Traumatic Shock: The Fifth Shock

Maighdlin W. Anderson, MSN, ACNP-BC, CCRN ■ Gregory A. Watson, MD, FACS

ABSTRACT

Although, historically, shock associated with traumatic injury has been evaluated through knowledge of the 4 recognized shock patterns—cardiogenic, obstructive, distributive, and hypovolemic—many trauma practitioners view traumatic shock as a unique fifth shock pattern. Although secondary to a systemic inflammatory response syndrome triggered by endogenous danger signals, traumatic shock represents a unique pathological condition that begins with multiple, usually blunt, trauma and may conclude with multiple organ dysfunction syndrome and death. While varying mechanisms of injury may lead to different presentations of shock and cardiovascular decompensation, a unifying theme of traumatic shock is an overwhelming inflammatory response driven by proinflammatory cytokines, and the downstream results of this cytokine storm including, but not limited to, acute respiratory distress syndrome, coagulopathy, sepsis, and multiple organ dysfunction syndrome. Treatment is primarily supportive; however, research into novel therapeutics for traumatic shock is ongoing and promises some direction for future care.

Key Words

MODS, SIRS, Traumatic shock

Simply stated, *shock* is defined as a state of inadequate oxygen delivery relative to the metabolic needs of the host. This may result from either a decrease in the amount of delivered components (red blood cells, hemoglobin, and oxygen) or from altered distribution of flow (depressed cardiac output and vasodilatory states). Left untreated, this can lead to widespread ischemia, and a systemic effort to compensate that often causes additional harm to the patient (Figure 1). The nature of the shock state stems directly from its etiology, and characteristic patterns of dysfunction and compensation may reveal the type of shock that is present.[2] Historically shock has been classified into 1 of the 4 types based primarily upon its etiology—obstructive, cardiogenic, hypovolemic, or distributive (Table 1).[2,3]

Author Affiliations: School of Nursing (Ms Anderson) and School of Medicine (Dr Watson), University of Pittsburgh, Pittsburgh, Pennsylvania.

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Correspondence: Maighdlin W. Anderson, MSN, ACNP-BC, CCRN, Department of Critical Care Medicine, University of Pittsburgh, 3550 Terrace St, Pittsburgh, PA 15261 (andersonmw@upmc.edu).

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SHOCK TYPES

Hypovolemic Shock

This is the most common type of shock present in trauma patients and is generally due to acute blood loss.[2]

Obstructive Shock

In this type of shock, there is a physical obstruction preventing blood from flowing into or out of the thoracic vasculature from or to the rest of the body. Classic causes in the trauma patient include tension pneumothorax and pericardial tamponade, while pulmonary embolus is the prototype in noninjured patients.[2]

Cardiogenic Shock

This may appear very similar to obstructive shock, but it is caused by mechanical cardiac dysfunction leading to an acute and significant decrease in cardiac output. The heart does not pump blood efficiently, leading to a decrease in the mean arterial pressure as blood pools in the precardiac spaces (right atrium and periphery).[2] Myocardial infarction and severe blunt cardiac injury are potential causes.

Distributive Shock

This type of shock state results from widespread vasodilatation and encompasses septic, anaphylactic, and neurogenic shock. Unlike the other types defined earlier, distributive shock does not present with decreased cardiac output and is commonly referred to as "warm shock," especially in the early stages before compensatory functions fail.[2] Spinal cord injury and sepsis are classic examples.

Common causes of shock in trauma patients are listed in Table 2. In most cases, patients in shock can be described by one of the classic syndromes discussed earlier. However, some trauma patients (particularly the multiply injured) will display components of more than one if not all of these syndromes. *Traumatic shock*, the "fifth shock," is increasingly recognized as a distinct syndrome with features overlapping many of the classic syndromes defined earlier.[3-12]

CASE PRESENTATION

Mr Doe, a 15-year-old white adolescent boy, presented to emergency department via air ambulance following an

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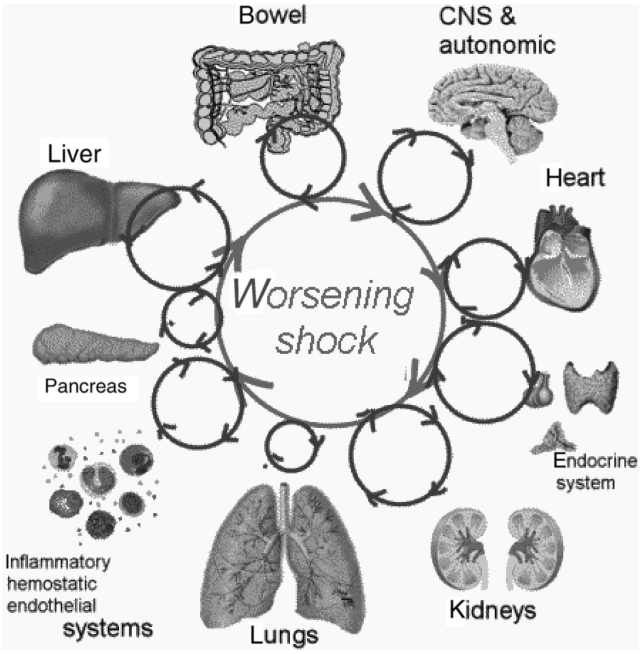

Figure 1. Compensatory mechanism in shock often leads to further organ hypoperfusion and ischemia. From Ref. 1. Used with permission from Striped Giraffe Press. CNS indicates central nervous system.

all-terrain vehicle collision with a coal truck. He had been intubated in the field. Initial hemodynamic instability was treated with fluids and uncrossmatched packed red blood cells. Bilateral chest tubes were inserted, and there was no large hemo-/pneumothorax. The Focused Assessment With Sonography for Trauma examination result was negative. Plain radiographs showed a right iliac wing and bilateral rami fractures as well as an open (grade IIIb) tibia fracture with no active bleeding. His hemodynamics normalized, and computed tomographic scans were performed. Injuries included a traumatic subarachnoid hemorrhage, multiple rib fractures, and a large pelvic hematoma with active contrast extravasation. He was placed in a pelvic binder and taken emergently to interventional angiography where a completely disrupted right hypogastric artery was identified and treated with coil and Gelfoam embolization. He later became hemodynamically unstable after being transferred to the intensive care unit (ICU) and was transfused with several units of packed red blood cells as well as fresh frozen plasma, platelets, and cryoprecipitate for a developing coagulopathy. Repeat angiography failed to identify additional hemorrhage. He subsequently suffered a cardiac arrest, and an emergent left anterolateral thoracotomy was performed, revealing only a small amount of blood in the left chest and no pericardial tamponade. After internal compressions and defibrillation, he regained a perfusing rhythm and was taken to the operating room. At laparotomy, 400 to 500 cc of blood was evacuated from the peritoneal cavity. A minor hepatic laceration was noted but was not actively bleeding. A large retroperitoneal hematoma was identified but did not appear to be significantly larger than on the initial computed tomographic scan. Mr Doe's abdomen was packed, and he was taken back to the ICU. Over the next 17 days, he remained severely ill, and despite intensive support, he died from multiple organ dysfunction syndrome (MODS).

BACKGROUND

What is striking about the clinical picture is the speed of onset and the apparent disconnect between clinical symptoms and root cause. A sharp drop in blood pressure may look exactly like acute hemorrhage, but diagnostics may show limited or no areas of bleeding. Systemic vasodilatation seems to signal the onset of sepsis, but no source of infection can be located, and the early onset following injury makes infection less likely. There is no single

TABLE 1 Nonunique Hemodynamic Pattern Associated With Traumatic Shock[a]

	Distributive	Traumatic	Hypovolemic	Cardiogenic	Obstructive
CO	↑↔	↑↓↔	↓	↓	↓
MAP	↓↔	↓↔	↓	↓	↓
CVP	↓↔	↓↔	↓	↓↑	↑↔
PA	↑	↑↓	↓	↑	↑
PAOP	↓↔	↔↓	↓	↑	↓↔↑
SVRI	↓	↓↑	↑	↑	↑
Warm/cold	Warm	**Cold/warm**	Cold	Cold	Cold
PP	↑	↑	↓	↓	↓

Abbreviations: CO, cardiac output; CVP, central venous pressure; MAP, mean arterial pressure; PA, pulmonary artery (pressure); PAOP, pulmonary artery occlusion pressure; PP, pulse pressure; SVRI, systemic vascular resistance index.

[a]Elements may mimic distributive and/or hypovolemic patterns during the evolution of the syndrome and depending on the primary etiology of the syndrome.

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TABLE 2 Causes of Shock in the Trauma Patient[a]

Cause	Pathophysiology
Lost airway or pulmonary injury	Inability of O_2 to reach the circulation
Tension pneumothorax	Diminished blood return to heart
Cardiac tamponade	Diminished blood return to heart
Hemorrhage	Inadequate oxygen-carrying capacity
Cardiac injury	Inadequate pump function
Spinal cord injury	Inappropriate vasodilatation Inadequate pump function
Poisoning	Direct failure of cellular metabolism Inappropriate vasodilatation
Sepsis	Inappropriate vasodilatation Direct failure of cellular metabolism

[a]*From Schroeder et al.[24] Used with permission from Elsevier.*

neurogenic, cardiogenic, or anaphylactic cause that seems to be great enough to explain the degree of instability present. As you work to stabilize organ perfusion with fluids, blood, and vasopressors, you find that acute respiratory distress syndrome (ARDS) sets in despite your best efforts.[6,7] If this shock state continues unabated, MODS may occur and an intrinsic, systemic effort to counter the proinflammatory surge with anti-inflammatory cytokines leaves the immune system vulnerable and greatly increases the chances of infection and sepsis.[10,13]

Traumatic shock is best described as a distinct shock state arising in the setting of severe, multiple trauma.[8] The direct association between shock and trauma has been recognized since the 18th century and was most evident during wartime in patients coming off the battlefield with hypotension and end organ dysfunction. Reports from the American Civil War and World Wars I and II differentiated between the symptoms of severe blood loss and the state of shock brought on by multiple wounds and injuries.[5] Hardaway[5] found that fatal traumatic shock was present in pigs with normal blood volume. Systemic vasodilatation secondary to a profound release of proinflammatory cytokines was observed in this scenario. Although a specific trigger is yet to be identified, Hardaway[5] has hypothesized that an endogenous compound(s), released by ischemic and dying cells, acts as a trigger for the inflammatory response. This "danger model" of inflammation and disease proposes that there are danger (damage)-associated molecular patterns that drive the immune response.[14-16]

PATHOPHYSIOLOGY AND CLINICAL MANIFESTATIONS

Systemic Inflammatory Response Syndrome in Trauma

The systemic inflammatory response syndrome (SIRS) is an innate response of the immune system to tissue injury and infection. Blunt tissue trauma leads to adenosine triphosphate release from damaged epithelium, which in turn activates the complement system, resulting in a flood of proinflammatory cytokines that, among other things, leads directly to systemic vasodilatation and oxygen-use abnormalities.[7,11,14,15,17] A secondary hypovolemic state ensues, and hypoperfusion of end organs leads to further ischemia, pushing the body into anaerobic metabolism and increasing the lactic acid byproduct. Monocytes are considered the expression engines of a large number of immunomodulators, including the proinflammatory cytokines TNF-α, IL-1β, IL-6, and IL-8, and hyperactivation of them following trauma is triggered by a danger-signal cascade catalyzed directly by cellular/tissue injury. High levels of proinflammatory cytokines occur early following injury, and high early levels have been correlated with severity of organ dysfunction and mortality.[11,18,19] This *cytokine storm* pushes the body into SIRS, defined clinically as 2 or more of the following conditions:

1. Temperature higher than 38°C or lower than 36°C;
2. Heart rate greater than 90 beats per min;
3. Respiratory rate greater than 20 breaths per min or $PaCO_2$ less than 32 mm Hg;
4. White blood cell count greater than 12 000 cells mm^{-3} or less than 4000 cells mm^{-3} or greater than 10% immature (band) forms.[20]

Three clinical stages of SIRS are recognized. Stage 1 is mainly a local response with increased recruitment of neutrophils and monocytes.[7,15] In stage 2, there is a spillover of activated cytokines into the circulation, but the dampening effects of anti-inflammatory cytokines maintain balance. This balance is lost in stage 3, and there is a massive proinflammatory swing characterized by a loss in capillary barrier function and generalized organ dysfunction.[11] The terminal state is characterized by severe hypotension that is refractory to fluid and inotropic support. As the ischemic insult progresses, there is worsening lactic acidosis and, ultimately, MODS.[11]

In a nonpathological response to injury, stress, or disease, there is a balanced expression of pro- and anti-inflammatory mediators. These factors work to trigger the

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perfect amount of immune function to fight off invaders and danger while leaving the body capable of normal homeostatic function. After the proinflammatory cascade that follows polytrauma, there is an innate effort by the body to return to this state of balance and function. A compensatory anti-inflammatory response syndrome occurs, which is mediated primarily by cells of the adaptive immune system.[11,21] In many cases, however, the secondary response is as much overkill as the initial response. A state of acute immune depression can occur, leading to an overall immune paralysis, placing the patient at extremely high risk for secondary infection and sepsis.[10]

ARDS in Trauma

The development of ARDS may be one of the most visible clinical markers of the onset of SIRS and the progression of traumatic shock following polytrauma. Inflammatory damage to alveolar epithelium decreases surfactant levels, resulting in atelectasis and hyaline membrane formation; whereas inflammatory damage to capillary endothelium attracts neutrophils, which secrete mediators, leading to further increases in capillary permeability, resulting in widespread pulmonary edema, cellular necrosis, and hemorrhage. Clinically, ARDS is divided into 3 phases—exudative, proliferative, and fibrotic—each with a variable course.[22-24]

The exudative phase is characterized by damage to the alveolar epithelium and vascular endothelium, which results in leakage of water, protein, and red blood cells into the interstitial space and alveolar lumen. Type I alveolar cells are irreversibly damaged, and their space is filled by the deposition of proteins, fibrin, and cellular debris producing hyaline membranes. In the proliferative phase, type II cells proliferate with some epithelial cell regeneration, fibroblastic reaction, and remodeling. In some patients, this progresses to tissue fibrosis, which is irreversible and fatal.[22,23] Treatment for ARDS is primarily supportive at each phase, and outcomes are largely dependent on successful treatment of circulatory shock, SIRS, and MODS.[25]

Coagulopathy in Trauma

Although there is some contention over the presence of disseminated intravascular coagulation as a confounding/additive factor within the SIRS state, there is evidence for its existence in cases of traumatic and septic shock. In pig models, for example, treatment with tissue plasminogen activator has restored oxygenation, leading to the theory that platelet function and fibrinogen availability are directly related to the signs and symptoms of circulatory shock.[5,26] The extrinsic coagulation pathway is activated following release of epithelial factors from damaged blood vessels and proinflammatory activation of monocytes, and the intrinsic pathway is activated by local and systemic factors. During the acute phase of SIRS, the procoagulation factors are used up, and there is a simultaneous decrease in the necessary inhibition factors usually produced by the liver.[27] Alternatively, increasing evidence from controlled trials supports the concept that tissue hypoperfusion and injury (as in trauma) results in thrombomodulin expression across epithelial boundaries and, through a complex with thrombin, leads to protein C activation and consequent inhibition of factors V and VII. Diffuse bleeding ensues secondary to the decreased production of fibrin.[28] Thromboelastograms can be useful in this setting to reveal that nature of the coagulopathy and suggest routes of treatment (Figure 2).[29]

MODS in Trauma

The presence of MODS after trauma is closely correlated with the severity of shock and the mortality of ICU patients. Multiple organ dysfunction syndrome describes the state resulting from progressive shock, when the ability of the body to compensate for hypoperfusion lessens and ischemic changes to end organs translate into clinical signs of a deteriorating condition. The exact biological progression from initial insult to onset of MODS is not well understood, although there is an international effort to map this progression in the hope that a greater understanding will elucidate an optimal time for intervention and reversal of damage.[13,16] There appears to be a

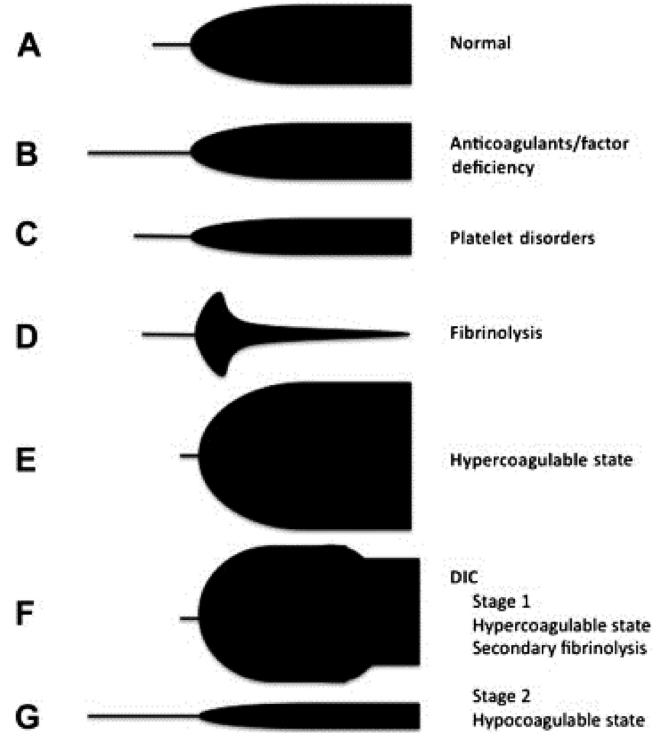

Figure 2. Thromboelastogram patterns of coagulation dysfunction. From Harr et al.[28] DIC indicates disseminated intravascular coagulation. Used with permission from Elsevier.

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temporal pattern to the onset of MODS that is correlated with the severity of injury and the size of the proinflammatory cascade. Because of the association between MODS development and poor clinical outcomes, there are a plethora of studies attempting to correlate the clinical picture with levels of pro- and anti-inflammatory cytokines as well as to identify metabolic signatures predictive of outcome in the critically ill patient with traumatic shock. For example, levels of certain cytokines like IL-6, IL-8, and TNF-α have been evaluated for their ability to predict outcomes and help determine management choices.[13,16,30-35] Other suggested predictors of MODS include Injury Severity Score, International Normalized Ratio, hemoglobin level on admission, age, and others. None of these markers are ideal or currently accurate enough to allow clinical application.[30]

TREATMENT OF TRAUMATIC SHOCK

The syndrome of traumatic shock should be viewed as a pathophysiological time line with time-specific complications as measured from the onset of injury. The immunomodulator combinations change as the syndrome develops, as does the resulting pathological dysfunction (Figure 3).[4,18,13,16] *Compensated traumatic shock* may have increased heart rate and catecholamine-driven vasoconstriction of nonessential tissue beds; prolonged survival and relatively easy recovery will follow adequate resuscitation. *Decompensated traumatic shock* can then be defined by the existence of cellular damage secondary to hypoperfusion with associated toxic metabolic effects. Shock is still reversible, but recovery may be extended. If resuscitation is complete but the patient later develops MODS secondary to ischemia and reperfusion, this stage is understood as *subacute irreversible shock*. *Acute irreversible shock* describes the severe syndrome with ongoing inflammation, compensatory decompensation, acidosis, and coagulopathy that results in death.[4] Treatment, although primarily supportive, must be instituted early and aggressively to avoid irreversible shock.

Blood Pressure Control

As in septic shock, SIRS secondary to trauma causes cell membranes to become leaky and there is a shift of fluid from the intravascular space to the extravascular tissues.[11] This compounds an already unstable hemodynamic picture secondary to vasodilatation, and blood pressure and organ perfusion become highly variable. Add in the possibility of blood loss with its associated decrease in oxygen-carrying capacity and the situation becomes very sensitive to slight changes in clinical management.

Fluid resuscitation is controversial, and there are 2 competing theories regarding optimal management. Some authors suggest that fluids be restricted while urinary output is maximized with the use of diuretics to decrease interstitial and pulmonary fluid burden, in turn limiting the duration of mechanical ventilation in the treatment of ARDS. The downside of this approach may be underresuscitation with decreased cardiac output and increased chance of MODS. An alternative approach stratifies risk in favor of end organ perfusion and preaches a liberal fluid approach.[36,37] A randomized controlled trial from 2006 revealed that there is a significant benefit for acute lung injury patients treated with a conservative fluid management approach (7-day cumulative fluid balance of −136 ± 491 mL as compared with 6992 ± 502 mL in the liberal management group). Along with an increased oxygenation index, the patients in the conservative fluid management group had an increase in ventilator-free days ($P < .001$) and days spent outside the ICU ($P < .001$) during the first 28 days without an increased incidence or prevalence of shock ($P = .06$).[37]

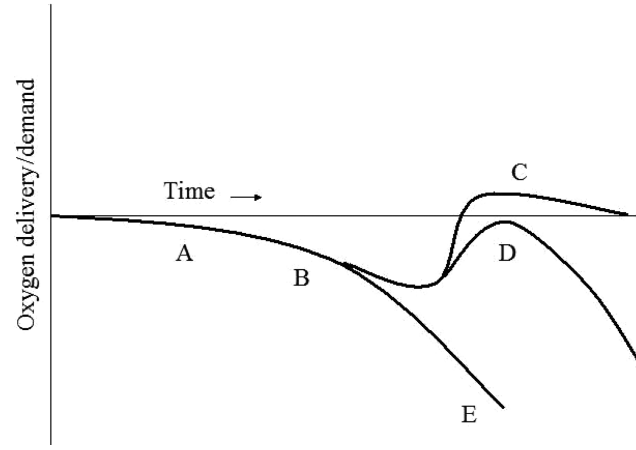

Figure 3. Stages and outcomes of traumatic shock. Curve A represents compensated shock. Curve B is acute decompensated shock. Once decompensation has occurred, 3 outcomes are possible: Curve C represents subacute reversible shock (the patient survives), curve D represents subacute irreversible shock (the patient dies of multiple organ system failure), and curve E represents acute irreversible shock (the patient dies of hemorrhage and cardiovascular collapse). From Dutton.[3] Used with permission from TraumaCare International.

A Cochrane review of 23 randomized controlled trials carried out from inception to March 2010 concluded that there is no preferential vasopressor for treatment of circulatory shock. The appropriate agent to use in each circumstance is best left as an individualized choice made with the discretion of the treating practitioner.[38] Factors such as pump sufficiency, fluid status, adrenal response, and blood pressure goals should guide decisions about the need for one vasopressor and/or inotropic agent over another from a similar class or type.

Glucose Control

Current research is building upon reliable evidence that tight glucose control with intensive insulin therapy in the

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critical care setting is associated with significantly improved outcomes. A 2001 study with critically ill patients (primarily surgical) found that intensive insulin therapy and tight glycemic control (blood glucose concentration 80-110 mg/dL) led to decreased ICU stay and decreased mortality.[39] A follow-up study enrolling primarily medical ICU patients did not measure the same significant benefits, although there remained a measurable mortality benefit.[40] Use of insulin drips and tight glycemic control are being evaluated in the setting of traumatic shock, and early evidence suggests improved outcomes for trauma patients with MODS, perhaps because of protection from hyperglycemic organ insult as well as the anti-inflammatory benefits of insulin.[41]

Infection

The onset of sepsis should always be considered when caring for a trauma patient in whom the clinical development of SIRS is present. Even early on, the shock syndrome may be secondary to an infectious process. After several days in the hospital, however, the risk of nosocomial infection increases dramatically. At the first suspicion of infection, a directed hunt for the culprit should begin and broad-spectrum antibiotics initiated. Differentiating between a noninfectious and infectious etiology for SIRS may be difficult, and in 50% of recorded septic shock cases, a specific organism could not be found despite serial cultures from multiple sites.[42] Differentiation between infectious and noninfectious etiologies may be aided by early measurement of procalcitonin and interleukin-6 levels. Elevated levels during days 1 to 5 postinjury were strongly correlated with the later development of sepsis in trauma patients.[43]

Immunomodulation

Attempts to modulate the immune system after traumatic injury may be either direct or indirect. In the former, agents are used to either dampen or heighten the immune/inflammatory response.[44] Corticosteroids are extensively used, particularly in the setting of secondary adrenal insufficiency where endogenous hormones are depleted following extended shock states or critical illness. However, if SIRS occurs early in response to a cytokine storm initiated by multiple traumatic injuries or massive blood transfusions, corticosteroid therapy is less helpful and may even be harmful if it suppresses an already fragile immune system.[44,45] Similarly, the use of monoclonal antibodies to combat early inflammation is an alternate strategy, but there has been limited success with this approach.[46] Conversely, efforts to support or enhance the immune system during the immunosuppressed stage of traumatic shock have shown limited success, but recent trials are few.[47] An indirect approach to modulating the immune system includes optimizing the timing and delivery of other necessary treatments in such a way so as to lessen the inflammatory response. This includes limiting the use of blood transfusion if possible, early initiation of enteral feeding following resolution of hemodynamic instability, tight glycemic control, and optimal timing of surgery.[41,44]

CONCLUSION

The human body's response to injury is a multifaceted and extraordinarily complex reaction that strives to reestablish homeostasis and protect the host from further insult. As is the case in many disease states, the compensatory mechanisms used to wall off and correct dysfunction can, when in excess, be harmful. Shock, a state of global hypoperfusion secondary to injury, foreign invaders, or organ dysfunction can be the driving force behind these compensatory mechanisms that may lead to worse damage and disease. The "fifth shock," traumatic shock, is a clear example of this tenet and is best viewed as a distinct shock syndrome unique to the multiply injured patient. Its features include components of many or all of the 4 classic shock syndromes. Central to its pathophysiology is a profound proinflammatory response. Early, aggressive, and complete resuscitation is necessary to avoid irreversible shock and to optimize outcomes.

As our understanding of the initiation and progression of traumatic shock and the underlying SIRS response expands, it is hoped that practitioners will be able to intervene in a timely fashion, perhaps by aiding in balancing the inflammatory response and restoring homeostasis. Research into immunomodulating treatment modalities continues and may offer new solutions and management options for those patients who present with this complex problem.

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