HYPERTONIC GUM ACACIA AND GLUCOSE IN THE TREATMENT OF SECONDARY TRAUMATIC SHOCK

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At the time this country was drawn into the world war the Committee on Physiology of the National Research Council decided to interest our physiologists in a coöperative investigation of surgical shock. Since then this laboratory has devoted all of its facilities and all of its research time to the study of that problem. One line of our experiments led us to the use of a strong solution of gum acacia and glucose in water in the treatment of shock. It is the purpose of the present paper to review briefly the experiments that led us up to that point,* and to present in detail the results, still quite limited, that have been obtained through the use of the solution in the treatment of shock and allied states in man.†

REVIEW OF EXPERIMENTS ON THE MECHANISM OF SHOCK

The first experiments done here were planned with the idea of familiarizing ourselves with the state that has been called shock by those who have worked on the subject, and of determining which manifestations of the state are fundamental to its development. These objects we hoped to attain by studying shock as produced in diverse ways. For, if it could be demonstrated that certain disturbances were constantly present there would be presumptive evidence that they were essential to the state of shock, and we would then be provided with a basis for the development of rational methods of treatment.

We believe we have succeeded in producing in the anæsthetized dog a condition resembling so-called secondary shock (*a*) by the usual method of exposing and manipulating the intestines;[1] also (*b*) by so occluding the inferior vena cava, between the diaphragm and the liver, as to hold the arterial pressure down to about 40 mm. Hg. for a period of about two hours;[2,3] (*c*) by occluding the thoracic aorta, distal to the origin of the left subclavian artery, so as to keep the arterial pressure beyond down to

* This phase of the work was begun in collaboration with my associates, Robert Gessell and Herbert S. Gasser, and was carried to completion by the latter and the author. Formal reports were submitted to the Committee as the work progressed and preliminary reports have been made before the Washington University Medical Society. It is being prepared for publication in full in the American Journal of Physiology.

† The results have been reported to the Committee and before the Washington University Medical Society. Doctor Gasser was prevented by war exigencies from participating in some of the preliminary experiments and in the clinical studies.

20–40 mm. Hg for a period of about two hours,[3] and (*d*) by the continuous intravenous administration of adrenalin at such a rate as to maintain a high arterial pressure for a period of twenty or more minutes.[4, 5] The symptoms eventually exhibited by animals exposed to these four forms of treatment are very similar; in all there is a characteristic apathy, usually with persistent eye reflexes, an inefficient circulation, as evidenced, when the condition is fully developed, by a low arterial pressure, a reduction in blood volume accompanied by concentration of the blood, and a reduction in reserve alkalinity. Furthermore, the pathological pictures, in certain respects, also are alike in all.

THE CIRCULATION IN SHOCK

In an effort to ascertain the *cause of failure of the circulation,* a study was made of (*a*) the arterial pressure, of the venous pressure, both (*b*) jugular (right auricular) and (*c*) portal, and of (*d*) the peripheral resistance.

A. Arterial Pressure.—The usual criterion of shock is a low arterial pressure. In the absence of this sign most laboratory workers, and perhaps clinicians, also, would not feel justified in making the diagnosis of shock. Yet, in agreement with Gesell[6], we are of the opinion that, in animals, at least, the circulation may be markedly reduced before the arterial pressure begins to fall. Thus in experiments on caval shock, after de-occluding the inferior vena cava the arterial pressure rises for a time to mount as high as, often higher than, the normal initial level. Observations on over 200 instances of this kind of shock have shown that if the arterial pressure begins to fall consistently before two hours have elapsed after decompressing the cava, the fall continues (there has been but one exception) until the circulation completely fails. If, in such instances, the animal is not in shock at the time its arterial pressure is still high, it at least seems justifiable to assert that shock is then developing. One of our cases of shock in man, as will be seen, possibly belongs to this category.

B. The *jugular pressure* is supposed to be an index of the effectiveness with which the heart pumps on the blood that is returned to it. We have been impressed, however, by the uncertainty of this method of judging the efficiency of the heart. However this may be, it can be asserted that in none of the types of shock we have studied has there been any material increase in jugular pressure, and yet we are convinced that in shock the heart may not preserve its normal efficiency. While it is true that against the extreme constriction produced by a large dose of adrenalin, or against a closed aorta, the heart in shock often is capable of raising the arterial pressure quite as high as can the heart of normal animals,[6] yet we have obtained evidence indicating that the shocked heart may be incapable of such sustained efforts as is the normal heart.

C. The *portal venous pressure* during shock induction is elevated by some of the procedures (markedly by adrenalin, slightly and temporarily by caval occlusion), and lowered by other procedures (intestinal exposure

and aortic occlusion). Therefore, increased filtration of blood from the splanchnic and portal areas, or sequestration of blood in these areas by mechanical distention of the veins and capillaries[2] through local constriction of the portal radicles [7, 8] cannot be regarded as essential to the development of shock. It is, however, possible to bring on shock by mechanically interfering with the outflow of blood from the portal area. Thus shock develops after plugging the smaller radicles of the portal vein in the liver by injecting into the portal vein a suspension of lycopodium spores.[8] But unless the obstruction so produced is much more complete than any that could possibly develop through any known physiological mechanism, the time required for the onset of shock greatly exceeds that elapsing during the induction of the types of shock that are seen in the laboratory.

D. The *peripheral resistance,* as followed by a modification of a method first used by Bartlett in this laboratory, also in a study of shock,[9] does not behave similarly during the induction of shock by the different procedures. Thus, as a result of exposure of the intestines, the peripheral resistance in both the somatic and splanchnic areas at first usually is increased; later, and usually only after the arterial pressure has started downwards, dilatation occurs. During caval occlusion the peripheral resistance is first increased, but soon becomes subnormal. During aortic occlusion the resistance is decreased, but it increases after de-occlusion, and usually remains high practically until the animal dies. Finally, those doses of adrenalin that bring on shock produce, through local action, an extreme and long-lasting peripheral constriction.

These observations clearly indicate that the condition in which the vasomotor centre finds itself in fully developed shock, namely, whether hyperactive or hypoactive, depends very largely upon the procedure employed for the purpose of inducing shock. Neither reduced nor enhanced vasomotor activity is an essential condition of shock. But in any event, the center is apt to become hypoactive after the circulation has been deficient for some time.

Analysis of the data derived from this study of the circulation in shock, while indicating that the low arterial pressure in advanced shock may in part be due to some inefficiency of the heart, and sometimes, also, to some decrease in the activity of the vasomotor centre (though increased tone is more common), clearly demonstrates that these two deficiencies, even when present, are not in themselves sufficient to account for the failure of the circulation. If, then, the efficiency of the heart is but little reduced, and if increased vasomotor tone is the rule, there is left as the only other possible explanation of the low blood-pressure of shock an insufficient return of blood to the heart.

Blood-Volume.—In an effort to ascertain whether there is a deficient blood supply, a study was made of the blood-volume in animals in shock.[10] For this purpose the method of Meek and Gasser [11] was employed. This method consists in allowing a known amount of gum acacia to circulate in the blood stream for a period of ten minutes and then in determining the per cent. of gum in the blood. The method, therefore, determines the amount

of blood participating in the circulation in the course of ten minutes. The blood-volume changes were followed also by counting the red corpuscles and by estimating the per cent. of hæmoglobin. The latter two methods have shown that depletion of the blood plasma occurs in all types of shock, indicating a reduction in blood-volume averaging 20.3 per cent. But the acacia method of determining the blood-volume brings out the fact that the loss in volume by this concentration of the blood (disappearance of plasma) in many instances does not account for the total reduction in blood-volume. The blood unaccounted for by concentration must therefore be out of circulation; it must be stagnant somewhere.

These results confirm the well-known fact [12] that but little blood can be obtained by bleeding an animal in shock. The following experience is cited by way of illustration of what is meant: An animal weighing 15 kilo was put into shock. At a time when it still had a fair arterial pressure, 70 mm. Hg, as much blood was drawn from the carotid artery as it was possible to obtain by the use of all of the devices for obtaining a maximum yield. Only 100 c.c., or one-twelfth of the estimated normal volume, were obtained, whereas at least three-fifths could easily have been obtained from a normal animal. It follows from such observations that the volume of blood that is in the body of a shocked animal and which is thoroughly mixed in the course of ten minutes is very much larger than the quantity that effectively participates in the circulation.

In this connection attention should be called to an observation indicating that the animal in shock attempts to combat the reduction in blood-volume by adding tissue fluids to the blood. Refractometer estimations have shown that even while plasma is disappearing from the blood stream, its protein content may be diminishing [13]; that is to say, the plasma is becoming more dilute. It would, therefore, seem that all parts of the vascular bed are not affected alike during the induction of shock; in some parts the normal reaction to decreased volume, namely, the passage of fluids from the tissues to the blood stream, is possible, whereas in other parts the alterations are such as to allow of outward transudation only. Our observations furnish some reasons for believing that the ability of the organism to thus make good the loss in blood plasma diminishes as shock deepens.

Reserve Alkalinity.—The reserve alkalinity, as indicated by the CO_2 in the plasma of arterial blood (Van Slyke method), is reduced in all types of shock; but in our experience the reduction is extremely variable.[8] The volume per cent. of CO_2 may be below 20, that is, extremely low, or it may not be below a figure often obtained in estimations made before starting to induce shock. We have seen heavily morphinized animals with 20 volume per cent. of CO_2 and an arterial pressure of 103 mm. Hg, only 3 mm. below the initial arterial pressure. Therefore, acidosis, though probably always present to some degree, can scarcely be regarded as a cause of the low arterial pressure of shock, as some have believed [14], or even as an essential feature of the shock complex.[15]

PATHOLOGY.—At autopsy, which in our hands, unfortunately, has never been as thorough as pathologists might desire, the organs of the animals dead of all of the types of shock we have studied, present a very similar picture.[8] The intestines are apt to contain some bloody material; and the mucosa, especially of the upper end of the jejunum, usually is deeply injected and of a bluish-red color. The spleen may be uniformly or unevenly enlarged and may contain hemorrhages. The liver usually is not enlarged and may contain less than the normal quantity of blood. Rarely the gastric mucosa shows hemorrhagic areas. The most remarkable feature, though, is brought to light by microscopic examination of the intestines: *in all types of shock the capillaries and venules of the villi are tremendously distended* by solid masses of red corpuscles.

THEORETICAL.—If, now, we pause to consider the methods by which we have succeeded in producing shock, we are struck by the fact that at least three of the four, namely, caval occlusion, aortic occlusion, and massive doses of adrenalin, involve reducing for some time the rate of movement of the blood through a considerable portion of the body; and if we accept the prevailing view that the blood stream eventually is slowed in regions that are the seat of an inflammatory process, it is to be presumed that as a result of intestinal exposure also, the blood stream in the splanchnic area is slowed. Furthermore our experiments, showing that, as a rule, traumatizing the abdominal viscera results in a certain amount of general constriction, and Gesell's observation [5] that the volume flow of blood through the salivary gland under similar circumstances is markedly reduced, indicate that during the development of this type of shock, also, the blood stream is slowed throughout the whole of the body.

Mall and Welch have followed under the microscope the changes in the flow of blood occurring in the smaller mesenteric vessels of the dog when the rate of blood-flow through them is slowed by partial obstruction of the mesenteric artery. In his classical article on Embolism and Thrombosis, Welch [16] describes these changes about as follows: The smaller and then the larger (microscopic) veins become more and more distended with red corpuscles and all of the phenomena of an intense venous hyperæmia appear. The red corpuscles accumulate in clumps or in solid columns. *This change may become permanent, producing an evident obstacle to the forward movement of the blood.* The same phenomena of distention with red corpuscles, clumping, and stasis appear gradually in the capillaries. With this partial blocking of the veins and capillaries the corpuscles begin to pass through the wall of the vessels by diapedesis.

Although Mall and Welch seem inclined to attribute this clumping of corpuscles to the absence of pulsation, their evidence does not preclude mere slowing of the blood-stream as the cause of the phenomenon. Assuming that slowing is the cause, we have in the peripheral mechanism thus started by a slowing of the blood-stream a means of accounting for all of the characteris-

tic changes in the circulation that occur in experimental shock. The concentration of the blood and the reduction in blood-volume are explained by the transudation of plasma which must precede the diapedesis observable under the microscope. The failure to obtain by bleeding, as much blood as the blood-volume methods indicate is present in the body is accounted for by the dilatation and plugging of the capillaries and venules. Reduction in reserve alkali is known to accompany deficient oxygenation of the tissues. While the low blood-pressure, naturally, is to be referred to the reduction in effective blood-volume due in part to the actual reduction by transudation and in part to the stasis in the capillaries and venules.

II. Review of Experiments on Treatment

Preliminary Experiments.—While making estimations of the blood-volume in shock by the acacia method it was observed [10] that the concentration of the blood that ordinarily occurs during the development of shock, did not occur, or, at least, was not nearly as marked as usual, in animals that had received a preliminary dose of 20 per cent. gum acacia. This observation forms the basis of our experiments on the treatment of shock. An investigation of this action of strong gum acacia led us [18] to conclude that in all probability it is referable in part, at least, to the osmotic pressure it exerts, and possibly in part to other properties.

By following the changes in hæmoglobin content of the blood it was found that when 25 or 30 per cent. gum acacia is quickly injected into the circulation the blood dilutes slowly, the maximum dilution being attained in from 25–30 minutes, the subsequent return to the normal concentration requiring many hours. This reaction to the injection of a hypertonic solution of the colloid gum is very different from that given by the injection of hypertonic crystalloid solutions. Thus a hypertonic (18 per cent.) glucose solution injected into the same animal some days subsequently led to a similar dilution of the blood; but in this case the maximum dilution was attained practically instantaneously, and within five minutes practically all of the water that had been drawn into the circulation by the glucose, had again returned to the tissues. By first injecting a strong gum solution and following it immediately with the strong glucose solution we found it possible, both in normal and in shocked animals, to expand the blood-volume as rapidly as injected crystalloids (glucose) are known to attract water into the blood-stream, and to maintain that expansion as long as colloids (gum acacia) are known to maintain dilution of the blood.

A series of experiments on animals in shock was then performed in order to ascertain whether the course of shock could be influenced by the administration of gum alone or of gum in combination with crystalloids. It was found that such solutions as simple isotonic [17] * (7 per cent.) gum acacia, 6 per cent. gum acacia in 2 per cent. $NaHCO_3$, 25 per cent. (hypertonic) gum acacia (sodium salt) and 5 per cent. (hypertonic) $NaHCO_3$ given in succession, and 25 per cent. (hypertonic) gum acacia and 18 per cent. (hypertonic)

* Recent estimations indicate [19] that 7 per cent. gum acacia is hypertonic.

glucose, also given in succession, all restore and maintain with equal effectiveness the blood-volume and the blood-pressure, while the bicarbonate solutions (at least the stronger of the two) restore the alkali reserve also. The ultimate result, however, that is, whether or not the animal recovered from shock, did not seem to be influenced by thus successfully treating these symptoms of shock. It followed that the efficacy of any proposed treatment of shock cannot be judged, or at least not solely, by the effect it may have upon these manifestations of shock during the limited period of observation of an experiment as ordinarily performed. An empirical study of the ultimate effects of administering these and similar solutions to animals after standard traumatization seemed, therefore, to be the only way of obtaining the desired information.

Experiments on the Treatment of Standardized Traumatization.—The ideal test would have been to have inflicted that amount of damage from the effects of which animals could just not recover; that is to say, the minimal fatal dose of damage, and to have determined whether treatment of animals so prepared saved life. It was found, however, that when this amount of damage was done the animals invariably died, irrespective of the treatment administered. After many trials we [8] adopted, as the standard damage, so clamping the inferior vena cava as to hold the arterial pressure at 40 mm. Hg for two and a quarter hours. It was found that if the arterial pressure did not fall within two hours after removing the clamp, animals so treated stood a 52 per cent. chance of recovering. It might be added that if the arterial pressure began to fall consistently before two hours had elapsed, again, no form of treatment whatever prevented a fatal issue. It is needless to state that aseptic precautions were carefully observed.

Large numbers of animals, after exposure to this measured traumatization, were treated with (*a*) 6 per cent. gum acacia in 2 per cent. $NaHCO_3$, 12 c.c. per kilo of body weight; (*b*) 25 per cent. gum (sodium salt) followed by 5 per cent. $NaHCO_3$, of each 5 c.c. per kilo; (*c*) 25 per cent. gum followed by 18 per cent. glucose, of each 5 c.c. per kilo, or (*d*) 25 per cent. gum in 18 per cent. glucose, 5 c.c. per kilo.

Our reasons for trying just these therapeutic measures were as follows:

Solution *a* we took as representative of a solution of gum and of a salt practically isotonic with the blood (though to be sure it was alkaline also). An additional reason for using it was that it was then the solution recommended by the English committee [17] for the treatment of shock at the front. More recently the English committee have given their support to a solution consisting of 6 per cent. gum acacia in 0.9 per cent. NaCl.[18] The efficacy of this solution we have not had the opportunity to test.

Treatment *b* was used mainly for the purpose of determining the effect of a hypertonic salt, which at the same time was strongly alkaline, in combination with hypertonic gum. It served to test not only the effect of restoring the blood-volume by osmotic action, but also the efficacy of alkalies, which were then being employed in the treatment of shock [19] and which have from

time to time been advocated for that purpose on the basis of their effect upon the blood-pressure [20, 21, 22, 23] and on the basis of theoretical considerations.[5] In order to obtain the desired osmotic effect the bicarbonate, as used by us, was in slightly greater concentration than it was being employed in man; but the dose per unit of body weight was less and the rate of administration was slower. The fact that the alkali was used in combination with gum acacia complicates somewhat the inferences our results seem to justify, though gum acacia in other combinations has not proved harmful.

Treatment *c* involved the use of hypertonic glucose, which experiments with Woodyatt [24] had let us to believe acts beneficially in shock. It has been shown by Woodyatt and co-workers [25] and more recently by Litchfield [26] that man, even when desperately ill, is not injured, indeed is benefited, by extraordinarily large doses of hypertonic glucose solution given at a subtolerant rate. Furthermore, hypertonic solutions in general (urea, glucose, NaCl) increase the cardiac output and dilate the arterioles, apparently through some specific action.[27] These, and other responses to be referred to later, are exactly the ones best calculated to counteract the mechanism which we believe is at the basis of the vascular failure of shock.

Treatment *d* was used for the same reasons and also for the reason that by it the deleterious effects of the high viscosity of the strong gum solution, which are operative for a time during the injection of the gum in treatments *b* and *c*, are completely obviated by the immediate dilution of the gum by the water attracted from the tissues by the hypertonic glucose. Solution *d* was so given (5 c.c. per kilo an hour) that the glucose entered the circulation at a rate that is just subtolerant for the normal animal.[25]

TABLE I

RESULTS OF TREATING MEASURED TRAUMA

Treatment	No. of animals	Deaths		
		Total, per cent.	After excl. abd. hem., per cent.	After excl. cardiac cases, per cent.
Controls	23	48	37	45
(*a*) 6 per cent. gum in 2 per cent. bicarbonate, 12 c.c. per K	20	45	35	42
(*b*) 25 per cent. gum and 5 per cent. bicarbonate, 5 c.c. of each per K	16	56	50	53
(*c*) 25 per cent. gum and 18 per cent. glucose; 5 c.c. of each per K	20	45	31–35	39
(*d*) 25 per cent. gum in 18 per cent. glucose; 5 c.c. per K. hr.	21	24	6–11	20

The essential results that came of this study are collected in Table I. This table shows, 1, that treatment *b* unquestionably is harmful; 2, that treatment *d* unquestionably is beneficial; and 3, that while treatments *a* and *c* seem to accomplish some good, the variations from the results of the control series are so slight that they unquestionably fall within the limit of the experimental

error. It should be added that the harmful effects of treatment *b* were also clearly manifested by the shorter span of life of the fatal cases.

No ill effects of giving gum acacia have been seen except early in our work when the strong gum solution was run very rapidly into the vein of an animal almost moribund. In several instances of this kind the heart became irregular and stopped as though it had passed into fibrillation. Since then we have given the gum solution to at least 200 animals, including those collected in Table I, animals so seriously injured that their lives actually were in the balance, and not a single bad effect has been observed. If there is any one thing we are convinced of, it is that gum acacia when given slowly is entirely innocuous.

Hemorrhage Does Not Contra-indicate the Use of Hypertonic Solutions.—Shock in man often, in war surgery perhaps always, is complicated by hemorrhage. The use of the strong gum-glucose solution in the treatment of cases complicated by dangerous hemorrhage would therefore not be justifiable unless it could first be shown in animals that such a hemorrhage is not a contra-indication to its administration. The results of a series of experiments planned for the purpose of testing this matter have been to show[8] that even when the corpuscles are reduced to an extremely low level by a hemorrhage that ordinarily proves fatal, the gum-glucose solution accomplishes a certain amount of good; deleterious effects were never observed.

III. Observations on the Use of the Hypertonic Gum-Glucose Solution in Man

Methods.—Preparation of the Solution.—The gum-glucose solution that was employed in most of the animal experiments described above and in the treatment of the cases of shock and allied states, to be described below, was made up as follows:

Two hundred and fifty grams gum acacia, "extra select," in pearl form (gum arabic, U.S.P.) are ground up and dissolved in 720 c.c. hot water, freshly distilled from glass. Constant stirring is necessary to prevent gumming of the acacia into a very slowly dissolving mass. To this solution 180 gm. pure glucose are added. The whole will amount to about 1000 c.c. The solution is filtered under pressure through a thick pad of glass wool, heated in an autoclave to a temperature of 120° C. for a few minutes, preferably in a sealed, high pressure, flask and then filtered under pressure through an alundum filter dish of a porosity of R. A. 98.

The filtered solution is then filled into tubes of the shape shown in Fig. 1, made to fit the cup of our largest (100 c.c.) centrifuge. Larger tubes, holding about 350 c.c. would be preferable, for then the maximum dose for man would be in one container; but we have been unable to obtain the use of a centrifuge of sufficient capacity to take larger tubes. In order to avoid the formation of bubbles, which, in such a viscid solution, are apt to persist for some time, the solution should be made to run down the side of the tube.

The tube, when filled, is sealed hermetically at *A*, and sterilized by heating to 120° C. in an autoclave for fifteen minutes (no longer).* A slight flocculent precipitate is apt to form during sterilization. This is thrown down firmly against the bottom of the tube by centrifuging the material for about an hour.

Administration.—The ampoule is opened by filing a scratch and breaking

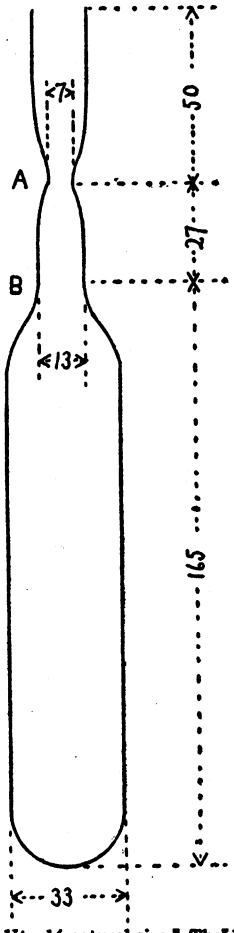

FIG. 1.—Ampoule. Reduced to ⅓ natural size. The dimensions are given in mm.

at *B* (Fig. 1). The opening thus made is flamed and the contents of the tube are so decanted as not to stir up the sediment. The sediment is usually firmly fixed to the bottom of the tube, but in order to avoid the danger of pouring it off, the last few cubic centimetres should not be decanted.

* In order to avoid the change that occurs in both glucose and gum acacia solutions as indicated by a slight deepening of color when they are sterilized under pressure, we at first sterilized them by pasteurization. Our experiments have shown, however, that the solution, even after several heatings to 120° C., is quite as efficacious and quite as innocuous as the pasteurized material. We, therefore, have come to employ the autoclaved solution only.

For the slow and steady intravenous administration of such a viscid solution special apparatus is needed. The apparatus devised by Woodyatt[25] probably would answer every requirement, but it is expensive and can be used only where electricity is available. We have designed for the purpose a burette with a capacity of 350 c.c. and a bore of 35 mm., calibrated upwards from the stem in small divisions (5 c.c.). Owing to the high viscosity of the fluid, its rate of inflow can be nicely controlled simply by varying the elevation of the burette; while the calibration of the burette from the stem upwards, makes it possible to utilize the last drop of the material. In order to avoid trapping air bubbles in the solution during the transfer, it should be made to run down the side of the burette.

Again owing to the high viscosity of the gum-glucose mixture, the injection needle must have an unusually large bore. It need not, though, be quite as large as the needles that have been recommended for use in the transfusion of blood.[28] The needle we have used (Fig. 2) is of silver, with inside and outside diameters at least at the point of 1.5 and 1.8 mm. respectively. Ordinarily it is not at all difficult, if it is properly pointed and sharpened, to insert a needle of this size into the vein through the skin. The author has convinced himself of this through use of the needle in a large series of cases

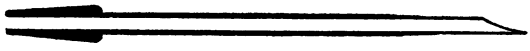

FIG. 2.—Injection needle. Natural size.

for the purpose of drawing blood samples for the Wassermann test. If, in any case, difficulty is anticipated on account of the smallness of the veins, the vein should first be exposed. After the burette and tube have been filled with the solution to the total exclusion of air, the needle is inserted into the vein, allowed to fill with blood without permitting of any loss, when the tube is rapidly slipped over the end of the needle which is so shaped as to facilitate this step. It is needless to add that all of the apparatus must be carefully sterilized and that the usual aseptic precautions must be observed.

The dose we used in the animal experiments was 5 c.c. of the solution for each kilo of body weight, and in order not to exceed the tolerant rate of glucose administration (0.8–0.9 gm. per kilo and hour), this dose was given in one hour. This particular dose was selected because it was found by experiment to be about the amount necessary to restore to normal the blood-volume of shocked animals. As no ill effects were produced by twice this dose administered at twice this rate, it may be regarded as a perfectly safe one for man. Experience has confirmed this conclusion. We have never repeated the dose, mainly, as will be seen, because we have not had the opportunity in instances in which a second dose was indicated. We feel convinced, though, that it would be perfectly safe to give, say, one-half the maximum dose some 8 to 10 hours after a maximum dose has been given.

Criteria of Effects.—The animal experiments made it clear that the immediate effect upon certain of the manifestations of shock, namely, the blood-

pressure, the blood-volume, and the reserve alkalinity, is of no value as an index to the ultimate efficacy of any treatment of shock. It was on this account that our conclusions were based solely upon the number of animals surviving a measured amount of damage. Complete recovery from the state of shock must be and is our final criterion of the efficacy of treatment of shock in man also. But while it is true that the state of these signs at any given moment is no sure index to the ultimate outcome, nevertheless, it is obvious that continuous changes in them must be indicative of a corresponding change in the condition of the patient. The arterial pressure is employed almost universally as a measure of the grade of shock. Furthermore, of the recognizable signs of shock, the arterial pressure is the easiest to gauge and to follow in man. For these reasons, and though we agree with Gesell [5] in believing that the circulation may be very seriously disturbed at a time when, through compensatory processes, the arterial pressure is still normal, the arterial pressure has been carefully followed in all of our cases.

For the purpose of following *the arterial pressure* the sphygmomanometer of the author [29] has been employed. The arm band is adjusted to the arm, and, unless it is stated to the contrary, its position is not changed, nor is it tightened or loosened during the entire series of readings. Likewise all of the other conditions affecting the registration of the pressures are kept constant throughout the observations in any given case. The variation in the amplitude of the oscillations, graphically recorded by the instrument in the successive readings, therefore, is an *absolutely objective index* to variations in the condition of the circulation. And, as the amplitude of the maximum oscillation as recorded by the sphygmomanometer under any fixed set of conditions is affected by the pulse-pressure alone, we have in the records as they stand an indication of the condition of the patient's circulation that is quite as significant as the blood-pressure itself.[30] In this respect we are in full accord with Maury and Soulé.[31] While obtaining each record the effort, of course, was made to read the systolic and the diastolic pressures, employing as the criterion of the former the change in the form of the wave [32] and of the latter the first abrupt and consistent diminution in amplitude. It not infrequently happened, however, when the circulation was poor and the recorded pulse amplitude, consequently, was very low, that the diastolic pressure alone could be read. It may be of interest to add that in such instances the pulse either could not be felt at all, or was scarcely palpable, and that attempts to read the pressure by the auscultatory method also failed, and not alone in the case of the systolic pressure but of the diastolic pressure as well.

Blood-pressure readings are subject to a rather large experimental error, especially when the pulse amplitude is small. We therefore desire to emphasize the data that are furnished directly by the pulse amplitude as recorded graphically, rather than those derived indirectly by the readings of manometer. The former, to repeat, are subject to no experimental error and can be interpreted from reproductions of the originals; whereas, the latter

depend upon a judgment made by the observer, which cannot be evaluated by the reader. All of our records, therefore, are published herewith.*

CLINICAL CASES.—Despite the fact that the clinical material of four large St. Louis hospitals has been at our disposal, we have had, since August, 1918, only ten opportunities to administer the gum-glucose solution. As will be seen, many of the cases were really not suited to the purposes of this study. Some of them, without doubt, were not cases of traumatic shock properly so called; pure hemorrhage, fat embolism, toxæmia, and general infection, probably, are amongst the etiological factors. But the cases have not been selected. At first (Cases II–VIII) the gum-glucose solution was given when the surgeon, through whose kindness I was called to see the case, regarded the condition of the patient as desperate, and provided consecutive blood-pressure readings made by myself bore out this opinion by indicating a continuing impairment of the circulation from which spontaneous improvement seemed unlikely to occur. More recently (Cases XI and XII), after experience had given us confidence, the solution has been given when the circulation was seriously impaired, without waiting to see whether the condition was going to be able to take care of itself. Many of the cases I was called to see were not treated because the condition of the patient, as indicated by the arterial pressure, did not seem to be sufficiently aggravated. In every instance, excepting one very flagrant one, cited below, the decision not to proceed with treatment has been justified by the subsequent course of the case. In one instance, in which the patient definitely was in shock, treatment was not given because of internal bleeding. Preparations in this instance were made to start the injection just as soon as the bleeding should be controlled, but the patient died during the operation.

CASE I.—*Crushed foot; shock; not treated.* The first case we were called to see we were unable to treat on account of an accident to the solution on the way to the hospital.† The patient was a colored boy whose foot had been crushed. Apparently there had been relatively little hemorrhage, yet the shock was extreme. The diastolic pressure was about 40 mm. Hg, the systolic pressure could not be determined The pulse amplitude (Fig. 3, records A, B, C) of 1.3 mm. was quite as high as, indeed considerably higher than, in many of our other cases of shock. The patient died about four hours after I had been called to see him.

* The conditions obtaining at the bedside, especially when the patient is desperately ill, are not conducive to the obtaining of unblemished records on smoked paper. The nurse's apron strings, the hand of the restless patient, etc., etc., seem to seek contact with the smoked paper; and the muscular contractions of the patient often cause the recording lever to sweep over the recording surface. The present experiences have led the author to add to the sphygmomanometer certain simple devices which should have the effect of minimizing difficulties of this character. The records reproduced as figure 9 *et seq.* had the advantage of these devices. We ask the indulgence of the reader in respect to the smirches upon the records published herewith.

† This happened before the solution was put up in hermetically sealed containers.

CASE II.—*Gunshot wounds of thigh and buttocks; typical shock.* The patient, a colored male, had suffered considerable loss of blood, though the hemorrhage was not regarded as dangerous. The temperature on admission was 96.8°, but rose to 100.6° just before treatment. The patient was cold, but perspiring freely; his pulse very small, 120 to the minute; the arterial pressures, systolic, 80, diastolic, 70 (records 1, 2, 3, Fig. 3). The diastolic pressure, therefore, was not very low but the pulse pressure was dangerously small. As the patient had been in this condition for some hours without showing any improvement it was decided that something should be done.

It was estimated that the patient weighed 70 kilo. The dose of gum-glucose solution, on the basis of our animal experiments, might therefore have been as large as 350 c.c. given in one hour. As a matter of fact the dose given was 270 c.c. in the course of one hour forty-five minutes. During the administration of the solution the recorded amplitude increased from 1.5 mm. (record 4) to 5.5 mm. (record 35), the pressures, especially the systolic, rising constantly and finally reaching, systolic, 120, diastolic, 85. The pulse-rate, as may be seen by the spacing of the pulses in the successive records, decreased steadily, reaching 77 at 4.20. Three hours later, and the next morning, the pressures were 120, 80–85, the pulse amplitude (new adjustment of arm band), 6.5 mm. All of the shock symptoms disappeared during the injection, the patient falling asleep before its conclusion. There was no temperature reaction to the injection. Recovery was uninterrupted.

CASE III.—*Panhysterectomy; hemorrhage; shock* (?); *infection* (?). White, female. The patient was seen a few hours after panhysterectomy during which there had been considerable and extensive soiling of the peritoneum. Her skin was of a dusky hue, the extremities cold and clammy, the pulse, when palpable at all, thready and uncountable. The diastolic pressure was 50 when the patient was first seen (Fig. 4, records 1–4), falling to 40 later (record 7), and to 30 mm. Hg (record 8) when the needle was inserted into the vein. The systolic pressure was undeterminable. The respirations were rapid, alæ nasi dilating, the temperature 105.6°.

The patient's weight was estimated at about 50 kilo. She was given 200 c.c. of the gum-glucose solution in the course of 1 hour 15 minutes. The recorded pulse amplitude increased from less than 1 mm. (record 8) to over 2 mm. (record 18); and the diastolic pressure rose to 50 mm. Hg, the systolic pressure at the same time becoming legible at 80 mm. Hg. There was possibly a slight improvement in the patient's general condition. The improvement in circulation was not sufficient, however, to hold out much hope for recovery, and it was not maintained. An hour and a half later (record 21) the pressures were 75–45, the amplitude irregular, the temperature 106°. The general condition of the patient was now getting worse again and she died four and a half hours after terminating the injection. There was no autopsy.

CASE IV.—*Primary carcinoma of the liver; splenectomy; shock* (?); *primary and secondary hemorrhage.* White, male. On October 13 splenectomy was done for what seemed to be Banti's disease. The

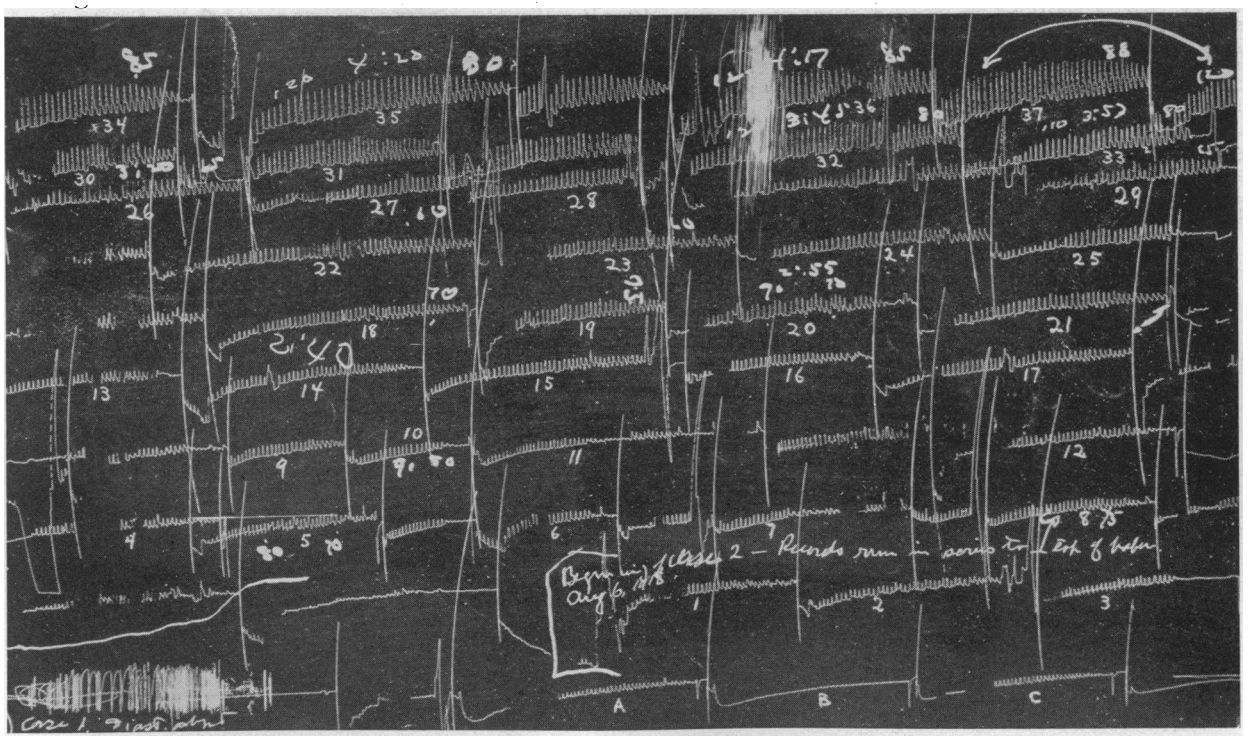

FIG. 3.—Blood-pressure records of Cases I and II. Reduced ⅓, approximately. Read from left to right and from below upwards. Description in text.

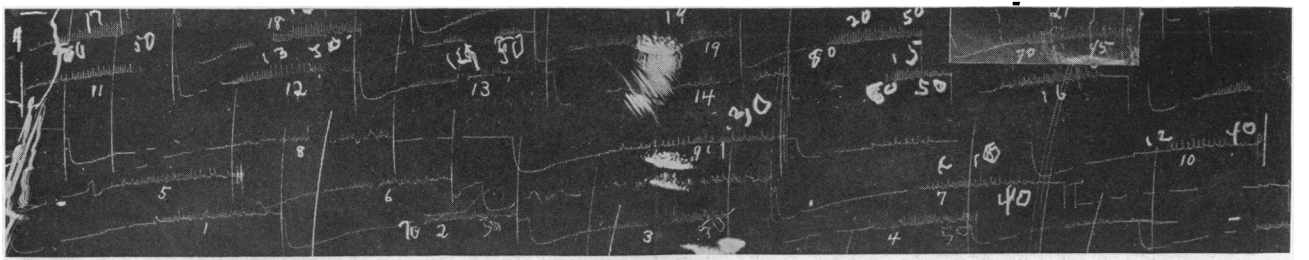

FIG. 4.—Blood-pressure records of Case III. Reduced 1/6, approximately. Read from left to right and from below upwards. Description in text.

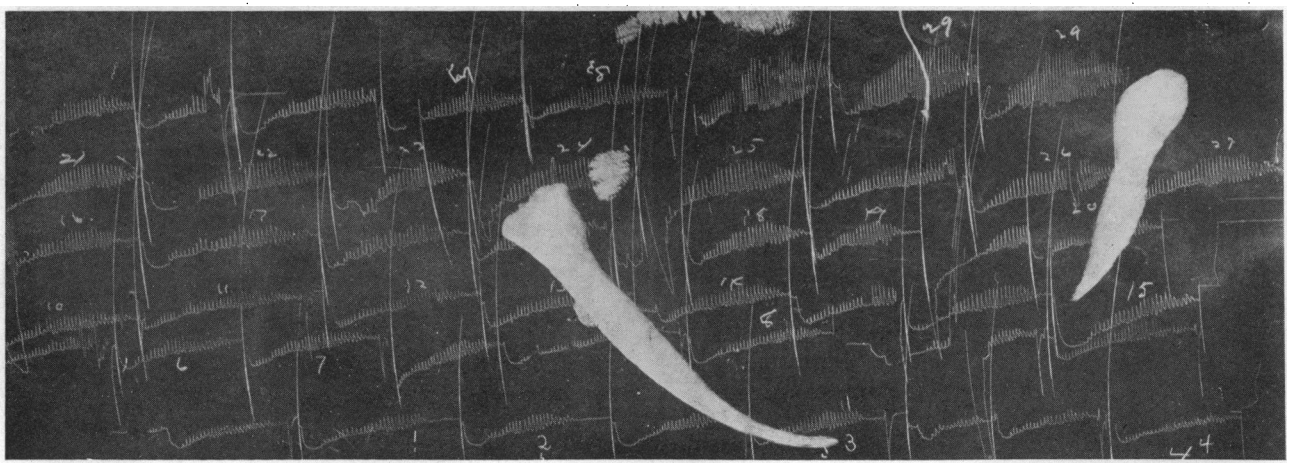

FIG. 5.—Blood-pressure records of Case IV. Reduced 1/6. Read from left to right and from below upwards. Description in text.

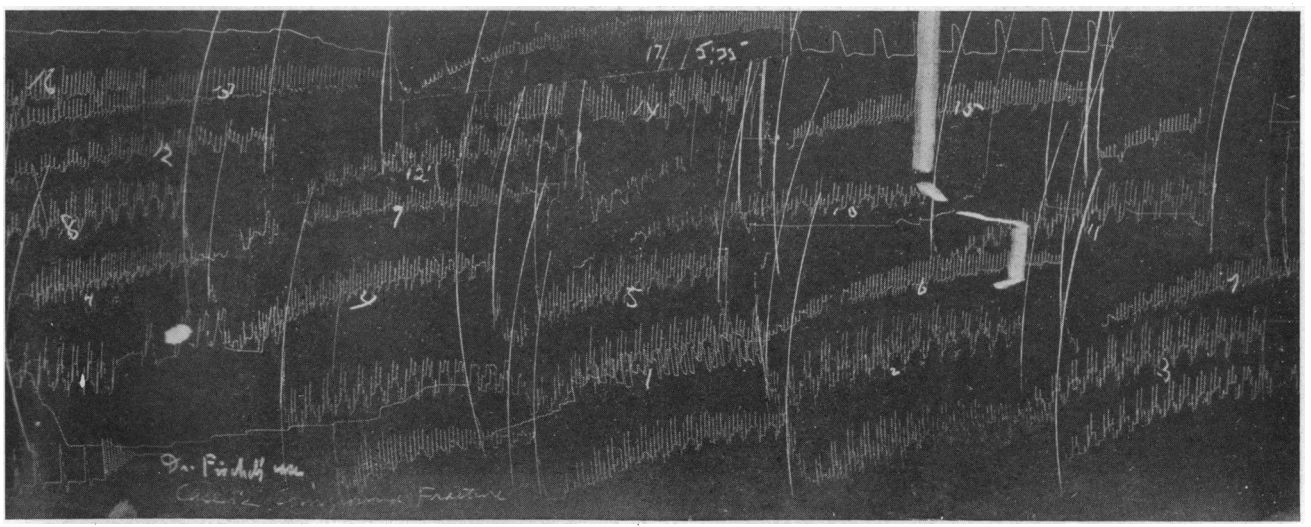

FIG. 6.—Blood-pressure records of Case V. Reduced ⅓, approximately. Read from left to right and from below upwards. Description in text.

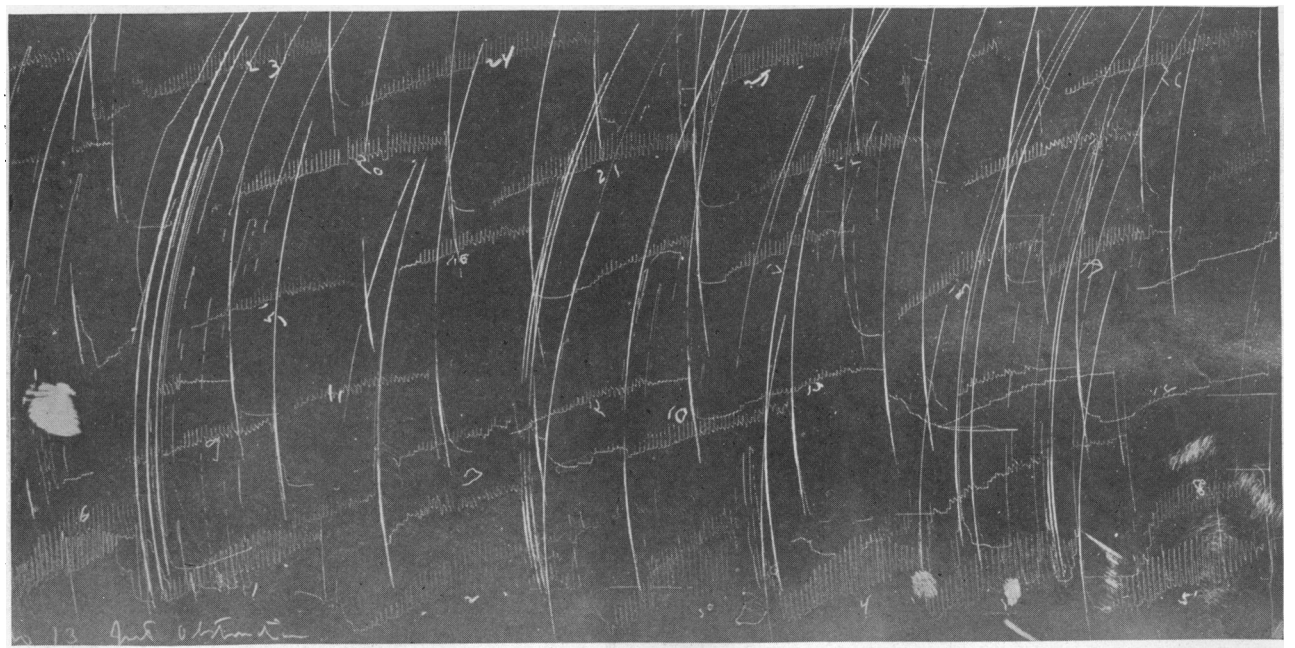

FIG. 7.—Blood-pressure records of Case VI. Reduced $^1/_{10}$. Read from left to right and from below upwards. Description in text.

spleen was everywhere firmly adherent; the operation, consequently, was difficult, and the patient lost a great deal of blood. He did fairly well on the first day. On the second day, the note was made—"At 9 A.M. to-day the patient was *in extremis*. His pulse was thready and almost imperceptible; he looked pale and cold. This condition developed about 2 A.M. Though the patient was a little better at 1.15 P.M., it seems wise to try Doctor Erlanger's treatment."

When the patient was first seen by the author his condition seemed serious. His pulse was weak—120 per minute—he was cold, and he felt that he was going to die. He was vomiting some bloody material. His pressures were 100–80. The amplitude of oscillation (Fig. 5, up to record 4) varied somewhat from record to record; it was not as small, however, as in some of our other cases. If the patient was not in shock, he was in what was regarded as a condition closely approaching it. It was, therefore, decided to administer the gum-glucose treatment.

The patient received 200 c.c. in the course of one hour ten minutes. More might have been given, but it was not regarded as necessary. Hypodermoclysis also was started while the solution was being administered. The pulse amplitude increased steadily during the injection, growing from 2.0–3.0 mm. (record 4) at the start to 5.0–5.5 at the finish (records 25, 26). The pressure readings at this time were 110, 80–85. The pulse-rate also diminished somewhat, from 120 to 105. The patient fell asleep toward the end of the period. Some three hours later (record 28) the pulse amplitude and the blood-pressures had receded somewhat; they were 4.0–4.5 mm. and 100, 80. The clinical note on the patient's condition reads: "Doctor Erlanger called to see the patient, advised gum-glucose treatment, treatment given, patient rallied."

The next morning (October 16) the patient's circulation was much improved, the pulse amplitude (new adjustment of arm band, see record 29) was 8.5 to 9.0 mm., the pressures 120–80; the pulse-rate, though, was still quite rapid, 120 per minute. The patient did fairly well during the 17th, though some blood continued to appear in the vomitus. On the morning of the 18th, he vomited 300 c.c. bright red blood; on the 19th he became irrational and violent, and as a result his wound broke open, and he died that day. There was no temperature reaction to the injection, the temperature remaining normal for twenty-four hours, rising to 101°, 100°, 100°, respectively, on the three following days.

TABLE II

ESTIMATIONS OF THE RED CORPUSCLES, HÆMOGLOBIN AND CLOTTING TIME, CASE IV

Date	R. B. C. per mm.³	Hb., per cent.	Clotting time
October 14	5,340,000	85	..
October 15	4,032,000	65	..
October 15 (2.00 P. M.)	4,608,000	75	5′
October 15 (9.15 P. M.)	4,056,000	75–80	7′
October 16	3,860,000	70–75	4′–20″
October 17	2,720,000	65–70	..
October 18	2,816,000	70	..
October 19	1,912,000	40–50	..

Estimations of the red corpuscles, hæmoglobin and clotting time are shown in Table II. It is seen, if allowance be made for experimental error, that the patient steadily lost blood, and that the clotting time was not affected by the injection.

At autopsy there was found primary carcinoma of the liver with metastases to the diaphragm and lung; cirrhosis of the liver; ruptured œsophageal varices; hemorrhage into the stomach and at the site of the splenectomy; general arteriosclerosis; and chronic interstitial nephritis.

To summarize, during the injection of somewhat less than 3 c.c. per kilo of body weight, 200 c.c. in all, of the solution, the circulation was decidedly improved though part of the improvement was lost subsequently. Some twelve hours later the pulse amplitude and the blood-pressures were found to be normal, though the pulse-rate remained high. These changes occurred despite evidence of continuous secondary hemorrhage which had begun before treatment and which apparently was not aggravated by the treatment. It is obvious that the whole of the recovery of the circulation was not attributable to the gum-glucose; it is quite possible, though, that by the treatment the patient was tided over the critical stage of the post-operative period. Death was due to secondary hemorrhage from ruptured vessels.

CASE V.—*Compound comminuted fractures; shock or fat embolism.* White, male. At midnight I was called to see a " case in shock with low pressures." The patient was a man who had been struck by an automobile and had sustained compound comminuted fractures of the left thigh and of the right leg. I saw him at about 1 A.M. He was then under ether and the operation was well advanced. The pulse was good, the arterial pressures 140, 90, the recorded amplitude 6.0 mm. (Fig. 6, record 1). I decided that the patient was not in shock despite the insistence of the surgeon to the contrary, who now based his opinion upon the observation that the skin incisions did not bleed. Table III and the records (Fig. 6) show that for a time the circulatory conditions remained constant. Later (record 4 *et seq.*), the pressures and the recorded amplitude started downwards. At 2.35 (record 12) the pressures were 90 (palpatory), 65, the amplitude 3.8 mm. The patient now began to struggle, so that pressure estimations could not be made until he was quieted, one hour twenty minutes later, by repeated doses of morphine. In the interval, judging by the pulse, the patient's condition grew steadily worse and preparations were made to inject the gum-glucose solution. The records, therefore, do not show the patient's circulation at its worst. At 3 A.M., when injection of the mixture was started, the patient was blue, pulseless, and gasping. By 3.42, 90 c.c. had been given, and the pulse was better and constantly improving. By 3.56 the patient had quieted down and we succeeded in obtaining record 13. The diastolic pressure alone was legible; it was 60 mm. Hg the amplitude 6.0 mm. Record 14 was obtained at 4.12, the pressures being 95 (palpatory), 60, the amplitude 6.0 mm.; record 15 at 4.23, the pressures being 90 (palpatory), 65, the amplitude 5.2 mm. At this time the injection was ended, the patient having received 265 c.c. The pulse was now fair, but did not feel normal and it was still quite

rapid. Neither were the pressures normal; the respiration, though, was much improved. It was decided not to give more of the solution, however, but to wait and see how the patient reacted. The pressures, though, started to fall again immediately after terminating the treatment, the diastolic pressure being 60 and the amplitude 4.5 at 4.42 (record 16); and 55 and 4.0 at 5.35 A.M. The interne was instructed to follow the pressure and to inform me if it fell any further. This was not done, despite the note in the history made at 7.15 A.M.—"pulse very weak, 136, respiration somewhat labored." It was not until 12 M. that I was called to the hospital. It was 1 P.M. when I reached the

TABLE III

DATA OF CASE V

Record No.	Time A. M.	Pressures		Ampl. mm.	Remarks
		Syst. mm. Hg	Diast. mm. Hg		
1	1.08	140	90	6.0(?)	
2	1.09	140	95	8.0	
3	1.15	140	95	7.5	
4	1.30	135	90	5.5	
5	1.31	135	90+	6.0	Arm band tightened here.
6	1.45	120 (?)	80	5.0	Anæsthetic off. Applying plaster casts.
7	1.50	115 (?)	80	5.3	
8	2.00	110 (?)	80+	5.0	
9	2.10	?	70 (?)	4.0	
10	2.20	?	60–70	5.0	
11	2.30	?	70	4.5	
12	2.31	90 palp.	70	4.0	
12′	2.35	90 palp.	65	3.8	No more records until 3.56 on account of struggling of patient. Pulse steadily becoming worse
	3.00				Patient pulseless and gasping. Starting gum-glucose.
	3.42				Pulse better. 90 c.c. in.
13	3.56	?	60	6.0	
14	4.16	95 palp.	60	6.0	Patient quieter, has had gr. ½ morphine. 215 c.c. solution in.
15	4.23	90 palp.	65	5.2	265 c.c. in. Injection ended. Carotids throbbing, pulse still rapid. Started giving 21 oz. saline hypo.
16	4.42	?	60	4.5	
17	5.35	?	55	4.3	In bed. Has had 1 gr. morphine

ward and the patient then was dying. It was too late to start a second injection. There was no autopsy. This note occurs in the history: "The patient passed into a state of shock and was treated for the same while in the emergency room, and later was sent to the ward in fairly good condition, but became progressively worse and died at 1.25 P.M."

The cause of the collapse in this case is not entirely clear; it may have been shock, properly so called, or it may have been fat embolism.[88] But whatever the cause, it is clear that, though the gum-glucose solution undoubtedly improved the circulation, the gain was not as complete as might have been desired, nor was it maintained. There was no temperature reaction to the injection.

CASE VI.—*Intestinal obstruction; shock* (?). White, female. This was a case of intestinal obstruction of over five days' duration. There had been fecal vomiting. The temperature was 97°. I was asked to be present at the operation because the surgeon anticipated trouble. The operation, consisting of a lateral anastomosis of the small intestine, was performed under morphine-scopolamine anæsthesia. The upper part of the bowel was greatly distended; no attempt was made to draw off its contents. The patient was quite restless, and it therefore was difficult to obtain good blood-pressure records, especially toward the close of the operation.

In Table IV are given the blood-pressure readings and the maximum amplitude of the records shown in Fig. 7. It is seen that at first the readings were well within the normal range. At about the time the operation began the pressures and the oscillation amplitudes (record 5) started to fall, and it was not long before the pulse could not be felt and before the systolic readings became very difficult. The diastolic pressure, though, could be read with a fair degree of accuracy at all times; it fell from 100 to somewhere between 70–80 mm. Hg, where it remained, possibly rising a bit toward the end of the injection. With the diastolic pressure as a basis, the variations in the systolic pressure can be inferred from the variations in oscillation amplitude. It thus can be seen that the systolic pressure, and consequently the pulse pressure, were lowest at about the time (record 13) the administration of the gum-glucose mixture was begun. They then increased more or less constantly during the injection which terminated with record 23. It is obvious, therefore, that the injection caused a decided improvement in the circulation, though it did not bring it back to normal. At 10 A.M., that is, seven and a half hours after terminating the treatment, the report was received that the patient was doing well. But the notes in the history show that, whereas at 4 A.M., and again at 5.30, the pulse was of "fairly good volume, 140," at 8 A.M. it was "very weak and irregular." The temperature now, about five and a half hours after terminating the injection, was 99.4°. At 12 M. "the skin was cold and clammy, pulse almost imperceptible, the respiration slightly labored." At 1 P.M., almost eleven hours after treatment, the rectal temperature was 105.8°, and at 2.15 P.M. the patient died.

The rise in temperature requires a word by way of comment. There are a number of reasons for not regarding it as a reaction to the injection. The most important of these are: (*a*) The phases of an anaphylactic reaction are very much shorter than in this case; (*b*) the temperature reaction to bacteria-containing salt solutions is not so severe.[84] As there was no autopsy it is impossible to reach a definite conclusion with regard to this question.

CASE VII.—*Cerebral exploration; hemorrhage; shock* (?). White, female. At 9.30 A.M. an extensive, rather bloody brain operation had been performed. Immediately after the completion of the operation, at about 12 M., the patient's pulse was weak and I was called to see her. The records marked "12.30" (Fig. 8) were then obtained. The pressure readings corresponding with them were 105, 80 and 100, 75.

TABLE IV

DATA OF CASE VI

Record No.	Time P. M.	Pressures		Ampl. mm.	Remarks
		Syst. mm. Hg	Diast. mm. Hg		
2	11.38	130	100	8.0	Before operation, patient on table under morphine-scopolamine
3	11.40	130	100	8.0	
4	11.45	125	100	8.0	
5	11.47	125	100	7.0	Operation started
5′	11.49	125	100	7.0	
6	11.52	120	100	5.5	
	A. M.				
7	12.07	...	90	2.5	Pulse 140
8	12.39	110	90	4.5	
9	12.53	?	80	2.5	Pulse 150
10	1.02	90 palp.	80	3.0	
11	1.20	...	80	1.5	After this tightened arm band.
12	1.22	...	80	2.0—	
	1.30	...	...	...	Starting gum-glucose
13	1.31	...	80	1.3	
14	1.40	?	?	1.0	
15	1.48	...	70	2.5	
16	1.50	...	80	2.5	
17	1.55	...	80?	2.5	
18	2.03	...	80	3.0	100 c.c. in.
19	2.04	100	80	3.0—	
20	2.15	...	70	3.5	
21	2.16	...	70	4.0	
22	2.17	85	70	3.0	
23	2.24	90	75	3.5	
	2.29	...	...	...	200 c.c. in. Injection ended
24	2.30	...	75	4.0	Pulse 150
25	2.31	...	80	4.0	
26	2.35	...	80	3.5	Record not satisfactory

As the patient presented none of the symptoms of shock, and as the circulatory conditions did not seem to be especially threatening, it was decided to do nothing except administer fluids in the usual way. At 6 P.M. the patient's pulse was found to be "imperceptible" and I was asked to see her again. The records marked 6.20 were now obtained. The systolic pressure could not be determined accurately but it is obvious from the record, both on account of the low amplitude and of the shortened phase of oscillations, that it was very close to the diastolic pressure which was 75. Her pulse pressure obviously was dangerously small.

Preparations were immediately made to administer the treatment. Owing to the inconspicuousness of the veins it was necessary to cut through the skin in order to insert the needle. At 6.30 the injection was started. The records (numbers 3–6) made during the first ten minutes showed such great variability that instability of the pressures, such as cerebral cases commonly exhibit, was suspected. Record 7, made with a constant, optimum (diastolic) pressure upon the arm, confirmed this suspicion. The patient received 250 c.c. of the solution

in the course of one hour twenty minutes. This was close to the maximum dose, for the patient probably did not weigh more than 45 kilo. Fig. 8 shows the continuous improvement in the circulation during the injection, which terminated with record 24. The readings made with this record were 100, 78. Records 25–27, made two hours later, showed further improvement in the circulation, the pressures with these being 110, 75. The next morning record 28 was obtained; as this was made after a readjustment of the arm band the amplitude of oscillation is not entirely comparable with that of the previous records. It is obvious, however, that in this respect the circulation was quite normal. The corresponding pressures were 105, 78. There was no temperature reaction to the injection, the temperature before being 99.6°, and after, 99.2°. During the same night and the succeeding night the temperature rose to 100.8° On the day following the treatment the note was made—" patient in good condition." The patient recovered completely from the effects of the operation, and was discharged from the hospital.

CASE VIII.—*Carcinoma of the rectum; hemorrhage; shock.* White, female. At 12.05 P.M., January 20, a Kraske operation was performed involving resection of the coccyx, a piece of the sacrum, about a foot of the rectum, and the posterior vaginal wall. It was necessary to enter the peritoneum. There was considerable loss of blood and " the patient was considerably shocked." I was called to see her at 3.30 P.M. and made the records labelled A (Fig. 9). The pressure readings were 80, 65. Her condition evidently was serious but it was decided to observe the trend of things before interfering. At 4.20 P.M. her pulse was 170, her " respiration jerky and shallow; " it was scarcely possible to get a pulse with the sphygmomanometer (see record 1). The diastolic pressure, roughly, was 5 mm. Hg, the systolic pressure could not be estimated. At 4.35 the administration of the gum-glucose solution was begun and in the course of two hours twelve minutes 220 c.c. were given. Owing to mechanical difficulties the rate of injection was much slower than was necessary. It was estimated that the patient received somewhat less than 5 c.c. of the solution per kilo of body weight. The injection terminated at 6.47 (record 28), when the blood-pressures were 100, 78, the pulse amplitude 3.0–4.0. The steady improvement during the treatment is clearly indicated by the figure. Records 29–33, made three hours later, with readings of 95, 70, and 3.0 mm., show that little, if any, of the improvement had been lost in the interval. Records 34–37 were made the next morning while the patient was nauseated. The systolic pressure ranged in the different estimations between 95 and 100 mm. Hg, the diastolic, between 75 and 80; the amplitude was 3.0 mm. In the evening the pressures were 110, 80. There was no temperature reaction to the injection. The clinical note made at 11 P.M. on the night of the operation reads, " Patient improved, condition now fair, pulse of fair quality—130–140." It should be added that the patient received 1000 c.c. salt solution subcutaneously while the gum-glucose solution was being given. A similar dose of salt solution was again given at 11 P.M.

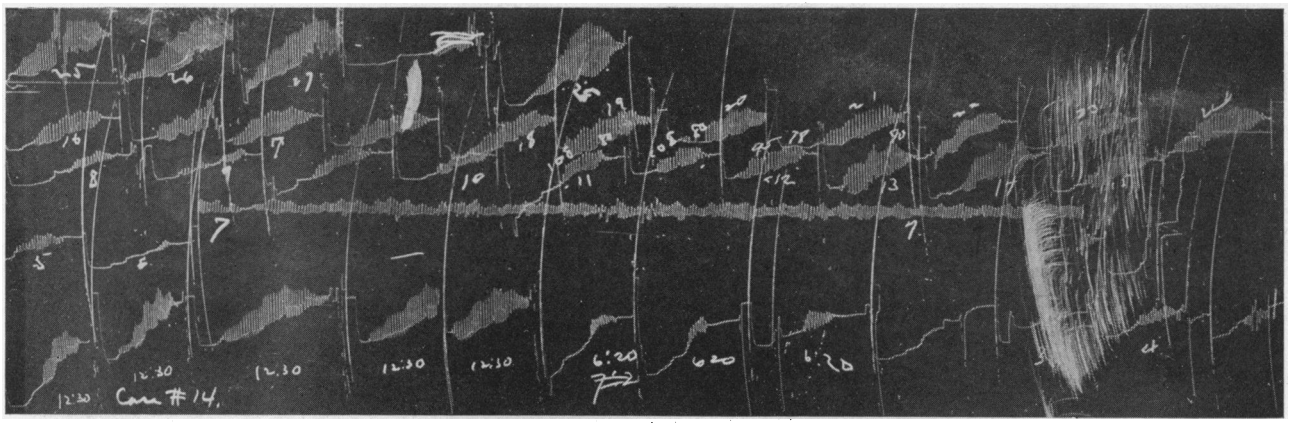

FIG. 8.—Blood-pressure records of Case VII. Reduced ⅓. Read from left to right and from below upwards. Description in text.

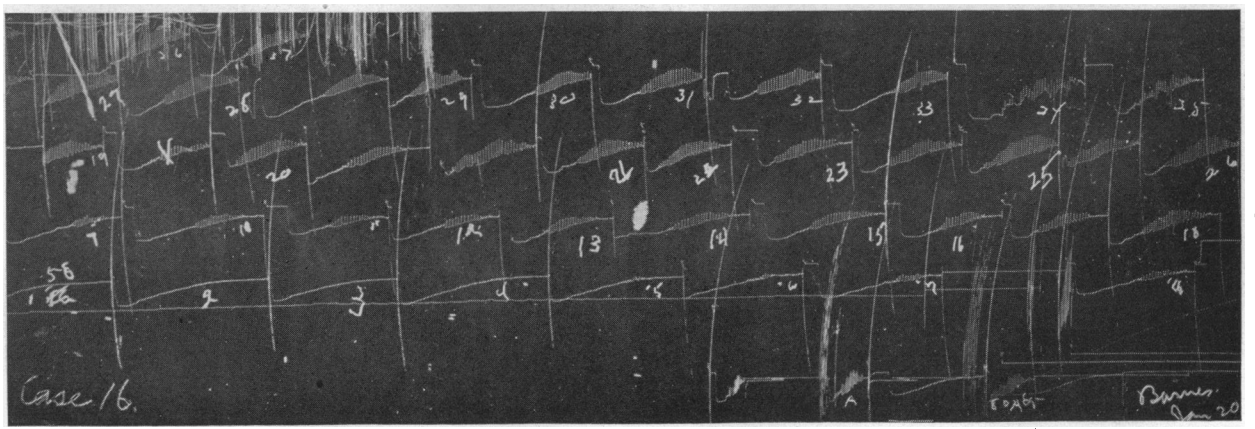

FIG. 9.—Blood-pressure records of Case VIII. Reduced ⅓, approximately. Read from left to right and from below upwards. Description in text.

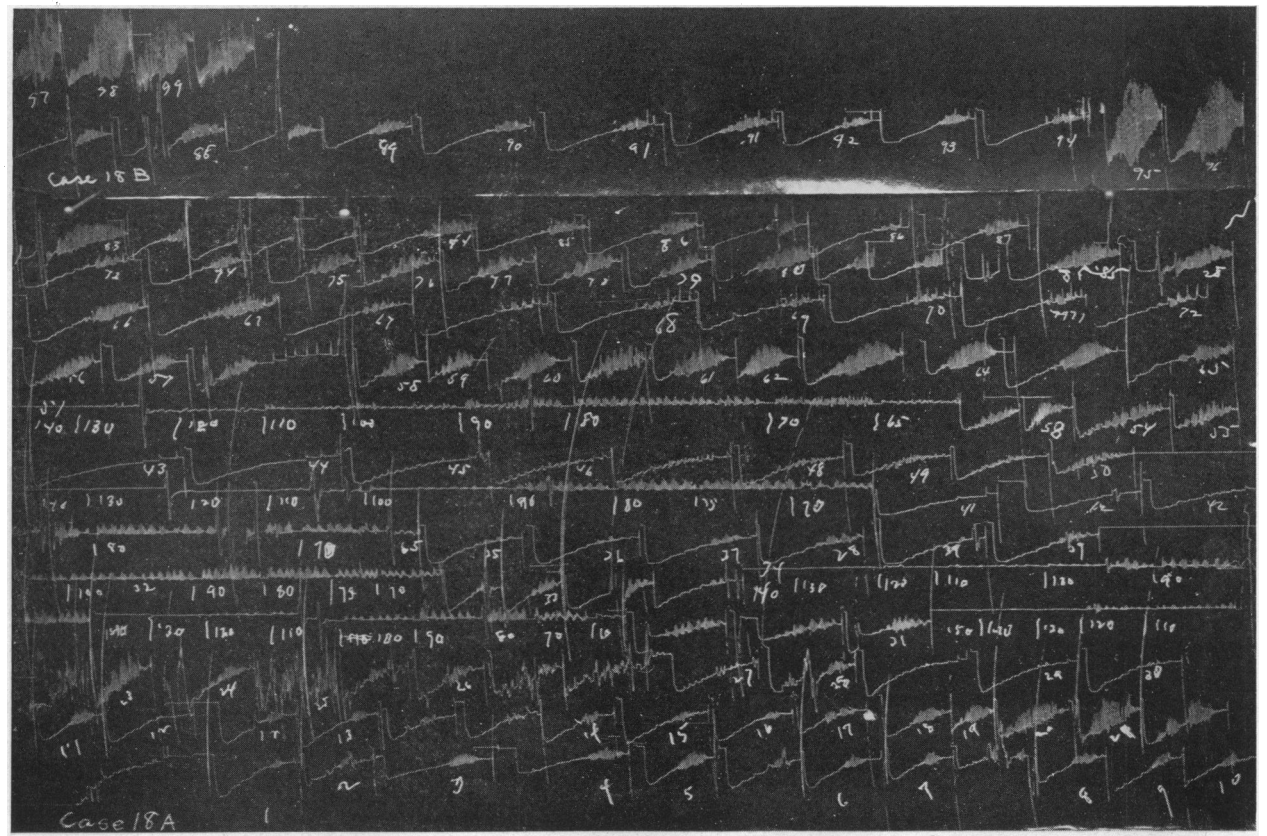

FIG. 10.—Blood-pressure records of Case X. Reduced ¼, approximately. Read from left to right and from below upwards. Description in text.

The patient did well for four days, when symptoms of peritonitis developed. She gradually lost ground and died two weeks after the operation. Blood cultures made on the fifth day were negative.

CASE IX.—*Vaginal resection of cervical stump for carcinoma; hemorrhage; not treated.* White, female. The operation consisted of a very difficult vaginal resection of the cervical stump for recurrent carcinoma. There had been considerable hemorrhage during the operation, and an apparently profuse secondary hemorrhage from the vagina, subsequently. I saw the patient at 2.15 P.M. The pulse could scarcely be felt at the wrist and the sphygmomanometer recorded only the faintest flutter of a pulse. The arterial pressure could not be determined by any method whatever. The patient was conscious and somewhat restless. The skin did not feel cold. It was obvious that she was suffering from an extreme, acute hemorrhage, and transfusion of blood was advised. I was told that the preparations would require about a half hour. As I felt the patient could wait that long the gum-glucose solution was not given. But there was one unavoidable delay after another, and after each it seemed as though the transfusion would be started without further delay. But the result was that the transfusion was not started until 4.58 and the patient then was dying.

This unfortunate experience teaches the lesson that even when, in any given case, transfusion of blood is clearly the preferred treatment, the thing to do, pending preparations for blood transfusion, is to at once transfuse a blood substitute, such as simple saline, or better, isotonic gum-saline or hypertonic gum-glucose solution (cf. Case X). This case, in a way, may be regarded as another control (see Case I) to our series of treated cases. It will be noted that death occurred about three hours after I had been called to see the patient. It was the earliest death of the whole series.

CASE X.—*Excision of osteoma of cranium; extreme hemorrhage; shock* (?). White, female, age sixty-one years. On March 3 an attempt to excise a bony tumor overlying the superior longitudinal sinus had to be interrupted on account of hemorrhage. I was called to see the patient immediately after this operation and after she had been transfused with blood. But her pressures were systolic 140–130, diastolic 100–90; and she presented none of the symptoms of shock. On March 6, the operation was completed. The hemorrhage again was extreme. Although the patient had already received 250 c.c. of blood, the pressures at 11 A.M. were about 85 (systolic) and 70 (diastolic), and the recorded amplitude (records 1–11, Figs. 10 and 11) was only 2 mm. Compared with those obtained three days earlier, these values were extremely low.

At 11.53, when her pulse pressure had decreased to 10 mm. Hg and the recorded pulse amplitude was decreasing, a second transfusion of citrated blood, taken from a matched donor, her son, was begun. In the course of ten minutes the patient received 450 c.c. of blood. During the injection (records 15–21) the pressures rose to 110, 80 mm. Hg, the amplitude becoming 6 mm. These pressures, however, did not hold. Within twenty-one minutes (record 24) they had fallen to 90, 75; the

amplitude to 2.5 mm.; and the pulse was 180 per minute. The patient now had a chill which for some time interfered with the obtaining of blood-pressure readings. Her temperature, which had been normal, at 1.30 was 102.4° F., at 7 P.M. 104°, and at 10 P.M. 100.8° (see Fig. 11). After the chill the recorded pulse amplitude diminished, to all intents and purposes, progressively (records 28–42) until, by 2.58 (record 42), the recording lever showed only the faintest oscillation on a diastolic pressure of about 65. The respirations now were 38 per minute and often periodic; the skin wet and cold. The patient was completely unconscious; there was no corneal reflex and no reaction to incision of the leg for the purpose of exposing the vein.

The injection of gum-glucose solution was started at this time. In the course of one hour eight minutes she received 275 c.c., when, on account of a leak in the vein, the injection was temporarily discontinued. During the injection the diastolic pressure rose (records 43–54) from 60 to 70 mm. Hg, the systolic to 105, the recorded amplitude increasing from practically nothing to 2.5 mm. The patient regained consciousness and did not again lose it. Later (4.45–5.37) the injection was completed. The total dose amounted to 300 c.c.; but the amount given after 4.05 was so small and the rate of its administration so slow that to all intents and purposes 4.05 marks the end of the injection. From about 3.25 (record 47) and until 5.37 (record 63) there was a progressive improvement in the circulation, the amplitude of oscillation and the pressures becoming quite as good as during the twelve-minute period of rapid blood injection. This improvement occurred despite the concurrent reaction to the blood injection. But now, during the height of the temperature reaction, the pressures fell (records 63–71), reaching the low point of 48 mm. Hg (diastolic) at 6.15. At this time the recorded amplitude was 1.6 mm.; it was not nearly so small as it had been during the period of low pressure that developed after the blood injection. Now the circulation began to improve again (records 71–83), so that by 7.55, the pressures had risen to 100, 70, the amplitude to 3–4 mm. The pulse-rate was 148; the respirations, 32. This improvement again was succeeded by a recession, the pressures, by 9.55 P.M., falling (records 84–94) to 70, 55, the amplitude to 1.5 mm. Periodic respirations were again noted.

During the remainder of the night systolic blood-pressure readings were made by the nurse by the palpatory method. Checked against the readings by the recording sphygmomanometer the former were about 10–15 mm. Hg too low. Bearing this in mind, it becomes obvious (see Fig. 11) that a slow and steady improvement in the circulation began within two to three hours of the termination of my readings, the systolic pressure rising from 70 at 10.30 P.M., March 6, to reach 118 at 6.30 A.M., March 7. At 8.40 A.M. readings with the recording sphygmomanometer (new adjustment of arm band, records 95–97) showed pressures of 120–130 (systolic), 70–80 (diastolic) and a pulse amplitude of 23 mm. The circulation evidently had become normal and it remained so. The patient's temperature reached normal on the third day, and remained normal for twenty-four hours; her pulse-rate remained at the high

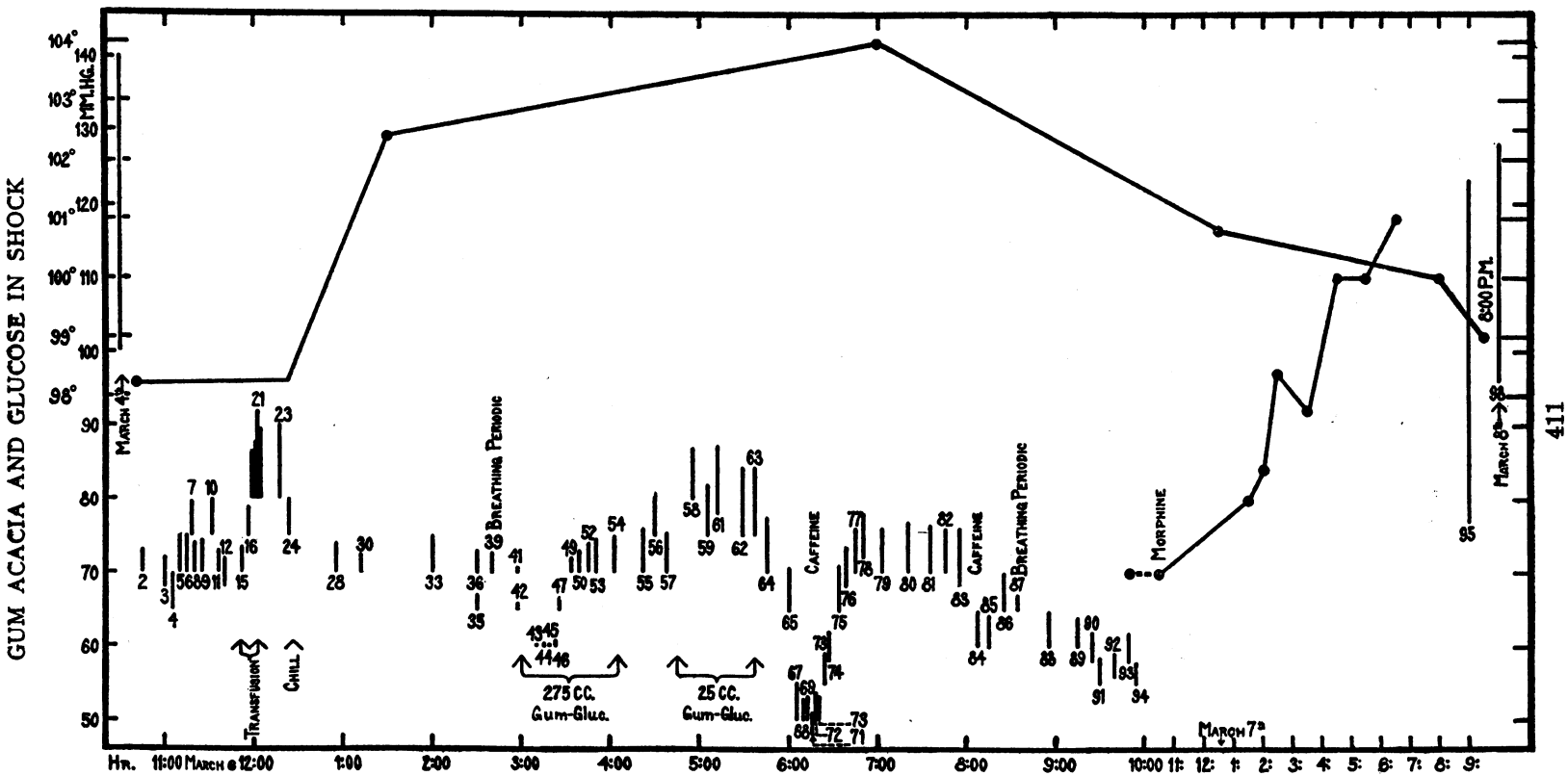

FIG. 11.—Curve made by erecting on the diastolic pressures the maximum amplitudes of oscillation recorded in Fig. 10. The ordinates give the diastolic pressure in mm. Hg. The scale of amplitude is such that 1.0 mm. of amplitude is subtended by 20 mm. Hg. Note that after 10:00 P.M. the time scale changes; this has the effect of making the final rise in pressure appear much steeper with respect to the rest of the curve than it actually was.

level of 120–130. On March 9 jaundice was first noted; this was disappearing on the 11th. Whether or not the patient had hæmoglobinuria cannot be positively stated, for the urine was voided involuntarily for several days. The nurse, however, states that the urine was dark brown in color.

The curve constructed by plotting the oscillation amplitude on the diastolic pressure (Fig. 11) clearly shows the three long blood-pressure waves, with troughs at 3.10, 6.08 and 9.40, respectively. Without doubt the circulation was at its worst during the first of these troughs. This is indicated both by the mental condition of the patient (consciousness was lost during the first fall only) and by the amplitude of oscillation (the patient actually was pulseless). It was at this time that the gum-glucose solution was given. In the second trough the blood-pressures fell lower than in the first, but the oscillation amplitude remained considerably larger. The latter is a matter of some significance, since, in general, the oscillation amplitude is a relative measure of the amount of blood put out by the heart per beat, and, therefore, of the blood flow. In this trough the patient received a dose of caffeine. One might be inclined to attribute the subsequent improvement in the circulation to the action of this drug were it not for the fact that a second dose of caffeine, given at 8, did not stay the fall in pressure which then was under way. The third trough was not as deep as the second, while the pulse amplitude in both was the same. It was from this trough that the arterial pressure steadily rose to reach normal in the course of about nine hours.

The etiology of these troughs is quite obscure. The only suggestion that seems to have any degree of plausibility refers them, not to anything that was being done at the time, but rather to some effect of the cerebral decompression upon the medullary centres. The fact that the patient at times had Cheyne-Stokes respiration, possibly lends some support to this view. Leaving these sharp depressions out of consideration, examination of the general trend of the curve (Fig. 11) shows that the blood transfusion was quite ephemeral in its effects. The gain was quickly lost and for three hours subsequently the pulse amplitude steadily declined; there is no question but that the circulation was insufficient to sustain life. The gum-glucose solution caused the circulation to improve for about two hours; then, again disregarding the (presumably) fortuitous troughs the circulation slowly but steadily declined through a period of over four hours; but at the end of this decline the circulation was not any worse, at least as regards pulse amplitude, than it had been forty minutes after the blood transfusion nine hours earlier. Then the final turn for the better occurred. It is possible that the waning of the reaction to the blood transfusion, as indicated by the fall in temperature, here facilitated the recovery of the circulation. There can be no question but that the gum-glucose solution markedly improved the circulation. We are inclined to believe that it tided the patient over her critical post-operative period, which was also the period of her reaction to the transfusion.

The results of the blood examinations, taken from the history, are given below in tabular form. The hæmoglobin estimations are somewhat more consistent than the red cell counts. We, therefore, base our discussion upon the behavior of the former alone. If we leave out of consideration, as being difficult of evaluation, the influence of the blood transfusions and of destruction and regeneration of red-cells, and regard the dilution of the blood as an index to the restoration of the blood-volume, it seems justifiable

Date	R. B. C. per mm.³	Leuc. per mm.³	Hb. per cent.
February 28	4,432,000	11,800	85
March 4	3,424,000	15,600	76
March 6	2,048,000	6,100	56
March 7	2,496,000	.....	49
March 8	1,798,000	.....	43
March 9	1,504,000	20,150	39
March 11	1,728,000	16,850	40
March 12	1,776,000	.....	42
March 13	1,952,000	15,000	42
March 14	1,964,000	16,700	42
March 15	1,620,000	12,400	36
March 16	1,760,000	11,800	37
March 18	1,824,000	12,500	41
March 19	1,312,000	9,750	38
March 20	2,048,000	9,980	38
March 21	2,853,000	10,500	20
March 22	2,240,000	8,750	23
March 22	1,744,000	14,950	42
March 23	2,112,000	16,080	25
March 24	.....	29,450	..

to infer that with the first hemorrhage (March 3) the patient lost about one-ninth of her total blood-volume, and with the second hemorrhage (March 6) a bit less than one-half of the blood-volume remaining. In the two hemorrhages considerably more than one-half of the total blood-volume was lost. The count of March 6 was made about twelve hours after the second hemorrhage and shortly after the administration of the gum-glucose solution. It shows that considerably more than 57 per cent. of the blood-volume finally attained had by then been acquired. Just how much of this rapid restoration of blood-volume is to be attributed to the action of the gum-glucose solution and how much to natural processes it is impossible to say. Nucleated red cells were found March 8.

On the fourth day the patient's temperature started on a more or less steady rise and reached 102°–103° on the eleventh day, where it remained until the nineteenth day. At, or shortly after, the time the temperature began to rise, a badly infected sore developed on the patient's buttocks; by the thirteenth day this had broken down; and on the sixteenth day it had to be incised. On the thirteenth day some sero-sanguinous fluid was removed from the wound in the leg from which the piece of muscle, used to stanch the hemorrhage from the longitudinal sinus, had been removed. On the twentieth day a small area of the patient's scalp was found to be sloughing. A blood culture, made on the

fourteenth day, proved negative. A thorough physical examination seemed to exclude all of the common causes of the febrile condition excepting the skin infections and the anæmia, which had persisted despite the administration of iron. The convulsions, which had been a part of the patient's pre-operative clinical picture, persisted after the operation.

On the nineteenth day the patient, now in an extremely weakened state, was again transfused with blood taken from a rematched donor, again a son. The temperature rose immediately to 106°, fell to 101° eight hours later, and then rose steadily to reach 106.8° in three days, when the patient died, twenty-two days after the second operation. There was no autopsy.

CASE XI.—*Excision of endothelioma of the dura; shock* (?). White, female. During the excision of the tumor, under ether anæsthesia, the patient's systolic pressure, taken from the leg by the auscultatory method, fell from 160 to 92 mm. Hg, and then could not be estimated at all. There had been relatively little hemorrhage. At this time the diastolic pressure, taken in the leg by the oscillatory method, was 75 mm. Hg, the systolic pressure could not be determined (records A to E, Fig. 12). Records F to I were taken from the arm while the patient was still in the operating room. The diastolic pressure was 70, the pulse amplitude 1.0 to 1.5 mm. Records 1 to 4 were taken between 12.12 and 12.18, after the patient had been put to bed (readjustment of arm band). The diastolic pressure was still 70 and the pulse amplitude 1.5 mm.

I felt that the patient's condition was not urgent and that it would do no harm, before interfering, to determine her trend. But in view of the results of treatment previously observed, the surgeon requested that the gum-glucose solution be given at once. At 12.18 the needle was inserted into the vein transcutaneously and the injection started, but as the fluid seemed to be going into the tissues, the injection was discontinued after about 50 c.c. had left the bottle. At 12.30 the injection was started again, now, into the exposed vein. The pressure and the pulse amplitude had not changed in the interval. In the course of an hour, 212 c.c. more of the solution were injected. During this time (records 5 to 16) the pulse amplitude increased steadily until it became 4 mm. The diastolic pressure rose to 80. The systolic becoming legible at 90, at 12.38, increased steadily and reached 110 at 1.31. The blood-pressure readings made after terminating the injection were as follows:

Record No.	Time	Syst. mm. Hg	Diast. mm. Hg	Max. ampl. mm.
18	1.35 P. M.	115	85	3.5
19	2.00 P. M.	110	85	3.0
20	2.20 P. M.	115	88	3.4
21–22	3.50 P. M.	105	75	3.5
23–24	5.20 P. M.	110	80	4.0
25–27	8.00 P. M.	125	90	5.5
28–29	9.00 A. M.	115	85	6.0 arm band readjusted

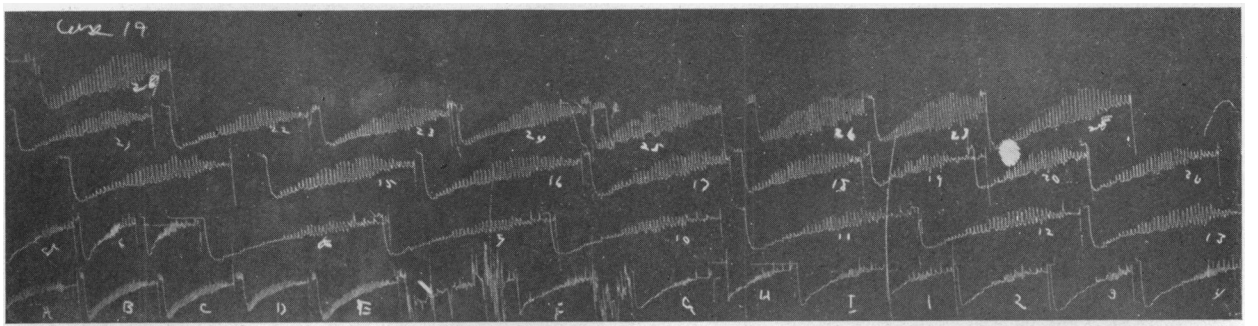

FIG. 12.—Blood-pressure records of Case XI. Reduced ¼, approximately. Read from left to right and from below upwards. Description in text.

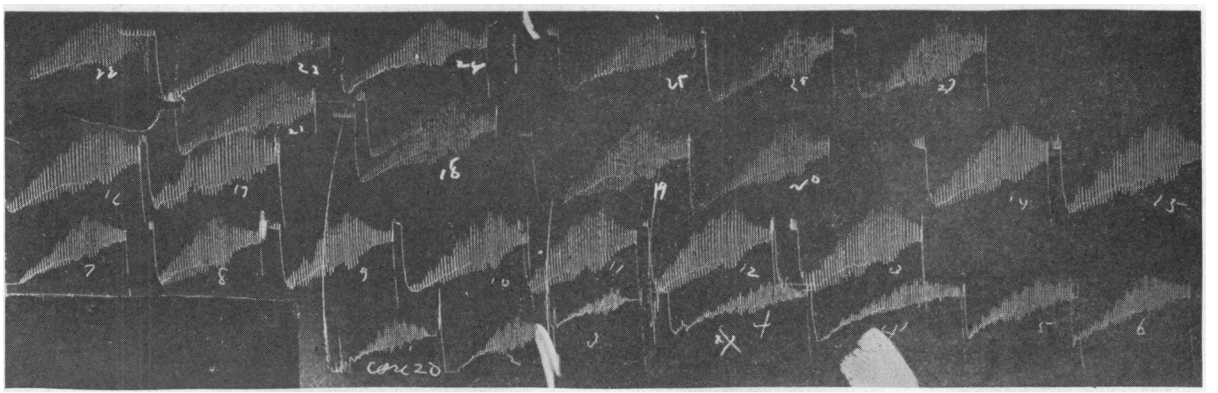

FIG. 13.—Blood-pressure records of Case XII. Reduced $^{2}/_{9}$. Read from left to right and from below upwards, as numbered. Description in text.

These readings show very slight, if any, retrogression during the first two hours or so, and then a steady improvement.

The patient's temperature rose gradually to reach a maximum of 102.6° at 8 P.M. on the first day. It remained there for about twelve hours, then slowly and steadily fell, and became normal on seventh day. The slow defervescence indicates that the rise was not in the nature of a reaction to the injection.

CASE XII.—*Operation for sarcoma of the uterus; hemorrhage; shock* (?). Colored, female. The operation consisted in the partial removal of a huge sarcoma of the uterus, which seemed to be aggravating a mitral regurgitation and to be causing, or aggravating, a marked renal insufficiency. During the operation an infected ovarian cyst was accidently ruptured. There was considerable hemorrhage. I was called to see the patient during the operation, when her pulse could no longer be felt nor her pressure determined (auscultatory method). Records 1 and 2 (obtained at 9.25 A.M.) showed the pressures to be 75 (systolic) and 50 (diastolic); the amplitude was 4.5 mm. (Fig. 13). Twelve and fourteen minutes later (records 3 and 4) the pressures were 65, 50 and 60, 45, respectively, the amplitudes, 3.5 and 4.0 mm.

Again I felt that it would do no harm to follow the trend of things before interfering, but the surgeon requested that the gum-glucose solution be given. Between 9.40 and 10.50, 210 c.c. were administered. The pressures (records 4 to 14) improved promptly, and more or less steadily, so that when the injection was terminated they were 105, 80, and the pulse amplitude 10.5 mm. About a half hour subsequently the pressures fell somewhat to reach 85 and 65, but the amplitude diminished very slightly, to 9.0 mm. (record 20). They then improved so that by evening (arm band readjusted) they were 100, 5 mm. Hg and 8.5 mm. The next morning (readjustment of arm band) they were 105, 76 and 10.0 mm. The pre-operation pressures had been 104, 70. Despite an unabated renal insufficiency indicated by 83–86 mgr. non-protein nitrogen per 100 c.c. blood, and by a phenolsulphonephthalein output of only 5 per cent. in two hours, the patient made perfect progress for 21 days, when she contracted pneumonia and died on the 25th day. At autopsy a fresh lobar pneumonia and very marked hydronephrosis were found.

Cases of Cholera Infantum.—The two following cases are included in this paper, not because they bear on the treatment of shock, but because they furnish valuable evidence of the harmlessness of the gum-glucose solution. The reasons for administering the solution will probably be published in due time. These cases were not seen by the author. They were in the service of Dr. W. McK. Marriott to whom we are indebted for the following note:

"We have injected the 18–25 per cent. glucose-acacia solution into two infants suffering from alimentary intoxication (cholera infantum). Both were in a state of collapse with feeble pulse, gray skin, great desiccation. The clinical results were good. One of these infants at the time of injection

was in a semicomatose state. He became conscious shortly after the injection. In both instances there was a distinct change in the character of the pulse. From a weak, thready pulse, it changed to a full one. One of these infants had previously received a glucose solution with good effect; but the effect was not so lasting as that of the glucose-acacia mixture. One child received approximately 5 c.c. of the solution per kilo of body weight, the other between 10 and 15 c.c., the solution being injected slowly over a period of some 50 to 65 minutes. No ill effects were observed. The infant receiving the larger amount of solution developed a slow, deep respiration which persisted for several hours after the administration of the solution. This respiration was not due to acidosis as was shown by laboratory tests."

We call attention to the fact that one of these cases received inadvertently more than twice the usual dose without ill effects.

SUMMARY OF CASES.—All ten of the cases treated by the author (see

TABLE V

SYNOPSIS OF CASES

Case No.	Nature of trauma	Condition immediately before	Dose		Immediate result	Ultimate result
			Amt. c.c.	Rate c.c. / K. / hr.		
I.	Crushed foot.....	S., ? D., 40; P. A., 1.3	0	...	Not treated.....	Died in about 4 hours.*
II.	Gunshot wounds. Hemorrhage	S., 80; D., 70; P. A., 1.5	270	2.2	S., 120; D., 80–85; P. A., 5.5. Circ. seems normal	No retrogression. Discharged well.
III.	Panhysterectomy. Hemorrhage. Infection	S., ? D., 30; temp. 105.6; P. A., 1.0 –	200	3.2	S., 80; D., 50; P. A., 2.0+. Slight improvement (?) Temp. 106°	Died in 6 hours†
IV.	Splenectomy. Primary carcinoma of liver. Primary and secondary hemorrhage	S., 100; D., 80; P. A., 2.5–2.8	200	1.9	S., 110; D., 80–85; P. A., 5.0–5.5. "Patient rallied"	Slight recession, then improvement. Next day, S., 120; D., 80. Continuous secondary hemorrhage. Died 4th day
V.	Compound comminuted fractures. Fat embolism (?)	Pressures unobtainable	205	3.0	S., 90; D., 65.....	Died in 10½ hours†
VI.	Intestinal obstruction	S., 90; D., 80; P. A., 1.3	200	2.6	S., ? D., 75–80; P. A., 4.0	Pressures not followed. Died in 10½ hours†
VII.	Cerebral exploration. Hemorrhage	Pulse imperceptible. S., very low; D., 75; P. A., 0.5–3.0	250	4.2	S., 100; D., 78; P. A., 4.0. Circulation much improved	No retrogression. Recovered
VIII.	Kraske operation for carcinoma of rectum. Hemorrhage	S.? D., 58; P. A., 0.3. "Respiration jerky and shallow"	220	2.2	S., 100; D., 78; P. A., 3.5. Circulation much improved	No retrogression. Peritonitis on 4th day. Died on 14th day
IX.	Vaginal resection of cervix. Profuse primary and secondary hemorrhage	Almost pulseless. Pressures undeterminable. P. A., 0+		...	Not treated.....	Died in about 3 hours*
X.	Excision cranial osteoma. Extreme hemorrhage; transfusion reaction	S.? D., 60; P. A., 0+ Unconscious	300	?	S., 105–110; D., 70–80; P. A., 7.5–12.0. Conscious	Circulation normal after periodic falls. Persistent anæmia. Skin infection; died (after transfusion), 22nd day
XI.	Excision dural endothelioma	S.? D., 70; P. A., 1.5	262	4.0	S., 110–115; D., 80–88; P. A., 4.0; circulation improved	Slight, temporary retrogression. Well
XII.	Excision sarcoma, uterus. Hemorrhage	S., 50; D., 45; P. A., 3.5–4.0	210	4.0	S., 105; D., 80; P. A., 10.5. Circulation good	Slight retrogression in pressures, not in P. A. Died 25th day.

Abbreviations: S. = systolic pressure; D. = diastolic pressure; P. A. = maximum oscillation amplitude.
* After being called to hospital.
† Timed from beginning of treatment.

Table V) showed a greater or less immediate improvement in the circulation as a result of the administration of the gum-glucose solution. But in three of the cases (III, V, VI) the improvement was by no means satisfactory at the conclusion of the treatment and did not hold. These cases behaved very much like animals in deep experimental shock, in which the injection temporarily raises the pressure though death is inevitable. Of these three cases, one (III) was a case which undoubtedly was overwhelmed by an infection dating from the operation; the second (V) was a case of compound comminuted fracture of both legs and might have been complicated by fat embolism; while the third (VI) was a case of long-standing intestinal obstruction, which might have been complicated by a general infection, by peritonitis or by toxæmia. All three died within twelve hours after beginning the treatment.

The circulation of Case X was improved much more by the gum-glucose injection than by the blood transfusion, but a considerable fall occurred after the injection of the gum-glucose before the circulation became normal. Subsequently, she had an extreme anæmia and a skin infection to contend with. Death occurred on the twenty-second day after a severe reaction to a blood transfusion. In the remaining cases, six in number (II, IV, VII, VIII, XI, XII), the improvement in the circulation that occurred during the injection held or continued subsequently; they, as well as Case X, recovered from the circulatory disturbance and from shock. The fact that the main improvement occurred during the treatment furnishes presumptive evidence that the latter was the cause of the recovery. A much larger series of cases than we have thus far succeeded in collecting, though, is necessary to prove this beyond peradventure.

Of the seven cases that recovered of shock, or of a condition approximating shock, four died subsequently—Case IV on the fourth day, of secondary hemorrhage; Case VIII on the fourteenth day, of peritonitis; Case X on the twenty-second day, probably of anæmia and skin phlegma, aggravated by a reaction to blood transfusion, and Case XII on the twenty-fifth day of lobar pneumonia and hydronephrosis. These deaths unquestionably were due to causes that were not referable to, or influenced by, the treatment. Seven of the cases (II, III, IV, VII, VIII, X and XII) were complicated by hemorrhage, which, in one case (X), was extreme.*

Two cases that might have received treatment did not; one (Case I) because of an accident to the solution; the other (Case IX) because it was decided that blood transfusion was the preferred treatment, and unavoidable delays resulted in the unfortunate failure to give any intravenous treatment at all. These patients died in about four and three hours, respectively, after I had been called to see them. Although we realize how difficult it is to gauge shock, we feel that the condition of Case I when first seen by us was not any worse than that of some of the cases that received treatment. It is also

* NOTE.—(At time of proofreading.) We have had another case of marked shock, with very satisfactory results. Up to now (eleventh day) the patient has made normal progress.

difficult to gauge hemorrhage; but we are of the opinion that the condition of the circulation of Case IX, when first seen by us, was no worse than that of our other hemorrhage case (X) at the time the administration of the gum-glucose solution was begun. But however this may be, these are the only cases in our series that we can cite as untreated controls; death occurred earlier in these two cases than in any of the treated cases.

No ill effects of any kind have been noted. During the injection, the circulation always has steadily improved and the anxiety of the patient, when conscious, always has diminished, two of them falling asleep before the close of the injection. With one possible exception (Case VI), there have been no temperature reactions that can reasonably be referred to the injection.

Utilization and Excretion of the Injected Gum Acacia.—Substances similar in composition to gum acacia are widely distributed in the plant kingdom and are very important factors in the nutrition of herbivorous animals, which seem to be able to use 50 to 60 per cent. of the amount ingested. Gum-like substances are, however, a far less important constituent of the diet of man, though those ingested are very largely utilized.[35] Chemically, gum acacia is a pentosan. On hydrolysis it yields a number of sugars of which the pentose, arabinose, is the most important, some samples yielding as much as 50 per cent. of this substance.[36] A certain amount of the ingested pentose always escapes metabolism and appears in the urine in the form of pentose.

We have followed the pentose quantitatively in the urine of Case VIII, using for the purpose the technic described by Testoni.[37] The color produced by this reaction was compared in a colorimeter with the color produced by a standard solution of arabinose treated in exactly the same way. As long as the amount excreted was fairly large the colors could be readily matched; but when the color produced in the urine was faint, it was no longer of the same tint as that of the control, and the readings then became quite inaccurate.

Table VI shows that about 0.7 gm. pentose was excreted in all. Just what this means in terms of gum acacia it is impossible to say. It is obvious, however, that of the 55 gm. gum acacia injected, practically all was utilized. It would also appear that about one-half of the gum injected is taken care of by the organism in the course of twelve hours, but that some of the gum

TABLE VI

EXCRETION OF PENTOSE AFTER INTRAVENOUS INJECTION OF 54 GM. GUM ACACIA

Catheterized sample of	Amount of urine, c.c.	Pentose, gm.
January 21, 3.00 A. M.	170	0.232
January 21, 3.45 P. M.	231*	0.208
January 22, 11.25 A. M.	366	0.079
January 22, 7.20 P. M.	575	0.058
January 23, 4.00 A. M.	500	0.079
January 23, 3.00 P. M.	625	0.035(?)
January 24, 11.00 A. M.	1150	None (?)
Total excreted	....	0.691

* Small amount lost.

remains in the body for over forty-eight hours. These facts should be of some assistance in determining how long the interval between repeated doses of gum should be (see p. 418).

SUMMARY

It is concluded on the basis of the animal experiments of the author and collaborators, and of others, on the mechanism and treatment of shock, that slowing of the circulation in a considerable part, or in the whole, of the body is commonly, if not always, the factor that leads to the development of experimental shock. It is believed that as a result of the slowing of the blood-stream the corpuscles clump in the venules and capillaries which then become choked with solid masses of corpuscles and dilate. The blood flow is thus curtailed still further, indeed, to the point of interfering seriously with the processes of tissue respiration and nutrition. The effective blood-volume is reduced, not alone by the dilatation, but also by transudation of plasma. The organism strives to combat this real and effective reduction in blood-volume by the usual mechanism of pouring tissue fluids into the blood-stream. Largely, if not exclusively, as a result of the deficient general circulation resulting from the reduction in effective blood-volume, the medullary centres, including the vasomotor centres, and the heart, eventually may show some signs of functional insufficiency.

The administration of a combination of hypertonic gum acacia and hypertonic glucose under these circumstances acts beneficially, we believe, in several ways: (*a*) By drawing fluids from the tissues into the blood-stream, thus assisting the normal mechanism in restoring the blood-volume. It is possible that such an *internal transfusion,* as Gesell [5] has suggested calling it, carries from the tissues into the blood-stream a certain amount of proteins and of salts [38, 39] so that the fluid thus added to the blood might resemble much more closely the composition of the plasma than could any artificial solution. (*b*) By maintaining this increased volume through some property of the gum acacia. (*c*) By dilating the arterioles through some specific action of the hypertonic crystalloid.[27] (*d*) By increasing the energy of the heart beat in the same way,[27] and also through direct action of the glucose on the muscle. And (*e*) by augmenting metabolism through the increase in the supply of glucose to the organism between the limits of basal metabolism and self regulation.[40]

There is no need of providing salts with this injection, because the solution is given in relatively small quantity (5 c.c. per kilo of body weight) and very slowly. It can be assumed that it is given so slowly that the salt balance of the blood can be maintained by interchange with the tissues, while the salt balance of the tissues, since the body contains 700 c.c. of fluid per kilo,[41] would not be appreciably affected. The withdrawal of water from the tissues seems to do no harm, probably because of the large supply available; and the loss that does occur can easily and should be made good by the administration of water by mouth, by rectum, and hypodermically.

But even if our views with regard to the cause of the circulatory dis-

turbance of shock should not withstand the test of time, and even if the theoretical reasons for using glucose or gum acacia should prove wrong, there would still remain the empirical tests which show definitely that the gum-glucose solution saves a certain number of animals from death by trauma. The results obtained through the use of the solution in the treatment of shock-like states in man, and after hemorrhage, are not so easily interpreted as are those of the animal experiments. But they show conclusively that the solution is innocuous and they are strongly suggestive, to say the least, of beneficial action.

We here desire to express our thanks to the surgical staffs of the Barnes Hospital and the St. Louis City Hospital, and especially to Dr. Ernest Sachs, Associate Surgeon, acting in charge of the surgical service of the former, and Dr. Ellis Fischer, Associate Surgeon in the Washington University Unit of the latter, who have made this investigation possible by keeping us informed with regard to, and by placing at our disposal, the clinical material suited to our purposes.

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