MANAGEMENT OF HYPOVOLEMIC SHOCK*

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BEFORE shock can be treated, its underlying cause must be discovered. Hemorrhagic shock, common in trauma patients, requires prompt recognition and treatment to prevent complications and to reduce mortality from prolonged and inadequate tissue perfusion. Although losses of functional extracellular fluid associated with hemorrhagic shock may aggravate the condition, these losses are difficult to recognize and measure. This paper will attempt to present a clinical classification of shock, to review several cogent research studies, and to outline the therapeutic concepts of fluid management in patients with hemorrhagic shock due to injury.

CLINICAL CLASSIFICATION OF SHOCK

During the 1930s the late Dr. Alfred Blalock devised a physiologic classification of shock still considered an excellent clinical classification in our own era.[1] The four etiologic forms of shock that Dr. Blalock described are hematogenic (oligemic), neurogenic (primarily caused by nervous influences), vasogenic (initially decreased vascular resistance and increased vascular capacity), and cardiogenic, including failure of the heart as a pump and other unclassified categories (including diminished cardiac output from various causes). Using the four etiologies of shock described by Dr. Blalock, these can in turn be categorized in three functional groups, namely, cardiogenic shock, reduction in blood volume, and changes in resistance vessels.

Cardiogenic shock. Primary myocardial dysfunction resulting from either myocardial infarction, serious cardiac arrhythmias, or myocardial depression can cause the heart to fail as a pump. Other factors—including venous obstruction, such as occurs in the mediastinum with tension

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pneumothorax, vena caval obstruction, and cardiac tamponade—may also cause cardiogenic shock.

Reduction in blood volume. Losses of whole blood, plasma, or extravascular fluid—either alone or combined—reduce blood volume.

Changes in the resistance of vessels. Spinal anesthesia, pain-induced or other neurogenic reflexes, or, possibly, the end stages of hypovolemic shock may all change the resistance of blood vessels. Likewise, septic shock—whether from a change in peripheral arterial resistance, in venous capacitance, or in peripheral arteriovenous shunting—may modify vessel resistance.

A single common denominator underlies the pathophysiology of shock: low-flow state. Reduced organ flow probably also accounts for the biochemical aberrations that indicate anaerobic metabolism. Treatment of shock obviously revolves around the etiologic type or combination of etiologies present in a given patient.

Experimental Laboratory Research

Hypovolemic shock is the most common form of shock. Hypovolemic shock has been intensively studied both in clinical situations and in the laboratory. Most studies have used hypovolemic shock from hemorrhage as the model. A method was developed that permits simultaneous measurement of total red cell mass, total body plasma volume, and total extracellular fluid, using, respectively, ^{51}Cr-tagged red cells, ^{125}I-tagged human serum albumin, and ^{35}S-tagged sodium sulfate.[2] The isotopes are injected together intravenously, and, using appropriate energy-differentiating counting instruments, all three isotopes are determined following equilibration. Volumes are then determined by the dilution principle using multiple sampling.

In one early study, the three spaces were measured. Splenectomized dogs were then bled a sublethal, subshock amount of 10% of the measured blood volume for two hours, when the three spaces were remeasured. The measured loss of plasma and red cells, removed during the blood letting, could now be detected. Results indicated that the decrease in extracellular fluid volume was identical to that lost as plasma during the two-hour bleeding.[3]

Using the same model, the three spaces were measured before and after hemorrhage of 25% of the measured blood volume. Again, the bleeding was sublethal and produced hypotension. Results again confirmed that loss

of plasma and red cells can indeed be measured by the method used. Further, the functional extracellular fluid volume, measured by an early ^{13}S-tagged sodium sulfate space, decreased by 18% to 26% of the original volume. Because no external loss of ^{13}S-sulfate was measured, the reduction was presumed to mirror an internal redistribution of extracellular fluid.

External hemorrhaging of 35%, 45%, and even above 50% in subsequent studies always produced a similar reduction in functional extracellular fluid as long as the splenectomized dogs were in shock.

In later studies, irreversible hemorrhagic shock was induced in splenectomized dogs according to a modified method devised by Wiggers, using a reservoir.[4] When the shed blood was replaced in this group of dogs, blood pressure returned to near control levels, only to be followed by a blood-pressure drop within one to 16 hours, resulting in a standard 80% mortality.

After the three volumes were measured in another group of animals, investigators subjected the dogs to shock by the Wiggers method. The three spaces were then remeasured by reinjecting isotopes during the period of shock as well as after the shed blood had been replaced. The initial decrease in blood equaled the volume that had been removed. Concurrently, functional extracellular fluid exhibited a marked reduction. When the shed blood was returned, both plasma volume and red cell mass returned to essentially normal levels, but a deficit in functional extracellular fluid remained.

Even when the dogs were treated with shed blood to which 10 ml./kg. plasma was added, losses during shock were similar. Although the blood volume returned to normal after this treatment, functional extracellular fluid volume decreased.

Balanced salt solutions. Dogs treated with a balanced salt solution and shed blood—a combination that mimics extracellular fluid—showed return of functional extracellular fluid volume to control levels and return of blood volume to normal. Restoring the extracellular volume also affected survival rate. Only 20% of splenectomized dogs treated with shed blood alone survived more than 24 hours. When plasma was added to the shed blood, the survival rate increased to 30%. But, when therapy consisted of lactated Ringer's solution plus the shed blood, 70% of the treated dogs survived. Thus, restoring functional extracellular fluid volume reduced mortality from standard irreversible shock from 80% to 30%.

All these early studies were based on volume-distribution curves of

sulfate, which were measured for a maximum of one hour. At any point in the course of this curve a reduction in extracellular fluid (in the untreated state) will take place.

More recently, shock-volume distribution curves were followed for many hours.[5] These studies demonstrated that in true untreated hemorrhagic shock the early equilibratable extracellular fluid is reduced, as is the total extracellular fluid, or final diluted volume of radiosulfate, when compared to preshock volumes. Even when a less severe shock preparation is used, early equilibrating extracellular fluid or early available extracellular fluid remains reduced, whereas the total anatomic extracellular fluid may remain normal.

Other recent studies also demonstrate that if shock does not last long enough to reduce both functional and total extracellular fluid, then only the functional fluid may be reduced. Further, if therapy rapidly returns blood pressure to normal, a long sulfate equilibration curve may fail to reveal the acute reduction that had been corrected at an earlier stage. Therefore, the present status of sulfate as a measure of the functional extracellular fluid must be interpreted with caution. One must keep in mind that although early sulfate space measurement does reveal functional or available extracellular fluid, only prolonged measurement will reveal the total extravascular fluid values. It is also important to remember that when successful therapy has been instituted or when therapy has been completed, the total (or even the available) extracellular fluid reduction may not be measurable.

Although some plasma or transcapillary refilling occurs in response to hemorrhage or to hemorrhagic shock, this refilling is initially limited. Moreover, in severe hemorrhagic shock the reduced interstitial fluid cannot be explained by plasma or transcapillary refilling. Because there was no source for external loss, the question arose whether interstitial fluid might move into the cell mass in an isotonic fashion.

More recent studies of ion transport across the cell membrane have attempted to determine whether hemorrhagic shock might result in intracellular swelling in skeletal muscle.[6] Intracellular transmembrane potential recording has been performed with glass tip diameters of less than 1 micron, using a Ling-Gerard ultramicroelectrode. A modified electrode has recorded intracellular transmembrane potentials *in vivo* before, during, and after shock.[7]

In acute hemorrhagic shock skeletal muscle measurements demonstrate a

constant and sustained fall in the normally negative intracellular transmembrane potential.[8] This fall, which may represent reduced efficiency of the sodium pump caused by tissue hypoxia, is present only when shock produces hypotension. Additional studies in splenectomized dogs show that change in such variables as pH, P_{CO_2}, and bicarbonate do not influence the transmembrane potential in shock.[8] Even when progressive metabolic acidosis and its subsequent correction were studied the potential still followed the blood pressure and the shock state.[8]

Studies with ultramicroelectrode measurement of transmembrane potential combined with a direct skeletal muscle interstitial fluid aspiration, by modification of the technique of Hagberg, were also performed.[9,10] With this technique it was shown that as blood pressure fails and transmembrane potential is reduced, plasma potassium slowly rises during the shock period. However, during the same time, when interstitial fluid potassium was directly aspirated, a rise to above 15 mEq. per liter of interstitial fluid occurred. This study also explained where potassium, moving out of skeletal muscle cells, is being sequestered, as sodium chloride and water move into muscle cells.

Other studies also document essentially the same phenomenon in primates. These studies further reveal that the cellular membrane transport is a reversible phenomenon: that is, once the shock state is treated, the transmembrane potential recovers.[11] Concomitant muscle biopsies made during primate studies clearly document that muscle cells gain sodium, water, and chloride while losing potassium. Thus, these data reveal isotonic swelling of skeletal muscle cells in response to shock injury. Studies currently being conducted in humans demonstrate a similar response to shock injury. Reported investigations in primates reveal interesting corroborative changes in action potentials of single cells in skeletal muscles.[12] These studies show decreased resting membrane potential, decreased amplitude of action potential, and prolongation of both repolarization and depolarization time. At resuscitation only repolarization time was not reversed, and changes persisted for several days. These findings offer *in vitro* confirmation of altered intracellular sodium and potassium concentrations, as measured by skeletal muscle biopsy and resting membrane potential measurements.

These results confirm that the cellular membrane transport changes in response to hypovolemic shock and that these alterations can be reversed. However, it is still not known whether these transport changes come about

as a reduction in an electrogenic pump, as a change in sodium-potassium exchange, or as a change in cellular permeability. But current data suggest the likelihood of reduced efficiency of an electrogenic sodium pump.

With a reset membrane potential, extracellular fluid electrolyte concentrations are constant. Therefore, using the Nernst equation, intracellular Cl^- must rise from 3.5 to 10 mEq. and intracellular Na^+ must rise from 10 to 22 mEq. Or, using the previously cited measurements in hemorrhagic shock, intracellular Cl^- must rise from 3.9 to 11.1 mEq., while intracellular Na^+ must rise from 9.9 to 18.5 mEq. per liter. This equation allows a 10% isotonic swelling of muscle cells to account for the reduction in extracellular fluid measured in hemorrhagic shock. The involvement of cell masses other than muscle during the course of hemorrhagic shock is still being investigated.

Present data suggest that skeletal muscle cells may be a major site of fluid and electrolyte sequestration following severe, prolonged hemorrhagic shock. Adjunctive studies by Grossman suggest that hypovolemic shock triggers similar changes in the intracellular mass of neurons in the brain.[13] Further, an increase in the water content of both cellular and connective tissue components after hemorrhagic shock has been demonstrated by Slonim and Stahl.[14] Fulton has also suggested that some sodium and water may be sequestered in the connective tissue.[15]

Another study shows that severe hemorrhagic shock of significant duration is associated with elevated internal sodium concentration in red blood cells.[16] Both the severity and the duration of the shock appear to influence the magnitude of these changes, and this also correlates with changes seen in the clinical course of shock when sequential sampling procedures are performed.

Based on present knowledge, sustained hemorrhagic shock seems to trigger a measurable reduction in extravascular fluid, and the cellular response to hypovolemic hypotension demonstrates a consistent change in active transport of ions. Evidence obtained directly from living cells indicates that sodium and water enter muscle cells, with a resultant loss of cellular potassium into the extracellular fluid, and that the interstitial fluid holds the extruded potassium.

The Clinical Management of Shock

Definitive diagnosis. The management of shock depends on identifying its cause while supporting the stricken patient. Only after the causative

mechanisms are identified can an attempt be made to treat shock. Thus, one sees again the utility of a practical classification of shock, which is worth repeating: oligemic shock, cardiogenic shock, and neurogenic shock and septic shock (caused by changes in peripheral resistance and capacitance vessels). It is also worthwhile to bear in mind that a patient who has experienced major injury may have more than one type of shock. Once the diagnosis of shock has been made and supportive therapy begun, a diligent search for the etiologic factor or factors can be made.

Fluid losses. The management of shock is related to the specific type of shock present. The pathogenesis of hypovolemic hypotension is quite varied and can present treatment problems. Recognition of deficits of total body water and electrolytes is often subtle, and correction requires specific therapy with crystalloid solutions. Primary reductions in extracellular fluid volume—plasma and interstitial fluids—is more straightforward and thus more easily recognized. Specific therapy should be started with electrolyte solutions; infrequently, patients also need plasma or some other source of protein. External blood loss (e.g., from lacerations) should be corrected immediately: fluid therapy is begun with first-aid measures, including pressure tamponade, and surgical procedures may then be carried out. Similarly, internal blood loss (e.g., bleeding from a duodenal ulcer) should be treated with the usual measures, including decompression of the stomach, while supportive therapy is begun.

Patent airway. The other immediate concern besides controlling the injuries caused by the trauma itself is maintenance of a patent airway. Although pulmonary insufficiency rarely occurs from shock alone, concomitant problems may include crushing injuries to the chest, pneumothorax, hemothorax, or specific airway obstructions from injuries to the head and neck. In these cases adequate respiratory exchange must be promptly restored.

Volume Replacement

Whole blood replacement. Early replacement of whole blood—properly cross-matched and type-specific—is the primary therapy in patients with hermorrhagic shock. Type-specific or Rh-negative type O blood—the universal donor blood—with low anti-A titer can also be administered in the absence of properly cross-matched and type-specific whole blood.

Extracellular fluid replacement. As soon as hemorrhagic shock patients are admitted to the emergency room, a large-gauge needle or catheter is

inserted in an appropriate vein, usually in the arm, and an infusion of lactated Ringer's solution is promptly started. Blood for type and cross-matching can be drawn at the same time. The rate of infusion of the Ringer's solution should be extremely rapid: between 1,000 and 2,000 ml. in 45 minutes.

The fast infusion is an effective therapeutic trial to determine the preexisting or continuing degree of blood loss. In patients with marked hypotension, blood pressure often returns to normal, becomes stable, and remains so after an infusion of one to two liters of a balanced salt solution. When this response is correlated with measurements of red blood cell mass, plasma volume, and extracellular fluid volume, the degree of pre-existing blood loss proves to be relatively small. Thus, if blood loss is minimal and hemorrhaging stopped, infusing the balanced salt solution may alleviate hemorrhagic hypotension.

When blood loss has been severe or when the patient continues to hemorrhage, the elevated blood pressure and the decreased pulse rate that usually occur with rapid intravenous infusion of lactated Ringer's solution may be only transient. When this occurs, accurately typed and cross-matched whole blood—which should be available by this time—can be given immediately. In other words, the initial use of the lactated Ringer's solution allowed enough time for whole blood typing and cross-matching.

Initially infusing lactated Ringer's solution from the standpoint of both therapeutic trial and therapeutic adjunct proved effective in several thousands of patients. The isotonic solution does not portend serious side effects, nor is there danger of aggravating other fluid and electrolyte aberrations. Administering a balanced salt solution also reduces the requirement for whole blood in a patient with hemorrhagic hypotension, both in terms of proper hemoglobin and hematocrit concentrations and in terms of recovery from renal failure.

Some critics contend that lactated Ringer's solution may aggravate existing lactate acidosis. However, previous experiments and clinical studies do not support this view.[17-20] Experimentally, using whole blood plus the isotonic solution to treat hemorrhagic shock resulted in a more rapid return of lactate, excess lactate, and pH to normal than did the administration of shed blood alone.[21] In a group of 52 patients in hemorrhagic shock recently studied, serial determinations of lactate, excess lactate, pH, and base excess were obtained.[22] All 52 patients received lactated Ringer's solution in addition to whole blood during the period of

resuscitation. Lactate and excess lactate levels were significantly reduced, and pH and base excess values returned toward normal while the solution was infused during the period of shock. All values returned to normal rapidly after resuscitation.

The possible relation between the use of crystalloid solutions in hemorrhagic shock and the development of progressive pulmonary insufficiency has also been raised. But, in a recent study of 978 patients operated upon for injury, significant pulmonary dysfunction occurred in only 2.1% and "classic shock lung" in only 1.4%.[23] In this series, as well as in two separate studies conducted in Vietnam,[18,24] no positive correlation could be demonstrated between hemorrhagic shock and the development of pulmonary dysfunction. It is also interesting to note that the highest incidence of pulmonary dysfunction and/or "shock lung" was found in patients with sepsis, regardless of the presence or absence of shock.

The use of crystalloid solutions in several thousand patients in hemorrhagic shock has reduced the need for uncross-matched blood and the number of transfusion reactions. The reduced rate of transfusion reactions plus prompt correction of associated extracellular fluid volume deficits and restoration of blood flow has virtually eliminated the complication of oliguric renal failure in these shock patients. The use of local renal hypothermia during surgery of patients with hemorrhagic shock, as suggested by Baxter et al.,[25] has been of additional benefit in these individuals.

SUMMARY

Proper management of patients in shock depends on initially classifying the clinical type of shock present. Therapy then aims at reversing the shock process while the patient is fully supported. Although whole blood replacement remains the mainstay of managing hemorrhagic shock, the initial administration of lactated Ringer's solution has a positive therapeutic effect. Patients with endogenous or exogenous bacterial contamination require effective antimicrobial therapy as soon as they are stabilized.

In light of the marked reduction in the extravascular extracellular fluid as demonstrated in animals and in humans, alleviating functional extracellular fluid reductions is an important aspect of the management of hemorrhagic shock. This, however, neither ignores nor diminishes the importance of necessary blood-loss replacement, but makes management more complete.

Discussion

QUESTION: Dr. Shires, could you comment on the use of steroids in the treatment of shock?

DR. SHIRES: There is presently little argument that steroids have no role in the treatment of neurogenic, hypovolemic, or cardiogenic shock. The real controversy is whether steroids are indicated in the treatment of septic shock, and the answers are not yet known. In a patient with mild septic shock—the warm-septic shock with early phase-dilated peripheral flow—there is little doubt that steroids can be given along with other drugs. Sometimes there is a dramatic increase in blood pressure, but this form of septic shock usually responds to therapy without steroids in a few minutes.

The question then is whether steroids are of any real therapeutic benefit in low-flow sustained septic shock. The control studies in man simply do not demonstrate any such benefit. On the contrary, during the last three years some studies have demonstrated immunological deficits produced by prolonged administration of steroids and that sustained high doses may actually be detrimental. So the next question would be whether to give one high therapeutic dose of steroids in the early treatment of septic shock. Opinions around the country are equally divided. Personally, I think there is no dramatic effect that can be attributed to steroids. In our own studies of cell function in patients with septic shock given steroids, there is no question that the membrane potential will jump up to normal, but it remains normal for only 10 or 15 minutes and then decreases to where it was initially. The same can be said of vasopressor and vasodilator drugs: they produce temporary improvement in cell function, but with repeated administration, that response is lost. Therefore, I believe that the best that could be gained with the administration of steroids would be a short pharmacologic effect. Data by Schumer indicate that, as an across-the-board adjunct, steroids may perhaps be helpful, but this work is not based on prospective clinical studies and therefore is very hard to evaluate clinically.

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