THE SHOCK SYNDROME AND THE THERAPEUTIC USE OF BALANCED SALT SOLUTIONS*

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The oldest surgical procedures are those for the treatment of trauma, and it seems that this branch of surgery will always remain an essential part of the practice of medicine. It is perhaps in parasurgical activities that the special knowledge of the anaesthetist can contribute most to the steady improvement in results. The most obvious problem is that of pre-operative fluid and blood replacement, the more so because during operation the anaesthetist's own problems are so much aggravated by an inadequate blood volume.

Most of the advances in the understanding and treatment of shock have taken place during the past 25 years. During this period specific physiological, biochemical and biophysical alterations in shock have been studied by leaders in these basic disciplines. As more investigators have taken an interest in shock, and with the concurrent development of new drugs and more refined measuring techniques for the study of cardiovascular haemodynamics, much useful information has accumulated.

The purpose of this paper is to define shock and to elaborate on the progression of the shock syndrome. Parameters to be measured in the management of a shocked patient will be discussed and the role of balanced salt solutions in the treatment of haemorrhagic shock will be considered.

PATHOPHYSIOLOGY OF SHOCK

Shock is an abnormal clinical state arising when the cardiac output is insufficient to fill the arterial tree with blood under sufficient pressure to provide organs and tissues with an adequate blood flow.[24] Shock appears to be invariably related to inadequate tissue perfusion; this low-flow state in vital organs is the final common denominator in all forms of shock.

While survival of a patient in shock is dependent upon excellent medical and surgical care directed at the clinical diagnosis, prompt therapy of the shocked state based on the haemodynamic diagnosis may be life-saving. A wide variety of clinical ailments at times are associated with shock, and establishing a clinical diagnosis does not ascertain the haemodynamic cause.

In the haemodynamic diagnosis of shock, 3 abnormalities are possible:[16]

1. Peripheral vascular failure.
2. Blood volume abnormality.
3. Cardiac failure.

It is the understanding and appreciation of the pathophysiological mechanisms in shock that has provided a rational basis for treatment. Above all, it must be realized that what might start due to, for example, a volume deficit, may progress to cardiac failure and finally an abnormal vascular tree may complete the circle of causative factors.

The Progression of the Shock Syndrome

A pathological vascular tree. The normal regulatory mechanism for the circulation[2] is geared to cope with varieties of a minor nature. Adrenergic responses regulate blood pressure, blood distribution, venous capacity and the force and rate of cardiac contraction. Supplementing this primary sympathetic effect is a secondary release of adrenaline and noradrenaline from the adrenal medulla and paraganglia. Major loss of volume or pumping ability tends to render this normal regulatory mechanism inadequate.

There is increasing evidence that the adrenergic response and exogenous reinforcement with amines may be entirely inappropriate in shock. The price paid for the adrenergic maintenance of blood pressure is prolonged reduction of visceral microcirculatory perfusion, with its sequelae.

Measurement of individual organ blood flow during shock shows that the splanchnic organs suffer a profound decrease of arterial and portal venous blood flow. This decrease is proportionately greater than the decrease in carotid or coronary blood flow, emphasizing the sensitivity of the splanchnic circulation to adrenergic vasomotor activity and the priority of blood flow to the brain and the heart. As the hypotension progresses, the ischaemic visceral tissues become congested in appearance and reach a state of stagnant anoxia. Although the target organ in which the change is most marked varies among various species of mammals, all show some capillary engorgement and stasis in visceral organs. Man shows most stagnant anoxia in the lungs, kidneys and bowels.

The formation of metabolic acidosis is a further result of shock. Under normal conditions of oxygenation, glucose is broken down to carbon dioxide and water in order to provide sufficient energy for cell metabolism. When insufficient oxygen is available at the cellular level due to excessive vasoconstriction, the oxygen-sensitive enzymes of the tricarboxylic cycle are paralysed. The metabolic fate of pyruvic acid is temporarily altered and lactic acid forms. Accumulation of lactic acid accounts, in part, for the progressive acidosis in the shocked state.

Metabolic acidosis may lead to the following problems:

1. There is a decrease of effective circulating volume since acidosis causes relaxation of precapillary sphincters with pooling and engorgement of the capillaries.
2. There is a reduction of myocardial contractility and the facilitation of arrhythmias.[4]
3. Hyperkalaemia may occur.[4]
4. Hypercoagulability of capillary blood may occur.[11]
5. The response to adrenaline, noradrenaline, isoprenaline, hydrocortisone and calcium is decreased.[4,18]

Weil[27] and others suggest that intestinal bacteria play a major role in the lethal outcome of prolonged reduction in visceral perfusion. The toxic factor, however, is not restricted to bacterial toxins and metabolites; acidosis and hypoxia lead to parenchymal cell destruction, with potentially lethal metabolic consequences. In regions of diminished blood flow, metabolites such as lactate, pyru-

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vate, ketones and tissue protein breakdown products accumulate and are slowly released into the general circulation. Electrolyte and water shifts are invariable with the leakage of potassium from the injured cells. Anoxic cells as well as those actually dead and undergoing autolysis seem to propagate injury from cell to cell by releasing lysosomal enzymes.

As the reduction of tissue blood flow is the lethal factor, the emphasis at this stage is on increasing tissue perfusion; if the abnormal states of tissue anoxia and acidosis are not corrected promptly, there is a rapid progression of the shock syndrome with blood volume deficits becoming grossly aggravated and the pumping function of the heart severely affected.

Volume Deficits

Lewis and Mellander[15] believe that in tissues affected by reduced perfusion with arteriolar vasoconstriction, the precapillary sphincters which control the opening and closing of the individual capillaries lose their tone as they are bathed by the metabolic products of glycolysis. As acidosis increases within the capillary bed, the precapillary sphincters lose their ability to respond to adrenergic neural and humoral stimulation and relax, allowing free ingress of blood into the dilated capillaries. The venules which control outflow from the capillary bed appear to constrict with adrenergic stimulation. The state of free inflow, obstructed outflow and capillary engorgement allows increased hydrostatic pressure within the capillary bed to produce transudation of fluid to the extracellular space, further depleting the effective circulating volume.

Rushmer[23] has shown that capillary beds of the body normally contain only 5 - 7% of the circulating blood volume, and that at any given moment only about one-third of the available capillaries are open, taking turns at being filled or emptied by local auto-regulatory processes. The filling of the other two-thirds of the capillaries during acidosis or ischaemic anoxia can account for a 10 - 15% loss of effective circulating volume.

Gelin[9] suggested that alterations in the stability of the suspensions of formed elements in the blood may lead to intravascular aggregation or sludging of blood cells. As blood flow decreases, viscosity rises, and hence the microcirculatory stagnation and slow blood flow in shock lead to increased blood viscosity. Hardaway[11] proposed that in areas of low microcirculatory flow, a transient clotting of blood in the capillaries with microthrombus formation may further intensify the stagnant anoxia of shock. However, attempts at treating this hypercoagulability in shock with heparin or fibrinolysins have not yet given proof of this theory.

It is recognized that the extracellular fluid volume is a major component of the body, comprising approximately 20% of body-weight. It is a large pool of water, electrolytes and metabolic components, and is a mobile and functional fluid which responds quickly to changes accompanying trauma or the manipulations of surgery. Furthermore, it is recognized that one-quarter of the extracellular fluid is normally in the intravascular compartment and three-quarters of the volume is extravascular.

Shires[25] has demonstrated that in haemorrhagic shock there are extracellular fluid deficits out of proportion to external blood losses. With radioactive isotope studies he has shown that a blood loss of 1,131 ml. from the intravascular compartment can be associated with a 4,414-ml. loss from the extravascular fluid. It is believed that the disparate extracellular fluid reduction is due to the following:

1. The shift of fluid from the extravascular to the intravascular compartment to replace external blood loss: a reduction of 1·5 - 2 litres of interstitial fluid may accompany a 30% loss of blood volume.[8]

2. A shift of fluid into the area of trauma: for example, in a bruise, fluid is lost from the intravascular to the extravascular compartment, but it is not functional. This fluid is sequestrated, cannot compensate for bleeding and leads to a decrease in functional extracellular fluid.

3. There is continuing fluid loss via the skin, lungs and urine.

4. Dillon[6] suggests that collagen fibres in the extracellular space may soak up or absorb fluid.

5. Shires[25] suggests that an intracellular fluid shift may contribute to decreased extracellular fluid volume.

Other workers[17] using radioactive isotope methods have not found the same degree of extracellular fluid deficits as reported by Shires. Nevertheless, there is general agreement that extracellular fluid deficits out of proportion to external blood losses occur in haemorrhagic shock.

Cardiac Failure

No one has clearly defined the relative contributions of central (cardiopulmonary) and peripheral circulatory disturbances to the production of shock. By custom the handling of the central mechanisms has usually been relegated to the cardiologist, while the peripheral ones have been left to the surgeon. As a result, there has grown up a dichotomy between cardiogenic and peripheral forms of shock which does not deserve perpetuation. Wiggers and Werle[28] were among the first to point out that progressive deterioration of the heart played a significant role in sustaining haemorrhagic shock. Guyton and Crowel[10] understood this evidence by demonstrating that dogs develop acute progressive left ventricular failure after shed blood is reinfused following a prolonged period of hypovolaemic hypotension. Regan[22] and others have demonstrated a progressive deterioration of myocardial contractility in dogs with haemorrhagic shock despite enterectomy which prevents development of lethal visceral microcirculatory changes.

Bloch and Lillehei[3] have shown pronounced left ventricular failure with deterioration of contractility in haemorrhagic, endotoxic and cardiogenic shock. The effects of hypoxia and metabolic acidosis are responsible, in part, for the production of cardiac failure.

The role of the heart in shock is just beginning to be critically examined, since it requires sophisticated and complex measuring techniques, but there is little doubt that cardiac deterioration is a sustaining mechanism in shock.

There are several salient features of the concept of shock. The major initiating and sustaining mechanisms are increased systemic peripheral resistance, decreased effective circulating volume, and decreased cardiac output, each of which feeds back either directly or through the

sympathetic nervous system, to perpetuate the shock cycle. The circulatory derangements are rarely attributable to dysfunction in a single circulatory component. Progressive deterioration of the pump or vascular integrity ensues in spite of compensatory efforts if the underlying aetiological factor is not removed.

This deterioration is hastened by changes in flow characteristics and the products of tissue ischaemia and hypoxia. The normal mechanisms to combat the deleterious effects of the hormonal and toxic products are depressed.

Unless these consequences of reduced tissue perfusion are energetically dealt with, the system is no longer capable of recovery and death occurs.

MONITORING IN HAEMORRHAGIC SHOCK

Patient-monitoring implies the continuous observation of physiological functions. Accurate indications of changes in a function can be of greater value than periodical measurements and can give an immediate warning if a significant change has taken place. However, monitoring instruments cannot replace sound clinical judgement. Their value lies in their ability to demonstrate quantitative changes which could not otherwise be adequately observed. In order to obtain the maximum value from such measurements, they must be integrated with other findings to produce an accurate and comprehensive clinical picture.

What Parameters Should be Monitored?

(i) *Clinical.* The appearance of the patient with manifestations of sweating, pallor, cyanosis and a cold clammy skin, together with other evidence of poor tissue perfusion, such as mental apathy, confusion and restlessness, must be noted.

(ii) *Pulse, arterial blood pressure and respiration.* The failure of these measurements to furnish more than the coarsest estimation of blood flow must be emphasized, and a sense of dissatisfaction is evident in the literature. Pulse and blood pressure readings within normal limits have been observed in the presence of recent blood loss of 35% of the blood volume. The heart rate in the elderly patient becomes relatively fixed and tachycardia is often lacking as a sign of shock.[20]

(iii) *Central venous pressure.* Central venous pressure monitoring is thought to be the most useful simple index available. In practice, it helps to answer the question: 'Does a hypotensive patient need more circulating volume expansion, and if so, how much?'[5]

Central venous pressure monitoring indicates the competence of the heart to accept or expel blood returned to it, that is, the relationship between the blood volume and cardiac competence. It is not a direct measure of blood volume. Central venous pressure measurements must always be correlated with other clinical data. For example, in cardiogenic shock where the breakdown of the circulation is due to impaired function of the heart, the central venous pressure may be low, normal or raised, the level depending on the presence of vasoconstriction, the duration of shock and the occurrence of congestive failure.

The venous pressure can be estimated by peripheral cannulation, but it is more accurate if the tip of the catheter is advanced, via an arm vein or the external jugular into a large vein in the chest. Pneumothorax and other complications make subclavian vein cannulation a poorer choice.

The procedure is greatly facilitated by using a commercially available disposable set (Fenwal HB12 set). The use of the 3-way stopcock on the set permits continuous administration of intravenous fluids and eliminates the need for heparin to keep the tubing patent.

The zero of the scale must correspond to a suitable reference point on the patient, and the most popular is the midaxillary line at the 4th intercostal space. Some investigators use the junction of the manubrium and sternum as the reference point. No readings should be accepted unless a respiratory fluctuation of the fluid column occurs.

Serial measurements will usually show a trend that is useful for assessing the haemodynamic abnormality. A low central venous pressure (0 - 5 cm. water) in a hypotensive patient suggests hypovolaemia or peripheral circulatory failure.[5] A high central venous pressure (above 15 cm. water) in a hypotensive patient suggests cardiac insufficiency.

When the central venous pressure is between 5 and 15 cm. water and the patient is hypotensive, the effects of trial infusion are important. A useful test is to administer fluid in 100-ml. increments every 5 minutes, measuring the venous pressure after each increment.[20] If the venous pressure does not rise more than 5 cm. water within 5 such trials and return to within 2 cm. of the original value, cardiac failure is unlikely.

If the central venous pressure remains low and the hypotension persists in spite of large volume replacement, peripheral circulatory failure is the likely diagnosis. In practice, when treating hypotension with volume replacement, a central venous pressure of 10 - 12 cm. of water will reflect an effective circulating volume.[7]

The concept of blood volume replacement of measured or estimated loss is no longer valid. Too much is known of fluid shifts in tissues and pooling in the microcirculatory bed to accept empirical data as a good guide to replacement therapy.

(iv) *Urinary output* below 30 ml./hour suggests inadequate renal tissue perfusion. Urinary output depends on proper renal blood flow, adequate blood volume of proper osmolality, and functioning renal parenchyma. Oliguria is an early warning and, if ignored, the kidney tubules may progress to an irreversible stage of pathological renal involvement.

(v) *Blood sampling* should be done before starting treatment. Arterial blood is ideally used for measurements of pH, PO_2, PCO_2, base excess, standard bicarbonate and buffer base. 'Arterialized' venous or capillary blood may be available, but the figure obtained must be interpreted with the knowledge that poor sampling technique may invalidate the results; the reason is that the blood sample might not be representative of tissue perfusion of the body as a whole, but might merely reflect the local tissue state, particularly when the sample is obtained while the patient is cold with superficial venous constriction.

Venous blood sampling will supply suitable material for basal levels of haemoglobin, haematocrit and electrolytes such as Na^+, K^+, Ca^+ and chloride.

While the arterial blood levels of lactate are elevated because of anaerobic metabolism in poor tissue perfusion states, Huckabee[13] has suggested that the lactate/pyruvate ratio, rather than the lactate level alone, is a more accurate index of inadequate tissue perfusion.

Less commonly employed methods, such as blood volume studies and cardiac output estimations, are beyond the scope of many hospitals.

(vi) *Temperature recordings* of the oesophagus and rectum may be useful. Correction of the acid-base estimation is necessary in the presence of hypothermia. Hypothermia *per se* might be the aetiological factor of the 'shock' state and might be an aggravating feature of a complex clinical problem. In the presence of hypothermia, massive blood transfusion of cold blood might precipitate ventricular fibrillation.

(vii) *Electrocardiography* as a monitor is widely accepted, but the appreciation of its value during shock is underrated. The onset of arrhythmia or S-T segment change is an excellent sign of insufficient perfusion when other causative factors are eliminated. Corrective measures, taken early, may prevent a refractory state.

THE ROLE OF BALANCED SALT SOLUTIONS IN THE TREATMENT OF HAEMORRHAGIC SHOCK

Several investigators have found that in the treatment of haemorrhagic shock, the use of balanced salt solutions and blood replacement gives better results than the use of blood alone.

A balanced salt solution contains the major electrolytes as present in the intravascular extracellular fluid, and in similar proportions. The latest balanced solution, Plasmalyte B (Baxter), differs from the older solutions such as Ringer's lactate in that the former contains 28 mEq./litre of bicarbonate, whereas the latter contains 28 mEq./litre of lactate ions. In the shocked state, the blood-bicarbonate levels are decreased and the lactate levels are raised, and therefore bicarbonate is preferred to lactate when treating haemorrhagic shock.

The aims of treatment with balanced salt solutions are to restore the effective circulating volume, i.e. the intravascular component of the extracellular fluid, and thus to establish adequate tissue perfusion; to restore the extravascular compartment of the extracellular fluid and thus to replace the deficit due to losses and shifts; and to combat the metabolic acidosis.

The experimental work of Wolfman *et al.* and Shires is of particular interest. Wolfman *et al.*[29] demonstrated that in the treatment of haemorrhagic shock in dogs, the administration of a balanced salt solution such as Ringer's lactate, followed by blood replacement, resulted in a higher survival rate than when treatment was limited to blood replacement alone. Treatment with blood resulted in an 80% mortality rate, whereas the use of a balanced salt solution and blood resulted in a 20% mortality rate.

In his animal studies Shires[25] found that, in the treatment of haemorrhagic shock, blood replacement or the use of plasma and blood restored the blood volume to normal, but extracellular fluid deficits were not corrected unless the treatment consisted of the administration of a balanced salt solution followed by blood replacement. He also found that the method of volume replacement affected the mortality rate of the treated dogs. The shocked dogs treated with blood replacement had a mortality rate of 80%, and those that received plasma and blood had a mortality rate of 70%, whereas the dogs that received a balanced salt solution followed by blood had a mortality rate of 30%. On rebleeding, the dogs that were treated with a balanced salt solution followed by blood replacement showed the lowest mortality.

In haemorrhagic shock in man, Shires demonstrated that extracellular deficits were out of proportion to external blood losses, a 1-litre blood loss being associated with a 4-litre deficit of functional extravascular extracellular fluid. After treating 1,200 cases of haemorrhagic shock, Shires recommended that treatment should start with a balanced salt solution and if the response is transient, as is evidenced by central venous pressure estimations, blood is given, together with further volumes of a balanced salt solution.

Thal and Wilson[26] reported that the rapid loss of more than 1 litre of blood is usually followed by severe clinical changes and that the use of a balanced salt solution will often bring about homeostasis, provided that bleeding has ceased. When bleeding is continuing, replacement with blood is mandatory. Even here, however, the combined use of a balanced salt solution and blood appears to have considerable merit. Thal and Wilson suggest that because of the narrowed calibre of the terminal vessels in shock and the tendency to red blood-cell aggregation, it is advantageous to reduce the viscosity of blood. Expansion of the plasma volume with solutions such as Ringer's lactate will accomplish this purpose by haemodilution; and in shock it appears advantageous to maintain a haematocrit level between 30% and 35%. Once the blood volume has been expanded to the point where there is adequate atrial filling pressure, the necessity for red blood-cell replacement can be judged by the haematocrit level.

With regard to blood replacement, Hardaway *et al.*[11] suggest that blood should be given only up to a normal red-cell mass. Volume replacement in excess of normal should be fluid other than blood, to allow for its easy removal from the circulation when shock is over. As a guide to effective volume replacement, they recommend that replacement therapy should raise the central venous pressure to the upper limits of normal.

The administration of a balanced salt solution can expand the intravascular and extravascular extracellular fluid spaces. The dispersal rate of an infused balanced salt solution out of the circulation is of interest. In the treatment of haemorrhage, Moore[19] found that with total infusion rates of approximately 8·33 ml./minute (2,000 ml. in 4 hours), the dispersal rate out of the circulation was about 5 ml./minute. The outward movement of fluid accelerated the shift of albumin into the circulation, and this may be one reason why balanced salt solutions can effectively replace intravascular deficits provided blood losses are not very severe. Moore has established that following haemorrhage, albumin in large amounts enters the circulation during the first 4 hours, when it may achieve rates of 40 G/hour. This early rapid phase involves the appearance of

preformed albumin from extravascular sites. The subsequent slow ingress of new albumin at a much slower rate suggests the appearance of albumin newly synthesized in the liver.

The administration of balanced salt solutions, with or without blood, is of importance in the treatment of the metabolic acidosis. While acidosis is treated by adequate volume replacement to improve tissue perfusion, it is advisable to give sodium bicarbonate for its rapid buffering effect. Sodium bicarbonate must be used promptly, because by improving tissue perfusion with fluids, acid metabolites are washed into the circulation and there may be a temporary aggravation of acidosis.

The administration of banked blood may also aggravate an existing acidosis. Howland and Schweizer[12] have reported that a unit of bank blood may contain 5 - 8 mEq. of acid and they advise that 44·6 mEq. of bicarbonate, i.e. about 90 ml. of 4·2% sodium bicarbonate, should be used with every 5 units of blood.

The Dosages of Balanced Salt Solutions

Shires's method is of particular interest because it is based on clinical experience with more than 2,000 patients.[24] He recommends that patients who are in a state of haemorrhagic shock should receive between 1,000 and 2,000 ml. of a balanced salt solution in a period of 45 minutes. If the blood loss is minimal and haemorrhage is not continuing, the haemorrhagic hypotension can be alleviated simply by the infusion of a balanced salt solution. Parameters of pulse rate, blood pressure and, above all, central venous pressure will indicate when an effective circulating volume has been established.

If the blood loss has been severe and haemorrhage is continuing, the elevation of blood pressure, decrease in pulse rate and elevation of central venous pressure which occur with rapid infusion of a balanced salt solution will usually be transient and blood replacement will be necessary. Particular emphasis must be placed on the necessity for warming all transfused blood.[1,21] At the same time, balanced salt solution therapy should continue. On reviewing their experiences, Jenkins *et al.*[14] recommend a volume equivalent to the volume of blood replaced, *plus* an additional 10 ml./kg. body-weight/hour if the resuscitative procedure extends for more than an hour.

The initial administration of a balanced salt solution acts as a very effective therapeutic trial to determine the pre-existing degree of blood loss, or the presence of continuing blood loss. If the response is a transient one, whole blood which has been accurately typed and cross-matched will have become available and can be given immediately. Consequently, the initial use of the balanced salt solutions allows typing and cross-matching, thus avoiding transfusion reactions which may occur with rapid administration of untyped or unmatched whole blood. Shires is of the opinion that the use of balanced salt solutions in this fashion significantly reduces the requirement for whole blood in the patient with haemorrhagic hypotension.

SUMMARY

The shock syndrome is a very complex problem and is invariably related to inadequate tissue perfusion. The assessment of the severity of shock and the response to treatment requires careful interpretation of clinical signs and symptoms assisted by monitoring procedures, particularly the frequent check of the central venous pressure.

Major disturbances in haemorrhagic shock are a decrease of effective circulating volume, a reduction of functional extracellular fluid and the development of metabolic acidosis.

Extensive experimental and clinical experience has demonstrated the value of balanced salt solutions in the treatment of haemorrhagic shock.

Replacement therapy starts with the infusion of 1 - 2 litres of a balanced salt solution in 45 minutes. If blood loss has been minimal and haemorrhage has ceased, blood replacement is unnecessary. If the response is transient, blood replacement is mandatory and the administration of a balanced salt solution is continued at a dose equivalent to the volume of blood replaced, plus an additional 10 ml./kg./hour if the resuscitative procedure extends for more than an hour.

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