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The Etiology of traumatic shock

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A Senior Thesis presented to the
College of Medicine, University
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INTRODUCTION

Traumatic shock, as defined by C. J. Wiggers, is a generalized body state which occurs following injury, and in which there is a progressive failure of body functions, usually leading more or less rapidly to death. It is characterized by the symptom complex typical of circulatory failure due to oligemia: "A cold, moist skin; white, pale, grayish or slightly cyanotic appearance; great thirst and often vomiting. The respiration is usually rapid, but may be either deepened or shallow. Patients are first restless and very anxious, but lapse gradually into a listless or apathetic state. Reactions to painful stimuli are reduced. The pulse is always rapid and feeble, the heart sounds are weak, and body temperature is subnormal". (65)

A better understanding of the term can be obtained from a clinical description of a typical case of shock. Of the many such descriptions to be found in the literature, the following one given by J. C. Warren in 1900 is excellent:

"A patient is brought into the hospital with a compound comminuted fracture or with a dislocation of the hip joint added to other injuries where the bleeding has been slight. As the litter is gently deposited on the floor, he makes no effort to move or look about him. He

lies staring at the surgeon with an expression of complete indifference as to his condition. There is no movement of the muscles of the face; the eyes, which are deeply sunken in their sockets, have a weird, uncanny look. The features are pinched and the face shrunken. A cold, clammy sweat exudes from the pores of the skin which has an appearance of profound anemia. The lips are bloodless and the fingers and nails are blue. The pulse is almost imperceptible; a weak, thread-like stream may, however, be detected in the radial artery. The thermometer, placed in the rectum registers 96° or 97° F. The muscles are not paralyzed anywhere, but the patient seems disinclined to make any muscular effort. Even respiratory movements seem for the time to be reduced to a minimum. Occasionally the patient may feebly throw about one of his limbs and give vent to a hoarse, weak groan. There is no insensibility, but he is strangely apathetic, and seems to realize but imperfectly the full meaning of the questions put to him. It is of no use to attempt an operation until appropriate remedies have brought about a reaction. The pulse, however, does not respond; it grows feebler, and finally disappears, and 'this momentary pause in the act of death' is soon followed by the grim reality. A post-mortem examination reveals no visible changes in the internal organs." (63)

Two types are recognized: Primary shock, which occurs

immediately after the injury; and secondary shock, which develops several hours later. The primary type is either a transient condition, resembling the nervous phenomenon of fainting, or is associated with such extensive destruction of tissue as to make continuence of life impossible. "Such cases either recover without treatment, or are hopeless and, consequently, do not constitute a clinical problem". (65)

Accordingly, little experimental work has been done on primary shock. It has been considered, however, in the absence of marked hemorrhage, to be due to some derangement of the nervous system, but since, for humane reasons, this condition cannot be readily produced in the laboratory, it has not been adequately inveetigated by experimental methods. (43)

About the only experimental work done on this type of shock is that of F. L. Goltz in 1862. He demonetrated that a reflex cardiac and vasomotor paralysis or inhibition resulted from striking a frog on the mesentery. His experiment was as follows: With a frog suspended with its legs down, it was sharply tapped on the mesentery. The heart suddenly stopped, and after a few minutes resumed its beat, but was paler than before, because the dilatation of the abdominal vessels allowed the blood to accumulate there and prevented sufficient blood from reaching the heart. (18)

Secondary shock, on the other hand, can be readily approached by experimental methods, and it is toward this type that investigators have directed their researches. It is with a discussion of the etiology of this type that this paper deals, and since there is still no agreement on the physiology and pathology of the condition, a discussion of these topics will be taken up only as concerned in each theory.

THE THEORY OF VASOMOTOR EXHAUSTION

Although G. W. Crile's theory that vasomotor exhaustion is the cause of shock has been quite thoroughly disproved, modern experimental research really began upon the publication in 1899 of his monograph, "An Experimental Research into Surgical Shock." (18)

After a series of numerous animal experiments in which he found that shock was most readily caused by trauma to those parts most richly supplied with sensory nerves, and that the more intense the trauma, the more rapid the shock, he came to the conclusion that shock was a state of exhaustion, and that since a low blood pressure was the most vital phenomenon accompanying shock, that shock must therefore be caused by exhaustion of the vasomotor center, and that the cardiac and respiratory failures and their associated phenomena were simply secondary consequences or subsidiary factors to this primary cause. In support of this, he claimed that shock could be prevented by blocking the nerve supply to the areas traumatized. (20)

In connection with his claim that shock could be prevented by thus blocking the nerve supply, he stated that ether anesthesia offered no protection to the brain cells from the effect of trauma, because under ether (or other lipoid-solvent anesthetics) afferent stimuli reached the brain as before, and the brain cell changes in shock were due to the discharge of energy in a futile effort to escape

from the injury. He claimed that lipoid-solvent anesthetics broke the arc of consciousness beyond the brain cells somewhere in the efferent path, but offered no experimental proof of this somewhat astounding claim. (19)

In one article he explained his theory in the following manner: He first postulated a "kinetic system" made up of a group of organs (brain, thyroid, adrenals, and muscle) whose function was to convert potential into kinetic energy, and it did this in response to adequate stimuli. When these stimuli were overwhelmingly intense, the kinetic system - especially the brain - became exhausted and even permanently injured, and the condition known as shock resulted. (19)

He demonstrated, to his own satisfaction, morphological and conduction changes in various tissues of rabbits following exhaustion. He pointed out that all cells are composed of two colloids (nucleus and cytoplasm) separated from each other and from neighboring cells or medium in which they are immersed by selective semipermeable membranes. He said that since the nucleus was acid and the cytoplasm alkaline, the nucleus compared with the cytoplasm was therefore positive, and each cell thus constituted an electro-chemical unit or an electric cell. The whole body was thus made up of these units and each tissue and organ was an electro-chemical mechanism. He then stated that normal conditions in the body obtained

when the brain acted as the positive pole and the liver as the negative. He stated that he found that the effect of stimulation within the organism was a slow increase in the conductivity of the cerebrum followed by a gradual continuous decrease, and a slight decrease in the conductivity of the liver followed by a rapid continuous rise to above normal as the state of exhaustion approached. (21)

He also demonstrated to his own satisfaction that there were actual changes in the cells - especially of the brain - corresponding to the degree of shock and to the changes in conductivity. These changes were hyperchromatism followed by chromatolysis. He said that when the differential stainability of the nerve cells was lost they ceased to be efficient batteries, and a state of exhaustion and shock resulted. To quote Crile's own words,

"The conception that man is an electro-chemical mechanism supplies an interpretation of the principle phenomena of quiescence, stimulation, and exhaustion which constitute normal life; it supplies a new basis for the analysis of pathological phenomena. In accordance with this conception, exhaustion is the result of a diminution of the difference of potential between the poles of the organism, due to a decrease in the brain, which in turn results from a decreased difference in the potential in its constituent cells. This conception explains the identity of the phenomena of exhaustion and the progressive

degrees of exhaustion to 'shock'. When the difference in potential reaches zero, the organism is dead." (21)

Other investigators have shown quite conclusively that the vasomotor center is not exhausted in shock. If this center were exhausted, there should be no peripheral vasoconstriction. Seelig and Lyon, as early as 1909, found by ophthalmoscopic examination of fundi of dogs before and after the induction of shock that during shock the blood vessels of the fundus were markedly contracted. (55)

They later confirmed this finding by experiments on dogs in which they found that no matter how profound the shock, the percentage rise in blood pressure upon stimulation of the central end of the vagus was equal to the percentage rise in the normal animal. They then showed that this was due chiefly to vasoconstriction and not to augumentation of the heart's action, by cutting the accelerator fibers to the heart through removal of both right and left stellate ganglia and still getting a rise in blood pressure upon stimulation of the central end of the vagus. They also achieved the same result with the celiac plexuses as well as the stellate ganglia removed. (56)

F. C. Mann confirmed their work as to the state of the peripheral vessels in shock. In the rabbit, a large number of the vasoconstrictor fibers to the ear run in the cervical sympathetic nerve. The blood vessels in the ear of an albino rabbit show vasomotor changes quite distinctly,

and in shock these vessels can be seen to become constricted until they are small faint lines. That this is not a passive condition is shown by the fact that the ear can be lowered below the level of the splanchnic area without it becoming congested, and section of the cervical sympathetic nerve produces noticeable dilatation of these vessels. He concluded that these vessels are under vasomotor control in shock. (42)

Janeway and Ewing were unable to produce shock or exhaustion of the nerve centers even after prolonged afferent electrical stimulation for two hours. (36)

F. C. Mann found that he could not produce shock by intermittent and simultaneous stretching of both sciatic nerves, both anterior crurals and both brachial plexuses for a period of four hours; nor could he produce shock by long continued electrical stimulation of afferent nerves.

He also found that typical shock could be produced after section of the spinal cord in the lower cervical or upper thoracic region. Such section does produce a great fall in blood pressure due to section of vasoconstrictor fibers, but the animal is not is shock as can be shown by withdrawing the anesthetic, whereupon the animal will regain consciousness and respond to stimuli about the head. (42)

That there must be some other cause than vasomotor paralysis is also shown by Carrel's experiments. He succeeded in removing all the abdominal and thoracic organs

from animals and keeping these "visceral organisms" alive for many hours immersed in Ringer's solution. Oxygen was supplied by artificial respiration. These visceral organisms could digest food and excrete feces and urine, and, although the blood pressure usually remained low, in some of his experiments it rose and remained at an almost normal level. (67)

W. T. Porter most vigorously opposed Crile's theory, and was very emphatic in his assertion that the vasomotor cells in shock were neither exhausted, depressed nor inhibited. He was unable to bring about any significant fall in blood pressure by such experiments as electrical stimulation of spinal nerves for almost four hours, by crushing or electrical stimulation of testes of dogs, or by electrical stimulation of brachial and sciatic nerves for two hours. (51)

He then determined that stimulation of the depressor nerve of cats caused about a 45% fall in blood pressure, and found that after the animal had been brought to a state of shock by painting the exposed intestines with nitric acid, and had remained in this state of shock for eight hours, stimulation of the depressor nerve still caused a 45% fall in blood pressure. From this he concluded that, since the depressor nerve can affect the blood pressure only through the vasomotor center, this center could not be exhausted during shock. (50)

Crile's contention that there are definite morphological and histological changes in the brain cells in shock has not been accepted by other observers. R. A. Kocher, in a series of experiments performed on dogs, cats, pidgeons, sparrows, frogs and rats, showed that there was no constant difference in the size of nerve cells or nuclei, nor was there any constant deviation in histological structure. The animals were reduced to varying degrees of exhaustion and shock, and each experiment was controlled by a resting animal. The control and fatigue animals were killed at the same time, the nerve tissue removed immediately, immersed in the same fixing solution, imbedded in the same block of paraffin, cut and mounted on the same slide, and stained together. He found that there was just as much variation between the cells of resting animals as there was between those of shock and resting animals.

He states in his conclusion that some very sweeping generalizations have been drawn from inadequately controlled experiments - i.e., that fatigue, exhaustion and shock may lead to permanent damage or even disintegration of nerve cells - and cites Crile's theory as an example of to what extremes such deductions have led. (39)

Porter concludes: "Experimental evidence shows that failure of the vasomotor center is due to anemia rather than stimulation. If the blood pressure in the nutrient capillaries falls below the critical nutrient level - a

very low level - the vasomotor cells are at once affected. Bulbar anemia may be a consequence of prolonged shock, especially when the bulb is allowed to be higher than the trunk, for a man with shock is a gravity animal and his cerebral circulation then depends chiefly on small differences in hydrostatic level, but an injury after shock is not to be confused with an injury causing shock. In short, exhaustion of the vasomotor center is a taking phrase but it is nothing more". (54)

THE THEORY OF INHIBITION

In 1908, S. J. Meltzer, on the basis of his own observations that irritation of the skin of the abdomen of rabbits by simple dissection caused a reflex inhibition of normal peristalsis, offered as an explanation of shock his theory of inhibition. He stated that the various injuries which were capable of producing shock did so by "favoring the development of the inhibitory side of all the functions of the body." This inhibitory action, he thought, made its first appearance in those functions which were of less immediate importance to life and therefore less well safeguarded. Later with increasing injury this inhibition spread to the more vital and therefore better protected functions of the nervous system. He went on to say that the early inhibition of the functions of lesser importance could be looked upon as measures for the protection of the more important functions. Thus the restlessness of the body, the painlessness and mental indifference would be most desirable conditions for the management of shock of the more vital functions. (44)

This theory, although attractive in its simplicity, had never been given much serious consideration. As Cannon pointed out, the chief phenomenon upon which Meltzer based his theory - the cessation of peristalsis - although indeed an inhibition of the activity of the intestine, is brought

about by overactivity of the nervous system and not by any inhibition. (11) Cannon and Murphy found that stimulation of afferent nerves resulted in an inhibition of the contractions of the intestine, but that this was caused by excess delivery of impulses over the sympathetic nerves. (14)

Cannon further pointed out that Meltzer did not take into consideration the most significant aspect of shock - the low blood pressure - nor did he consider that, in shock, there is no inhibition of the heart or respiration. Cannon concluded that this theory had very little support. (11)

THE THEORY OF ACAPNIA

In 1908, Y. Henderson advanced the theory that the exhalation of carbon dioxide was responsible for the development of shock.

In performing a series of experiments on dogs, he was puzzled at the fact that frequently, in extensive operative procedures, tachycardia and fatal shock developed; while in other cases where equally extensive operations were performed, this did not happen. Since this was so similar to what happens in surgery on man, he was stimulated to investigate the cause.

He noticed that in dogs under artificial respiration, the development of shock was apparently not dependent upon the extent of the trauma or the intensity of stimulation of afferent nerves, but upon the rate of pulmonary ventilation. He then found that hyperventilation of the lungs caused an increase in the heart rate, and that if this was continued there resulted a cessation of the pumping action of the heart. The ventricles were in complete tetanus with almost complete obliteration of the ventricular chambers. If a more moderate hyperpnea was used, the animal gradually passed into a condition of typical surgical shock. The animal could then be brought out of this condition, provided the shock was not too severe, simply by increasing the carbon dioxide in the air breathed. (29)

In support of this conception, he pointed out that

voluntary forced breathing in man, so far as the experiment could be safely carried, induces symptoms similar to those of shock, and that pain, ether-excitement, fear, and other conditions inducing shock, involve excessive respiration. (32)

In shock from ordinary trauma, the acapnia, which is responsible for the development of the condition, is produced by the hyperpnea, which in turn is the result of intense afferent stimulation. In abdominal operations, carbon dioxide is not only thus lost from the lungs, but is also lost, to some extent, by exhalation from the exposed viscera. He demonstrated this by measuring the amount of carbon dioxide given off by exposed peritoneal surfaces, and found it to be from 0.15 to 0.20 cc. per square centimeter. He also found that the congestion and loss of tone which abdominal viscera underwent when exposed to the air, could be remedied by the restoration of the body's store of carbon dioxide. This was accomplished by such measures as inhalation of carbon dioxide, intravenous injection of normal saline solution saturated with carbon dioxide, and by the introduction into the peritoneal cavity of Ringer's solution saturated with carbon dioxide. In addition, he showed that shock could be produced simply by exposure of the abdominal viscera to a current of moist warm air, and that shock thus induced could be relieved by these same measures. (31)

In the cases of shock from moderate hyperpnea that ended fatally, he found that death was due, not to cardiac tetanus, as in the cases where excessive hyperpnea was used, but to a "failure of vascular tonus", and that this was venous and not arterial in character.

He explains this as follows: The failure of the circulation in shock is due to failure of the "veno-pressor mechanism". This consists in part of the tonus of the tissues and in part of osmotic processes. The tonus of contractile tissue is dependent to a large extent upon their carbon dioxide content, and this tonus prevents stasis of blood by preventing a relaxation of the capillary bed. When this carbon dioxide content is diminished, as it is in shock, the tonus is lost, the capillaries become dilated, and blood tends to stagnate.

The osmotic portion of the veno-pressor mechanism consists in the regulation of the water content of the tissues and blood by the amount of carbon dioxide they contain. Acapnia upsets in some way the osmotic balance between the blood and the tissues, and permits the passage of fluid from the blood stream into the tissues. After the blood volume and therefore the circulation has thus been impaired to the point that oxygen is inadequately supplied to the tissues, an asphyxial acidosis results. The tissue proteins then imbibe water and swell. Under such conditions a fatal oligemia soon results, and if, in an attempt to

replenish the blood volume, saline is injected into a vein, it rapidly passes out of the blood into the tissues and is of very little benefit. (34)

To summarize briefly, shock, according to this theory, is produced as a result of the following series of events: hyperpnea, acapnia, failure of the veno-pressor mechanism, venous anoxemia, tissue asphyxia, and oligemia.

This theory, convincing as it sounded, was soon shown by other investigators to inadequately explain shock. F. C. Mann (42) attempted to produce shock by Henderson's method of hyperventilation, and failed in all but one case. He concluded that shock could not be produced in this way except by artificial respiration greater than would be possible for the animals to do themselves by the greatest possible forced respiration.

C. J. Wiggers found that in no instance after afferent stimulation such as crushing the testis and spermatic cord, or stimulation of the sciatic nerves (which caused a marked increase in the rate and depth of respiration), was there produced, even after two hours of such respiration, any case of shock or death from respiratory failure as Henderson described following intense artificial respiration. (64)

Janeway and Ewing (36) also repeated Henderson's experiments, and found that, while they could produce shock by hyperventilation, it took a rate of seventy breaths a minute to produce a significant fall in blood pressure,

and that in those cases where death was produced, there was an interstitial emphysema of the lungs because of the excessive pressure needed.

Still more conclusive was their series of experiments in which they produced identical results even though the carbon dioxide content of the air breathed was maintained at a proper level by adding carbon dioxide from a tank.

They concluded that diminution of carbon dioxide was not the factor which produced shock in hyperventilation of the lungs, and looked for another cause. They found that by hooking a bronchus to a water manometer, and hooking a cardiometer in circuit with a recording tambour, that a rise of intrabronchial pressure above 8 or 10 mm. Hg. always caused a fall in the blood pressure proportional to the rise of intrabronchial pressure, and a corresponding diminution in the cardiac output. They concluded that the excessive intrabronchial pressure which accompanies excessive artificial respiration is sufficient of itself to account for the lowering of blood pressure, diminished cardiac output, and shock.

They then demonstrated that exposure of the intestines to a current of warm air did not produce shock nor any significant lowering of the carbon dioxide content of the blood, nor did it even produce any significant lowering of the blood pressure, even after a period of three hours.

W. B. Cannon (11) points out that Henderson's primary

assumption that severe wounds are associated with sufficient pain to cause vigorous respiration and consequent acapnia is not borne out by observed facts. The severely wounded do not experience any immediate great pain; it is only when inflammation sets in that severe pain occurs. Also, although respiration in shock is often faster than normal it is usually so much shallower that it actually brings about a less effective ventilation of the lungs.

He also points out that in cases of such intolerably severe pain as in trigeminal neuralgia, no symptoms of shock are produced.

Finally, Cannon found that treatment of shock based upon this theory is of no benefit. He found that, although in animals in shock, the breathing of carbon dioxide did actually cause a rise in blood pressure, the effects were only temporary. Similar results were obtained in human cases, and in some of these a disastrous fall in blood pressure took place, and in none of them was any permanent benefit rendered.

THE THEORY OF ACIDOSIS

In 1917, A. E. Wright, while studying gas gangrene, observed that symptoms of shock often occurred, and that in these cases there was a definite reduction in alkali reserve, and that in cases where such symptoms did not develop, there was no such reduction. He suggested that the acidosis might be the cause of these symptoms. (66)

W. B. Cannon found that in shock cases received at the clearing stations at the front during the World War, there was a definitely diminished alkali reserve, and that there existed a rough correspondence between the degree of acidosis and the degree of depression of the blood pressure. He further stated, at that time, that surgery on shock cases caused a further drop in an already low alkali reserve, in addition to further lowering the blood pressure, and thus favored a fatal issue, but that if a solution of sodium bicarbonate was injected intravenously before operation, these unfavorable conditions were obviated - the alkali reserve was raised and with it the blood pressure. (10)

N. M. Keith found, however, that while there was this reduction in alkali reserve, it never reached the level at which symptoms of acidosis might be expected to arise. (38) Cannon, after further investigation, came to the same conclusion, and further states that an increase in the H-ions of the blood necessary to bring about such a

change would have to be much greater than would naturally be produced by any bodily changes. (11)

C. C. Guthrie, in experiments on dogs, found that definite symptoms typical of shock could not be produced by intravenous injections of lactic acid, and that recovery from an otherwise fatal lactic acid intoxication took place when sodium bicarbonate was given intravenously; and that there was no recovery from shock (produced by trauma) upon injection of sodium bicarbonate. He concluded, therefore, that acidosis could not be a primary causative factor in shock. (28)

Dale and Richards (working with the Medical Research Committee of Great Britain) showed that the alkali reserve of the plasma could be reduced to a very low figure (from 44 volumes percent to 8.6 volumes percent) without producing any significant change in the blood pressure. Subsequently divergent results were obtained in other experiments by this committee, but they finally came to the conclusion that, "simple acidosis, in the sense of a reduction of the alkali reserve of the blood, even though it be severe and prolonged, does not cause shock, or, indeed, any perceptible impairment of the circulation or other vital functions in an otherwise normal animal at rest." (22)

THE THEORY OF FAT EMBOLISM

W. T. Porter (50) on the basis of personal observations made on over a thousand consecutive cases fresh from the front line trenches during the World War, came to the conclusion that, aside from abdominal cases, "the only shock was that caused by fracture of the femur or by multiple wounds through subcutaneous fat - conditions in which fat embolism is known to take place." He then proceded to work out a series of experiments which proved to his satisfaction that fat embolism of the vasomotor center was a cause of shock.

In his early experiments in 1917, (49) he simply injected varying amounts of olive oil, cottonseed oil or cream intravenously in animals and found that he could thereby produce a marked fall in blood pressure accompanied by symptoms of shock.

In his later experiments, completed in 1925, (50) he apparently demonstrated quite conclusively that it was embolism of the vasomotor center and not of any other part of the body that produced the shock.

He injected neutral olive oil into the vertebral artery of animals and found that the injection of but 0.2 cc. would produce a lowered blood pressure and shock. That it was the bulbar vasomotor region that this affected and not portions of the brain anterior to the bulb was demonstrated by the fact that the whole of the brain anterior

to the bulb may be separated from the bulbar region without lowering the blood pressure. In cases in which shock was thus produced, fat emboli were demonstrated in the bulbar region by microscopic sections stained with Scharlach R.

The shock thus produced could not have been due to pulmonary fat embolism because the amount of this 0.2 cc. of oil which would have passed through the bulb into veins and thus to the lungs would have been too minute to have had any such effect. In addition he showed that massive fat embolism of the lung did not produce shock provided the oil was prevented from reaching the medullary center. He did this by means of a crossed circulation between two cats, arranged so that the brain of cat A was supplied with blood from cat B. Then 1 cc. of olive oil was injected into the jugular vein of cat A. The systemic blood pressure of cat A did not fall even though its lungs were so filled with oil that the resulting pulmonary edema caused foam to pour from its trachea.

Finally he demonstrated that after an animal was reduced to shock by fat embolism of the vasomotor center, this center was definitely damaged, for stimulation of the depressor nerve no longer brought forth any response.

Porter did not contend that this was the only cause of shock, but that it was simply one among a number of

causes such as hemorrhage, dilatation of the abdominal vessels, vibration injuries (concussion of brain), poisons, etc., but he overemphasized it. It appears rather strange that he should in criticism of Crile's theory insist so strongly that the vasomotor center is intact to almost the very end in shock, and then turn around and try to show that shock is due chiefly to embolism of that center - a condition which, as he demonstrated himself, definitely damages the center.

Moreover, as Cannon (11) points out, if shock is to be attributed to the plugging of the vessels of the vasomotor center, it is surprising that one should think that of all the vital centers so closely related to one another in the floor of the fourth ventricle, the vasomotor center should so exclusively suffer. One would expect, in damage to this region, to also get marked disturbances of, for example, swallowing and respiration. This does not occur. Furthermore, in proved cases of fat embolism of this region, there are also other disturbances such as stupor, cramps, paralyses, and usually a high temperature, even up to 104° to 105° F. These symptoms are not characteristic of clinical shock.

MINOR THEORIES

There have been a number of minor theories advanced as to the etiology of traumatic shock. On none of these has much work been done, yet they do bring out certain features of the problem, and some of them have been embodied and more completely worked out in later theories.

In 1893, J. D. Malcolm had already made the observation that the arteries are actively contracted in shock, and in 1905, he advanced his theory, based almost entirely on clinical experience, that shock was the result of prolonged constriction of the arteries, produced as a result of traumatic irritation of nerves. This constriction, he thought, caused the blood to accumulate in the veins, and in plasma being mechanically expressed from the vessels into the tissues. This brought about a decrease in blood volume and a reduction in blood pressure, with their attendant symptoms of shock. Death resulted from a deficiency in the nourishment of the vital nerve centers. (41)

In 1907, E. Boise endeavored to demonstrate that the essential cause of shock was excessive sympathetic irritation, manifestated mainly by a tonic contraction of the heart and arteries. He did demonstrate, in a series of experiments on rabbits, that in shock there was increased systole of the heart, decreased diastole, lessened output of blood from the heart, and therefore low blood pressure. (9) Essentially the same theory was more completely

worked out by N. E. Freeman. This will be discussed under a separate topic. (26)

L. Hill, 1910, was of the opinion that shock was caused by a paralysis of the sensory synapses. He reasoned that since the stimulation of a reflex arc left it momentarily depressed, excessive stimulation would result in paralysis and the development of a primary nervous shock, with a secondary fall in blood pressure. (35)

E. H. Starling, 1919, believed that the essential factor in shock was the stagnation of the blood in the dilated capillaries. These, by a process of exclusion, he assumed as being in striate muscle. In explanation of this, he suggests that a man in battle is under a state of great tension, and the arteries and arterioles have an increased tonicity. When a man in injured, this hypertonicity is suddenly increased, and at the same time there is an inhitibion of all striate muscle. The result is stasis of blood in the muscle capillaries, less blood in the circulation, a fall in blood pressure, anoxemia, acidosis, and further dilatation of the capillaries. A vicious circle is thus set up which eventually results in death. (58)

Erlanger and Gasser, 1919, found that the capillaries and venules of the intestinal villi were enormously distended and solidly packed with red blood corpuscles, and made the suggestion that the failure of circulation was, at least in part, due to the resultant mechanical obstruction to blood flow. (23)

THEORIES OF AN ADRENAL FACTOR

Two opposing theories have been advanced as to the role played by the adrenals in shock: one, that shock follows exhaustion of the adrenals; the other, that shock is due to overactivity of the adrenals.

In 1907, Bainbridge and Parkinson found, after an examination of the adrenal glands in fifty consecutive post mortems, that adrenalin had entirely disappeared in cases of death from acute general infections and from postoperative shock, whereas it was normal or almost normal in amount in cases of death from chronic diseases. Control observations showed that the amount of chromaffin substance was not appreciably lessened in the interval between death and the post mortem. This apparently indicated exhaustion of the adrenals in shock. (1)

In 1915, J. F. Corbett found that the epinephrin content of the blood of animals in shock was reduced to 8% of normal. He concluded that epinephrin exhaustion was the predominant factor in shock. However, he gave no details of his experiments. (17)

In 1918, J. E. Sweet made the statement that the only way in which he could experimentally bring about a condition comparable to surgical shock was by the complete removal of both adrenals. Upon this finding, and upon the fact that in Addison's disease, in which the adrenals are affected, there is a low blood pressure,

and upon the fact that the injection of adrenalin raises blood pressure, he based his assumption that shock was the result of exhaustion of the adrenals. (60)

Other observers have been unable to confirm these findings. A. R. Short could find no significant change in the epinephrin content of the adrenals in shock. The method he used for testing the amount of epinephrin in the adrenal glands was able to detect one part in five hundred million of Parke, Davis and Company's adrenalin. There was no appreciable difference between the shock cases and the control cases. (57)

Gley and Quinquard ran a large series of experiments to determine what part, if any, epinephrin, as secreted into the blood stream by the adrenals, played in maintaining the tonus of the sympathetic nervous system, and in maintaining the arterial blood pressure. They obtained the following results: The arterial pressure was maintained at a normal level after bilateral adrenalectomy, and after bilateral ligature of the adrenal veins. The splanchnic nerves retained all their irritability after either of these two operations. (27)

F. C. Mann found that animals could live for several days after removal of all suprarenal tissue, and be kept in an apparently normal condition. (42)

The theory that overactivity of the adrenals might be a cause of shock was first advocated by Bainbridge and

Trevan in 1917. They injected adrenalin slowly intravenously into anesthetized dogs for twenty minutes or longer, at a rate sufficient to maintain the arterial pressure at a supranormal level comparable with that obtained by moderate stimulation of a sensory nerve. During the injection, the portal pressure rose and remained at a high level, while the systemic venous pressure was not significantly altered. Meanwhile, hemoglobin and hematocrite readings showed a steady decrease in volume of plasma compared with corpuscles, and an increase in the viscosity of the blood. When the injection of adrenalin was stopped, the arterial pressure fell rapidly to a low level, while the portal pressure remained high, and the animal passed into a state of shock. The relation of portal and systemic pressures indicated some obstruction, but they had not investigated what this might have been.

With the injection of adrenalin stopped, the splanchnic vessels dilated sufficiently to allow a large amount of blood to accumulate therein, and because of the inadequate amount of blood returned to the heart, there was a diminution of cardiac output and symptoms of shock. (2)

Erlanger and Gasser also found that they could produce symptoms of shock following the continuous injection of epinephrin. However they attributed the failure of the circulation to the constricting action of the epinephrin on the arteries. They considered this to be simply

a mechanical effect similar to the effect of partially occluding the aorta or vena cava. (24)

Investigators have not been able to come to an agreement as to whether there is or is not an increased output of epinephrin in shock. E. A. Bedford tested the blood taken from the adrenal vein before and at successive periods during shock, and found that increased quantities of epinephrin were thrown into the blood stream during conditions of low blood pressure and shock. He thought that this was due to an actual increase in the activity of the glands and not simply to a release of stored material. (4) Stewart and Rogoff, on the other hand, found that after the blood pressure had been lowered by such procedures as exposure and handling of the intestines, partial occlusion of the inferior vena cava, hemorrhage, and by injections of peptone, there was no difference in the amount of epinephrin produced. (59)

In 1935, Swingle and Parkins still further complicated the question as to the role played by the adrenals in shock, by apparently demonstrating that the cortical hormone of the adrenal gland played an important part in shock. They worked out a series of experiments on the effect of trauma on dogs with and without adrenal glands. They found that if both adrenals were removed, the dog soon went into shock and died, unless daily maintenance doses of cortical hormone were given. If this was done,

together with the injection of adrenalin to prevent hypoglycemia (the injection of adrenalin alone did not prevent shock), the animals could be restored and maintained in an apparently vigorous healthy state. They found, however, that such adrenalectomized animals went into shock after a negligible amount of trauma - trauma which had no demonstrable effect on dogs with the adrenals intact. They then found that the injection of cortical hormone would restore these animals to normal, and that if previous to the traumatization, the animals were primed with a large dose of cortical hormone, the same amount of trauma did not produce shock. They concluded that the cortical hormone must play an important role in the prevention of and recovery from traumatic shock. (61)

THE THEORY OF HYPERACTIVITY OF THE SYMPATHETIC NERVOUS SYSTEM

Related to the adrenal theories is the theory that shock is brought about by hyperactivity of the sympathetic nervous system. This theory was advanced by N. E. Freeman in 1933. He reasoned that, if all factors at present known to produce shock, or to aggravate the condition if present, were examined, it would be found that they have one physiological action in common, that is, that they are all adequate stimuli for producing hyperactivity of the sympathetic nervous system. Vasoconstriction and increased output of adrenalin, both of which are indices of generalized sympathetic hyperactivity, have been found to be produced by each of the following: hemorrhage, cold, fear, pain, asphyxia, and low blood pressure.

The question which was the basis of this author's investigation was: Does hyperactivity of the sympathetic nervous system in itself result in a diminished blood volume; since shock is characterized by a reduction in the circulating blood volume, and since shock-producing factors stimulate the sympathetic nervous system.

He found that he was able to produce an average decrease in blood volume of 14%, in cats, by the continuous intravenous injection of adrenalin in physiological amounts (0.001 to 0.006 mgm. per kilogram per minute), and that such a decrease did not occur if the vasoconstrictor action of the sympathetics was inhibited by ergotoxin.

He also found that there was an average drop in blood volume of 21.9% in cats brought into the pseudoaffective state by decortication via the orbits. In this pseudoaffective state there is evidence of a greatly increased production of adrenalin: a rise in blood pressure, a rise in blood sugar, and sham rage - evidenced by struggling, clawing, panting, lashing of tail and erection of hairs. However, if ergotoxin was administered in such experiments, the drop in blood volume was prevented, even though all the above mentioned symptoms were present.

Then, to rule out any action of ergotoxin, he repeated the experiments on the pseudoaffective state in completely sympathectomized cats, and found that here also there was no drop in blood volume.

He concluded that prolonged hyperactivity of the sympathetic nervous system, whether resulting from the injection of adrenalin in physiological amounts, or from the spontaneous emotional activity of the pseudoaffective state, caused a decrease in the volume of circulating blood.

He suggested that the following sequence of events took place in the development of shock: hyperactivity of the sympathetic nervous system, vasoconstriction, tissue asphyxia, increased permeability of the capillaries, passage of fluid from the blood stream into the tissues, lessened blood volume and increased concentration of the blood, increased resistance to the flow of blood, a slowing of

the blood stream and eventual stagnation, and shock. (36)

THE THEORY OF TRAUMATIC TOXEMIA

In 1918, W. B. Cannon, together with other members of the Medical Research Committee of England, brought forth the theory that toxic material was formed in damaged tissues, and that this material, upon being carried throughout the body in the blood and lymph, so injured the blood vessed walls or their control as to result in a lowering of arterial pressure and the bringing on of a state of shock. There was considerable experimental and clinical evidence to support this theory.

Back in 1903, Vincent and Sheen performed a series of experiments in which they injected various tissue extracts (nerve, muscle, kidney, etc.) intravenously in dogs, cats and rabbits, and found that this caused a temporary fall in blood pressure. (62)

The experimental evidence upon which this theory is based consists chiefly in the following work of Cannon and Bayliss: Under urethane anesthesia, the thigh muscles of a cat, while supported by an iron block, were struck repeatedly with a hammer. The muscles were thus severely traumatized and occasionally the femur was broken, but usually no break in the skin resulted. After a period of twenty minutes or a little longer, the blood pressure would begin to fall and usually within about an hour it had fallen to shock level. That the urethane was not a factor was shown by repeating the experiments under

ether and gradually lightening the anesthesia as the symptoms of shock increased. (13)

It was suggested that there might have been sufficient loss of blood and lymph into the damaged tissues to account for the fall in blood pressure. They tested this by removing the normal and traumatized limbs post mortem by symmetrical cuts through the upper thigh region, and found that the difference in weight between the two was in some cases only 10% of the estimated blood volume. This amount of blood loss would be insufficient to account for a fall in blood pressure to shock level.

To rule out the shock being due to afferent nervous impulses, the experiments were repeated with the nerves to the injured limb severed, and the same results were obtained.

Acapnia as a factor was ruled out by keeping the breathing uniform by artificial respiration.

To prove that the lowered blood pressure must be caused by toxic products carried in by way of the blood stream, they repeated the experiments with the blood vessels to the limb tied off. No shock resulted. Then when these ligatures were removed, shock developed.

To further demonstrate this, they traumatized the muscles as before, and after the blood pressure had begun to fall, they clamped the vessels to the injured limb. The fall in blood pressure ceased, and in many cases even

a little rise took place. They supposed therefore that whatever the substance originating in the damaged tissues was, it was fairly promptly eliminated and the effect was therefore not permanent.

They also found that massaging the traumatized limb caused a more marked fall in blood pressure, and assumed that the reason for this was that the massaging facilitated the absorption of the toxins. (13)

The work of McIver and Haggart tended to support this theory. They established a crossed circulation between two cats. One of the cats was traumatized in the thigh region by the method of Cannon and Bayliss, and the effect on the blood pressure of the other cat noted. In nine cases out of twelve, shock developed in the other cat. They concluded that some substance capable of producing shock was produced in the traumatized area. (47)

An explanation of the mechanism of shock, based on this theory, is found in the work of Dale, Laidlow and Richards. In experiments on cats under ether anesthesia, they found tha the injection of 1 to 2 mgms. of histamine per kilogram body weight caused first a steep fall in the blood pressure, associated with a dilatation of the right chambers of the heart, then a rise because of a constriction of the arteries, and finally a steady moderately rapid decline from a normal of abour 150 mm. Hg. to 40 or 50 mm. in four or five minutes. The respiration failed at about

60 mm., and the institution of artificial respiration failed to arrest the downward course of the blood pressure. With artificial respiration continued, the chest was opened, and the heart was found to be beating strongly, but there was very little blood in it. The venae cavae were found to be flaccid and half empty, and, upon opening the abdomen, the abdominal vena cava was seen to be poorly filled, and the portal vein was flat and almost empty. The arteries similarly appeared to contain little blood, and were constricted. The liver and spleen were pale. They thought therefore that the blood must be in the capillaries. Inspection of the bowel showed that, while the arteries and arterioles contained but little blood, the bowel was of a diffuse dusky red congested appearance. This appeared to confirm their supposition. And, since the same lowering of blood pressure could be produced after removing the viscera, it was assumed that, although the muscles showed no macroscopic changed, the capillaries here were in the same condition. Moreover, if the volume of blood was increased by transfusion before the production of the shock, the accumulation of blood in the capillaries of the muscles became very apparent.

They explained the action of histamine as follows: Normally only a small portion of the capillary network is functioning at any one time. Under the influence of histamine, the capillary tone, which permits only this small

portion to function, is lost, and the whole of the potentially patent capillary bed becomes open. There is then a rapidly diminished venous return to the heart, its output declines, and the arterial pressure falls. In addition, the histamine causes a change in the permeability of the capillary walls, allowing the passage of plasma from the blood stream into the tissues.

This sequence of capillary dilatation, with an opening up of channels which under normal conditions have only a potential existence, plus an abnormal permeability of the capillary walls, leading to transudation of plasma, and finally the tendency of the blood thus concentrated by loss of plasma to stagnate in the widened channels, is familiar as a local effect, namely, inflammation. It is such an effect as occurs in the formation of a wheal from the lash of a whip, or in the formation of a boil from bacterial action. It is also known, they argued, that bacterial toxins, which locally produce an intense inflammatory reaction, will produce shock-like collapse when suddenly disseminated throughout the body.

Histamine produces a reaction of the inflammatory type when locally restricted, and shock-like failure of the circulation when its action is generalized by injection into the blood stream. Thus by analogy, they reasoned, products from injured tissues, which locally cause an inflammatory reaction like that of histamine, like

histamine, produce a shock-like condition if liberated in such quantity as to be rapidly absorbed into the general circulation. (22)

Considerable clinical evidence accumulated during the World War in support of this theory. In 1917, previous to any experimental work on this theory, E. Quenu had already made the suggestion that shock was probably due to the absorption of toxic material from the wounded area. He based this idea upon clinical experience, and cited a case illustrative of this. A soldier was severely wounded in the foot and was brought in with tourniquet tightly applied around the leg. At this time there was no evidence of shock, and the patient appeared to be in good condition. A conservative operation was done and the tourniquet removed. Three hours later, although there had been no hemorrhage or other untoward complications, the man was in intense shock. Quenu explained this as probably being due to the absorption of toxic products from the wound upon the removal of the tourniquet. (52)

Cannon cites a case in which a tourniquet had been in place on the upper arm for an undetermined period. The wound, which was on the hand, was so slight that the surgeon simply cleaned it and removed the tourniquet. Before removal of the tourniquet the patient was in good condition; a short time after removal he went into profound shock and died.

Cannon also cites the experiences of numerous surgeons during the World War, who found that amputation proximal to a tourniquet prevented the development of shock, and that the earlier damaged tissue was removed, the less likely was shock to develop, and often the removal of damaged tissues was followed by the recovery of patients already in shock.

The theory of traumatic toxemia may be summed up as follows: As a result of tissue injury, histamine-like bodies are formed. They at once cause a dilatation of the capillaries and a change in the permeability of their walls. The resultant tendency toward a lowered blood pressure is at first compensated for by an arterial vasoconstriction and an increased heart rate. However, as the condition progresses, this compensation begins to fail. This further aids capillary stasis already begun by the relaxation of the capillaries, and venous return to the heart is reduced. There results an insufficient volume of blood to maintain the circulation, and tissue asphyxia and death results.

This theory for many years constituted the best explanation we had of the mechanism of shock. However, even before the development of this theory, Carlson, Woelfel, and Powell (15) had tested the effects of the intravenous injection of extracts of a number of different tissues of

the body, and had found that muscle extract was among those having the least effect. And, in 1928, J. B. Collip found that tissue extracts contained a pressor as well as a depressor principle. He was able by extraction with acetone to obtain a substance which would cause a rise in blood pressure up to 300 mm. Hg. (16)

Because Collip had found that the chemical extractions of tissues contained both pressor and depressor substances, Roome and Wilson (53) attempted to determine the effect of simple mechanical (hydraulic press) extractions. They found that the injection of the whole extract of tissue from a traumatized limb (after heparinization of recipient to prevent coagulation of the blood by the tissue extract) caused not a fall but a rise in blood pressure. Injection of the bloody fluid from the traumatized limb caused a slight rise usually, and the injection of muscle extract caused a slight fall in blood pressure. All these changes in blood pressure were only transitory.

Then, beginning in 1930, there has accumulated during the development of the "Theory of Blood Loss" a mass of experimental evidence which apparently quite conclusively disproves the "Theory of Traumatic Toxemia". A discussion of this theory follows.

THE THEORY OF BLOOD LOSS

In 1930, Parsons and Phemister advanced the theory that the symptoms of shock resulting from trauma to a limb were due to hemorrhage into the traumatized tissue. They ran a series of experiments on dogs in which they compared the results obtained by trauma to a limb with the results obtained by hemorrhage alone. They found the traumatized limbs to be considerably swollen, and when the limbs were removed by symmetrical amputations along lines of attachment to the innominate bones, that there was an increase in weight of the injured limb equal to from 42% to 59% of the estimated blood volume; and that in dogs that were brought into a state of "shock" from hemorrhage alone, from 44% to 52% of the estimated blood volume was drawn to accomplish this. They found the swelling to be due to hemorrhage and edema - chiefly hemorrhage. This apparently showed that enough blood was lost into the traumatized tissue to account for the symptoms of shock on this basis alone. Moreover, they also found that red blood cell counts after hemorrhage and after trauma decreased approximately the same amount in both cases. This further substantiated their contention that both cases are really simply cases of hemorrhage, rather than one being a case of hemorrhage and the other a case of shock. (48)

About the same time, Blalock and Bradburn began working

on the problem from a slightly different angle, and came to the same conclusions. They ran a series of experiments on dogs to determine the oxygen content of venous blood from different localities, in shock produced by histamine, by trauma to the intestinal tract, by trauma to the brain, and by trauma to one of the posterior extremities. Blood was obtained from the following sites: external jugular (from brain), portal vein (from intestines), femoral vein (from muscle), right heart, and renal vein (from kidney). They found that there was a striking similarity between the values of the oxygen content of the blood from the various sites in normal animals, and between the lower values obtained in cases of shock from hemorrhage, from the injection of histamine, and from brain trauma. This indicated that in shock by these methods, there is a fairly uniform diminution in the volume of circulating blood in all parts of the body.

In cases of shock produced by intestinal trauma, on the other hand, the oxygen content of the portal vein was markedly higher than that obtained elsewhere; and in cases of shock produced by trauma to a posterior extremity, the oxygen content of the femoral vein of the traumatized extremity was higher than that obtained elsewhere, including that of the opposite femoral vein. These results suggested that in traumatic shock, there was an accumulation of blood in the traumatized area, and a decrease of blood

in other areas.

Their conclusions were as follows: "It would seem that trauma to the intestinal tract or to an extremity produces its effect by a local accumulation of blood and not by an increase in capillary permeability in the general circulation with a loss of fluid into tissues such as is attributed to histamine". (8)

On the basis of the above work, Blalock worked out group of experiments to determine whether the low blood pressure following trauma was due to some substance exerting a general bodily effect, as advocated by Cannon and his co-workers, or whether it was due simply to local hemorrhage into the tissues.

He first repeated the experiments of Cannon and Bayliss, and found that he could produce shock by traumatization of the thigh muscles of an animal, but that this could not be done without there being a sufficiently large amount of blood lost into the injured tissues to account for the low blood pressure. He explained the discrepancy between his and Cannon's work as being due to the difference in methods employed in determining the weights of the traumatized and nontraumatized limbs. Cannon and Bayliss amputated the extremities by symmetrical cuts across the thighs. Blalock points out that there are a number of objections to this method. First, it is impossible to be sure that the level of amputation is the

same on both limbs because of the irregular contour of the thigh; second, that one cannot make such a cut through such traumatized tissue without some loss of blood; third, that trauma to the thigh results in some bleeding into the loose tissues of the groin as well as into the thigh. Blalock overcame these objections by amputating in the midabdominal region after ligation of the abdominal aorta and vena cava and clamping the iliacs on both sides. In control experiments, in which no trauma was done, the weights of the two limbs were practically identical. The difference in weight of the two limbs where shock was produced by trauma to one limb, amounted to at least 4% of the body weight, or almost one-half the calculated blood volume. In other control experiments, he found that a loss of blood amounting to only 1% of the body weight was sufficient to produce a low blood pressure and shock.

The fact that animals could withstand a larger loss of blood into tissues than by direct hemorrhage, he explained by the fact that there was a proportionately greater loss of plasma into the injured tissues than of red blood cells. He determined this by the fact that the hemoglobin content of bloody fluid from the traumatized tissues was less than that the blood.

He then ran a series of experiments to determine whether there was any toxic substance absorbed from the injured tissues.

In determining this he first ran some preliminary experiments as follows: He first showed that the absorption of histamine (and therefore of any other toxic substances) from a limb could be prevented with certainty only by removal of the upper part of the femur and then applying a tourniquet tightly at this point. Any absorption of histamine would have been demonstrated by a drop in blood pressure. Then he repeated this with the femoral artery dissected loose and not included in the tourniquet. There was still no absorption of histamine. In these experiments, there was no significant fall in blood pressure incident to the operation for removal of this portion of the femur, nor when the tourniquet was subsequently applied.

Then in dogs in which the upper part of the femur had been thus removed, the femoral artery and vein dissected loose (vein occluded by a clip), and a tourniquet applied around the thigh beneath these vessels, he tried the following set of experiments:

The removal of the clip on the vein resulted in a temporary rise in blood pressure, followed by a fall to the level that existed before the clip was removed.

Then, with both artery and vein occluded, the limb was traumatized. No fall in blood pressure took place until the clip was removed from the artery. The blood pressure then declined rapidly at first, then slowly,

and when the blood pressure had thus been reduced by varying amounts, the clip was removed from the vein. There was an immediate small rise in blood pressure, followed by a gradual decline which was not so rapid as that which had been taking place before the vein was released.

In order to demonstrate that toxic products, had they been present, could have been absorbed from the injured limb, histamine was injected into the limb, with the vein closed, and when the vein was then released, there was a prompt and rapid fall in blood pressure.

Cannon's theory that the fall in blood pressure after trauma is caused by absorption of toxic products was thus apparently proved to be erroneous, since the greatest fall in the pressure took place upon allowing blood to flow into the injured limb, rather than when the blood was allowed to flow from the limb into the general circulation.

To add further proof, he reduced a dog to shock by trauma, and then injected its blood intravenously into normal dogs, and found that, instead of a fall, a rise in blood pressure took place. (5)

Freedlander and Lenhart repeated and confirmed Blalock's experiments, and in addition they excluded the nervous system as a factor. They accomplished this by severing all the peripheral nerves to the limb, severing the sympathetic chain, doing an arterial sympathectomy, and

cutting the lower dorsal cord. This was done aseptically in stages, and the animal was allowed to recover before doing the shock experiments. The same results were obtained as with the nerves intact. (35)

Beard and Blalock, after examination of the fluid that escaped from the blood vessels after trauma to an extremity or to the intestine, found that the chlorides, sugar, nonprotein nitrogen, and total proteins were practically the same as in blood plasma. From this they reasoned as follows: In ordinary hemorrhage, the blood lost is rapidly replaced by fluid from the tissues, because the reduction in blood pressure no longer offsets the greater osmotic pressure of the plasma, as compared with the lymph, and fluid passes into the blood stream. In shock, on the other hand, there has been an escape of whole plasma from the injured capillaries at the site of trauma, with the result that the escaped fluid has the same composition and osmotic pressure as plasma. The fluid that has escaped cannot therefore be reabsorbed. The diminution in capillary pressure probably does draw fluid into the blood stream from the noninjured areas, but the increase in mechanical pressure simply results in further fluid loss at the site of injury. (3)

Blalock then attempted to show that the mechanism of shock produced by trauma to the intestines was the same as he had already demonstrated in shock from trauma

to muscles.

He proceded as follows: The average weight of the intestinal tract between the ligament of Treitz and the appendix was determined on a group of normal dogs. Then dogs were brought to a state of shock by pinching repeatedly this portion of the gut and by pulling on the omentum. The fluid that accumulated in the peritoneal cavity during the course of the experiment was gathered in weightd sponges. These were then reweighed afterwards and the amount of fluid lost in this manner thus determined. Then at the end of the experiment, the portion of gut between the ligament of Treitz and the apendix was removed and weighed and compared with the average normal weight of this section of gut, as previously determined. From this, the loss of fluid into and from the traumatized area was determined, and was found to average 4.48% of the body weight. The variation in the different experiments was from 1.89% to 6.22%. As he had determined in previous experiments, this amount represents a sufficient loss of blood volume to account for the lowered blood pressure and shock.

The average increase in the hemoglobin of 38% indicated a marked concentration of the blood due to the tremendous loss of plasma in this type of trauma.

He concluded that "the loss of fluids into and from the traumatized area was the chief if not the sole cause for the reduction in the blood pressure". (6)

In spite of the fact that this theory most adequately explains traumatic shock, and rests upon thorough and well controlled experimental work, it has not been accepted without question. W. B. Cannon warns against the unreserved dropping of the theory of toxemia. He states that even though proof of the presence in damaged tissue of a specific shock inducing agent, there still remains the clinical testimony that "material absorbed from dead and dying tissues and distributed in the organism may be toxic - so toxic as to play a role in lessening the quantity of circulating blood". (12)

N. E. Freeman, in working out his theory of the production of shock by hyperactivity of the sympathetic nervous system, states that it is impossible to account for the shock he produced, on the basis of the theory of blood loss, because where he simply injected adrenalin at a physiological rate, no trauma was produced; and where trauma to the brain was produced, the rigid cranial walls prevented swelling of the tissues, and moreover, this same amount of damage to the brain in the sympathectomized animal caused no decrease in the blood volume. (26)

And, in view of the support given the theory of toxemia by Moon and Kennedy, this factor must be considered. After a series of observations on shock in experimental animals and in human cases, they came to the following conclusions: "The shock syndrome is accompanied by gross

and microscopic changes opposite in character to those produced by hemorrhage. The changes include dilatation and engorgement of capillaries and venules, permeability of capillary walls, as indicated by petechial hemorrhages and edema, and frequently effusion into serous cavities. Increased concentration of the blood is a characteristic phenomenon in shock.

"These vascular phenomena are widespread, but are most prominent in the pulmonary and gastro-intestinal tracts.

"These circulatory effects can be produced by trauma, by intravenous or intraperitoneal injections of extracts of normal muscle, or by implanting muscle substance into the peritoneal cavity. This tends to corroborate the view that products absorbed from injured tissues produce the shock syndrome, and that these act by causing dilatation and increased permeability of the capillaries and venules". (46)

CONCLUSIONS

From a consideration of the foregoing theories of the etiology of shock, it is evident that, in spite of the large amount of work done on the problem, there is still no unanimity of opinion, even among equally competent observers.

V. H. Moon is of the opinion that shock is present as a terminal factor in the majority of deaths from all causes, and that the degree to which shock is operative varies within wide limits. For example, it is the dominant factor following extensive trauma, and a minor terminal factor in various diseases. He maintains that shock, instead of being of various types, is a definite entity, even though it may originate from various sources. He further maintains that it is accompanied by distinctive changes which are demonstrable both ante mortem and post mortem, that these changes are directly related to its mechanism of origin, and that this mechanism is one of toxemia.(45)

A. Blalock makes the suggestion that the terms primary and secondary shock be abandoned. He contents that a state of traumatic shock may follow directly the receipt of an injury, and there may be no intermission in the symptoms until the syndrome is terminated by recovery or death, and it is therefore unwise to classify the condition according to the time separating the injury and the decline in blood pressure. He suggests that the following terms

be used to designate different types of shock: hematogenic, neurogenic, and vasogenic. By hematogenic shock, he meant the type in which there was a decrease in blood volume, as a result of hemorrhage, dehydration or loss of blood or plasma into or from an injured area; by neurogenic, the type in which there was vasodilatation because of influences acting through the nervous system; and by vasogenic, the condition in which there was a loss of peripheral vascular tone caused by agencies which acted directly on the blood vessels. He concludes that the mechanism of the production of all types of shock is not the same, and that they cannot therefore be explained by one theory. He advises the abandonment of such attempts. (7)

F. C. Mann and H. E. Essex sum up the problem as follows: In an attempt to account for the cause of the clinical syndrome known as traumatic shock, theory after theory has been advanced. Each theory, when more thoroughly tested clinically and experimentally, has been found inadequate, but has served to focus attention on certain aspects of the problem, and has been of value as a stimulus to further research. Thus through the efforts of many investigators, the mystery that surrounded the problem at the beginning of this century, has been replaced by certain definite facts, although our knowledge concerning the condition is far from complete. (43)

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