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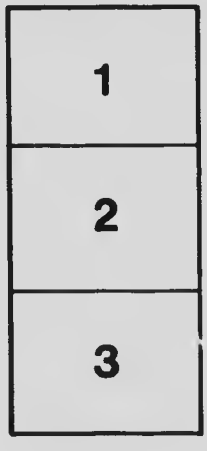

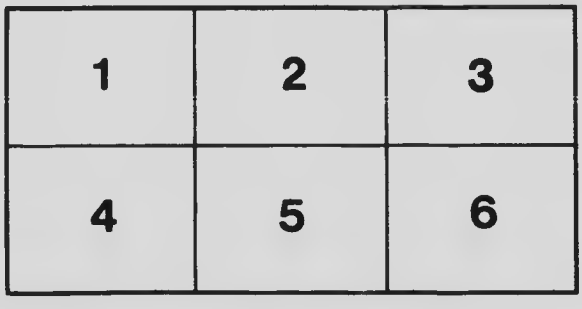

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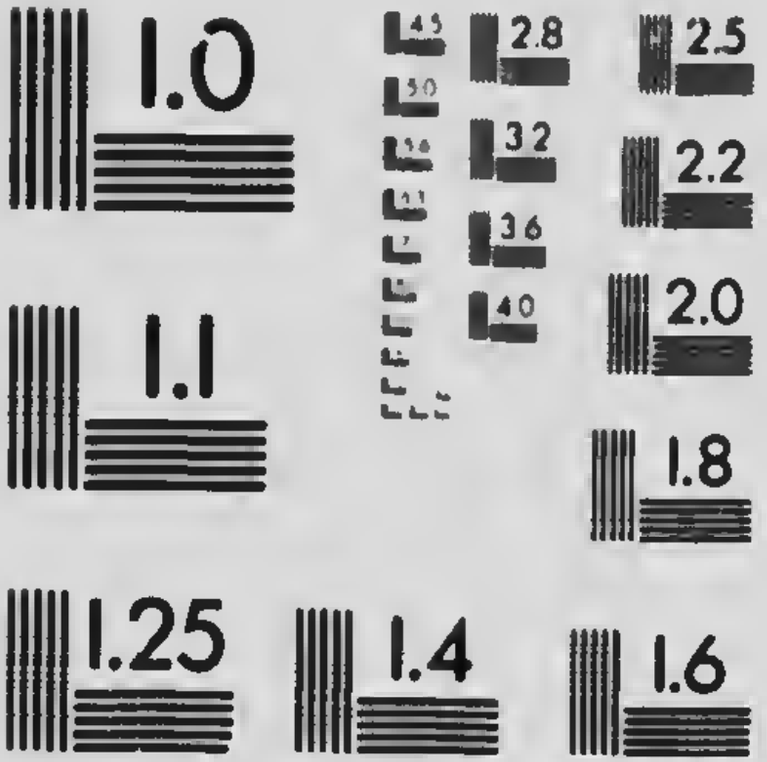

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THE FUNCTIONAL PATHOLOGY OF SURGICAL SHOCK

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The Functional Pathology of Surgical Shock

BY CONCERTED investigation in experimental medicine in England and this country, remarkable progress was made during the last two years of the war in the elucidation of the causes of the condition known as shock. There are several varieties of this condition, the two most characteristic of which are surgical shock met with in the operating room and after severe accidents in civil practice, and secondary trench shock met with at the battle front. In every essential particular these two conditions appear to be alike, and a condition apparently identical with them can be produced in laboratory animals by various experimental procedures. It is largely because of the availability of this experimental material that it has been possible to throw so much light on the problem. This but serves once again to illustrate the necessity of animal experimentation in the furtherance of medical and surgical knowledge. Had it not been for the work done on shock in the laboratory by Bayliss, Cannon, Dale, Erlenger and others, the war might have ended without our being any further advanced in our knowledge of this mysterious and fatal condition. It may be of interest here to review very briefly some of this experimental work.

We shall consider first of all the investigations by Dale,[1] and Laidlaw and Richards[2] on the shock-like condition which is produced by injection of histamine (iminazylethylamine). This substance is derived by removal of the carboxyl group, as CO_2, from histidine, one of the most important of the building stones of the protein molecule. Injected quickly into etherized animals in very minute dosage (1 mg. per kg. body weight) histamine soon causes the arterial blood pressure to fall to the shock level of 30-40 mm. Hg. For a brief period preceding the fall there is a rise in pressure due to constriction of the arterioles, and this constriction persists while the pressure is falling. So far as the obvious vascular changes are concerned, therefore, the condition is strictly comparable with those found in shock—low blood pressure and constricted arterioles. By the time the pressure has fallen to near the shock level the cardiac pulsations disappear from the tracing. The respirations also cease, but if the animal be kept alive by artificial respiration and the thorax opened for inspection of the heart this organ will be observed to be beating quite vigorously, with, however, a pronounced deficiency of blood in the auricles and in the large veins both of the thorax and abdomen. This observation affords positive proof that in this form of shock at least the fundamental cause for the condition is inadequate blood flow to the heart. The question is, what becomes of the blood? Either it must pass out of the blood vessels into the tissues, or the capacity of the former must be increased. Loss of blood itself could scarcely occur short of hemorrhage of which there is no evidence in histamine shock—but the water with some of the soluble constituents (plasma) might become extravasated, leaving in the vessels blood excessively rich in corpuscles. Such extravasation actually occurs in acute histamine shock, as revealed by measurement either of the concentration of hem-

globin or of the corpuscles, but this in itself can not explain all of the loss in circulating blood, for if the histamine be given slowly (over a period of 20-30 min.) it takes much longer for the shock to become established, and the blood does not show any increase in the percentage of hemoglobin or in the number of corpuscles. In these cases we are driven to conclude that much of the blood must be withdrawn from currency by stagnation in dilated vessels. Direct evidence for this important conclusion has been secured by determination of the volume of circulating blood, by means of the vital red method of Keith, Rowntree and Geraghty,[3] described elsewhere.

Although the oligemia is due in great part to dilatation of the capillaries and venules of the intestine, as can be shown by inspection, it is also partly dependent upon dilatation of vessels elsewhere, since histamine shock can be induced in animals from which all of the intestines have been removed. The vessels of the skeletal muscles are probably the chief extraabdominal vessels affected, for although no dilatation of these can ordinarily be seen in histamine shock, it becomes quite evident in animals which have been transfused before being shocked. The capillaries (and venules) in these areas evidently lose their tone so that they become too roomy for the available blood. As a matter of fact Dale and Richards[2] have shown that histamine abolishes the tone of capillaries at the same time that it increases the permeability of the walls and so permits the plasma to leak through. It is on account of this latter action that histamine when it is rubbed on the scarified skin soon causes the formation of a wheal like that following the lash of a whip.[4]

When histamine is given to unanesthetized animals about ten times as much can be withstood as in those that are anesthetized with ether.[5] At first sight this result might seem to discount the observations on etherized animals, but on the contrary they greatly enhance their importance. They indicate that whereas the normal animal is able to combat the toxic action of histamine, ether greatly depresses this power, an observation which agrees remarkably with the clinical experience that administration of ether is most dangerous in persons who are threatened with shock. The poisoning effect of ether persists for some time after the anesthetic is removed, and it is no doubt dependent upon a toxic action on the endothelium of the capillaries, for it is particularly in such animals that concentration of the blood is evident after histamine. It is of great significance that histamine did not readily produce shock in nitrous oxide anesthesia.

Hemorrhage also greatly predisposes to histamine shock, but in this case the blood is not nearly so concentrated as ordinarily because of the passage of plasma from the tissue spaces into the vessels, which, it will be remembered, is the natural reaction of an animal to hemorrhage alone. The cause of shock in such animals is mainly the opening up of the vessels.

Many bacterial toxins, both when applied to scarified skin and when injected intravenously, have effects very like those of histamine. It is also well known that shock is peculiarly common after injuries in which there has been extensive destruction of tissue. The facts warrant the suggestion that shock may be due to intoxication from damaged tissues, particularly the muscles and the viscera of toxic substances acting like histamine. This conforms with the fact that shock is most common when there has been extensive destruction of muscle, or when

the liver or intestines are roughly handled. It is possible also that the shock of intestinal obstruction is fundamentally due to absorption into the blood of such substances from the closed loop of intestine. Whipple and Hooper's discovery that absorption of a proteose is responsible for the shock like symptoms of intestinal obstruction are very suggestive in this connection.[6]

But to return to surgical shock. Is it possible that the condition is dependent upon intoxication by histamine-like substances absorbed from greatly damaged tissues? To test this hypothesis Cannon[7] and others have investigated the effects of crushing the muscles of the hind limbs, without external hemorrhage, by blows from a heavy hammer. It was found that an immediate fall in blood pressure occurred, followed by a more gradual decline to the shock level, with a decrease in the CO_2-combining power and a marked concentration of the blood. This result was not due to irritation of afferent nerves, causing excessive stimulation of the vasomotor centers, since it persisted in animals in which all nerves of the limb had been cut; neither was it caused by any local loss of circulating fluid (by dilatation of vessels or extravasation). It was due to the discharge into the circulation of some toxic material, since no shock resulted when the vessels of the damaged limb were clamped. Removal of the clamp some time after the damage resulted in the immediate appearance of the symptoms which could again be caused to disappear somewhat by its reapplication. As to the nature of the toxic material, the first possibility to be considered is that it is unoxidized acid (lactic), which, it is well known accumulates quickly in muscular tissue whenever this is destroyed, or when the circulation through the tissues is greatly curtailed. As a matter of fact it was found that the CO_2-carrying power of the blood became greatly depressed whenever the toxic material was permitted to enter the circulation by removal of the clamp, and it is well known that there is also a decided depression in the blood carbonates in surgical shock. Acid intoxication can not, however, be the main factor, and for the following reasons: 1. Injections of lactic acid intravenously do not cause shock, neither do they predispose an animal to it. 2. Copious injections of bicarbonate solution do not prevent shock. 3. Extracts of damaged muscle made with isotonic saline do have a shock-like effect, but this is just as great when the lactic acid in the extracts is neutralized with bicarbonate, as when they are unneutralized. Moreover the fall in the blood carbonate does not coincide with, but rather precedes, the development of the shock symptoms. An excess of lactic acid in the blood has been noted in the later stages of many cases of shock (Wiggers and Macleod[8]), but this is a secondary effect, and it is doubtful whether it is the only cause for the depressed CO_2-carrying power of the blood.

In one or two cases the muscles were crushed in unanesthetized cats, with the result that shock did not invariably follow, but this does not invalidate the observations on anesthetized animals; it only shows that, as in histamine poisoning, the anesthetic weakens the resistance. When the normal animals were bled before the crushing operation, shock supervened with certainty.

Taking the results as a whole and comparing them with clinical experience a very strong case is made for the hypothesis that surgical shock is essentially due to intoxication by materials derived from damaged tissue. Shock is particularly common after severe tissue damage; rough handling of the wound greatly

aggravates it, whereas rigid care to render the wounded part immobile is a valuable safeguard, the administration of ordinary anesthesia (ether) to a shock patient is notoriously dangerous, whereas rapid amputation under nitrous oxide often ushers in a steady recovery. All these clinical facts conform admirably with the experimental findings.

With regard to the diagnostic value of measurement of the blood volume, it has been shown by Erlanger, Gasser and Meek[9] that concentration of the blood becomes evident before the shock symptoms are pronounced. This concentration is no doubt a most important factor in causing curtailment of the volume of circulating fluid, not only because of loss of plasma, but also because it causes the corpuscles to become contiguous so that they have a tendency to jam in the capillaries and so lead to a progressively increasing under nutrition of the tissues and the production of more toxic material.

It remains for us to show that the foregoing conclusions drawn from observations made on laboratory animals are applicable to the clinical condition known as surgical shock. It will then be advantageous to consider the principles which determine successful treatment. The unusual opportunity afforded at the front to study shock has led to a furtherance of our knowledge of its causes, which might have taken many years of investigation in time of peace, and by far the most important contributions have come from those who have been intimately familiar with the experimental as well as the clinical aspect of the problem. N. M. Keith[9] estimated the total volume of circulating blood by the vital red method and the relative amounts of plasma and corpuscles by measurement of hemoglobin or by means of the hematocrit, and as a result of his investigations has divided the cases of secondary shock into three groups which vary from one another with regard to: 1. The total volume of blood in circulation and (2) the relative amounts of plasma and corpuscles in the blood. The differentiation is not only of great prognostic value, but also invaluable as a guide to the proper plan of treatment. In group I are the *compensated cases*, in which the blood volume is reduced to not more than 80 per cent of the normal, but in which the plasma is relatively greater, being reduced only to 85 or 90 per cent of the normal. In other words these cases have reacted like cases of hemorrhage, i. e., there has been a migration of fluid from the tissues into the blood. If kept warm and given fluid per rectum, the patients recover. In the second group, called *partially compensated*, the blood volume is reduced to 65-75 per cent, with little, if any, evidence of dilution of plasma (i. e., the plasma is also reduced to 65-75 per cent). Treatment by transfusion either with blood (citrated blood by Robertson's method,[10] or with gum solutions (*vide infra*) is necessary and in most cases, if the proper technic is followed in the transfusion, recovery is likely. It is important, however, that the plasma volume be measured a few hours after the transfusion to see whether the desired reaction, namely, a migration of fluid into the plasma, has set in. If not so, a second transfusion is indicated. In favorable cases the plasma volume increases more rapidly than that of total blood, and *per passu* the arterial blood pressure rises.

In the third or *uncompensated group*—the blood volume is below 65 per cent and the blood is more concentrated than normal, i. e., there is relatively a greater decrease of plasma. Treatment must be energetic in these cases, but the

prognosis is unfavorable because the transfused fluid readily leaves the vessels, causing the lungs and tissues to become edematous.

With regard to the rationale of the transfusions, it is clear that the added fluid makes good the blood that is lost by stagnation, etc., and so tends to maintain in the circulation a normal pressure for a sufficient time to enable the organism to destroy the toxic bodies. If the shock condition has existed for some time, so that the nerve centers are paralyzed, the injections are of no avail. Since many cases of shock in man have also suffered considerably from loss of blood, it is often difficult to decide whether shock really exists apart from the effects of hemorrhage, the cardinal symptoms of the two conditions being very much alike. The test is afforded by examination of the total blood and plasma volume, and by the reaction to transfusion. After hemorrhage alone there is great migration of plasma into the blood, making this very dilute, and transfusion has immediately beneficial results. In shock there is no migration of fluid into the blood, indeed the reverse is usually the case, and transfusion does not always succeed in re-establishing normal conditions.

Finally, with regard to the composition of the transfusion fluid, should this be human blood, or can a reliable substitute be found in saline solutions containing gum? There is much diversity of opinion over this question. Keith sums up by stating that there does not appear to be any decided advantage in blood over gum solutions, although the immediate restoration of natural color to the patient, which occurs with blood but not with gum solutions, may make the former appear to be the more satisfactory treatment.

Much painstaking work has been done by Erlanger and Gasser[8] to determine the exact conditions for success in using gum solutions. As their criterion for successful treatment, they did not merely see whether the blood pressure was restored, but they allowed the animals to recover from the effects of the anesthetic and then watched them to see whether they became restored to normal. Many animals might appear to be recovering, but nevertheless succumb within 24 hours. These workers point out that strong gum solutions owe their efficacy to the fact that they slowly attract water into the blood from the tissues, and once attracted the water remains in the vessels. Hypertonic solutions of crystalloids on the other hand, quickly attract water, but this is not retained long. These workers, therefore, devised the scheme of combining the two factors, and they found that success depended on how this was attempted. In the shock produced by partial clamping of the vena cava about one-half of the animals died within 48 hours. Neither weak gum (6 per cent) and weak alkali (2 per cent) given in large amount (12 c.c. per kg.) nor strong gum (25 per cent) in strong alkali (5 per cent) given in smaller dosage (5 c.c. per kg.) decreased the above mortality; but if strong gum (25 per cent) were given along with strong glucose solutions (18 per cent) at the rate of 5 c.c. per kg. an hour, many more animals survived. The alkali was chosen to furnish the crystalloid, in many of the experiments, so that it might incidentally combat any existing acidosis. We have already seen, however, that there is no reason to believe that acidosis is an important factor in shock. Two precautions are necessary to success in using the gum solutions, first they must be properly prepared, and second they must not be injected so rapidly

that their high viscidity would slow the circulation and so embarrass the heart's action.

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– *J. J. R. M.*

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