Pediatric Shock Review

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EDUCATION GAPS

Recognition and management of pediatric shock is essential for all clinicians. Although the basic pathophysiology and clinical signs and symptoms of shock have not changed, the diagnostic tests, monitoring devices, and management principles continue to evolve, requiring ongoing review, updates, and knowledge sharing.

OBJECTIVES *After completing this article, readers should be able to:*

1. Describe pediatric shock and the associated shock pathophysiology.
2. Identify the clinical presentation of shock, distinguishing features of early versus late presentations.
3. List the laboratory and diagnostic tools helpful in diagnosis and management of pediatric shock.
4. Describe general management principles, including different management based on different categories of shock, shock etiologies, and resource availability.

ABSTRACT

Shock occurs when there is energy failure due to inadequate oxygen/glucose delivery to meet metabolic demands. Shock is a leading cause of death and disability in children worldwide. Types of shock include hypovolemic, cardiogenic, distributive, and obstructive. This review provides an overview of the epidemiology, pathophysiology, and clinical signs and symptoms of each of these types of shock, followed by a discussion of advancements in diagnostic tests and tools and management/treatment principles for different categories of shock.

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ABBREVIATIONS

BP	blood pressure
CO	cardiac output
CVP	central venous pressure
DO_2	delivery of oxygen
ECMO	extracorporeal membrane oxygenation
NIRS	near-infrared spectroscopy
PI	perfusion index
POCUS	point-of-care ultrasonography
SvO_2	mixed venous oxygen saturation
VO_2	oxygen consumption

INTRODUCTION

Shock is a clinical manifestation of underlying pathophysiologic change at the cellular level in response to energy failure from inadequate delivery or utilization of oxygen and metabolic substrates (ie, glucose) to meet tissue metabolic needs. Initially, tissues demonstrate compensatory mechanisms to maintain adequate cardiac output; however,

without hemodynamic support, malperfusion culminates in a refractory stage, resulting in multiorgan failure and death.

EPIDEMIOLOGY

Shock is a leading cause of death and disability in children worldwide. The overall prevalence and incidence is difficult, if not impossible, to determine. (1) Worldwide, in children younger than 5 years, the leading causes of mortality related to shock include diarrheal illness, other infectious diseases, and motor vehicle accidents. (2) In neonates, common causes of shock globally include birth trauma, infectious diseases, and congenital heart disease. (3)(4) In older children and young adolescents (5–14 years old), causes of death globally shift toward unintentional injuries (motor vehicle accidents, burns, drownings, and falls) (5) versus the more recent rise in firearm injury overtaking as the leading cause of death in the United States. (6)(7)

Shock etiology is often divided by type or category of shock. Types of shock include hypovolemic, distributive, cardiogenic, and obstructive. Within these 4 main categories, shock causes can be further subcategorized as shown in Table 1. (8) Some clinicians reference dissociative shock as an additional rare category. (9)

The most prevalent type of pediatric shock is hypovolemic, (10)(11) predominating from diarrhea and vomiting due to gastrointestinal infection, with diarrhea accounting for approximately 9% of all deaths in children younger than 5 years globally. Additional etiologies of hypovolemic shock include hemorrhage (eg, trauma), burns, diabetic ketoacidosis, third space losses (eg, intestinal surgeries), and renal losses. (12) In addition, distributive shock, as is seen in sepsis, results in functional hypovolemia through inappropriate vasodilation and maldistribution of fluid. (13)

Septic shock carries the highest mortality rate (40%–60%) of all pediatric shock etiologies. (14) The World Health Organization's 2020 global report estimated that 20% of all global deaths were from sepsis or sepsis-related deaths, with almost half of those in children younger than 5 years, mostly due to infections related to neonatal disorders, lower respiratory infections, and diarrheal diseases. (15) Most pediatric death from sepsis is from refractory shock and/or multiorgan system dysfunction. (16) The COVID-19 pandemic has resulted in identification of multisystem inflammatory syndrome in children, a hyperinflammatory state contributing to significant cardiogenic and septic shock with consequences that include vasopressor use (45.3%), extracorporeal support (3.3%), and mortality (1.9%). (17)

Finally, as international travel and migration continue to increase, children may present to local hospitals with shock due to less familiar etiologies, such as dengue hemorrhagic fever, (18) enteric fever, (19) and Ebola. (20) Knowledge of the fundamentals of shock assists in identifying appropriate management and decreasing the incidence of complications, including death.

PATHOPHYSIOLOGY

The following discussion of pathophysiology was guided by critical care textbooks. (9)(13)(21)

Circulatory delivery of oxygen (DO_2) is dependent on cardiac output (CO) and arterial oxygen content, also referred to as oxygen-carrying capacity (CaO_2). Oxygen content is primarily determined by the amount saturated (Sao_2) on hemoglobin (Hb) molecules, with some additional oxygen dissolved in blood (Pao_2). Dissolved oxygen becomes more contributory to oxygen content in states of significant anemia. These principles are shown in the following equation:

$$DO_2 = CO \times CaO_2, \text{where } CaO_2 = (Hb \times SaO_2 \times 1.34) + (PaO_2 \times 0.003)$$

CO is provided by heart rate (HR) and stroke volume (SV). Stroke volume is dependent on cardiac myocyte stretch by the volume of end-diastolic ventricular blood (preload), the intrinsic resistances to the ejection of that volume (afterload), and the contractile force generated to perform systole (contractility).

$$CO = HR \times SV; \text{where SV is mediated by preload, afterload, contractility}$$

The amount of oxygen extracted (VO_2) from the blood varies by tissue type and is a general surrogate for oxygen demand. In healthy states the range of DO_2 is sufficient to meet the extraction demands and maintain optimal oxidative phosphorylation.

$$VO_2 = DO_2 \times O_2ER, \text{where } O_2ER = \text{extraction ratio of blood oxygen in \%}$$

In states of inadequate perfusion, however, a point may be reached where inadequate DO_2 prevents optimal oxygen extraction and compensatory autonomic mechanisms become overwhelmed. This is known as the critical point, as seen in Fig 1A, and represents a state where oxygen extraction is dependent on DO_2. Figure 1B offers a clinical differential diagnosis based on interactions of VO_2, DO_2, and oxygen extraction ratio. With ongoing ischemia, a host of molecular changes result in cellular injury and ultimately cell necrosis. Furthermore, if DO_2 is reestablished, reperfusion may cause further cellular injury by inflammatory reactions and resultant reactive oxygen and nitrogen species.

Table 1. Types and Features of Shock

SHOCK TYPE	PRINCIPAL FEATURES	CLINICAL SIGNS	PHYSIOLOGIC CHANGES	DISEASE EXAMPLES	LABORATORY/IMAGING CONSIDERATIONS	MANAGEMENT CONSIDERATIONS
Hypovolemic	Volume loss, including if relative to increased venous capacitance	Tachycardia, cool extremities, decreased UOP	Decreased CO, decreased preload, increased SVR, decreased CVP	Diarrhea, dehydration, burn, hemorrhage	Electrolytes, renal function; CBC count, INR, PTT, fibrinogen; POCUS–IVC	Targeted IVF, balanced blood product
Cardiogenic	Intrinsic cardiac defect	Tachycardia (if able), cool extremities, decreased UOP, crackles/pulmonary edema	Decreased CO, increased SVR, increased CVP	Heart failure, arrhythmia, myocardial infarction, valvular insufficiency, carditis	NT-proBNP, troponin, potassium, magnesium, iCa^{2+}; echocardiography	Cautious IVF, inotropy, chronotropy, lusitropy (rate of myocardial relaxation), ECMO
Distributive	Redistribution of blood flow, abnormal vascular tone, inadequate capillary recruitment, suboptimal oxygen utilization	Variable disease-specific findings; typically warm extremities, fast capillary refill	Decreased or maintained CO, tachycardia or bradycardia (neurogenic shock), decreased SVR	Sepsis, anaphylaxis, neurogenic (ie, spinal trauma), iatrogenic, endocrinopathies	Infectious cultures, CRP, procalcitonin, CBC count with differential count; serial glucose, thyroid studies, cortisol, ammonia, pH, iCa^{2+}	Targeted IVF, vasopressors, hormone repletion
Obstructive	Mechanical obstruction to cardiac output	Tachycardia, cool extremities, increased CVP	Decreased CO, increased afterload	Tension pneumothorax, Cardiac tamponade, pulmonary embolism, congenital lesions	Chest radiography, echocardiography, CT chest with contrast (spiral CT)	Procedural relief of obstruction; thrombolysis, anticoagulation
Dissociative	Inability to release delivered oxygen	Tachycardia, altered mental status, fatigue	Primarily maintained CO, volume, and vascular tone	Carbon monoxide, methemoglobinemia, cyanide poisoning, propofol infusion syndrome	Blood gas (methemoglobin, carboxyhemoglobin), lactate, cyanide level (confirmatory)	Oxygen and HBO_2, methylene blue, ascorbic acid; hydroxocobalamin, sodium thiosulfate, sodium nitrate

CBC=complete blood cell, CO=cardiac output, CRP=C-reactive protein, CT=computed tomography, CVP=central venous pressure, ECMO=extracorporeal membrane oxygenation, HBO_2=hyperbaric oxygen, iCa^{2+}=ionized calcium, INR=international normalized ratio, IVC=inferior vena cava, IVF=intravenous fluid, NT-proBNP=N-terminal prohormone of brain natriuretic peptide, POCUS=point of care ultrasonography, PTT=partial thromboplastin time, SVR=systemic vascular resistance, UOP=urine output.
Adapted from Fuhrman (13) and Rogers' (21) critical care textbooks.

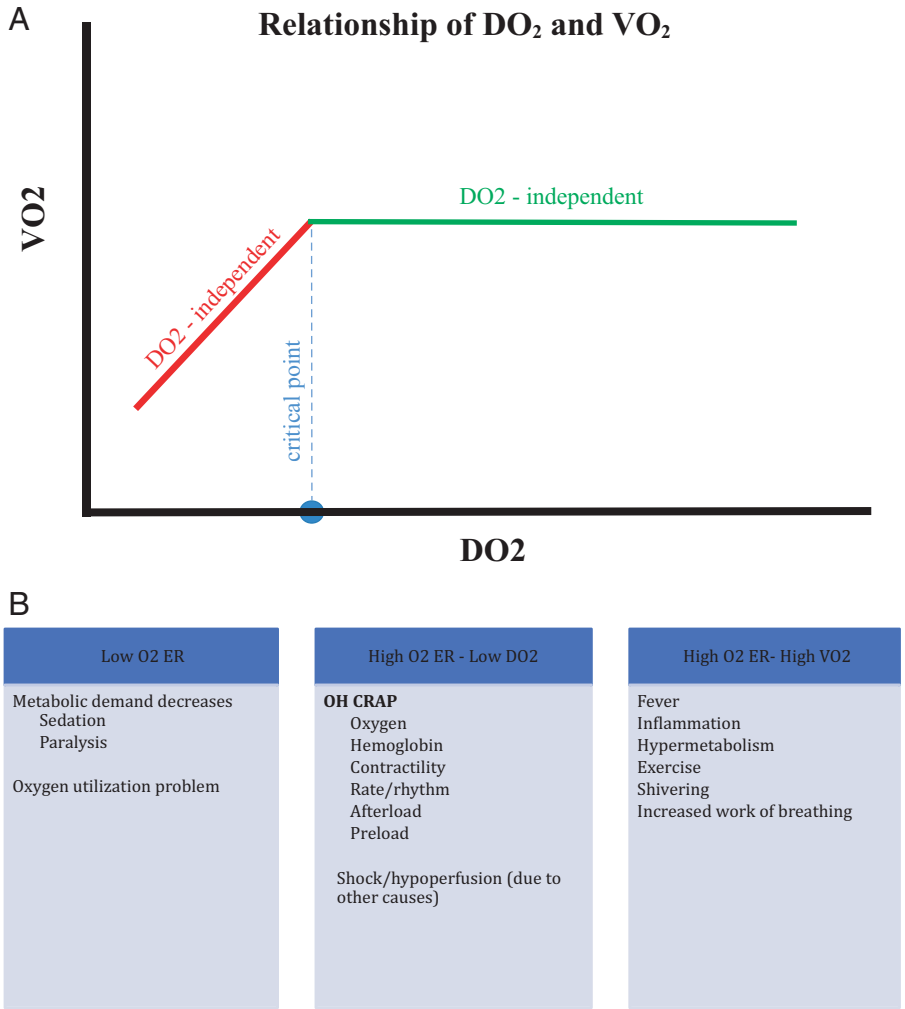

Figure 1. Consumption of oxygen (VO_2) and delivery of oxygen (DO_2). A, VO_2 is typically independent of DO_2. The critical point in shock is when VO_2 becomes dependent on DO_2. B, Shock etiology (and subsequent management) can be categorized as shock due to a low oxygen extraction ratio (O_2ER), high O_2ER due to low DO_2, or high O_2ER due to high VO_2. Examples are listed in the chart.

Shock is, therefore, a consequence of either decreased DO_2 to tissues or decreased extraction and utilization of delivered oxygen. Management principles are based on this concept (Fig 2). The pathogenesis of shock will vary by the underlying disease state, offering opportunity for classification; however, clinically there may be multiple mechanisms simultaneously. Types of shock and some common, pertinent identifying features are outlined in Table 1. (8)

CLINICAL PRESENTATION

Shock is a clinical diagnosis. Classically, pediatric shock manifests with signs/symptoms indicative of decreased organ perfusion or poor peripheral perfusion, many of which are subtle or have poor specificity, making it possible to miss the diagnosis initially. (22) As shown in Table 1, different types of shock have different clinical manifestations. There are some clinical features, however, that are common to most types of shock, and they can be divided into early versus late signs.

Early Clinical Signs of Shock

Children most often have tachycardia with normal blood pressure (BP) in early shock. In this "compensated shock" state, BP is maintained via increasing heart rate and/or increasing vascular resistance. Compensatory changes help

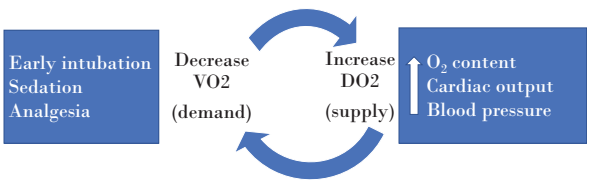

Figure 2. Shock management principles. The goal is to balance oxygen supply and demand while treating the underlying etiology/cause. DO_2= delivery of oxygen, VO_2=consumption of oxygen.

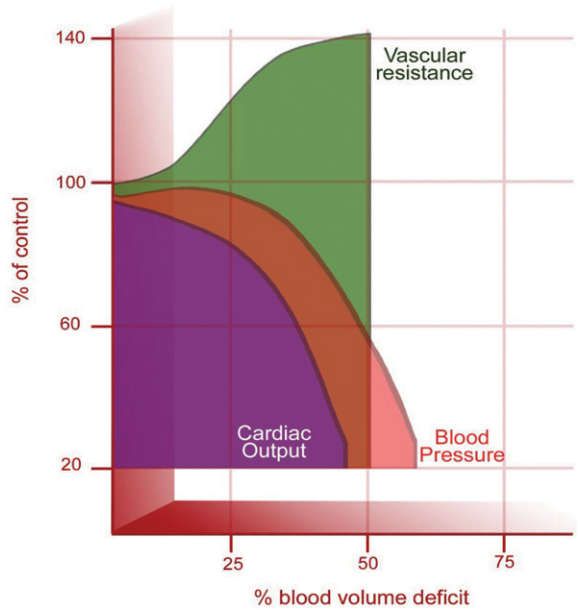

Figure 3. Hemodynamic response to shock hemorrhage model (based on normal data). ABC=airway patency, breathing mechanics, and circulation, CaCl=calcium chloride, CVL=central venous line, CSF=cerebral spinal fluid, ETT=endotracheal tube, iCA=ionized calcium, IM=intramuscular, IO=intraosseous, IV=intravenous, IVF=intravenous fluid, K=potassium, Mg=magnesium, MIS-C=multisystem inflammatory syndrome in children, MTP=massive transfusion protocol, PALS=pediatric advanced life support, PE=pulmonary embolism, PRBC=packed red blood cell, PTX= pneumothorax. Adapted from Schwaitzberg et al. (23)

maintain essential perfusion and augment CO. Figure 3 demonstrates the delay in decrease of CO and BP (y-axis) until a larger component of intravascular volume loss (x-axis). (23) Compensation often results in signs of poor peripheral perfusion such as decreased peripheral compared with central pulses, alteration in capillary refill (either "flash" or delayed >2 seconds), cool and/or mottled extremities, or decreased urine output. Additional signs of shock include tachypnea, hypothermia, or hyperthermia. As shock progresses, there can be early mild changes in alertness, such as irritability or agitation.

Late Clinical Signs of Shock

Hypotension is the hallmark late sign of shock in children. The compensatory mechanisms that maintain CO in early shock are overcome (Fig 3). (23) Late signs of shock also include loss of peripheral pulses and/or cold extremities with prolonged capillary refill (often 4–5 seconds) as well as worsening alteration in mental status, including lethargy, confusion, and obtundation. In addition, bradycardia and bradypnea/apnea are very late signs of shock.

Shock is often also divided into categories based on clinical assessment of vascular resistance and CO. Classically, these clinical shock syndromes referred to vasodilatory shock as *warm shock* and cardiogenic shock as *cold shock,* as shown in Fig 4. Children can change from one shock category to another (warm to cold or vice versa) throughout their course due to progression of illness or response to treatment. Frequent reassessment is essential.

Warm Shock: Signs of Vasodilation

Decreased vascular resistance may result in bounding pulses, flash capillary refill, warm extremities, flushed skin, and widened pulse pressure. A common misperception is that warm shock requires fever.

Cold Shock: Signs of Poor CO

Decreased CO is often compensated for with increased vascular resistance, which may result in absent or weak distal pulses, prolonged capillary refill, cool extremities, mottled or pale skin, and a narrow pulse pressure.

DIAGNOSTIC EVALUATION

There have been many advances in the technology and tools used to diagnose and manage shock. Many of the tools have been more extensively used and validated in adults, and this continues to be an area of ongoing research and development in pediatrics. The currently available tools add contextual information in assessment of

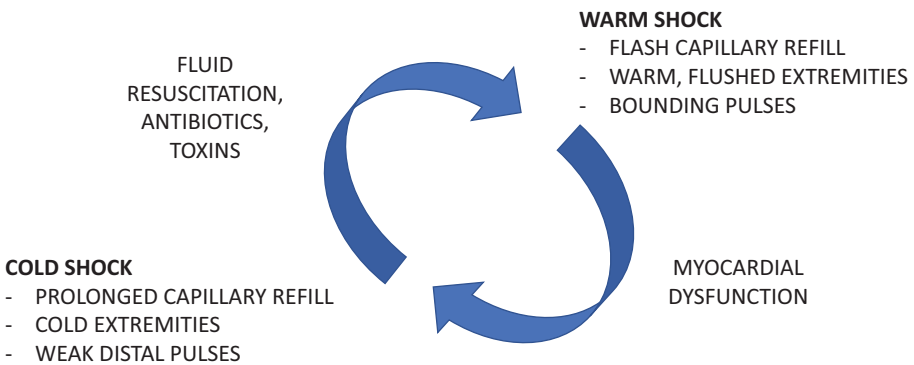

Figure 4. Signs of cold versus warm shock. It is not uncommon to change from one presentation to the other with treatment or progression of illness.

hemodynamics, volume status, and tissue oxygenation that can be paired with other clinical information for a diagnosis of shock.

Monitoring

Near-infrared Spectroscopy. Near-infrared spectroscopy (NIRS) is a noninvasive monitor that provides continuous information about tissue oxygenation, (24) which some consider an additional vital sign. An external adhesive probe is applied to the tissue that measures regional oxyhemoglobin and deoxyhemoglobin. NIRS had classically been used to monitor cerebral oximetry during cardiac bypass but has been extended to pediatric shock evaluation as a marker of regional tissue perfusion. NIRS data cannot be used in isolation but rather for trends over time. One recent study suggests that NIRS may have value as a noninvasive guide for assessing responsiveness to fluid resuscitation. (25) This is especially important to resource-limited or military settings and to prolonged transports when more invasive monitoring or laboratory sampling may not be available to assess CO in the setting of shock.

Pulse Oximetry and Peripheral Perfusion Index. Pulse oximetry is used to measure oxygen saturation. Commonly, in cases with delayed recognition of shock there are reports of not being able to obtain a consistent pulse oximetry reading. Pulse oximetry provides information about perfusion through a calculated perfusion index (PI). The PI is the ratio of the pulsatile blood flow to the nonpulsatile or static blood in peripheral tissue. As such, the PI can be used as a continuous and noninvasive measure of peripheral perfusion obtained from a simple, commonly used pulse oximeter. (26) A low PI is associated with shock and mortality. A recent study evaluated the PI, lactate level, and lactate clearance, demonstrating that all 3 were similar in predicting mortality in pediatric shock. The PI may be an inexpensive, noninvasive measure available for earlier detection and triage of patients with high risk of mortality in pediatric shock. (27) The PI has the potential to become a universal marker of shock if further validated in studies in both high-income countries and low- or middle-income countries.

Laboratory Evaluation

Mixed Venous Oxygen Saturation. Mixed venous oxygen saturation (SvO_2) can be helpful in assessing the whole body VO_2/DO_2 relationship. For SvO_2 to be a helpful measurement it must be obtained from a central venous catheter with the tip in the superior vena cava and in a child without intracardiac shunts.

- Normal SvO_2: Normal oxygen extraction in nonshock states is 25% to 30%. Assuming normal arterial saturation of 100%, a normal SvO_2 should be greater than 70%.
- Low SvO_2: In states of low CO or high metabolic rate there is increased oxygen extraction and a lower SvO_2 (<65%).
- High SvO_2: In higher CO states or states with minimal energy use (eg, sedated/paralyzed, brain death) SvO_2 may be supranormal (>80%–85%), reflecting a narrowed arteriovenous saturation difference. Of note, this can be falsely elevated in toxic exposures such as carbon monoxide poisoning. Lactate and urine output should be used as other markers of adequate DO_2 in these states. (9)(21)

Lactate. Blood lactate levels are a valuable indirect marker of tissue hypoperfusion, although they are not specific for tissue hypoxia. Adult sepsis guidelines recommend using lactate as a trigger for sepsis evaluation as part of the hour-1 sepsis bundle. A lactate level greater than 18 mg/dL (>2 mmol/L) is considered a marker of cellular/metabolic dysfunction. (28) In pediatric shock, optimal levels of hyperlactatemia have not been fully defined, and children can be in a shock state with normal lactate levels. However, if lactate level is high on the initial evaluation, and there are no reasons other than cellular hypoxia, a high lactate level has been shown to correlate with increased mortality. (29) In addition, decreasing lactate levels over time can be used to help track response to therapy. Elevated lactate level is considered a late sign in shock and is associated with increased morbidity and mortality. (30)(31)

Additional Laboratory Evaluation. Depending on signs, symptoms, and history, additional laboratory tests may be helpful in determining shock etiology or to guide ancillary treatment options. Table 2 is not all-inclusive but includes some initial screening laboratory tests to consider.

Imaging

Echocardiogram. A formal echocardiogram can provide detailed information about cardiac function and structure, including estimation of CO/cardiac index, ventricular filling status, and signs of a pericardial effusion, tamponade, or heart strain.

Point-of-Care Ultrasonography. Ultrasonography is a noninvasive imaging tool that is radiation-free and provides rapid real-time information for diagnosis and management of pediatric shock. (32) The use of point-of-care ultrasonography (POCUS) has gained popularity as the technology has become more accessible and physician training in

Table 2. Etiology-Based Targeted Laboratory Evaluation

SUSPECTED ETIOLOGY	LABORATORY EVALUATION	COMMENTS
Infection	Cultures (blood, urine, CSF) Inflammatory markers (CRP, procalcitonin, ESR) CBC count with differential count	Studies based on symptoms and risk factors.
Trauma (hemorrhagic shock)	CBC count Coagulation studies, including TEG/ROTEM	Hemoglobin level may lag behind clinical bleeding. In shock states, a hemoglobin level is often targeted to maintain oxygen delivery.
Endocrine	Cortisol Calcium level Thyroid studies Glucose Ammonia	Can be used in resuscitative efforts or diagnostic of cause of shock. May need to check glucose multiple times in resuscitation.
Cardiogenic	BNP Troponin I	Troponin I is released from damaged myocardial tissue in the setting of ischemia or injury. Elevated troponin level is not diagnostic of shock but is associated with cardiovascular dysfunction and, therefore, is often measured in shock evaluation.
Dissociative	Carboxyhemoglobin Cyanide level	Propofol infusion syndrome is a rare cause, and laboratory evaluation includes CK, lactate, and ABG.

ABG=arterial blood gas, BNP=brain natriuretic peptide, CBC=complete blood cell, CK=creatine kinase, CRP=C-reactive protein, CSF=cerebral spinal fluid, ESR=erythrocyte sedimentation rate, ROTEM=rotational thromboelastometry, TEG=thromboelastogram,

POCUS has increased. POCUS has now become an extension of the physical examination. (33) Some uses of POCUS are highlighted in the following subsections.

Focused Cardiac Examination. Cardiac POCUS can improve clinician understanding of hemodynamics and assist in management choices in pediatric shock. (34) Cardiac POCUS generally focuses on global biventricular function, presence of effusion and/or identification of cardiac tamponade physiology, and evidence of right heart strain. (35)

Inferior Vena Cava Evaluation. Standard measurement of the inferior vena cava and aorta is not as well established in children, but the ratio of the inferior vena cava to the aorta and respiratory variation/dynamic collapsibility have been studied and shown to correlate with hydration status. (10) These measurements should not be used alone as diagnostic but can provide additional information in the evaluation of shock states. (36)

Lung Ultrasonography. Lung POCUS can be used during volume resuscitation in shock to evaluate for signs of pulmonary edema/fluid overload. Lung POCUS can also provide information about pneumothorax, pleural effusion, and consolidation.

Invasive Hemodynamic Monitoring Tools

Placement of central venous access in a patient with shock facilitates safe use of vasoactive medications and can be useful in gathering more information about the patient's hemodynamics.

Central Venous Pressure Monitoring

Measurement of central venous pressure (CVP) should ideally be through a central venous catheter with its tip in the superior vena cava and is affected by both blood volume returning to the heart and cardiac function. Low values (<3 mm Hg) can be seen with hypovolemia and/or distributive shock. High values (>10 mm Hg) can be seen with volume overload, cardiac dysfunction, or causes of high intrathoracic pressure. Elevated CVP has been shown to be an independent risk factor for mortality in pediatric septic shock. (37) Pediatric shock management does not rely on CVP alone, and its use in guiding fluid administration is controversial. (38) Clinical trials have shown that titrating fluid administration to a goal CVP can result in fluid overload. (37)(39) Trending CVPs can still provide useful information about response to therapy; however, careful interpretation of the data in the context of other patient factors is essential. (39)

CO Monitoring

The gold standard for bedside CO measurement continues to be thermodilution techniques using a pulmonary artery catheter; however, given concerns in risk profile and questions of mortality benefit in critically ill patients, this technique has fallen out of favor. (40) Techniques have emerged that use algorithmic data from central venous and arterial catheters that take advantage of pulse contour and power analysis, including FloTrac® (Edwards Lifesciences, Irvine, CA), PiCCO Plus® (Pulsion Medical Systems, Munich, Germany), and LiDCO Plus® (LiDCO Ltd, Cambridge, UK). (41) These

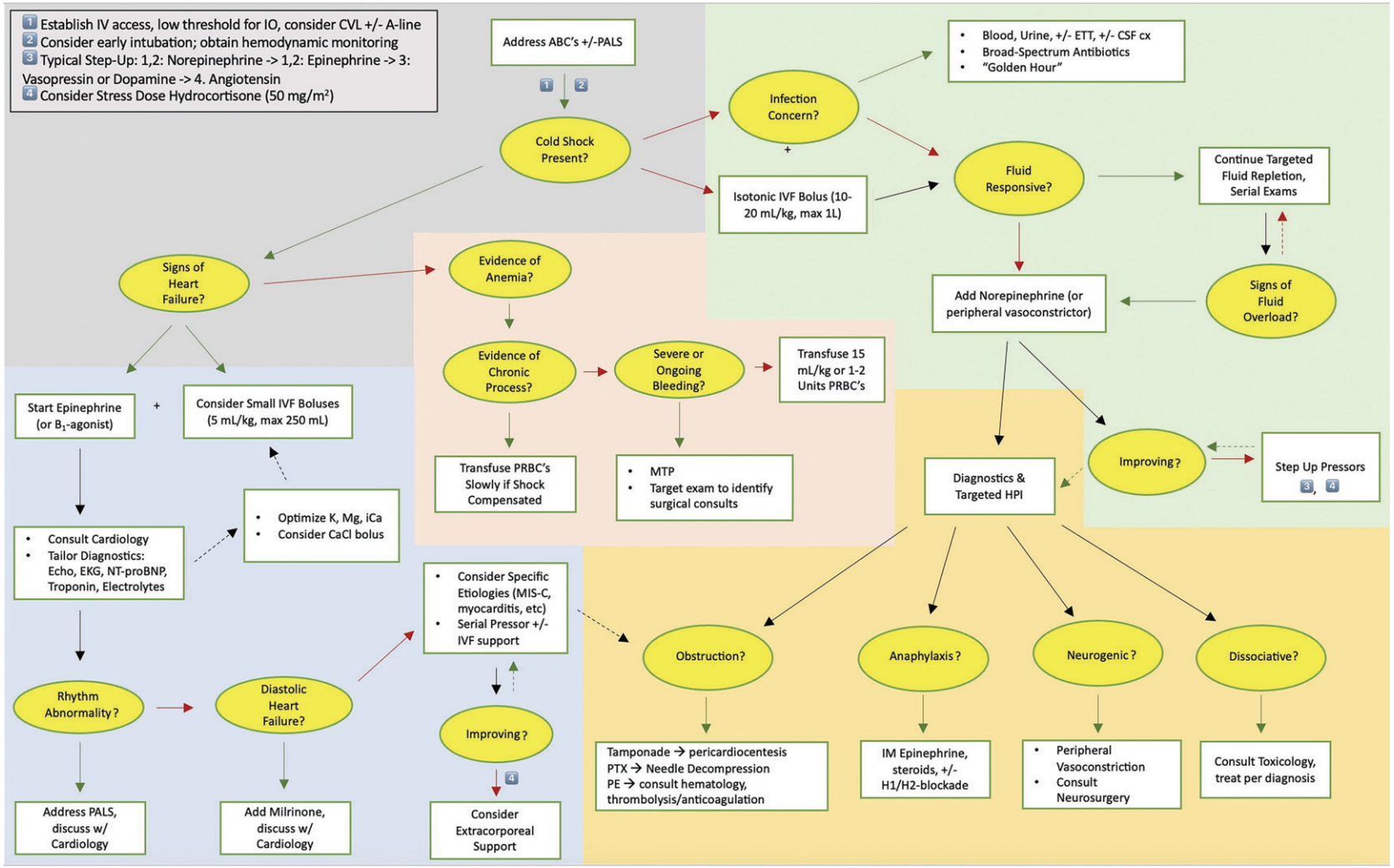

Figure 5. Flow diagram of shock management.

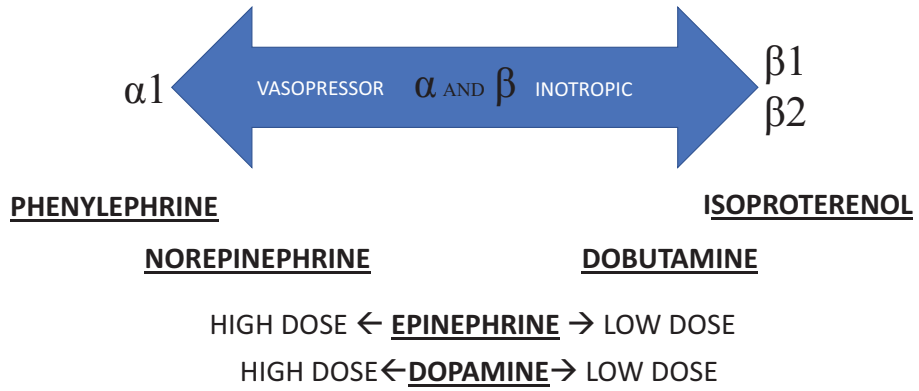

Figure 6. Vasoactive agents and relative receptor activation and hemodynamic effects.

devices provide measurements that include cardiac index and systemic vascular resistance, both indicators of mortality. (38) However, despite known normal values in children, there is no guidance on targets in shock. (1) Given overall sparse validation data, these devices are not yet recommended for routine hemodynamic monitoring in children. (38)(42)

Arterial Catheter

Continuous monitoring of BP via an arterial catheter can provide real-time information for management. The diastolic BP is more accurate from an arterial line than from noninvasive BP monitoring. Waveform analysis may provide clues to shock states due to tamponade, valvular regurgitation, and pulsus paradoxus, among others.

MANAGEMENT

Management of shock uses several concepts of caring for critical illness, including the pathophysiology discussed previously herein. The initial approach should acutely address airway patency, breathing mechanics, and circulation, as well as pediatric advanced life support for cardiac arrest if necessary. Individual variation is targeted toward the type of shock and available resources. (9)(13) Figure 5 is a flow diagram that depicts different management pathways.

General principles include 1) establishing adequate vascular access, which may include peripheral venous catheter, intraosseous needle, or central venous catheter insertion; 2) consideration of approaches to increase DO_2 and decrease overall metabolic and oxygen demand (empirical supplemental oxygen, blood transfusion, endotracheal intubation, sedation, paralysis); 3) intravascular volume assessment and repletion (fluid boluses); and 4) monitoring hemodynamic response and organ perfusion throughout interventions (repeat physical examination, cardiac monitoring, pulse oximetry, arterial access, serial laboratory monitoring, etc).

Use of vasopressors and inotropes, if indicated, is tailored to the individual hemodynamic profile. Epinephrine and norepinephrine, 2 adrenergic agents, are the mainstays of initial vasoactive therapy. (16) Dopamine has fallen out of favor unless other agents are unavailable based on multiple clinical trials. (43)(44) Several factors are used to choose the correct agent; however, generally, norepinephrine—a vasopressor—is used for vasoconstriction in vasodilatory shock (via α1-receptor agonism) and epinephrine—an inotropic agent—is used to improve cardiac contractility in low CO states/cardiogenic shock (via β1-receptor agonism). Figure 6 shows these mechanisms, receptor activation, and expected hemodynamic effect, as a more complete discussion is beyond the scope of this review. Supplementary Table 1, included as an additional resource, shows receptor activation and expected hemodynamic effects. Also note that multiple types of shock may exist simultaneously and require individualized adjustments in therapy. Administration of vasopressor or inotropic support should not be delayed due to lack of central venous access because early initiation may affect outcomes. (45)(46) Our own practice typically incorporates placement of central venous access within 24 hours because rates of complications with peripheral vasoactive medication may increase beyond this time. (47)

Hypovolemic shock management requires replenishment of intravascular volume to improve preload (and, therefore, CO). Replenishment of intravascular volume should be tailored to patient response, with particular attention given to signs of pulmonary edema or cardiac dysfunction throughout resuscitation. Excessive preload may paradoxically decrease CO. In hypovolemic shock demonstrating signs of poor end-organ perfusion, fluid should typically be delivered as a rapid bolus in 10- to 20-mL/kg aliquots. The "push-pull" method uses a 10- to 50-mL syringe, a stopcock, and a giving set to pull volume from a fluid bag and push it manually to the patient rapidly

through the point of vascular access rather than at maximum velocity on a medication pump. Pushing fluid through larger-diameter, shorter catheters (ie, large-bore peripheral intravenous catheters instead of peripherally inserted central catheters) may exploit the Poiseuille law (flow rate is proportional to the radius to the fourth power). Selection of fluid replacement depends on clinical presentation and fluid composition lost during illness. Options for fluid boluses include isotonic crystalloid (normal saline, lactated Ringers, plasma-lyte) and colloid (5% albumin), although blood products (packed red blood cells, platelets, fresh frozen plasma, etc) may also be given, particularly in hemorrhagic shock. Note that colloid use, despite physiologic plausibility of improving oncotic pressure, has not established mortality benefit in pediatrics (48)(49)(50)(51) and may increase mortality in trauma. (52) Choosing between balanced crystalloid (eg, lactated Ringers) versus normal saline may be more difficult given variable literature findings. (53)(54) Product replacement in hemorrhagic shock should maintain balanced repletion of blood components and be guided by institutional massive transfusion protocols. (13)(21)(55) Transfusion in hemorrhagic shock should be ongoing until source control and hemodynamic stability are achieved. (56) The hemoglobin level may lag in hemorrhagic shock; therefore, if signs of shock and bleeding are present, blood administration should not solely rely on hemoglobin measures. As noted previously herein, attention should be given to the development of signs of fluid overload. Vasopressor therapy targeting peripheral vasoconstriction may be required to accommodate BP support while preventing fluid overload.

Cardiogenic shock management centers on addressing clinical etiologies contributing to cardiac failure, supporting CO, and correcting arrhythmia. Early approach for cardiac dysfunction includes β-agonist infusions (eg, epinephrine, dopamine) to provide inotropic support. Volume repletion may help optimize preload but should be performed judiciously given the propensity for poor systolic ejection. Our group favors fluid delivery via approximately 5- to 10-mL/kg aliquots while monitoring signs of volume overload. In clinical presentations in which there is significant diastolic dysfunction, administering milrinone (a phosphodiesterase-3 inhibitor) may be beneficial due to milrinone's inotropy and afterload-reducing properties. Administering milrinone can result in peripheral vasodilation, thus it is important to evaluate for hypotension and vasodilation before milrinone initiation. In cardiac dysfunction with significant right-sided heart strain, including pulmonary hypertensive crisis, strategies to reduce pulmonary vascular resistance may be warranted, using inhaled and systemic pulmonary vasodilators (oxygen, inhaled nitric oxide, prostacyclin), while also normalizing pH, and providing appropriate sedation. Correction of calcium, magnesium, and potassium deficiencies may optimize cardiac function. Cardiology consultation is typically warranted, and echocardiography or POCUS, if available, is useful to aid both diagnosis and management. Refractory cases may necessitate extracorporeal membrane oxygenation (ECMO), such as venoarterial ECMO, or cardiothoracic surgery, and early transport to institutions with these capabilities should be considered in severe presentations.

Distributive shock has disease-specific nuances as to its treatment but universally includes fluid resuscitation and improving vasomotor tone via systemic vasoconstrictors (norepinephrine, phenylephrine, vasopressin, etc). Anaphylactic shock should rapidly be addressed with intramuscular epinephrine and may require epinephrine infusion if refractory, in addition to other antihistaminergic, glucocorticoid, and bronchodilator therapy. Neurogenic shock requires vasopressors for BP support to ensure spinal cord perfusion, and bradycardia may require atropine or cardiac pacing if unresponsive to treatment. Other etiologies and treatments of vasoplegia may be case specific, including consideration of methylene blue as a means of restoring vascular tone via inhibition of nitric oxide synthase and guanylate synthase. (57) Myxedema from severe hypothyroidism requires repletion of thyroid hormone. Adrenal insufficiency, which may be isolated or occur in the setting of other disease processes, requires administration of hydrocortisone. (58)

Septic shock deserves individual mention, although it is a subtype of other types of shock (distributive, hypovolemic). The depth of inflammatory physiology is beyond the scope of this paper. Recently the Surviving Sepsis Campaign issued guidelines for septic shock in children, (16) many of which align with the distributive principles previously herein. A useful diagram is available at http://www.sccm.org/survivingsepsiscampaign/guidelines/pediatric-patients. Additional highlights include use of systematic screening and management protocols, early cultures, empirical broad-spectrum antibiotic initiation within 1 hour of recognition, demonstration of antibiotic stewardship principles as cultures speciate and sensitize, targeted fluid resuscitation with (preferably balanced) crystalloid product, use of norepinephrine or epinephrine as first-line vasoactive agents (not dopamine), mean arterial pressure target of 5th to 50th percentile, avoidance of etomidate for sedation during intubation, early enteral nutrition (gastric if able), normocalcemia and normoglycemia, avoidance of hyperglycemia with insulin use unless there is a sustained glucose level greater than 180 mg/dL (>9.99 mmol/L), overall avoidance of mineral supplements except targeted supplementation in special populations such as children with severe acute malnutrition (ie,

zinc, vitamin C, selenium, etc), and availability of ECMO when clinically appropriate. (16) Based on results from the FEAST (Fluid Expansion As Supportive Treatment) trial demonstrating increased mortality, (59)(60) recommendations in low-resource settings without intensive care include crystalloid fluid boluses (maximum, 40 mL/kg) only in hypotensive patients. (61)(62)(63) Normotensive patients should otherwise receive only maintenance intravenous fluid for fluid resuscitation. When intensive care is available, targeted fluid resuscitation up to 60 mL/kg should be performed within the first hour. Both populations should receive 10- to 20-mL/kg fluid aliquots that are discontinued if any signs of fluid intolerance/overload, including simple physical examination findings such as new hepatomegaly or crackles, appear. (16)

Obstructive shock requires alleviation of the pathologic obstruction preventing adequate CO. Tension pneumothorax should be relieved with needle decompression followed by chest tube insertion. Pericardial tamponade may be amenable to pericardiocentesis. Pulmonary embolism should include thrombolysis, which may be systemic or catheter directed, although it may necessitate surgical thromboendarterectomy. Each of these are larger topics that require more dedicated discussion than this review can provide. While awaiting the definitive procedures needed in all obstructive shock pathologies, gentle fluid resuscitation should be provided to maintain preload and CO. Cardiac function should be supported with inotropic agents as needed.

Dissociative shock treatment involves restoration of appropriate oxygen utilization, either by normalizing a hemoglobinopathy or restoring oxidative phosphorylation. Carbon monoxide poisoning treatment includes delivery of high-concentration supplemental oxygen, with consideration of hyperbaric oxygen therapy once stabilized. Methemoglobinemia is generally treated with methylene blue and supportive care. Cyanide toxicity includes a complex, often multimodal approach, including administration of hydroxocobalamin, sodium nitrite, and sodium thiosulfate. Dissociative shock due to propofol infusion syndrome is considered irreversible; however, prompt discontinuation of propofol at the first sign of this syndrome and provision of supportive care are recommended.

There are some additional considerations broadly applicable to the management of shock. Although debated, hydrocortisone may be considered in fluid and vasopressor refractory hypotension, ideally with a pretreatment cortisol blood level analysis, (16)(64) recognizing that outcomes may be independent of random cortisol levels. (58) Establishing early nutrition as able, particularly gastric if feasible, may improve outcomes. (65)(66) ECMO support may target either primary refractory respiratory failure (venovenous) or refractory cardiac failure (venoarterial). Moreover, the potential sequelae of shock management are broad, requiring astute attention to evolving clinical parameters. Fluid overload may result in respiratory failure and/or renal failure necessitating continuous renal replacement therapy. Adrenergic and vasopressor medications may elicit peripheral ischemia. Inotropes may incite arrhythmias. Blood products may result in transfusion reactions.

CONCLUSIONS

Shock is a clinical manifestation of complex pathophysiology culminating in high multiorgan morbidity and potential mortality, necessitating a detailed approach to management and keen anticipation of rapid changes in a patient's condition.

Future QI work and research: There is ample opportunity for study and improvement in shock management. Some author suggestions include quality improvement targeting early culture sampling and antibiotic initiation in sepsis, improving timing of massive transfusion protocol initiation and compliance with product delivery, and improving clinical recognition of early fluid overload; research of noninvasive advanced hemodynamic monitoring reliability in various forms of shock, advancement of bedside imaging in unstable patients, and identification of biomarkers and diagnostics to aid in recognition of early or worsening shock.

Summary

- We recommend that fluid boluses should not be administered to children in limited-resource settings for septic shock without hypotension. (Based on strong research evidence and expert consensus, level B, strong recommendation) (16)(60)(61)(63)
- We recommend that initial fluid resuscitation in children with noncardiogenic shock should be 10 to 20 mL/kg up to 40 to 60 mL/kg, with examination between boluses for signs of fluid overload. (Based on some research and expert consensus, level C, weak recommendation) (9)(16)
- We recommend that fluid boluses in pediatric shock should be crystalloid not albumin. (Based on some research and expert consensus, level B, weak recommendation) (16)(48)(49)(51)
- We recommend that norepinephrine or epinephrine should be first-line vasopressors for septic shock

rather than dopamine. (Based on some research evidence, level C, weak recommendation) (16)(43)(44)

- Decreasing lactate level over time can be used to help track response to therapy. (Based on limited research, level C, weak recommendation) (30)
- Hydrocortisone may be considered in fluid and vasopressor refractory hypotensive shock, ideally with a pretreatment cortisol blood draw. (Based on some research and consensus, level C, weak recommendation) (16)(64)

References and teaching slides for this article can be found at https://doi.org/10.1542/pir.2022-005630.

PIR QUIZ

1. A child with shock is admitted to the PICU. The attending physician assessing the patient during rounds informs the clinical team that this patient has reached a critical point in his shock. Which one of the following pathophysiologic changes best describes the time at which the critical point of shock appears?

   A. When blood pressure (BP) falls below the 5th percentile for age.
   B. When further resuscitative measures will likely be unsuccessful.
   C. When oxygen extraction depends on oxygen delivery.
   D. When mixed venous oxygen saturation falls below 70%.
   E. When warm shock changes to cold shock.

2. You are taking care of a patient on the general pediatric floor who has been persistently tachycardic since admission earlier this morning. As you evaluate the patient, one of the concerning clinical diagnoses on your differential is shock. Which one of the following clinical patient findings is most consistent with the earliest clinical sign of shock?

   A. Capillary refill time greater than 3 seconds.
   B. Cold extremities.
   C. Decreased urine output.
   D. Loss of peripheral pulses.
   E. Tachycardia.

3. You are caring for a 14-year-old girl brought to the emergency department (ED) with fever. She has bounding pulses, flash capillary refill, tachycardia, and a BP of 92/40 mm Hg. Initial resuscitation included a 1-L normal saline bolus and placement of a central vascular catheter, through which central venous pressure was measured at 3 mm Hg. Serum lactate level was elevated at 21.6 mg/dL (2.4 mmol/L). Point-of-care ultrasonography demonstrated hyperdynamic biventricular function. She was admitted to the PICU. After additional fluid boluses, BP and physical examination findings have not significantly improved. Which one of the following is the best first choice for vasoactive medication in this patient?

   A. Dobutamine.
   B. Dopamine.
   C. Epinephrine.
   D. Norepinephrine.
   E. Vasopressin.

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4. A 3-year-old girl without a significant medical history is brought to the ED by her parents after a 3-day history of having vomiting and diarrhea. She is assessed and found to have evidence of hypovolemic shock. Regarding fluid resuscitation, which one of the following statements reflects best practice for fluid administration in this clinical scenario?

   A. Colloid fluids are the preferred initial resuscitating fluid.
   B. Fluid can be given faster through a peripherally inserted central catheter than any sized peripheral intravenous line.
   C. Fluid is best delivered in 20- to 30-mL/kg aliquots given over 15 to 30 minutes.
   D. Patients presenting in hypovolemic shock cannot develop fluid overload from aggressive fluid resuscitation.
   E. The "push-pull" method of manually delivering fluid is an effective and rapid strategy for resuscitation.

5. A 17-year-old boy is admitted to the PICU after initial resuscitation for multiorgan trauma from a rollover motor vehicle collision. He presented to the ED with a Glasgow Coma Scale score of 5 and was intubated. He received 2 L of crystalloid fluid in the ED, followed by a unit of packed red blood cells. You are awaiting bedside sign-out from the surgical team about the extent of the patient's injuries as he arrives at the PICU from computed tomographic scan. On arrival, the patient has the following vital signs: BP, 84/35 mm Hg; heart rate, 60 beats/min; pulse oxygen saturation, 93% on fraction of inspired oxygen 0.4; temperature, 99°F (37.2°C). The clinical findings in this patient are most consistent with which one of the following types of shock?

   A. Cardiogenic.
   B. Dissociative.
   C. Distributive.
   D. Hypovolemic.
   E. Septic.