

Pathophysiology of Traumatic Shock

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Dr. Dutton has no conflict of interest with any product named in this article.

Learning Objectives: 1) To learn the definition of “shock” and the common subtypes. 2) To understand the clinical diagnosis and progression of shock. 3) To learn the pathophysiology of shock at the cellular, tissue, organ, and whole body level.

Abstract

Shock is a systemic disease caused by failure of oxygen delivery or utilization at the cellular level. Shock occurring after a traumatic injury is due to hemorrhage with decreased cardiac output until proven otherwise, but may also be exacerbated by hypoxemia, mechanical impairment of blood flow (tension pneumothorax or tamponade), cardiac contusion or ischemia, poisoning, or acute spinal cord injury. Pain, anxiety, and hemorrhage combine to trigger systemic compensatory mechanisms designed to preserve perfusion of the most oxygen-sensitive organs: the brain and heart. Compensatory vasoconstriction leads to progressive ischemia in other organ systems, with progressive development of shock at the cellular and tissue level. Cells of different organs react differently to shock, but each contributes to the overall pathophysiology of the disease. Release of inflammatory mediators and organ system dysfunction and failure perpetuate shock as a systemic disease even after the inciting pathology has been identified and corrected.

“A rude unhinging of the machinery of life.”
 Samuel Gross, 1862¹

“Shock” is the systemic disease that results from any process that impairs the systemic delivery of oxygen to the cells of the body, or that prevents its normal uptake and utilization. Hemorrhage with decreased cardiac output is the most common cause of shock in trauma patients (Table 1), although it is not unusual for shock to result from a combination of events. Hemorrhage, tension pneumothorax, and cardiac contusion can all coexist in the patient with chest trauma, for example, with each contributing to systemic hypoperfusion. Iatrogenic contributors to shock may include anemia following vigorous crystalloid infusion, the use of tourniquets, and the use of systemic pressor agents. Underlying medical conditions can also play a part, with myocardial ischemia potentially contributing to decreased oxygen delivery, especially in older trauma

patients. The effects of alcohol, medications, and illicit drugs may contribute to a state of hypoperfusion and may block normal compensatory mechanisms. It is important to recognize that the traumatic shock seen clinically in severely injured patients may be quite different from the induced shock seen in laboratory animals hemorrhaged under controlled conditions.

Stages of Shock

The Advanced Trauma Life Support course of the American College of Surgeons defines traumatic shock as occurring in four stages, based on arbitrary levels of blood loss and vital signs.² A better approximation of the degree of shock, based on the patient’s symptoms, response to therapy, and prognosis, is represented in Figure 1. In *compensated traumatic shock*, an increase in heart rate and vasoconstriction of nonessential and ischemia-tolerant vascular beds will allow prolonged survival and easy recovery once hemostasis is achieved and resuscitation is completed. *Decompensated traumatic shock*, also known as progressive shock, is a transitory state in which lack of perfusion is creating cellular damage that will produce toxic effects. Shock is still reversible at this stage. In *subacute irreversible shock*, the patient is resuscitated to normal vital signs but succumbs at a later time to multiple organ system failure (MOSF) as the result of tissue ischemia and reperfusion. Finally, *acute irreversible shock* is the condition of ongoing hemorrhage, acidosis, and coagulopathy that spirals downward to early death from exsanguination.

Progression from compensated to uncompensated shock (usually due to ongoing hemorrhage) is a surgical and metabolic emergency. Successful recovery requires rapid diagnosis and control of the inciting event (i.e., hemostasis) facilitated by resuscitative therapy directed toward minimizing the overall “dose” of shock. A patient who experiences substantial blood loss and massive transfusion will experience some degree of organ system failure thereafter (i.e.,

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

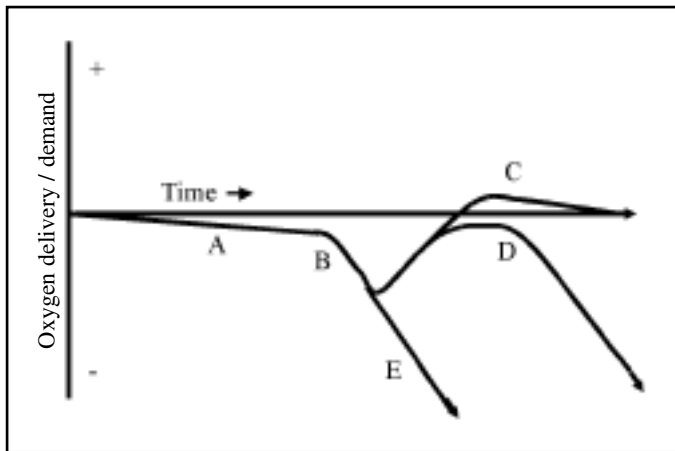


Figure 1. Stages and outcomes from traumatic shock. Curve A represents compensated shock. Curve B is acute decompensated shock. Once decompensation has occurred, three outcomes are possible: Curve C represents subacute reversible shock (the patient survives). Curve D is subacute irreversible shock (the patient dies of multiple organ system failure). Curve E is acute irreversible shock (the patient dies of hemorrhage and cardiovascular collapse). See text for a complete explanation of the stages of traumatic shock.

edema, pulmonary dysfunction). This is due to the systemic effects of tissue ischemia. Bleeding may be controlled and vital signs may be normal or even hypernormal, but the damage has been done on the cellular level. Ischemia can persist because of “no reflow” caused by cellular swelling and microcirculatory obstruction, while effects in nonischemic organ systems such as the lungs are actually a form of reperfusion injury.

Death in the first hours following trauma is generally the result of acute irreversible traumatic shock. Prolonged hypoperfusion depletes cellular energy stores, especially in the vascular endothelium. This is manifested by progressive vasodilatation, loss of response to fluids and catecholamines, capillary leak, diffuse coagulopathy, and cardiac dysfunction. These patients are usually said to exsanguinate, although in the presence of modern rapid-infusion techniques and aggressive transfusion, this is not strictly true. Rather, the patient dies from the acute metabolic consequences of failed perfusion, frequently in the presence of adequate control of surgical bleeding and voluminous blood product replacement. In patients without significant primary brain injury, death occurring in the days to weeks following injury is due to the persistent effects of systemic shock, manifesting as MOSF and recurrent sepsis.

The Systemic Response to Shock

The stages of traumatic shock are directly related to the physiologic response to hemorrhage. The initial response is on the macrocirculatory level and is mediated by the neuroendocrine system. Decreased blood pressure leads to vasoconstriction and catecholamine release. Heart and brain blood flow is preserved, while other regional beds are constricted. Pain, hemorrhage, and cortical perception of traumatic injuries lead to the release of a number of hormones as part of the “fight or flight” response, including renin-angiotensin, vasopressin, antidiuretic hormone, growth hormone, glucagon, cortisol, epinephrine and norepinephrine.³ This rush of chemicals sets the stage for the microcirculatory responses that follow.

On the cellular level the body responds to hemorrhage by taking up interstitial fluid, causing cells to swell.⁴ Edematous cells obstruct

adjacent capillaries, resulting in the “no-reflow” phenomenon that can prevent the reversal of ischemia even in the presence of adequate macro flow.⁵ Ischemic cells produce lactate and free radicals, which are not adequately cleared by the failing circulation. These compounds cause direct damage to the cell that produces them, as well as forming the bulk of the toxic load that will be washed back to the central circulation when perfusion is re-established. The ischemic cell also produces and releases a variety of inflammatory factors: prostacyclin, thromboxane, prostaglandins, leukotrienes, endothelin, complement, interleukins, tumor necrosis factor, and others.⁶ These are the ingredients of acute and subacute irreversible shock. Figure 2 summarizes the inflammatory response to cellular ischemia, demonstrating the amplification that occurs once active mediators reach other sensitive cells—especially in the lung. The realization that ischemia occurring in one organ system can cause a systemic disease that affects the entire body is an important advance in understanding the pathophysiology of shock and will help in creating effective treatments.

Organ System Responses to Traumatic Shock

Each individual organ system responds to shock in a specific fashion. Understanding how each system contributes to the overall systemic disease is important both for clinical management and for the development of preventive or mitigating therapeutic strategies.

The Central Nervous System

The central nervous system is exquisitely sensitive to hypoperfusion and is thus the prime trigger of the neuroendocrine response to shock, which maintains oxygen supply to the heart and brain at the expense of other tissues.⁷ Regional glucose uptake in the brain changes during shock.⁸ Reflex activity and cortical electrical activity are both depressed during hypotension; these changes are reversible with mild hypoperfusion, but become permanent with prolonged ischemia. The brain has a limited capacity to “hibernate” during hypoperfusion; the agitation and then loss of consciousness

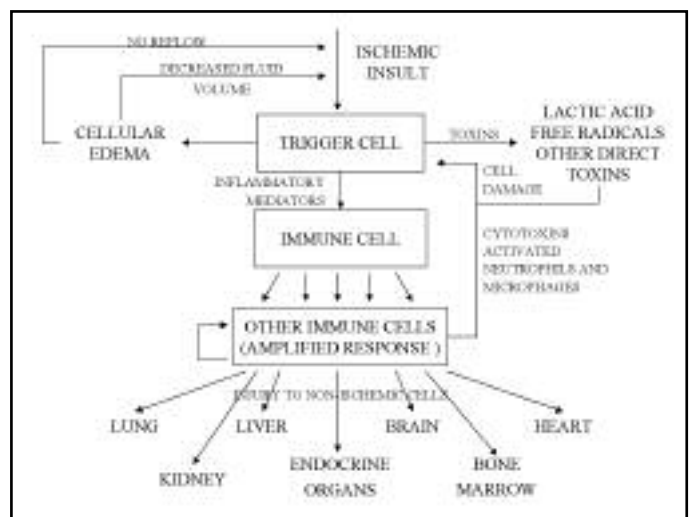


Figure 2. The Inflammatory Cascade. Traumatic shock produces an ischemic insult on the cellular level, which is then amplified into a systemic response. Trauma to one part of the body can lead to a fatal failure of multiple uninvolved organ systems.

seen in advanced shock are due to reductions in cerebral activity. Beyond this limited reserve, however, further decreases in tissue oxygenation will lead to permanent cell damage; either apoptosis (programmed cell death; cellular machinery is activated that permanently “turns off” the cell)⁹ or direct necrosis. Failure to recover preinjury neurologic function is a marker for subacute irreversible shock, even if the patient’s hemodynamic functions are normal.¹⁰ Further, neurologic outcome is the primary driver of long-term patient outcomes after traumatic injury.¹¹ For these reasons the brain has been cited as “the target organ of resuscitation,” and all candidate therapies for treatment of hemorrhagic shock must be evaluated in light of their ability to improve neurologic outcomes.¹²

Cardiovascular

The heart has little capacity to function anaerobically, and is relatively preserved from ischemia during hemorrhage because of maintenance or even increase of nutrient blood flow driven by the fight or flight response. Cardiac function is generally well preserved until the late stages of shock, and failure of adequate oxygen delivery to the heart itself will be rapidly fatal.^{7,13} Lactate, free radicals, and other humoral factors released by ischemic cells all act as negative inotropes, however, and in the decompensated patient may produce cardiac dysfunction as the terminal event in the shock spiral.¹⁴

Maintenance of vascular tone is critical to normal physiology because the actual fluid capacity of the blood stream—especially on the venous side—is many times the normal blood volume. Some of this tone is maintained by spinal reflex, which is why a high spinal cord injury can produce “neurogenic shock” characterized by hypotension due to inappropriate vasodilatation. Much of the vascular tone necessary to maintain blood flow and pressure is maintained at the regional level, however, by the opening and closing of arterioles feeding discrete vascular beds (veins distal to closed arterioles will passively collapse). This is an energy-dependent process. Persistent shock can produce ischemia in the vascular endothelium itself, which manifests as a loss of regulatory constriction. Clinically, the patient becomes hypotensive and progressively less responsive to resuscitative efforts. Although the first bolus of fluid or epinephrine in a patient in ongoing hemorrhagic shock will often produce an exaggerated response, because the patient is very vasoconstricted, later applications will have less and less effect and the patient will be persistently hypotensive and vasodilated.¹⁵ Death from acute hemorrhagic shock is thus death from vascular collapse. No therapy has yet been described that can reverse this phenomenon once it is established.

Kidney and Adrenal Glands

The kidney and adrenal glands are prime responders to the neuroendocrine changes of shock, producing renin, angiotensin, aldosterone, cortisol, erythropoietin, and catecholamines.¹³ The kidney itself maintains glomerular filtration in the face of hypotension by selective vasoconstriction and concentration of blood flow in the medulla and deep cortical area. Deeper levels of shock are tolerable because the kidney can “hibernate.” Energy-dependent filtration ceases in order to conserve oxygen for cellular survival. Prolonged hypotension leads to tubular epithelial necrosis, then diffuse necrosis (“patchy cell death”), and finally to complete and permanent renal failure.^{7,16}

The Lung

The lung is almost never the trigger of the shock syndrome because it cannot itself become ischemic. The lung is nonetheless the

downstream filter for the inflammatory byproducts of the ischemic body, and is itself an active immune organ. Amplification of the inflammatory response to shock occurs primarily in the lung, such that it is often the sentinel organ for the development of MOSF.^{17,18} Immune complex and cellular factors accumulate in the capillaries of the lung, leading to neutrophil and platelet aggregation, increased capillary permeability, destruction of lung architecture, and the acute respiratory distress syndrome.^{19,20} The pulmonary response to traumatic shock is the leading evidence that this disease is not just a disorder of hemodynamics: pure hemorrhage, in the absence of hypoperfusion, does not produce pulmonary dysfunction.^{18,21}

The Gut

Splanchnic perfusion is very strongly controlled by the autonomic nervous system, and the gut becomes vasoconstricted early in the course of hemorrhagic shock. The intestine is one of the earliest organs affected by hypoperfusion and may be a primary trigger of MOSF. Intense vasoconstriction occurs early and can be difficult to reverse, perhaps as the result of the “no reflow” phenomenon.²² Necrotic cell death causes a breakdown in the barrier function of the gut, which results in increased translocation of bacteria to the liver and lung.²³ The impact of this on the development of multiple organ failure is controversial at present, but the use of gut decontamination to reduce this risk in victims of severe shock has been proposed.²⁴

The Liver

The liver has a complex microcirculation and has been demonstrated to suffer both “no reflow” and reperfusion injury during recovery from shock.²⁵ Hepatic cells are also metabolically active and contribute to the inflammatory response to decompensated shock. Patients with pre-existing liver disease do very poorly with hemorrhagic shock, suggesting that the liver’s role as a moderator of inflammation and a reservoir for clotting factors is important to normal recovery. Irregularities in blood glucose levels following shock are attributable to hepatic ischemia.²⁶ Complete liver failure following hemorrhagic shock (more common in those with underlying liver disease) is almost uniformly fatal.

Skeletal Muscle, Bone, and Skin

Vasoconstrictive mechanisms in peripheral tissue are important to spontaneous hemostasis and tissues of the musculoskeletal system are ischemia-tolerant as long as motor function is not required. Isolated limbs can tolerate total ischemia (as from a surgical tourniquet) for periods of several hours without sequelae.²⁷ When ischemia persists to the point of tissue necrosis, however, the large volume of muscle in the body makes it an important source of lactate and toxins contributing to reperfusion injury. Further, injured muscle and skin become edematous at low levels of shock, and contribute to the free-fluid deficit seen after major trauma even in the presence of hemostasis and blood product replacement.⁴

Conclusion

Traumatic shock is a disease of tissue ischemia, and is characterized by a trigger that produces tissue ischemia (usually hemorrhage) and the inflammatory disease that follows. Surgical hemostasis and precision resuscitation can restore normal blood volume quickly after major trauma, but the patient can still die as a result of the systemic effects of shock. The future management of this

disease will depend on a clear understanding of the effects of shock in different organ systems, the ways in which inflammatory mediators can exacerbate ongoing ischemic distress, and our ability to support multiple failing organ systems simultaneously.

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