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The Pathogenesis and treatment of shock associated with myocardial infarction

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THE PATHOGENESIS AND TREATMENT OF SHOCK ASSOCIATED WITH MYOCARDIAL INFARCTION

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The progress made in recent years in the management of myocardial infarction has been in the treatment of arrythmias and congestive failure, in the accuracy of diagnosis, and in the prevention of thrombo-embolic complications. The treatment of shock accompanying myocardial infarction has been highly controversial. An important cause of death within the first 24 to 48 hours after coronary occlusion is profound hypotension and the development of shock. This state occurs in approximately 10% of all cases of myocardial infarction, and is associated with a mortality of 26 to 93% depending upon the severity of the shock. (1,2) Since the total mortality rate following acute myocardial infarction is 20% (1), the shock state occurs in 40 to 45% of those who die.

During the acute stage of myocardial infarction, transient moderate hypotension is frequent and is usually considered salutary. However, if the blood pressure falls to a critical level for a sufficient time, the clinical picture of shock supervenes, and the prognosis becomes grave. The shock picture is considered to exist when the systolic blood pressure falls abruptly and remains below an arbitrary level of 80 to 90 mm Hg., for at least one hour. (1) In previously hypertensive patients, shock may occur at a higher pressure (100 mm Hg.). During this time classic signs of circulatory collapse appear, viz., rapid pulse (sinus tachycardia), small pulse pressure, poor heart

sounds, gallop rhythm, pallid cyanosis, faintness, weakness, cold moist skin, and stupor or coma. (3) Often there is clear-cut evidence of both shock and congestive failure, even though many cases give the clinical evidence of shock alone. Since the clinical findings in cases of shock associated with myocardial infarction are identical with those of traumatic shock, many clinicians have become accustomed to thinking of both having a common cause. The therapuetic approach to this grave manifestation of infarction is necessarily guided by the correct understanding of its mechanism.

At the onset it should be emphasized that, save for the neurogenic component, none of the currently popular theories of traumatic shock can reasonably be applied to shock in myocardial infarction. Loss of enough fluid into the small area of infarction seems unlikely. The liberation of a histamine-like substance in sufficient quantity from the small area of infarction to produce paralysis of the capillary bed is also unlikely. The search for a toxic substance liberated from the area of infarction also has never been successful. (3) Green (4) found that the lethal dose of crude muscle extract required to produce clinical shock was equivalent to about one-fifth of the body weight of muscle. He also pointed out that the bulk of muscle that must be submitted to trauma or asphyxiation in order to produce severe shock in man and animals must be very

large. Furthermore, such explanations leave unaccounted for the fact that the size of the infarct at post-mortem cannot be adequately correlated with the degree of shock produced. As in traumatic shock, there is a slight decrease in the circulating blood volume. Freis et al (5) found, by use of the Hamilton Dye method of measuring blood volume, that there was a slight decrease in the volume, and that thiscould be explained on the basis of sweating, nausea, and pulmonary edema. Stead and Ebert (6), by studying the concentrations of serum and plasma proteins, concluded that the loss of volume was on the basis of loss of water alone.

Freis et al (5) found, by the use of ballistographic methods, that the cases of cardiogenic shock showed a decrease in cardiac output. The degree of shock was correlated with the decrease of stroke volume; e.g., those with only mild shock symptoms showed only a slight lowering of the blood pressure. The drop in pressure immediately results in the activation of neurogenic reflexes and possibly other compensatory mechanisms which produce an increase in total peripheral resistance and tachycardia. Thus, the hemodynamic response is not unlike the compensated phase of hypovolemic shock except that the disturbance is due to ineffectual contraction of the myocardium rather than blood loss.

The hemodynamic alterations accompanying myocardial

infarction may be explained by the fact that the ventrical may balloon out rather than contract during systole. In some animals, this phase is compensated by increased contractibility of the fibers but in some this is not adequate and the pressure falls progressively and the ventricles, atria, pulmonary vessels and veins fill with blood.

Along with these phenomena there is an increased venous pressure. This can be explained by inability of the myocardium to move the pool of blood. Another factor which seems to play an important part in elevation of venous pressure is the reflex vasoconstriction. This and the concomitant constriction of the skin resevoirs tends to increase the volume of blood flowing to the already "overtaxed" ventricle. Elevations of venous pressure may be obtained experimentaly in normal individuals by use of angiotonis or norepinephrine, thus it seems that the increased venous pressure may be due at least in part to the vasoconstriction. (7)

These combinations of "forward failure" and the reflex vaso-spasm tend to give the syndrome of shock and congestive heart failure. This has been shown very adeptly by McMichael (8) who states "The two factors determining arterial blood pressure levels (B.P.) are cardiac output (C.O.) and the total peripheral resistance (T.P.R.). Their relationship may be expressed by the proportional formula: B.P. is proportional to T.P.R. times C.O."

Orias (9) studied the dynamic changes in the ventricles following experimental coronary occlusion in dogs and offered a reasonable and probably important approach. He states that there are probably three different types of response to acute coronary occlusion. In a few animals, the aortic and left-ventricular pressures fell progressively with evidence of cardiac dilitation and failure. In another group of animals, there was an immediate fall in the aortic and ventricular pressures, followed quickly by recovery of the cardiodynamics to pre-ligation levels. A small group of animals showed no fall in pressures. Orias interpreted these responses as indicating that deletion of a portion of the ventricular muscle immediately resulted in a hypodynamic beat and consequent dilitation of the heart. If the non-ischemic muscles were unable to respond according to Starling's law, with increased vigor of contraction, progressive drop in blood pressure and heart failure occured. This may well explain why a fall in blood pressure is not a striking feature of experimental coronary occlusion, for in the majority of such experiments the blood supply and the cardiac reserve of the uninfarcted region were essentially normal. Unfortunately this is not obtained in patients with chronic hypertension and a limited reserve. Thus hope of compensation of a heart subject to depletion of a large portion of its muscle mass is slim.

Even if Orias's concepts are correct, it is still conceivable

that peripheral mechanisms play a contributory role. Two possiblities present themselves. (1) Primary or neurogenic shock may occur at the onset of the attack, and the resultant fall in blood pressure may so diminish blood flow to the occluded coronary arteries as to depress the uninfarcted muscle, thus preventing its normal compensatory response. The result would be a progressive hypodynamic action of the heart and shock persisting beyond the usual duration of primary shock. (2) The other possibility is concerned with whether true peripheral shock may not ultimately occur following a prolonged period of capillary anoxia secondary to cardiogenic shock. Against this is the fact that the state of shock induced by prolonged anoxia is largely an irreversible process and that recovery is rare. This is not true in cardiogenic shock, as recovery may occur even if shock has persisted for several hours to days. (10)

Since coronary blood flow is dependent upon the head of aortic pressureand the cardiac output, it seems logical that low aortic pressure would tend to further embarrass the already ischemic myocardium and even cause more extensive infarction. Secondarily, the cerebral ischemia associated with low aortic pressure may of itself operate to intensify the shock state by depression of the vital centers. (10)

Despite the universally grave prognosis of shock accompanying myocardial infarction, specific therapy remains ill-defined.

In fact, antishock therapy has even been discouraged by some, on the basis that low blood pressure relieves the work for the heart. This may be true in mild hypotension without signs of shock: however, prolonged severe hypotension with failure of perfusion of vital organs results in an irreversible state of shock. (3)

All measures designed to combat shock in myocardial infarction should be directed toward supporting the uninfarcted muscle. The objective of therapy is to restore the effective head of blood pressure in the aorta so as to enable the perfusion of coronary, cerebral, renal, hepatic, and other vital circulations. As far as the heart is concerned, elevation of the blood pressure (to 100 mm systolic in patients who were previously normotensive, and 120 mm in those previously hypertensive) improves the total coronary circulation, enhances the chances of survival of borderline myocardium and that supplied by stenotic arteries, and may decrease the size of the infarct. In many patients, the area of ischemic myocardium is relatively so large that death is inevitable regardless of the treatment. Similarly, there are some with moderate hypotension who recover without specific medication. Between these two extremes, there are many patients in whom the treatment of shock may be lifesaving. (10,3,12)

Specific therapy includes the use of digitalis glycosides, transfusion, venesection, vasopressors, and a combination of

vasopressors and digitalis.

If one accepts shock in myocardial infarction as a manifestation of heart failure, the use of digitalis and other cardiac glycosides must come in for very serious consideration. In general the use of digitalis has been avoided during the acute phase for the following reasons: first, it decreases cardiac output in patients without heart failure and it has been thought that this effect may aggravate the shock, second, the use of digitalis has been objected to on the ground that stimulation of the heart may increase the danger of cardiac rupture, and finally, the objection has been raised that digitalis increases ventricular irritablity and increases the likelihood of fatal fibrillation. Since the evidence favors the presence of congestive failure in some patients with myocardial infarction even though they may show predominant signs of shock, the first objection is insignificant and may be disregarded. (1) Since ventricular rupture is most likely to occur from the fourth to the seventh day after infarction and the shock picture is present during the first day or two, this second objection is probably overrated. (3) Although the last objection may be valid, it should be recalled that such ventricular irritability is usually attributed to excessive amounts of digitalis. It has not been demostrated that cardiac infarction sensitized the heart to therapeutic amounts of the drug. It has been shown that in the experimental animal, digitalis does not significantly alter the fibrillation threshold of the ventricles. (13) It has

also been demonstrated that the spontaneous ventricular fibrillation that occurs with toxic amounts of digitalis differs in several particulars from that which occurs with coronary occlusion. (13,14) Although myocardial ischemia lowers the fibrillation threshold, it has not been shown that this increases the tendency of digitalis to produce fibrillation. Indeed there is considerable evidence that this is not true. (10)

In 1925, Gold (15) found that the lethal dose of ouabain for cats subjected to coronary artery legation did not differ from that of normal animals. This study extended over a period of 24 hours following ligation. More recently, these findings were confirmed by Bellet, Johnston and Schecter (16) but the latter authors extended the period of observation and found that four days following ligation the tolerance to digitalis diminished by 23% of normal. Still later, Travell, Gold, and Modell (17) reported that the tolerance of cats to digitalis three weeks after ligation of the coronary vessels was diminished by 25%. Since shock in cardiac infarction is an early manifestation, it appears from these experiments that no great fear need be felt in the use of digitalis. (10) It must also be emphasized that in these experiments, lethal amounts of digitalis were used and no information concerning therapuetic amounts of the drug has been forthcoming. Therefore, it seems that there is little support to the belief that the use of digitalis in therapuetic amounts is

attended by any hazards in the cases of experimental coronary occlusion.

Certainly digitalis has been used in many patients with acute myocardial infarction accompanied by congestive heart failure. The number of sudden deaths in such patients is probably no larger than might be expected in a similar group not recieving digitalis. (10)

In view of the fact that the clinical picture of shock associated with myocardial infarction is similar to hypovolemic shock, many clinicians have in the past attempted to correct the underlying disturbance. As a whole, these men were disappointed with their results. If we are correct in assuming that the shock is one of decreased cardiac output, it seems very reasonable that any increase in the venous volume would aggravate the condition. "Such measures as the use of intravenous fluids or blood are not only uncalled for but are, of course, contraindicated". (10)

Silber, Levin, Becker and Levy (2) have been using an intra-arterial transfusion of whole blood. This group is using an apparatus which enables them to bubble oxygen through the blood before administrating it. The radial artery is cannulated so that the infusion is toward the heart and the pressure from the oxygen tank is used to supply the head of pressure to overcome the arterial pressure of the patient. It was the original intent to limit the total amount of blood administered to 250 to 300 cc, the theoretical capacity of the arterial tree. (2)

However, in practice it was usually necessary to employ considerably more blood in order to obtain the desired clinical response.

In every case, despite a decreased sensorium, the procedure provoked severe pain along the course of the vessels of the arm. This was particularly true immediately after the transfusion started. Spasm of the collapsed vessel in response to sudden distention by the blood infused under pressure is apparently the mechanism for the pathogenisis of the pain. Liberal infiltration with 1% procaine solution at the infusion sight was ineffective and the use of morphine was necessary.

In six of the nine cases upon who this method was used, the blood pressure was 9 immediatley prior to the transfusion. In the remaining cases the systolic pressure was 95 mm Hg. or less. A significant initial restoration of blood pressure in the eight of the nine was induced by 125 to 400 cc of blood administered in 10 to 20 minutes. Results are hard to evaluate since this method was used as a last resort when it was obvious that the patient would die. In some of the cases in whom there was no response, it was the impression of the staff that he was moribund before the transfusion was started. As a result, it is the impression of the authors that had the system been used at an earlier time, the results might have been better. Several of the patients upon whom this was used died at a later date (48-128 hours) after making a satisfactory response.

Advantages of intra-arterial transfusion according to the authors are: (1) Only a relatively small amount of blood is required to restore the blood pressure and a normal circulating blood volume. A much larger amount is required intravenously and would of course be contraindicated. Even in the presence of pulmonary edema, the authors found that intra-arterial infusion appears to have no deleterious effect. When shock following recent infarction is accompanied by venous engorgement, the procedure of choice is the removal of 200 to 300 cc of blood from a vein and following this by arterialization and the rapid introduction into the artery. It was the authors experience that failure of intra-arterial transfusion to cause a sustained elevation of blood pressure was an ominous sign indicative of irreversible shock due to peripheral vasodilatation. (2) Intra-arterial transfusion, by its improvement of coronary flow, tends to relieve hypoxia and to restore the normal contractile power to that portion of the myocardium that has not been infarcted. (3) Intra-arterial transfusion results in prompt stimulation of the respiratory center, as indicated by prompt improvement in respiration and sensorium. (4) Finally, intra-arterial transfusion results in a rapid return of kidney function by re-establishing adequate filtration pressure. (2)

There is good evidence to indicate that blood introduced into the radial artery reaches the arch of the aorta, the coronary arteries, and the cerebral circulation. Jones and his collegues (12) demonstrated by a series of arteriograms in dogs that

that when iodopyracetate concentrated solution (Diodrast) was injected into the femoral artery at levels less than 50 mm. Hg., all the arteries arising from the aortic arch were visualized, including the coronary and cerebral circulations. In experiments with exsanguinated dogs they were able to demonstrate a respiratory arrest. This was attributed to the perfusion of the respiratory centers.

Of greatest controversy in the field of therapy of shock associated with myocardial infarction is the use of some of the new vasopressor substances.

A few physicians have used epinephrine unhesitatingly in shock associated with myocardial infarction. Some have been goaded into its use by the necessity of some desperate circumstances. Several objections have been raised to its use. It has been thought to be contraindicated in any type of shock because of arteriolar constriction is already present, and if epinephrine does succeed in producing further constriction it will only serve to increase capillary anoxia and thus aggravate the shock. This may apply to traumatic shock, but is probably insignificant in the type of shock under consideration. (10) Another objection to the use of epinephrine has been its tendency to increase both the general and the cardiac metabolism. This effect is out of proportion to the increase in blood flow to the coronary arteries as a result of an increase in aortic pressure; in fact after the use of epinephrine, Green. Wegria

and Boyer (4) have found it to produce angina in supposedly normal individuals.

As of date, there are several sympathetic amines available. The ones which have been recommended by the manufacturer for the treatment of shock associated with myocardial infarction are, l-arterinol (Levophed), phenylephrine (Neo-synephrine), hydrochloride, N-methyphenyl-tertiary-butylamine (Wyamine), and desoxyphedrine. All that have been used show a clinical response manifested by an increase in arterial pressure. All of the synthetic amines have decreased or absent effects of the myocardial irritability, and also have no effect on the heart rate. Some have the added advantage of being used intramuscularly as well as intravenously. Thus, they would seem to be useful in the treatment of shock associated with myocardial infarction.

Ideally the substances should elevate the blood pressure, increase peripheral resistance, and increase coronary blood flow without decreasing the cardiac output or causing arrythmias or other serious side effects. (3) Miller and Baker (18) have shown that there was no change of the prevailing cardiac rhythm, the state of congestive failure, or the subjective status of the patient by the use of one of these pressor amines. Two of their patients manifested auricular fibrillation and auricular flutter, respectively, and showed no change in the rhythm with pressor therapy. These authors would advise that the therapy be continued until the patient's general status has shown a definite improvement

and that the infusion should be slowed gradually.

Miller and Baker (18) suggest that the use of pressor substances may be used along with intra-arterial transfusions. The transfusion would serve to fill the arterial tree and the pressor substance to induce, enhance, and/or maintain the peripheral vasoconstriction necessary to sustain an adequate blood pressure.

Fink, d'Angio, and Bildon (19) have also done some experimental work with pressor amines. They conclude that the use of these substances is contraindicated when the venous pressure can be observed throughout the treatment period. They maintain an entry into a forearm vein by means of a slow infusion consisting of 5% dextrose in distilled water to which heparin has been added. A three way adaptor was incorporated at the needle hub. By attaching a capillary manometer at this point and filling it from the infusion reservoir, frequent venous pressure readings were readily obtained. The point of reference was the manubrium sterni. Whenever desired the manometer was detached for the introduction of intravenous medication. The infusion rate was regulated to about 60 cc per hour. The total quantity of fluid administered thus was small and not considered to affect the readings significantly. Those patients with normal or low venous pressure were treated with a vasopressor whereas those with an elevated venous pressure were treated

with a rapid acting cardiac glycoside. In some cases there was an elevation in the venous pressure following the administration of the pressor substance. In these cases the digitalis preparation was used simultaneously. (19)

SUMMARY

The entity of shock following acute myocardial infarction is a problem of major importance to all clinicians. The pathogenesis has not been definitely established. It has been postulated that after infarction, the myocardium balloons out with each systole resulting in a hypodynamic beat. This results in a drop in aortic pressure which in turn causes the activation of the neurogenic reflex and possibly other compensatory mechanisms which cause tachycardia and possibly an increase in the total peripheral resistance. Thus, the hemodynamic response is not unlike that of a compensated phase of hypovolemic shock except that the disturbance is due to ineffectual contraction of the myocardium rather than blood loss.

Other secondary factors may then come into play as a result of the low aortic blood pressure. Coronary blood flow which is dependent upon aortic pressure decreases, thus further depressing the already embarrassed myocardium. Cerebral blood flow is also decreased leading to anoxia and depression of the vital centers thus intensifying the shock state. Renal blood flow and pressure is decreased leading to a decrease in the filtration rate.

The clinical picture may present itself in one of two ways. In one type, the picture is one of frank shock, characterized by rapid pulse, small pulse pressure, poor heart sounds, pallid cyanosis, faintness, weakness, cold moist skin, stupor and coma. In the second type, the same signs may be present but superimposed upon them are the classic signs of congestive heart failure. The elevation of venous pressure may be explained on the basis of engorgement of the ventricles, atria, pulmonary and systemic veins as a result of the inability of the myocardium to move the pool of blood, plus the reflex constriction of skin reservoirs which may in itself cause an elevation of venous pressure

Whether signs of clinical shock alone or shock plus congestive failure will occur cannot be predicted in any patient, nor has it been explained as to why one occurs in some patients and not in another.

It is evident that this is a grave situation requiring active therapy to restore the physiology to normal.

Despite the universally grave prognosis of shock accompanying myocardial infarction, specific therapy remains ill-defined. In fact, anti-shock therapy has even been discouraged by some, on the basis that low blood pressure relieves the work of the heart. This may be true in mild hypotension without signs of shock; however, prolonged severe hypotension with failure of perfusion of the vital organs results in an irreversible state of shock.

All measures designed to combat shock in myocardial infarction should be directed toward supporting the uninfarcted muscle. The objective of therapy is to restore the effective head of blood pressure in the aorta to perfuse the coronary, cerebral, renal, hepatic, and other vital organs. As far as the heart is concerned, elevation of the blood pressure (to 100 mm systolic in patients who were previously normotensive, and 120 mm in those previously hypertensive) improves the total coronary circulation, enhances the chances of survival of borderline myocardium and that supplied by stenotic arteries. In many patients, the area of ischemic myocardium is relatively so large that death is inevitable regardless of treatment. Similarly, there are some with moderate hypotension who recover without specific medication. Between these two extremes, there are many patients in whom the treatment of shock may be lifesaving.

At the onset, it should be pointed out that the regular treatment of hypovolemic shock is contraindicated in the treatment of cardiogenic shock in that any intra-venous infusion increases the venous pressure and the work load on the already overloaded myocardium.

All investigators advocate generally accepted methods of treating myocardial infarction such as oxygen, analgesics, bed rest, anti-coagulants, and other supportive measures. It is also the popular consensus of opinion that a short acting digitalis

preparation be used if the venous pressure is elevated significantly either before or during any active treatment of the shock picture. For many years, the use of digitalis in myocardial infarction has been contraindicated because of the hazard of causing rupture of the myocardium or else ventricular fibrillation. Current investigation shows that digitalis preparations may be used in therapeutic doses in the treatment of the acute phase of cardiogenic shock without fear.

One of the current methods of treating the shock picture itself is the use of intra-arterial transfusions. It is felt by the proponents of this method that it is both physiological and safe. It acts to elevate the arterial pressure directly by infusion of small quantities of whole blood, which has been "arterialized" by bubbling oxygen through it, directly into the radial artery. This method has been shown to increase the blood flow to the vital centers by direct elevation of aortic pressure. This method is advantageous in that small quantities of blood are effective and very little if any extra burden is placed on the already overloaded venous system. Therefore, this method may be used along with a digitalis preparation in the presence of congestive failure and/or pulmonary edema.

One of the most recent methods of treatment of cardiogenic shock has been the use of pressor amines. The validity of these in the treatment of cardiogenic shock has not yet been proved.

It is known that these drugs cause a constriction of the vascular bed, thus elevating the aortic pressure. Since it is not known whether or not the peripheral vascular bed is constricted in cardiogenic shock, the use of this drug has been empirical. There have been some good reports in the use of this drug in this type of condition.

In all of the methods which have been advocated for use by clinicians in the experimental field, the results are difficult to evaluate since the new methods of treatment are used as a last resort and many of the patients have been moribund. As a result the effectiveness of any of the methods is impossible to evaluate at this time. Proponents of the various methods are trying to begin the treatment as soon as signs of shock are evident, consequently more significant material will probably be forthcoming.

CONCLUSIONS

I. It is important to start active therapy as soon as evidence of shock is present.

II. Venous pressure should be taken and if elevated a short acting digitalis preparation, such as Digitoxin, should be administered.

III. If this fails to elevate systemic blood pressure, one of two courses may be taken:

1. Intra-arterial transfusion, which according to present concepts is most physiological.
2. Empirical use of a pressor amine.

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