THE NATURE OF SHOCK.

ITS RELATION TO ACAPNIA AND TO CHANGES IN THE CIRCULATION OF THE BLOOD AND TO EXHAUSTION OF THE NERVE CENTRES.*

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It is the object of this paper to present the results of a series of experiments which furnish information regarding the relative etiologic importance of acapnia, of reflex changes in the circulation of the blood and of exhaustion of the nerve centres in shock produced by three methods. Crile has concluded as a result of a long series of experiments that the primary change wrought by all causes of shock is a fatigue of the vasomotor centre. As a consequence of this fatigue there is a continuous lowering of the blood-pressure until the cerebral centres, particularly the medullary centres, no longer receive sufficient blood to enable them to functionate normally, and from this cause, in fatal cases, life becomes extinct.

This theory has received the recognition to which it is entitled by the high character of all the work of its chief advocate. The protocols of his experiment demonstrate the close relation between low blood-pressure and shock. At present the theory is made the basis of a method of anæsthesia which is believed to diminish shock in operations, and is rendered conspicuous by having been christened with a new name.

No one can fail to admit the important association of a diminution of blood-pressure with the onset and development

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of shock. Every writer has felt obliged to admit its bearing on the problem of shock. Nevertheless, a rather large number of writers since the publication of Crile's work have been unable to believe that any of the series of events, including the low blood-pressure itself, which may result in shock is, at the start, a process of fatigue of the nerve centres. Meltzer has discussed the whole question at length in a review of all the more recent theories of the nature of shock. He presents many observations of others and adds the results of his own experiments to show that the primary changes in the human body leading to the development of shock is not fatigue of the nerve centres but an inhibition of their activities. Differing from Crile, he quite justly questions the legitimacy of distinguishing etiologically between shock and collapse.

During the past winter we have performed experiments in connection with the production of shock by three methods. These experiments in agreement with the views of others, particularly of Howell, Porter and Meltzer, demonstrate, first, that a low blood-pressure is an important symptom of shock, but that an animal may pass into shock with a blood-pressure which is still far above a point below which the nervous system fails to functionate normally; and, second, that changes in the frequency of the heart and its output per beat always accompany shock, even in the earliest stages; but that it is very unlikely that changes either in the blood-pressure or in the force and output per beat of the heart are inaugurated by fatigue of the nerve centres. Our experiments indicate that shock in its incipiency in some cases is of reflex, and in other cases of local peripheral origin.

From the practical as well as the scientific point of view the causes inaugurating shock are the most important. It matters little that a low blood-pressure may cause the death of an animal already in fatal shock. We wish to know what are the causes leading to shock before the blood-pressure begins to fall, and how to prevent these causes from becoming active.

Yandell Henderson has sought an explanation different from that of all other writers. He concludes from a large

amount of experimental work that acapnia can be one of these causes. He believes it to be the essential cause in shock produced by artificial hyperrespiration and by prolonged exposure of the intestines, and may be a cause of that form of shock produced by severe stimulation of afferent sensory nerves.

In all experiments performed by us, dogs were used. Each animal received 0.005 mg. of morphin for each kilogram of body-weight. Sufficient ether was given during each experiment to produce full anæsthesia.

SHOCK AND ARTIFICIAL HYPERRESPIRATION.

In the first series of experiments that form of shock was considered which was produced by artificial hyperrespiration.

A suitable time after the injection of the morphin the animal was etherized and a rubber tube introduced through the larynx into the trachea. By means of two rotary blowers and an intervening slide-valve which regularly threw first the exhaust of one blower and then the intake of the other blower into connection with the intratracheal tube, air was alternately forced into and sucked out of the lungs. The slide-valve was operated by another electric motor than either of those turning the blowers. Its speed was regular and could be controlled by a rheostat, and the frequency of the interruption of the valve which it operated could be varied as occasion demanded. By means of by-passes in series with the exhaust of the blower used to inflate the lungs, and the intake of the blower used to deflate the lungs, the amount of air used for the artificial inspiration and expiration could be varied at will. In these experiments the intratracheal catheter did not tightly fit the trachea. Provision, therefore, was made for the escape of any excess of air forced into the lungs during the inspiratory phase around the intratracheal tube, and the same factor of safety controlled the expiratory phase. We found, without this provision for a certain latitude in the amount of air used to inflate and deflate the lungs, that sudden death from excessive variations of pressure within the chest could occur. As will be developed, this fact is in accord with our own belief as to the cause of shock produced by excessive artificial respiration.

In four of these experiments which we have performed, the artificial respiration varied from 60 to 70 times a minute, and the lungs were as completely inflated and deflated as is possible with a closed chest. In order to accomplish such a filling and emptying of the lungs at a rate of from 60 to 70 times a minute, the air must be forced into and sucked out of the trachea under considerable pressure. Two of the experiments were continued for three hours and two for two hours. In these experiments the blood-pressure fell 40 per cent. within a few minutes after starting

the artificial respiration and then decreased more slowly to between 40 and 50 mm. of mercury. After the cessation of the experiments, the blood-pressure rose from 60 to 90 per cent. within a few seconds.

The carbon dioxide content of the arterial blood at the end of the experiments was from 38 to 44 per cent. of its original amount. The amounts of carbon dioxide and oxygen were measured in all experiments reported in this paper by the Barcroft-Haldane method. At the end of the experiment the animals were in deep shock. One died the next morning, one in two days and the other two lived three days. None of them died of the immediate effects of the experiment, but from secondary effects. They had recovered from the shock and their lungs at necropsy showed interstitial emphysema. In all these experiments it was found that the amplitude of the pulse and the blood-pressure was proportional to the pressure at which the lungs were inflated and, therefore, to the intrathoracic air-pressure. The amount of shock which was produced was proportional to the length of time that certain pressures, which we may term critical intrathoracic pressures, were maintained. The carbon dioxide content of the arterial blood could be easily reduced to from 40 to 50 per cent. of its original amount within half an hour; but in four other experiments when artificial respiration was maintained for only this short period, we found that no shock resulted. It has been assumed by Henderson that a long-continued acapnia, lasting two to three hours, results in a depletion of the tissues' store of carbon dioxide by osmosis, and accompanying this osmosis of carbon dioxide from the tissues into the blood, water passes from the blood into the tissues. As a consequence, a diminution of the total volume of the blood ensues. The associated general muscular relaxation dependent on the changed chemical composition of the muscles contributes to the diminution of the general blood-pressure by no longer affording the proper support to the veins. Thus the veno-pressor mechanism is also disturbed and, with it, the proper balance of the distribution of the blood in the body.

In our experiments the force of the artificial respiration necessary to produce acapnia was so excessive and the degree of shock and the change of blood-pressure so closely proportional to the intratracheal pressure that the air-pressures, at which the artificial respiration was given, seemed to us to be the most important factor in the production of shock by this means. We therefore performed three experiments in which the same conditions of artificial respiration were maintained, but with the provision against the loss of carbon dioxide. In all three precisely the same conditions of artificial respiration were maintained as in the first set of experiments, but, by inserting a rebreathing bag in which the expired air was collected and from which that blower was supplied which furnished the

air to the dog's lungs, and supplying to the fresh air required to be added during the experiment a proper proportion of carbon dioxide from a tank, the amount of oxygen in the blood was unchanged at the end of the experiment and the amount of carbon dioxide raised only slightly above the normal. All of these animals presented the same degree of shock at the end of their period of artificial respiration (two hours) as the animals of the first series. In these experiments, also, the shock was directly proportional to the air-pressures used during the artificial respiration.

Clearly, then, the shock produced by artificial hyperrespiration was not due to a diminution of carbon dioxide but to some other factor which is dependent on increased intrathoracic pressure. Of the effects produced by increased intrathoracic pressure, the one first suggesting itself as the most important and, as far as we can conceive, the only one bearing on the problem of the cause of this form of shock, is the interference of the venous return to the heart. By venous return to the heart, not only the return from the systemic circulation is referred to, but also the return from the pulmonary veins. The latter is affected in two ways, first, by direct pressure around the pulmonary artery, and second, on capillaries and veins within the lungs themselves. The pressure on the pericardium required to alter the general blood-pressure is much above that which affects the circulation when applied to the great veins at the base of the heart. This factor, therefore, can be neglected in these experiments. The most direct manner of measuring the effects of increased intrathoracic pressure on the circulation is to measure the output of the heart; and a third series of experiments, four in number, were devoted to this investigation.

The thorax was opened laterally, and a T-tube connected with a water manometer was tied in a small bronchus. The heart was then enclosed in a Henderson's cardiometer in circuit with a recording tambour. The blood-pressure was recorded from the carotid artery. The thorax was then closed and the animal subjected to intratracheal insufflation from an apparatus provided with an exhaust-valve which reduced the pressure to approximately zero from four to twelve times a minute, or

could be made to furnish continuous insufflation. In one experiment taken as an example, with an increase of intrabronchial pressure from 8 to 30 mm. Hg, the blood-pressure sank from 122 to 55 mm. Hg and the volumetric tracings of the cardiometer showed a diminution of cardiac output of 44 per cent. In another experiment the blood-pressure rose 15 mm. Hg each time the interrupting valve reduced the intrabronchial pressure from 6 mm. to 0. These variations of blood-pressure were completed within a few seconds after the change in intrabronchial pressure and could be duplicated at will. A rise of intrabronchial pressure above 8 or 10 mm. Hg always caused a fall of blood-pressure proportional to the rise of intrabronchial pressure.

It is evident, therefore, that excessive intrabronchial pressure, such as always accompanies violent artificial respiration even at from sixty to seventy times a minute, is quite sufficient in itself to account for a continued diminished cardiac output and low blood-pressure.

VENTILATION OF THE ABDOMINAL CAVITY.

We next studied the relation of acapnia to that form of shock produced first by exposure of the intestines to a current of warm moistened air passed over them beneath a celluloid cover, and second, by evisceration and handling the intestines.

A portion of the anterior musculature of the abdomen was excised, the omentum cut away and a celluloid window fitted in place between the layers of the muscles left at the side in such a manner as to completely cover the intestines. A current of warm and moistened air was then passed beneath the celluloid over the covered intestines. The air entered through a tube piercing the celluloid at one end of the abdomen and passed out through an opening at the other end. Aëration of the abdominal cavity under these conditions for a period of three hours produced no shock in one experiment and little reduction of the carbon dioxide content of the blood. Through the celluloid it could be seen that no drying of the peritoneal surface occurred. The intestine remained a good color, and peristalsis was almost absent at the end of this time. The blood-pressure was 163 mm. Hg. The celluloid membrane was then removed, the intestines spread out and the aëration continued for forty-five minutes longer. The blood-pressure was then 153 mm. and the carbon dioxide content of the arterial blood was 38.8 volume per cent. The intestines were then handled and in ten minutes the blood-pressure had fallen to 80 mm., and in twenty minutes to 56 mm. After even ten minutes longer there was 31.6 volume per cent. of carbon dioxide in the arterial blood.

As a check to this experiment another experiment was performed. The abdomen was opened by cutting away the anterior wall. The in-

testines were exposed by cutting away the omentum and warm, moistened air passed over them. A long tube was inserted into the trachea in order to preserve the normal amount of carbon dioxide in the blood. At the end of one and one-half hours the blood-pressure had not changed and the animal was in good condition. The intestines were then handled and in ten minutes the blood-pressure fell from 122 mm. Hg to 60 mm. Hg. The carbon dioxide content was 45.1 volume per cent. In twenty-five minutes the blood-pressure was 46 mm. Hg, the carbon dioxide still undiminished and the dog was in pronounced shock. The sciatic nerve was then stimulated and a rise of blood-pressure to 96 mm. Hg was obtained, showing a strong medullary reaction.

These experiments, investigating the relative effects of aërating the intestines and of handling them, justify the conclusion that the manipulation of the intestines and not a diminution of carbon dioxide is the important factor in the causation of shock accompanying exposure and handling of the intestines. We have been unable to find any record among the experiments of Henderson of the production of shock by aërating the abdominal cavity alone within reasonable lengths of time.

SHOCK AND MANIPULATIONS OF THE INTESTINES.

In attempting to investigate the mechanism of shock produced by prolonged handling of the intestines, we first sought to establish definite controls. After some preliminary experiments we demonstrated that by handling the intestines violently for one hour, with, it should be remembered, complete anæsthesia, a deep degree of shock could always be produced. In some of these animals the degree of handling of the intestines was sufficient to produce actual rhexis from the peritoneal surface. In our subsequent work we attempted to avoid such a severe degree of handling. We aimed to secure a very intense congestion without actual rhexis. We satisfied ourselves that this degree of handling, in two hours' time could be counted on to produce fatal shock.

Having established this fact we next attempted to discover how far it would be possible to resuscitate dogs from a condition of otherwise fatal shock produced in this manner by transfusion from another dog.

Deep degrees of shock were produced by handling the intestines in six dogs, as described before, for two hours. At the end of this time each animal was in a deep degree of shock. Their eyes were immovable in the orbits and drawn down and inward beneath the conjunctiva. They were absolutely irresponsive to sensory stimulation. Their muscles were relaxed, respiration was shallow, the surface of the body cold, and the pulse rapid and diminished in amplitude. In one of the dogs the transfusion was given immediately after the period during which the intestines were handled, in the others it was given at varying intervals up to one hour after the intestines were handled. Recovery from the shock followed transfusion in all of the dogs. In four of them immediately after the transfusion their eyes regained the normal position in the orbit. The recti muscles of the eyes recovered from their previous relaxation. The dogs voluntarily moved their legs and became responsive to external stimuli. Immediately after the transfusion three of them ran around the laboratory so that they were obliged to be tied up in order to keep them confined. Running around seemed to cause them no discomfort whatever. In two of the dogs which were not transfused until an hour after the experiment, and with which the blood-pressure had been allowed to reach a very low point during this hour, the recovery was less complete, though unmistakable. Following this improvement all of the dogs remained for a long time in about the same condition but permanent recovery was never obtained. They gradually manifested signs of increasing abdominal distress, becoming in consequence more quiet, and died some time during the following night. The temporary improvement after the transfusion described was only the well-recognized improvement regularly following transfusion in shock from any cause. Nevertheless we believe that these transfusion experiments on animals in shock from evisceration of the intestines afford information regarding the nature of shock when carefully studied themselves, and when taken in connection with the control experiments and other experiments about to be described.

The first significant fact to note, and one previously emphasized by Howell and Meltzer, is the comparatively high blood-pressure at the end of the period of intestinal manipulation. Only two of the animals had a blood-pressure approximating 50 mm. Hg. In all the other animals the reduction of the blood-pressure had been as follows: from 104 to 90; from 114 to 54; from 119 to 75; from 115 to 46, and from 105 to 80. The same failure of the blood-pressure during the period of the production of the shock to fall to a dangerously low point was noted in the control experiments; namely, from 116 to 84; from 118 to 67; from 110 to 94; from 102 to 90; from 145 to 88, and from 129 to 101. The one animal

which recovered ran around the laboratory in an apparently normal condition with a blood-pressure of 50 mm. Hg.

These facts demonstrate that at the end of the period during which the intestines were handled the nerve centres must have been supplied with sufficient blood to enable them to functionate properly in the absence of any other disturbing factor.

The second significant point was the very rapid recovery by the animal of his normal condition after transfusion. In other words, an animal in a deep degree of shock which our control proved would have certainly died in a few hours' time with a progressively falling blood-pressure, and in a number of instances with a blood-pressure which had already shown the first steps of this progressive fall, could immediately be resuscitated by transfusion. This rapid recovery precludes the idea that the other disturbing factor to which reference has just been made was an exhaustion of the nerve centres. We cannot conceive of an exhausted centre recovering so quickly. The fact that in our experiments the dogs spontaneously got up and played around and responded normally, as they did, to whistling, indicates that their cortical centres had not been exhausted by sensory impulses. There is no reason to assume that these impulses evoke a greater response in the medullary centres than in the cortical centres. Our deduction, therefore, that the medullary centres were not exhausted or even fatigued is justified. We draw no distinction except in degree between exhaustion and fatigue.

This conclusion is in accord with the results of Porter's experiments which furnish strong evidence that the medullary centres are not exhausted in shock. Porter obtained in numerous experiments a greater percentage rise of blood-pressure by stimulating the sciatic or vagus or splanchnic, or a greater percentage fall by stimulating a depressor nerve after the blood-pressure had been reduced in shock than before the shock had been produced. With a low blood-pressure the same strength of stimulus would probably be more effective both because the vessels may be dilated and because their walls

meet less resistance during contraction. Nevertheless, the absolute rise or fall in Porter's experiments was very great and the experiments furnish strong evidence of the absence of fatigue in the primary stages of shock.

In one experiment we have confirmed the results of Porter's work. A dog was thrown into deep shock by one and one-half hours of violent artificial respiration. On afferent stimulation of the vagus, or sciatic, or stimulation of the splanchnic, a percentage rise of blood-pressure of almost 100 could be obtained. The absolute rise was practically the same as at the beginning of the experiment before the shock had been produced, namely, 30 mm. Hg.

Those who have explained shock as primarily an exhaustion of the nerve centres assume that the blood-pressure in an unconscious animal falls because the medullary centres respond to afferent sensory stimuli and thus dissipate their energy. Numerous experiments have been reported by others in which animals have been thrown into deep shock by prolonged crushing, tearing, and electrical stimulation of sensory nerves. The results of these experiments have been interpreted as demonstrating the power of prolonged and strong afferent stimulation to exhaust the nerve centres. They have been used to explain the shock following serious injuries or operations and of the various methods of producing experimental shock. If, however, these results are used to interpret other forms of shock, they should parallel, particularly as regards time, the actual conditions of the accidents, operations or experiments which they are used to explain.

We have performed experiments of this kind. The animals have received the usual dose of morphin which has been used in all the work presented in this paper. They were then etherized. The sciatic and brachial nerves were dissected out and a strong faradic current applied for two hours to the nerves. Much tearing and crushing of the nerves was incidental to the experiments. During the period of stimulation the medullary centres were certainly active and presumably dissipating energy. This was proved by the hyperpnœa and rise of blood-pressure maintained during the experiment. As soon as the stimulation was discontinued there was a definite fall of blood-pressure, never, however, to a degree which either indicated shock, or could be of any significance in its pro-

duction. The blood-pressure averaged, for instance, at the start of the experiment, during the period of stimulation and after the latter was discontinued respectively 150, 120 and 110 in the first animal; 90, 120 and 100 in the second; 130, 176 and 140 in the third, and 96, 116 and 74 in the fourth.

These dogs required considerable ether, which regularly lowered the pressure each time it was applied. At the end of the experiment all four dogs recovered promptly. Immediately after the experiment the frequency and amplitude of the pulse was good. It compared favorably with that at the beginning. In one hour's time one of the dogs responded normally to his environment; the other three in four hours' time.

There was certainly little difference in this manner of recovery from that which would be presented by another animal which had received an equal amount of morphin and ether.

These statements are emphasized by the differences presented by animals in which the same prolonged severe stimulation of the sciatic and brachial nerves was conducted after the animal had lost the power of controlling his blood-pressure by a preliminary division of the great splanchnic nerves. Three of these experiments were performed. In one animal at the end of fifty minutes' stimulation the blood-pressure had fallen to 14 mm. Hg, death following a short time later. The second withstood a continuous stimulation for two hours; at the end of this time the blood-pressure was 77 and the animal was in deep shock; in three hours' time he was in still deeper shock and he was killed in five hours' time. The third animal recovered from the immediate effects of the experiment.

The relation of diminished blood-pressure to the production of shock in association with the stimulation of sensory nerves was intensified by bleeding the dogs after the splanchnics had been divided. One of these experiments was performed after division of both splanchnics, 200 c.c. of blood were withdrawn, reducing the primary blood-pressure from 152 to 70. The sciatic and brachial nerves were then stimulated as in the preceding experiment. The animal died in deep shock before the conclusion of the experiment.

In four other experiments dogs were bled until the blood-pressure fell to a degree comparing favorably with the fall produced by dividing the splanchnics and the sciatic and brachial nerves were then stimulated for two hours. All four

of the animals developed deep shock; one of them recovered with the aid of an infusion and was alive the next day; another recovered spontaneously, though he did not stir when disturbed; another died during the experiment from excessive anæsthetization, and the fourth succumbed from the experiment. On the other hand, animals subjected to similarly caused reduction of blood-pressure and equal periods of anæsthetization by ether, but not to the prolonged sensory stimulation, suffered from a degree of shock which we were unable to distinguish from that of the stimulated animals which were similarly bled. It must be remembered in this connection that the latter required more ether. We have performed three such control experiments and are satisfied as to the truth of this statement.

As soon, however, as the animal's blood-pressure was reduced and the animal was deprived of his power of compensating for lowered blood-pressure by paralysis of the splanchnic area, serious shock developed but always in proportion to the diminution of blood-pressure and not greater than in animals in which the blood-pressure was reduced to a similar degree by hemorrhage alone.

In shock produced by prolonged handling of the intestines it seems that much less severe sensory impulses can be present than occur in stimulation of the sciatic and brachial plexus for the same length of time. Consequently, if sensory impulses in an unconscious animal were not effective in producing shock by causing exhaustion of the central nerve cells in the absence of vasomotor control, it is not likely that they are the important factors in the production of shock by prolonged handling of the intestines. Simple division of the splanchnic, as we ourselves have also experienced, does not in itself result in a lowering of the blood-pressure sufficient to produce shock. Within the time limit which we have adopted in these experiments, which is quite sufficient from the practical point of view of the operating surgeon, the exhaustion of the nerve centres by afferent stimulation of sensory nerves is a wholly negligible factor in the production of shock.

CAUSE OF SHOCK PRODUCED BY MANIPULATION OF THE INTESTINES.

Returning again to the interpretation of the experiments in which shock was produced by prolonged handling of the intestines and in which attempts were made to resuscitate the dogs by transfusion, the quick recovery precludes the idea that the nerve centres had been exhausted. It does not, however, negate the possibility of the condition of the animals at the end of the period of intestinal handling being due to cerebral anæmia in combination with the anæsthesia which had been used. While the blood-pressure was still far above a level which would prostrate an animal wholly out of anæsthesia, there was little difference in the condition of these dogs and similarly anæsthetized dogs whose blood-pressures had been reduced to a similar degree by hemorrhage. Cerebral anæmia, however, is a far different condition from exhaustion of the nerve centres, a state demonstrated to be absent, as we have repeatedly emphasized, by the rapid recovery after transfusion.

But as has been stated, with the fairly high blood-pressures recorded in these experiments cerebral anæmia could have contributed little to the degree of shock exhibited by the animals. Many facts indicate that coöperating with the cerebral anæmia, inhibitory impulses are important causes of the animal's condition at the end of the period during which the intestines are handled. On the cessation of the handling there would be a return of a reflex response of the animal indicating semiconsciousness. An immediate relapse into an insensitive comatose condition could be produced by continuing the handling. The blood-pressure usually fell when the handling was stopped and rose again under the stimulus of handling, though this was not a constant effect. We know that afferent impulses of possibly an inhibitory nature are present. It is due to them that these experiments of evisceration and intestinal manipulation may be performed at times without the continuous use of a specific anæsthetic other than morphin and the preliminary anæsthesia, and yet without any evidence whatever of feeling on the part of the animal. There

is no physiological reason for distinguishing between shock and collapse. The latter condition is entirely due to inhibition. Howell and Meltzer have presented additional evidence that inhibitory impulses are important factors in this stage. They unquestionably are responsible in the beginning of the experiment for the onset of shock and the first fall of blood-pressure. If they are then operative they must continue to be during the whole time during which the intestines are handled.

Following the period during which the intestines were handled in those animals in which the shock was produced for control purposes and which were not therefore transfused, there occurred a progressive fall of blood-pressure within the next few hours until death occurred. The progressive fall was often initiated by a considerable drop at the start. This progressive fall was unquestionably due to bleeding into an absolutely paralyzed splanchnic system. During this period we have found that stimulation of the splanchnic nerves produced no rise in blood-pressure, or change in a plethysmographic tracing measuring the amount of blood in the splanchnic area. There were even no indications of blood-flow through the intestinal vessels.

The local peripheral character of this vascular paralysis has been clearly shown by two experiments. A coil of intestines was protected in a plethysmograph during a period of handling of the intestines for one hour and one and one-half hours. The splanchnic nerve was stimulated and the diminution of volume within the plethysmograph recorded before and after the period during which the intestines were handled.

The protected loop and kidney showed a marked change in volume both before and after the period of intestinal manipulation, while after this period a loop of the handled intestine showed no change.

There can be no question therefore about the extreme paralysis of the splanchnic area after two hours' handling of the intestines. There is an absolute paralysis of every tissue of the intestines, of the muscles, of the intestinal walls and of the arterioles. There is an absolute abolition of all reflexes. The great means by which vasomotor changes in the body are

possible, that which the vasomotor centre uses to produce its rise and fall of pressure and without which it is powerless, is hopelessly unavailable.

The amount of blood which this area will contain is well illustrated by a number of experiments which we performed, in which during the period of handling the intestines, the brain of the same animal was supplied with blood from the carotids of another dog, and in one case from the carotids of two other dogs. Before the intestines were handled, an anastomosis was made between the carotids and external jugular veins of the donor and the recipient, which was to be shocked. The purpose of these experiments was to discover whether or not any diminution of shock could be obtained by supplying the dogs being shocked, with blood from a presumably normally beating heart, thus eliminating the small fall in pressure occurring in the other transfused dog, during the experiment. In general the dogs gave the same result as the dogs transfused at the end of the experiment. The main purpose of the experiment was defeated, however, by the fact that the splanchnic area of the recipient during the period in which the intestines were handled drained off so much blood from the donor and in one case from two donors, that the blood-pressure of all donors in the three experiments fell to a serious degree, so that at the end of the experiments the donors no longer supplied the brain of the recipient with blood under good pressure, and were themselves in a serious condition from exsanguination.

Animals shocked in the manner described are deprived of all vasomotor control solely because of a local peripheral paralysis of the splanchnic area. It is as though the branches of their mesenteric arteries emptied into a large reservoir with perfectly flaccid walls, into which they bled to death. The aptness of the comparison of the splanchnic area to a flaccid rubber bag is made more apparent by pressure on the abdomen. The blood-pressure can be raised at will by this procedure. The explanation of the secondary shock developing in the transfused animals, the intestines of which are paralyzed from one end to the other, introduces very complex questions which

are not concerned in this paper. Suffice it to say that the animals remained in good condition with high blood-pressure in one case—the only dog watched till death—for twelve hours, and that they rather suddenly passed into a moribund condition.

CONCLUSIONS.

Our conclusions, which we hope to support by more numerous experiments, and by reporting them in greater detail in the future than has been possible in this paper, are as follows:

1. As severe a degree of shock may be produced by artificial hyperrespiration, and by handling of the intestines when provision is made for keeping the carbon dioxide content of the blood high, as when it is allowed to fall to 40 or 50 per cent. of the normal.

2. Shock produced by artificial hyperrespiration is due chiefly to a long-continued, mechanical interference with the return of the blood to the heart.

3. There is evidence that the early stages of shock produced by evisceration and handling of the intestines is due to inhibitory afferent impulses.

4. At the end of the period during which the intestines were handled none of the animals' nerve centres were exhausted.

5. By such handling of the intestines a complete splanchnic paralysis of local peripheral origin is produced, and it is this paralysis which causes the subsequent fatal fall of blood-pressure and not exhaustion of the nerve centres.

6. In the presence of a good blood-pressure and unimpaired vasomotor compensatory mechanism, prolonged afferent electrical stimulation for two hours will not produce shock or exhaustion of the nerve centres.

7. If trauma to the sensory nerves is a factor in production of shock in an unconscious animal, it is wholly subsidiary to other factors, and it is questionable whether it was apparent in our experiments even when these other factors had rendered the nerve centres more vulnerable by toxic influences, as ether, or by a fall in blood-pressure.

8. The all-important factor in the development of shock, in so far as the forms which we have studied may represent shock in general, is loss of vasomotor control. It is, at least, the impossibility of regaining this control after it has reached a certain degree which determines the failure to recover. The mechanism of this loss and its maintenance is important. The loss of control and its maintenance is never caused by acapnia or central nervous exhaustion, but, aside from afferent impulses more especially splanchnic sensory impulses which may have initiated the shock and contributed to it, the loss of control was always due to local peripheral causes which in our work were mechanical obstruction, loss of blood and trauma to the viscera.

The practical conclusions from these observations emphasize the necessity, in attempting to prevent shock, of providing against a fall of blood-pressure and local trauma, particularly within the abdomen, as the most important of all precautions. The truth of this statement at present is so generally acknowledged that it is almost trite to make it. Nevertheless the conclusions, indicated by the experiments in which unsuccessful attempts were made to produce shock by trauma to peripheral sensory nerves, will not be generally accepted. They directly contradict grounds on which the method of anæsthesia known as anoci-association is based. We appreciate that our experiments are few. Nevertheless, a study of their details demonstrates that their results were decisive and that severe trauma both electrical and mechanical of peripheral somatic nerves in an unconscious animal within reasonable time limits did not result in either a reflex fall in blood-pressure or exhaustion of the nerve centres. Its influence as a cause of shock at least in so far as the three forms of shock which we have studied may serve as examples of shock in general is so small that it may be practically neglected. In this connection it must be remembered that shock following burns is toxic in its nature.

However valuable the blocking of sensory nerves during operation may prove, the explanation is not to be found in the protection which it may insure against fatigue of the nerve

centres, certainly within the time limits of the usual operation. It is doubtless a wise precaution, on account of the more complicated manner in which reflexes may be modified in the human being than in animals, to block the larger trunks of the sensory somatic nerves when these must be divided. Clinical experience certainly teaches that it is most desirable to block the sensory splanchnic nerves when their trunks or more particularly the region of their plexuses must be subjected to trauma. Such blocking will often spare a patient reflexes which may seriously lower the blood-pressure. But the harmful effects, if it persists, is not due to fatigue of the nerve centres but entirely to reflexes and peripheral changes which may be either secondary to them or the result of other local peripheral causes or both. It is equally important to recognize that vasomotor control may be impaired or lost by peripheral injury alone. The central mechanism seems capable of outlasting the peripheral mechanism every time.

The necessity of guarding against loss of blood is self-evident. Of equal importance is the selection of an anæsthetic which, aside from any consideration of toxicity, does not reduce blood-pressure. Ether does not always fulfil this condition. Clinically and experimentally, unless administered with the greatest care, it strongly reduces the blood-pressure. We have numerous illustrations of this fact among our tracings and are disposed to attribute much of the shock of long operations under ether to this fact and to its toxic effect on nerve tissue and the glandular organs. Nitrous oxide does not possess this disadvantage and is also much less toxic. Crile has in no instance shown his keen appreciation of those factors which make surgery more successful than in his advocacy of nitrous oxide anæsthesia. If the general blocking of sensory nerves only increases the efficiency of nitrous oxide anæsthesia it is for this reason valuable. Its effect in eliminating harmful reflexes caused by trauma, particularly in the region of distribution of the splanchnic sensory nerves, has been explained.

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