater than can be accounted for by the reduction of arterial pressure. This is interpreted as indicating vasoconstriction. Certain modifications of these perfusion experiments suggest that in muscle this vasomotor activity competes with the vasodilator effect of the muscle metabolism.

The balance struck and therefore the effectiveness of the vasoconstrictor activity is, furthermore, markedly influenced by the type of anesthesia. For example, while under chloralozane anesthesia very marked diminution of flow occurs; under barbital or pentobarbital the flow may decrease but still be greater than would be anticipated from the aortic pressure. In other words, the net result of the interaction of nervous and metabolic effects in muscle is often vasodilation under the latter anesthetic agents. Preliminary tests with adrenaline suggest that even under chloralozane the vasoconstriction which is observed in muscle is not maximal.

In many of our experiments any initial vasoconstriction appears to persist up to death. However, on a few occasions in which shock was induced by hemorrhage we have observed a weakening of the vasoconstriction as true shock developed. The brain and heart show also a reduction of flow during shock, but this reduction seems to be about what would be anticipated from the progressive lowering of arterial pressure.

Provided that hemorrhage is not simultaneously occurring, careful repeated determinations of the hematocrit usually show increasing concentration of the red cells during the initial stage and often during the progressive stage of shock, thus suggesting that progressive loss of plasma is occurring. Some of this increase of red cell concentration could be due to possible enrichment of the circulation by contraction of the spleen, but often the increase of red cell concentration continues and even becomes accelerated during the progressive stage when the spleen has already become fully contracted (8).

The observations on the hematocrit should be substantiated by the simultaneous measurement of plasma volume. Unfortunately, however, all the available methods of measuring plasma volume require administration of a known amount of substance, which will not leave the blood stream, and subsequent determination of the concentration of the injected substance in the blood. Diminution of plasma volume by loss of fluid to the tissue spaces should result in a smaller dilution volume and therefore higher concentration of the test substance. However, in shock the damaged capillaries are apparently permeable to the test substances so that the test may give figures which are relatively too high for the true plasma volume; in other words, they may fail to show reduction of plasma volume in shock.

Pathological examination occasionally shows evidence of increased tissue fluid. It is not difficult to see, however, why such findings are not always observed, since less than half of the blood volume—less than 4 per cent of the body weight—need be lost from the circulation to cause profound symptoms and this small percentile amount of fluid, if distributed throughout the body, would indeed be difficult to detect.

That accumulation of red cells does occur in the tissues is demonstrated by the finding first described by Erlanger and his collaborators

(15), and frequently substantiated in our laboratory, that the mucosa is intensely red and swollen in the upper part of the small intestine and duodenum up to the duodenal bulb, but *not* including the stomach, and that a hemorrhagic fluid is frequently present on the surface of the mucosa and in the lumen of this part of the gut in animals dying from shock induced by hemorrhage, trauma, adrenal decortication, intestinal stripping and other procedures.

We have found (8) in confirmation of previous reports (16, 17, 18) that coincident with the decline of aortic pressure during the initial stage, the metabolic rate of the whole animal—measured in terms of oxygen consumption—may begin to decline, and, associated with this the animal's rectal temperature starts to fall, thus indicating the beginning depression of tissue function. The depression of metabolic rate and rectal temperature usually becomes accelerated, however, when the mean aortic pressure reaches a level of around 70 mm. Hg. This is probably due to the fact that flow of blood through many tissues also almost ceases when the mean aortic pressure approaches this level.

Another example of the depression of bodily functions in shock is the decreased reactivity of the patient and experimental animal. Using a relatively rapidly destroyed anesthetic such as pentobarbital or morphine, repeated injections are required during the control period and during the early stages of induction of shock. However, by the time blood pressure starts to fall, and, in fact, sometimes even before, in the case of traumatic shock one can cease giving the anesthetic and the animal will remain quiet even though at this time the wink reflex and tendon jerks may still be obtained. With further fall of arterial pressure the animal becomes more depressed and even these reflexes may disappear in the absence of further anesthetic (8).

THE INITIATION OF SHOCK

As we see, shock appears to be a phenomenon of too little blood for the capacity of the available vascular bed, which, at least in its progressive stage, is associated with dilation and increased permeability of the capillaries and venules which tend to augment the discrepancy. Once the progressive stage has been started, treatment becomes almost hopeless. It is therefore important to analyze the factors operating in the initial stage not only in order to understand the initial mechanism of shock but also to provide a more rational basis for prevention and early treatment of shock.

A. Shock Initiated by Burns.—Many studies of shock initiated by burns have been made on patients. Certain of these have attempted to show that prevention of absorption of toxic products by various modes of treatment of the burned area diminished the tendency for shock to occur. More precise data have, however, been obtained by careful collection of the quantity and observation of the character of the fluid lost

through the burned area (19, 20). This fluid, resembling plasma, has, in severe burns, been shown to be of a sufficient quantity that, if lost entirely from the plasma of the blood, it could cause even greater decline of blood pressure than that observed. This loss of fluid is also consistent with the concentration of the blood seen in many such shock patients. While these studies suggest that fluid loss leading to reduction of circulating blood volume is the predominant initiating factor, it must be admitted that neither nervous nor humoral factors have been completely ruled out. A theoretical concept of the stages in the development of shock following burns is illustrated in figure 1.

B. Shock Initiated by Trauma.—Studies of the mechanisms by which trauma induces shock, made largely on experimental animals, have dealt chiefly with attempts to demonstrate the part played by local fluid loss at the site of the trauma, the part played by nervous reflexes initiated in the traumatized area, and the part played by hypothetical substances absorbed by the blood flowing through the traumatized area and distributed throughout the body.

a. Local fluid loss theory (see fig. 1).—In early experiments on traumatic shock, extremities were traumatized by various forms of pounding. After the animal had died of shock the weight of the injured extremity was compared with that of the untraumatized opposite extremity. The difference, assumed due to the loss of fluid from the blood, was considered to be insufficient to account for the observed changes of blood pressure. In later experiments, performed in essentially the same manner, more care was taken to weigh both the traumatized region and the adjacent soft tissues. The differences obtained when this was done appeared to be great enough to account for the observed circulatory phenomena. These latter experiments were interpreted as indicating that in all cases of traumatic shock, local fluid loss was the predominant factor (21, 22, 23). Undoubtedly, this was the case in these experiments, but they do not rule out nervous or humoral factors. Within the last few years additional experiments have been reported (7, 24, 25) which we have confirmed, showing that shock can still be caused by repeated trauma by blows with padded mallets even after the extremities are so bound that hemorrhage or local accumulation of fluid is prevented, thus confirming the earlier hypothesis that some factor other than local fluid loss can also be responsible for initiating the shock process. It should be noted in this regard that usually four to eight hours or more elapse following the trauma before the decline of arterial pressure becomes appreciable.

b. Afferent impulse theory.—Afferent nerve impulses from traumatized and burned areas are considered by some investigators to initiate shock. One theory, proposed by Henderson and his collaborators, states that reflex hyperpnea and hypocapnia induced by the pain impulses cause tissue atony and pooling of blood in the capillaries and veins. This theory has not been adequately substantiated as an initiat-

ing cause and has in fact been abandoned by its proponent. It has also been proposed largely on the basis of Gesell's experiments (10, 11) that the afferent nerve impulses caused extensive reflex vasoconstriction which diminished the volume flow of blood through many of the tissues and, because of the resulting ischemia, initiated the vicious shock cycle. It is highly doubtful whether such intense vasoconstriction actually occurs since it would cause much higher elevation of the arterial pressure than is seen during or after trauma. Erlanger and Gasser (26) and Freeman and his collaborators (27) and others (28) have caused death in animals, associated with hemoconcentration, capillary congestion and reduced blood volume by prolonged intravenous injections of epinephrine, but it is not at all certain that these animals died of shock. Cardiac failure due to excessive demands on the heart may have been the more important factor. In fact, with a little consideration it can be seen that generalized vasoconstriction, such as is seen in renal hypertension, could never cause ischemia, since, if the heart is able to maintain a normal output, the circulation through the tissues must also remain normal. In other words, the excessive generalized constriction will be automatically overcome by the elevation of the arterial pressure. This would, of course, not apply if it could be shown that intense arteriolar vasoconstriction occurred in some regions at the same time that vasodilation occurred in others.

Experimentally, shock can be produced by trauma to denervated extremities (20, 29), although this has been denied when local fluid loss is prevented (22, 30), but shock has not been produced by stimulation of pain fibers (31). These facts should not be taken as license to manhandle a traumatized or fractured extremity, however, since even though pain impulses may not induce shock, they may serve as a contributing factor. Another argument against the rough handling of traumatized tissue is the probability of enhancing the local fluid loss, and the possibility that such treatment may cause the formation and release into the blood stream of additional toxic substances, if such are ultimately proved to play a part in the initiation of shock. In this regard one might consider the possible deleterious effects of periodic release and replacing of tourniquets.

O'Shaughnessy and Slome (30) have been the chief proponents in recent years of the importance of afferent nerve impulses in the production of shock. They feel that they are unable to produce shock by trauma to denervated extremities under conditions which would cause shock without sufficient local fluid loss in normally enervated extremities, and that the shock state induced by trauma of a hind extremity is improved by spinal anesthesia. I am not aware that they have attempted to explain the mechanism by which afferent impulses play a part. Generalized decrease of peripheral resistance, like generalized increase of peripheral resistance, could not alone cause diminished minute volume flow of blood. If afferent impulses initiate or facilitate

the start of the vicious cycle they must do so by causing a reflex increase in the capacity of the vascular system. A diagram of the steps which theoretically might operate in the induction of shock by such reflex action is presented in figure 2.

c. Humoral theories (see fig. 3).—Production of shock by trauma which did not cause large accumulation of fluid in the traumatized area; prevention of such shock when the artery and vein were ligated but occurrence of shock when the ligatures are released; the gradual occurrence of the shock; and the development of shock following trauma to denervated extremities suggest that an initiating factor in traumatic shock is the development in the injured area of a toxic substance which, carried by the blood to all parts of the body, causes a generalized increase of permeability and dilation of capillaries analogous to the formation of wheals in hives (7). This results in a diminution of blood volume relative to circulatory volume and thus initiates the vicious cycle of shock. According to this theory, the impairment of the capillaries would precede the actual onset of shock. The most frequently suspected substances are histamine, the potassium ion, or some product of tissue autolysis, but no factor has been definitely established (32, 33). A modification of this theory proposed by Selye and his collaborators (34) is that the traumatized muscle removes from the blood excess quantities of some substance essential to the needs of the body as a whole.

A number of ingenious cross circulation and transfusion experiments have been attempted (30, 34, 35, 36, 37, 38, 39, 40, 41) to demonstrate a humoral factor in shock, but so far they have given negative results. Too much emphasis should, however, not be placed on the failure to demonstrate shock in the cross-circulation experiments, as one should always remember the many negative results obtained in the study of renal hypertension before formation of renin by the kidney became established.

The chief criticism of the toxic theory has come from those who have found sufficient local loss of fluid in the traumatized and immediately adjacent tissues to initiate the shock cycle. While these indicate the importance of local fluid loss as a factor in trauma they do *not* rule out the possibility of humoral or nervous factors. The emphasis should have been placed on trying to show that shock can *never* be induced by trauma in the absence of sufficient loss of local fluid which most opponents of the toxic theory have not done. It seems to me, therefore, that while a humoral factor has not been conclusively established, it is quite probable that in some way the blood flowing through the traumatized tissue may so affect the vascular system and tissues in distant parts of the body that the disturbances of blood volume, vascular volume and other accompaniments of shock are thereby initiated.

While probably not concerned in the initiation of shock, it is quite possible, as suggested by the work of Hamilton and Collins (42) and

Braun-Menendez, that part of the compensatory vasoconstriction during the stage of declining aortic pressure is due to the elaboration of renin by the kidney, and that the terminal events may be in part due to failure of this mechanism due to tachyphylaxis. Our experience suggests that a chemical constrictor is rarely seen in animals surviving less than six hours, but that in experiments lasting from ten to twenty hours increase in peripheral resistance in extremities due apparently to vasoconstriction is quite frequently seen even after denervation.

A rather intriguing possibility has recently been suggested by the incidental observations made by Knisely and his collaborators (43) during their studies of the behavior of the blood observed microscopically in malaria. They found that even mild trauma causes the appearance in distal parts of the body of sludge-like clumps of red cells. If this should be substantiated, and if this sludge should be shown to cause appreciable impediment to the flow of blood, then the initiating factor in traumatic and perhaps other forms of shock may be this change in the physical character of the blood.

C. Hemorrhagic Shock (see fig. 4).—Werle, Cosby and Wiggers (3) have shown that an animal may readily recover from a single hemorrhage, even if the arterial pressure be dropped suddenly to rather low pressures. If, however, these animals are repeatedly hemorrhaged so that their blood pressure remains at a level of 30 to 40 mm. Hg for from one-half to two hours then without further bleeding, and even after return of all withdrawn blood, the animals develop a progressively declining arterial pressure, hemoconcentration and decreased cardiac output measured with the cardiometer. In other words, they have died of what appears to be true shock. This work provides proof that an initiating factor, which causes an initial discrepancy between blood volume and circulatory volume, can bring about the progressive stage where this reduced blood volume seems to perpetuate and augment itself. Since most experimental animals in shock die of cardiac or respiratory failure before the arterial pressure falls to this low level it might be questioned whether the vicious cycle plays much of a part in the progressive nature of shock as seen in the clinic. Recently, in collaboration with Lewis and Nickerson (8) the author has been able to show that even in lightly anesthetized (morphine) animals it is possible to induce the vicious cycle at mean aortic pressures of 50 mm. Hg and above if one keeps the animal at this pressure by slow bleeding for somewhat longer periods (circa, two to four hours). While we have not completed the investigation, it seems probable that the vicious cycle may be induced even at higher pressures if maintained for appropriately increased lengths of time, but that at pressures as high as 70 to 80 mm. Hg twelve to twenty-four hours may elapse before shock develops.

D. Other Methods of Experimentally Inducing Shock.—Shock, or at least a state very closely resembling shock, has been induced by nu-

merous other types of experimental procedures which we can mention only briefly. Among these are: opening the abdomen and "stripping" the intestines (8, 31, 44, 45)—drawing them between the fingers, prolonged action of gravity in anesthetized animals (46), placing sterile muscle in the abdominal cavity (7), severe dehydration (47), injection of normal glucose into the peritoneal cavity, high intestinal obstruction (22), adrenal decortication (44), minor operations followed by intravenous injection of large doses of heparin (8), intravenous injection of large doses of the anticoagulant dye Chlorazol fast pink (8), massive venous thrombosis of a leg (48), prolonged periods of artificial respiration with the chest opened (8), and compression of both thigh muscle masses by tight wire ligatures which do not compress the femoral artery or vein or the sciatic nerve (8). The common initiating factor in many of these seems to be either capillary injury or loss of plasma. It seems just possible to me that normally small openings are constantly occurring in the vessel walls and that heparin and the anticoagulant dyes may favor shock by impeding the normal plugging of these holes by fibrin.

DEDUCTIONS REGARDING THE NATURE OF SHOCK BASED UPON THE RESULTS OF THERAPY

In the first World War the most effective agents proved to be intravenous injection of acacia solution and transfusion. In the present conflict it has been found, in addition, that use of some form of plasma —whole plasma, redissolved dried plasma or serum—is better than acacia and almost as good and in some cases better than transfusion of whole blood in preventing and in treating the initial stage of shock. The fact that administration of fluid containing protein is beneficial in the initial stage confirms the concept that shock is a state in which the vascular capacity no longer fits the volume of the circulating blood. However, everyone with much experience with shock has seen instances where therapy was postponed and have observed that the longer it is postponed the greater is the quantity of fluid needed, and that after considerable delay no quantity of fluid may avail. In the latter, we have found that the venous and arterial pressures may momentarily rise with each injection, but soon after the infusion is stopped the arterial and venous pressures again begin to decline and upon death large quantities of fluid may be found in the areolar connective tissues, to a small extent in the pleural and pericardial cavities, but particularly in the peritoneal cavity, intestinal mucosa, and lumen of the gut (8). Thus we are forced to conclude that once the progressive stage of shock has been entered, many difficultly reversible processes have set in with progressive deterioration of many of the tissues of the body.

In analyzing the differences between shock induced by hemorrhage and induced by trauma, it would be of interest to compare the quantities of plasma required in patients or experimental animals in whom the

blood pressure had been at shock levels for comparable periods of time. There is some suggestion that greater quantities are required after trauma (49). If this is substantiated, it would offer confirmation for the greater degree of capillary damage which one would be inclined to anticipate on the basis of a combined action of a circulating toxin or nerve reflex action plus the vicious cycle.

Of interest in regard to the part that tissue anoxia may play in the vicious cycle are two recent reports of the favorable effect of administering high O_2 concentrations (50, 51).

One of the time-honored procedures used in the army for treatment of shock deserves mention. This is the shock tent in which the patient, supposedly in shock, is placed on a bed, wrapped in blankets and warmed by lamps before any attempt is made at surgery. It is not clear whether this procedure is actually effective in overcoming shock or whether it merely serves to improve the condition of soldiers exposed for prolonged periods to cold. Within the last few months, several voices have been raised warning against the indiscriminate use of heat in shock (52). Certainly it is quite possible that excessive warming may induce dilation of compensatorily constricted cutaneous vessels and thereby impair one of the body defense mechanisms against loss of blood volume. It then becomes a question of determining whether the improved metabolism and general condition of the patient are of more benefit than the possible danger from the cutaneous dilation. Personally, I have not as yet seen any particular improvement from warming experimental animals whose rectal temperature had begun to drop in the late stages of shock.

Since the development of adrenal cortical extracts, much study has been given to the part the adrenals may play. Adrenal decortication in experimental animals causes the appearance after a few days of a more or less typical shock (44, 45). These animals may furthermore be cured by administration of adrenal cortical extract. Treatment of traumatic shock with extracts has, however, been less spectacular (45, 53, 54, 55, 56). Injection of the adrenal cortical extracts seems to be most successful if given just at or just before the trauma (48). If given too far in advance accentuation of the shock seems to occur. This latter has been interpreted as due to depression of the adrenal cortical activity by the injected extract. Injections do little good after the progressive stage has begun. Evidently the adrenal cortical secretions are important in maintaining the normal character of the capillaries, but are unable to reverse the shock process after it has become well established.

CONCLUSIONS

Shock represents a *progressive* self-perpetuating deterioration of the circulation characterized by progressively diminishing minute volume of circulation throughout the body, which is associated with in-

creased permeability and dilation of the capillaries and probably also of the venules, and which is also usually associated with terminal failure of the cardiac, vasomotor or respiratory mechanisms.

Shock appears to be initiated by any factor which causes an acute but persistent diminution of the minute volume of the circulation. This reduction may be of cardiac origin, as in the case of coronary occlusion; it may be due to loss of plasma externally, as in intestinal obstruction, cholera, burns or hemorrhage; or it may be due to a primary combined diminution of blood volume (due to increased permeability) and increase of the capacity of the circulation (caused by dilation of the capillaries and venules) such as appears to occur in trauma and perhaps also after burns. In the latter a change in the chemical or physical character of the blood may also serve to impair the circulation throughout the body.

The net result of these initiating factors is a diminished return of blood to the heart, decreased cardiac output, fall of arterial pressure, compensatory vasoconstriction in some parts of the body, and speeding up of the heart and decreased minute volume of circulation.

After the blood pressure has remained at around 70 mm. Hg or lower for a half hour or more, the diminished circulation throughout the body begins of itself to cause increased permeability and dilation of the capillaries and venules, and thus augments the impairment of capillary function already present. When this begins to occur true shock is said to be present.

In part at least, by direct effects on the capillaries such substances as anesthetics, heparin, dyes, toxins and other chemical agents in excessive quantities may also contribute to the induction of and may even induce shock.

Most of the symptoms of shock appear to be explainable upon the basis of the depression of the circulation and the associated depression of the functions of most of the tissues and organs of the body.

Because of the tendency for shock to perpetuate itself once the minute volume of circulation has become sufficiently decreased, it is most important to prevent, wherever possible, the operation of the initiating factors and to institute restoration of the blood volume before the vicious cycle has become firmly established and before irreversible damage has been done to the various body tissues.

The author is firmly convinced that it is better to give fluid, preferably blood, during an operation, even though it be continuously lost by unavoidable hemorrhage, than to allow the blood pressure to decline to dangerous levels and then attempt to restore the fluid loss after the completion of the operation.

The choice of the term shock for this condition is perhaps unfortunate since it seems to imply something sudden, whereas shock appears at the present time to be a relatively slowly developing progressive con-

dition. It is also unfortunate that the term is rather generally applied to any patient with low blood pressure regardless of the cause or duration of the symptoms. Since the term has been used continuously since its introduction by Latta in 1795, and since it has the advantage of brevity, it probably will be continued in use. The author would, however, prefer some such designation as *acute progressive circulatory failure.*

I should like to express my appreciation to my collaborators in the experiments reported briefly in this paper: Richard S. Cosby, Karl Radzow, Robert Lewis and Neil Nickerson; and to Professor Carl J. Wiggers in collaboration with whom the program of shock research is being carried out in the Physiology Laboratory at Western Reserve University Medical School.

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MEETING OF THE AMERICAN SOCIETY OF ANESTHETISTS, INC.

SQUIBB BUILDING, 745 FIFTH AVENUE, NEW YORK CITY

December 10, 1942—7:30 P.M.

1. Responsibility of the Anesthetist in Reducing Operative Complications in Thoracic Surgery. Lantern demonstration. 40 minutes.
   By Herbert C. Maier, M.D., Med. Sc.D., (by invitation) Instructor in Surgery, Columbia University, New York City.
   Discussion to be opened by Sidney Cushing Wiggin, M.D., Boston, Mass.
2. Comparative Clinical Results Using Various Drugs and Methods in Spinal Anesthesia. 40 minutes.
   By Harold F. Bishop, Capt., Army Medical Corps, Chief of Anesthesia and Operating Section, Walter Reed General Hospital, Washington, D. C.
   Discussion to be opened by Philip D. Woodbridge, M.D., Philadelphia, Pa.