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Septic Shock: Recognizing And Managing This Life-Threatening Condition In Pediatric Patients

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Abstract

Septic shock is a relatively rare but life-threatening condition in pediatric patients that can often be difficult to recognize in the emergency department. Once recognized, the emphasis of therapy is to reverse deficits in cellular respiration by increasing oxygen and other substrate delivery to tissue beds. Providing oxygen, improving tissue perfusion through augmentation of cardiac output, and administering antibiotics in a timely manner have all been shown to significantly improve outcomes in children with septic shock. Goal-directed therapy is relatively straightforward, emphasizes the need for effective surveillance and timely recognition of this disease process, and has the potential to significantly reduce morbidity and mortality. This review discusses how to identify specific populations at the greatest risk for septic shock, lays out the essential components of goal-directed therapy, examines potential pitfalls in management, and distinguishes additional ways that emergency clinicians can avoid the devastating consequences of septic shock in pediatric patients.

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CME Objectives

Upon completion of this article, you should be able to:
1. Identify the types of septic shock.
2. Evaluate the role of goal-directed therapy in the management of pediatric shock.
3. Explain management pathways for septic shock in pediatric patients.

Prior to beginning this activity, see "Physician CME Information" on the back page.

Case Presentations

During a busy shift in the ED, an adolescent girl is wheeled back from triage. Her right arm is resting on the arm of the wheel chair, and she is holding her head. Her eyes are downcast, and she appears weak. She saw her doctor the day before with complaints of fever, nausea without vomiting, and generalized muscle aches. Her pediatrician diagnosed her with a flu-like illness and recommended plenty of fluids and ibuprofen as an antipyretic and analgesic. Earlier that morning when her parents went in to check on her, she was weak and could barely get out of bed. Her vital signs in the ED are temperature 39.4°C, heart rate of 141 beats/min, and blood pressure of 80/30 mm Hg. You begin examining the patient as a nurse inspects her upper extremities for a site to place a peripheral IV. She has a generalized erythematous nonpalpable rash, a slightly red posterior oropharynx, supple neck, clear lung fields, tachycardia with an otherwise normal cardiac examination, lower abdominal tenderness without peritoneal signs, and extremities noticeable for 1+ peripheral pulses, 2+ central pulses, and a capillary refill time of 4 to 5 seconds. You ask the respiratory therapist to provide her oxygen by facemask, and now that the nurse has established an IV line, you ask for a rapid bolus of fluid and start to consider antibiotics. The nurse asks, "What type of fluid and how fast?" You think to yourself, "Which antibiotic should I use, and what will I do if her condition continues to decline?" Then you recall that you didn't ask when her last menstrual period occurred.

Just then, a nurse rushes back from triage with a 7-month-old boy who is minimally responsive, limp, mottled, and pale. The child's breathing is not labored, and his airway seems patent. The nurse quickly hooks up the monitors and then starts working to obtain IV access. The child has a pulse, and the monitor shows a heart rate of 190 beats/min, which matches what you feel on examination. The blood pressure cuff inflates, deflates, and re-cycles without giving a reading. The pulse oximeter shows a poor waveform and also seems unable to yield a reading. After several minutes of failed attempts, the nurse looks up and says, "I don't think I'm going to be able to get this IV in." You reach for an intraosseous needle driver and needle, and you drill into the infant's anterior tibia. You ask the nurse to check glucose on the aspirate from the intraosseous needle and start pushing normal saline into it. Realizing just how sick this infant is now, you ask the clerk to call the tertiary children's hospital to arrange transfer. You obtain a basic history from the mother, and she tells you that her baby is usually healthy, but he has had a fever and a couple of episodes of vomiting overnight. While standing over this child, a number of thoughts come to mind at once: "This kid is obviously in shock. Vomiting can be seen with hypovolemic shock, but his history doesn't suggest substantial volume loss. Why is this kid in shock? If not hypovolemic shock, what kind of shock is this? Should I go ahead and intubate this baby? Should I start antibiotics even if I don't know what is causing the infection? When is that transport team from the children's hospital going to call me back?"

A 3-year-old boy undergoing induction therapy for acute lymphoblastic leukemia presents to the ED, and initially, he looked pretty good. His mother brought him in because he had a fever of 39.1°C at home, and she had been instructed to bring him to the hospital for any fevers. He had been in reasonably good spirits when the nurse accessed his central line to obtain blood for laboratory work and cultures. Only a few minutes have passed when the nurse comes to you saying that she is worried about him because he is still febrile but is now tachycardic and sallow in appearance. You go back to his room and agree with the nurse's assessment. You ask for 20 mL/kg of normal saline to be rapidly pushed as you confirm that antibiotics have been given. After 2 more 20-mL/kg boluses of normal saline, there is little improvement in his tachycardia or pulses, and his blood pressure is starting to decline. He has developed "flash" cap refill, and he is less interactive. You ask the nurses to prepare a dopamine infusion and start it at 10 mcg/kg/min. You ask yourself, "What else will help with his tachycardia and hypotension? I've given him fluids and antibiotics, and I'm starting inotropes. Are there other things that have been shown to help in this situation?"

Introduction

For an emergency clinician, there may be nothing more anxiety-provoking than caring for an infant or young child who presents in septic shock. Signs and symptoms concerning for septic shock include fever, tachycardia, evidence of decreased perfusion (such as poor pulses, mottled skin, or delayed capillary refill), decreased urine output, and altered mental status. Conditions that place a child at increased risk for shock include younger age, immunocompromised state, chronic medical conditions, or surgically placed hardware or devices.

Once a child's condition has progressed to this point, it can be very difficult to determine the exact cause. Shock is a common pathway for a multitude of life-threatening illnesses and injuries, and septic shock is one of the most common forms of shock in developed countries. Fortunately, the fundamental principles of early goal-directed therapy for children in septic shock have been shown to reduce the mortality of this condition. These include: (1) providing oxygen, (2) aggressive fluid resuscitation, (3) early antibiotic administration, (4) inotropic support for fluid-resistant shock, and (5) stress-dose steroids for inotropic-resistant shock.

Now more than ever, septic shock is best approached as a "team sport" in which the emergency medicine physician coordinates the initial care with a team of practitioners in the emergency department (ED). Additionally, children whose shock state does not improve with initial interventions, there must

be effective coordination with transport teams and colleagues in pediatric tertiary care centers' intensive care unit (ICU) to ensure that, when indicated, further therapies are initiated and appropriate monitoring is performed while this transition of care proceeds.

Critical Appraisal Of The Literature

Studies of septic shock in pediatric patients in the ED are somewhat limited. Most research on children with septic shock are usually studies of "pediatric shock," which is a heterogeneous clinical entity of which septic shock is only one cause. Individual cases of pediatric shock are not common, and a single institution would have to study data spanning many years to have a reasonably sized study.

The cause of shock is often not immediately apparent on presentation to the ED or the ICU. Therefore, studies tend to be retrospective and rely on information that is only available as the case unfolds over time, which leads to studies that have limited applicability to ED care.

Children in shock are often critically ill, and some clinicians consider interventional or experimental studies to be unethical.[1-3] Performing a study that substantially increases a child's risk for death is unappealing (to say the least) to many researchers, patients, and families.[3] This leads to a paucity of relevant studies. Given the severity of illness, exceptions from informed consent may be needed to allow the performance of a study. Obtaining an exception from informed consent is an arduous process that few researchers have the resources or willingness to endure.[3-5]

It is impossible to compare treatments, for example, since many of the study populations assessing the treatment of shock in children include not just septic shock but also hemorrhagic shock from trauma, hypovolemic shock from a diarrheal illness, cardiogenic shock in children with congenital heart disease, and distributive shock from anaphylaxis. Any discussion of the literature on the treatment of septic shock in children must include the Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012.[6] These guidelines were initially published in 2004, revised in 2008, and then revised again most recently in 2012. They contain the most updated evidence-based recommendations on the approach to managing septic shock and include specific considerations for treating children based on information available through early 2012, but it must be noted that these are consensus expert recommendations based on somewhat limited studies, which has lead to continued use of ineffective or even harmful therapies, simply because evidence is not available to refute their use.[7,8] Some reasons cited for using these ineffective therapies include: a "love of the pathophysiological model (that is wrong)," "a need to do something," and "clinical experience."[8]

Another problem arises when the results of studies involving adults only are applied to the care of children. An example that illustrates this point nicely are the studies demonstrating that activated protein C is an effective therapy for adults in septic shock.[9-11] However, a multicenter study of activated protein C for the treatment of children in septic shock was suspended due to excessive complications and a lack of demonstrated benefit over placebo.[12] In this case, there was an increase in intracranial bleeding, particularly in children aged < 2 months. Reliance on adult data to guide the care of children in this instance would have been harmful.

Finally, some of the most fundamental concepts in the management of shock are supported by very small studies. For example, critically ill children are often found to be hypoglycemic on presentation. Studies that directly address this, however, are rare. One of the best known studies is by Losek, who reported on 49 children undergoing resuscitation, 9 of whom were discovered to be hypoglycemic.[13] Another example involves fluid resuscitation. Although nearly universally recommended, few studies have directly explored whether or not fluid resuscitation is beneficial in management of shock. An early and widely cited study by Carcillo et al addresses fluid resuscitation, but it only included 34 children.[14] Systematic reviews regarding fluid resuscitation seldom evaluate the unproven "facts" and instead compare 2 similar therapies.[15,16]

Epidemiology, Etiology, And Pathophysiology

Epidemiology

Previously, there has been limited information available on the incidence of shock (specifically septic shock) in children, but new data have allowed better understanding of how this process develops. A 2010 study by Fisher et al revealed that the incidence of children presenting in shock was approximately 1 for every 1600 general patients who presented to the ED of a pediatric hospital. The age of the patients tended to be < 3 years, but all ages were significantly represented.[17] In this study, 31% were aged 0 to 3 months, 32% were aged 3 to 36 months, 21% were aged 3 to 12 years, and 16% were aged > 12 years. Of those patients, 57% of the children were classified as having septic shock.

When looking specifically at pediatric sepsis and septic shock, there has been an increase in the number of cases of severe sepsis as well as the prevalence of sepsis in the population.[18] In 1995, the national age-adjusted annual incidence of pediatric sepsis was found to be 0.56 cases per 1000 children, suggesting an estimated 42,364 cases per year nationally.[19] This increased to 0.63 cases per 1000 children

(53,410 cases nationally) in 2000 and to 0.89 cases per 1000 children (75,255 nationally) in 2005.[18,19] The most significant increase in the incidence of severe sepsis was seen in very low-birth-weight infants, but there was also an increase among adolescents (aged 15-19 years) from 0.37 per 1000 in 1995 to 0.48 per 1000 in 2005. Boys were also found to have a significantly higher incidence compared to girls, at approximately 3300 more boys than girls per year nationally.[19] Hospital mortality decreased from 10.3% in 1995 to 8.9% in 2005.[18,19] Throughout these time periods, there was an increase in the prevalence of severe sepsis in children with underlying comorbidities.[18,20] Mortality due to shock in critically ill children is highly associated with multiple-organ dysfunction syndrome, as it is common for multiple organs to fail early, acutely, and simultaneously.[21]

Etiology

Data in children with septic shock and organ failure are limited, and most data analyze the incidence of sepsis, septic shock, and multiple-organ dysfunction syndrome in the pediatric ICU rather than in the ED.[22] In most cases of septic shock described in the ED, a specific etiology is not identified. Among those cases in which an infecting organism is identified, viral as well as gram-negative and gram-positive bacteria are represented.[17] In other studies, gram-negative bacteria were responsible for 50% of the total cases of culture-proven bacterial sepsis, with approximately 115,000 deaths/year.[19,20] Most deaths due to sepsis are caused by central nervous system infections, endocarditis, and gram-negative bacteria. Recently, more gram-positive cases of septic shock have been seen, likely due to the increased use of intravascular devices. The remainder of sepsis cases can be attributed to fungal, viral, and idiopathic causes.

Probable factors contributing to the increasing incidence of sepsis are the widespread use of corticosteroid and immunosuppressive therapies for organ transplants and inflammatory diseases and the fact that patients predisposed to sepsis from an underlying disease process now live longer lives due to medical care, such as the increased use of chronic ventilator support, gastrostomy tubes for providing enteral nutrition, and central venous lines for parenteral nutrition. This rise in bacteremia and sepsis is also related to the increased use of invasive devices, such as surgical prostheses, home mechanical ventilator equipment, and percutaneous intravenous catheters. The overuse of antibiotics, which creates conditions for overgrowth, colonization, and subsequent infection by aggressive, antimicrobial-resistant organisms, contributes as well. The most frequent sites of infection include the lungs, abdomen, and urinary tract. Other sources include the skin, soft tissue, and central nervous system. **Table 1** outlines risk factors for septic shock.

Pathophysiology

Shock is caused by inadequate substrate for aerobic cellular respiration, and the limiting substrate is almost always oxygen. When the cardiopulmonary system no longer adequately supplies the mitochondria with glucose and oxygen to create adenosine triphosphate (ATP), a shock state has developed. This shock state occurs when decreased oxygen delivery limits oxygen consumption and energy production becomes dependent on anaerobic metabolism. Oxygen delivery is dependent on cardiac output and the oxygen-carrying capacity of blood. By increasing heart rate and stroke volume, cardiac output can be increased.[23] In addition to maximizing cardiac output, oxygen delivery can be augmented by providing 100% inspired oxygen, rapidly infusing isotonic fluids to attain an adequate circulating volume, and transfusing packed red blood cells, until there is an appropriate hematocrit level.

Destruction Of Cellular Integrity

If substrate supplies remain inadequate for cellular respiration, cellular integrity will be lost. The normal ion gradients are not maintained and intracellular fluid increases. The resulting cellular edema and energy deficit cause cell death and organ dysfunction. Damage to the endothelial cells of the vasculature causes widespread release of cytokines and immunomodulators, resulting in the systemic inflammatory response syndrome (SIRS), a systemic response to a variety of insults in which hypothermia or hyperthermia, tachycardia, tachypnea, and abnormalities in white blood cell counts are seen. Further interruptions in substrate delivery are seen as microcirculation becomes severely damaged. Eventually, as organs fail, the premorbid condition

Table 1. Risk Factors For Septic Shock

- Neonates
- Victims of trauma
- Immunosuppression
  - Primary oncologic process
  - Human immunodeficiency virus/autoimmune deficiency syndrome
  - Treatment with chemotherapy or immunomodulators
  - Asplenia (eg, sickle cell disease)
  - Congenital immunodeficiency
  - Other disease which decreases activity of immune system
- Children with chronic medical conditions
- Presence of surgically placed hardware or other devices
  - Tracheostomy
  - Percutaneous or tunneled central venous catheter
  - Surgical prosthesis
- Recent use of corticosteroids (due to both effects on immune function and adrenal suppression)
- Chronic use of antibiotics
- Severe malnutrition

termed multiple-organ system failure occurs.

At cellular, microcirculatory, organ, and systemic levels, all manifestations of shock can be explained by a lack of oxygen or glucose utilization in the mitochondria and by limitations in the production of ATP. At the cellular level, this results in anaerobic metabolism, decreased ATP production, and the formation of lactate. The resulting decrease in energy production leads to loss of cell integrity, cellular swelling, and cell death. As energy production and cell integrity are failing, marked damage and dysfunction occur at the microcirculatory level. The loss of function that is seen at the cellular level results in mechanical obstruction of microcirculation, as fluid shifts and cellular swelling cause a loss of lumen diameter and a greater osmotic concentration of intravascular material. There is further damage to the endothelium and activation of multiple inflammatory cascades, including the complement system, cytokines, and interleukins. This causes further endothelial damage and further activation of both the cellular and humoral immune systems, which also contributes to third spacing. This vicious cycle of damage leads to worsening dysfunction.

Organ Dysfunction

Normally, organs autoregulate blood flow within a broad range of perfusion pressures. Once perfusion pressure falls below a certain threshold, the individual organ begins to suffer from a substrate-deficient state. Organ function declines, and, as individual cells swell, the entire organ becomes edematous. As shock worsens, individual organ failure further complicates the clinical scenario. Liver failure results in a deficiency of clotting factors, which potentially exacerbates the bleeding seen in hemorrhagic shock and disseminated intravascular coagulation. The decrease in perfusion of the kidneys results in a decrease in fluid elimination, and, therefore, an increase in both intravascular volume and extravascular volume (increased third spacing). This increase in whole-body fluid most dramatically affects the lungs, resulting in poor compliance, an increased work of breathing, and an elevation in the ventilating pressures required for children being mechanically ventilated. Increased cardiac edema decreases contractility and increases the risk of dysrhythmias and cardiac conduction defects. The hyperkalemia seen in renal failure can cause cardiac dysrhythmias and asystole, while elevated blood urea nitrogen causes decreased platelet function. A vicious cycle of worsening tissue hypoxia, worsening organ dysfunction, and increased inflammatory response occurs throughout the body.

Onset Of Septic Shock

Although septic shock is often considered a form of distributive shock, a more appropriate classification would be as a combination of distributive, hypovolemic, endocrinologic, and cardiogenic shock. Although it was once thought that the specific causative organism involved in a shock state made a significant difference in treatment and outcome, now the actual host response to the insult is recognized as the key factor dictating the clinical course.[24,25]

Septic shock occurs as a response to an infectious agent, mediators from the infectious agent, and the response of the immune system. This creates signs and symptoms of SIRS, sepsis, and septic shock. The myriad responses that occur in sepsis are predominantly the result of mediator release.[25] Some of the mediators involved include interleukin-1 (IL-1), tumor necrosis factor-alpha (TNF-alpha), cytokines, platelet-activating factor, eicosanoids, and nitrous oxide.

Often, increased cardiac output, decreased systemic vascular resistance, a wide pulse pressure, and hypotension characterize the initial stages of this clinical syndrome, a state known as "warm shock." As the shock state continues, there is often a transition to cold shock, in which cardiac output declines, systemic resistance increases, metabolic acidosis is more pronounced, and hypotension worsens. The time course over which warm shock becomes cold shock, and the relative length of time that a child may be in either one of these states, is highly variable and impossible to predict.

As the shock state progresses, multi-organ system failure develops, requiring increasing levels of support. The initial stages of respiratory and renal dysfunction are often seen in the ED, but the full manifestation is often not encountered until the child enters the ICU. Because of the prolonged and extreme disturbance of cellular energy production, the development of organ failure can be rapid and severe. Respiratory failure can occur for a variety of reasons: atelectasis, increased intrapulmonary shunt, and, eventually, decreased oxygen saturation, all of which worsen the cellular hypoxic-ischemic state of the child.

From Systemic Inflammatory Response Syndrome To Septic Shock

The ways in which the body reacts to the insulting infection causing septic shock occur on a continuum from SIRS to sepsis to severe sepsis to septic shock. The continuum contains a number of specific definitions to allow for accurate treatment, communication, and research. Consensus definitions for SIRS, sepsis, severe sepsis, and septic shock were developed and published by International Consensus Conference on Pediatric Sepsis in 2005.[26] **(See Table 2, page 6.)**

SIRS is defined as at least 2 of the following criteria: (1) fever/hypothermia, (2) tachycardia/bradycardia for age, (3) tachypnea/respiratory failure, and (4) leukopenia/bandemia. Sepsis is defined as SIRS in the presence of suspected or proven infection.

Severe sepsis is sepsis and at least 1 of the following: (1) cardiovascular dysfunction, (2) acute respiratory distress syndrome, or (3) ≥ 2 other organ dysfunctions. Septic shock is defined as sepsis and cardiovascular dysfunction presenting as hypotension, the need for vasoactive agents despite the administration of ≥ 40 mL/kg intravenous fluids, or other indicators of hypoperfusion (unexplained metabolic acidosis, lactic acidosis, oliguria, prolonged capillary refill time, or a core-to-peripheral temperature gap). Although formal definitions stress the presence of hypotension, hypotension is not required to be present in children for the diagnosis of septic shock to be made.

Differential Diagnosis

Hypovolemic Shock

The most common cause of shock in children worldwide is hypovolemia, as seen with fluid losses caused by diarrhea and vomiting. These losses are often exacerbated by decreased oral intake. Hypovolemic shock can occur from a variety of illnesses, including viral and bacterial gastroenteritis. Some viral causes of acute gastroenteritis include rotavirus and enterovirus, while bacterial causes include *Escherichia coli*, *Salmonella* species, *Shigella* species, and globally, *Vibrio cholerae*. Hypovolemic shock also occurs in the setting of hemorrhage due to trauma, plasma losses due to burns, environmental exposure, and peritonitis as well as increased urine loss as seen in diabetic ketoacidosis and diabetes insipidus. Hypovolemic shock causes a decrease in cardiac preload, which decreases stroke volume and cardiac output. Due to an increase in sympathetic discharge and catecholamine release, peripheral vasoconstriction and tachycardia are often adequate in mild or moderate volume loss to preserve relatively normal blood pressure.

Table 2. Sepsis, Septic Shock, And Shock Syndromes Definitions

Disease Entity	Definition
Infection	An inflammatory response to invasion of a normally sterile tissue by a microbial organism
Bacteremia	Bacteria in the blood
Systemic inflammatory response syndrome (SIRS)	A systemic response to a variety of insults evidenced by at least 2 of the following: 1. Temperature < 36°C or > 38.5°C 2. Tachycardia • Newborn-1 y: HR > 180 bpm • > 1-5 y: HR > 140 bpm • > 5-12 y: HR > 130 bpm • > 12-18 y: HR > 110 bpm • > 18 y: HR > 90 bpm 3. Tachypnea • Newborn-1 wk: RR > 50 breaths/min • 1 wk-1 mo: RR > 40 breaths/min • 1 mo-1 y: RR > 34 breaths/min • > 1-5 y: RR > 22 breaths/min • > 5-12 y: RR > 18 breaths/min • > 12-18 y: RR > 14 breaths/min 4. White blood count < 4000 cells/mL^3, >12,000 cells/mL^3, or > 10% bands
Sepsis	SIRS occurring simultaneously with or due to infection
Severe sepsis	Sepsis in which organ dysfunction, hypotension, and tissue hypoperfusion exists
Septic shock	Sepsis in which hypotension exists despite adequate fluid resuscitation; evidence of tissue hypoperfusion exists, such as lactic acidosis, decreased urine output, and altered mental status
Multiple organ system failure	Alterations in the function of multiple organs in a critically ill patient
Cold shock	Signs of decreased perfusion, including altered mental status, capillary refill > 2-3 sec, diminished peripheral pulses, mottled, cool extremities, or decreased urine output (< 1 mL/kg/h)
Warm shock	Signs of decreased perfusion, including altered mental status, flash capillary refill, bounding peripheral pulses, or decreased urine output (< 1 mL/kg/h)
Fluid-refractory/dopamine-resistant shock	Shock persists despite 60 mL/kg fluid resuscitation in the first hour and dopamine infusion of 10 mcg/kg/min
Catecholamine-resistant shock	Shock persists despite use of catecholamines, such as epinephrine or norepinephrine
Refractory shock	Shock persists despite goal-directed use of inotropic agents, vasopressors, vasodilators, and maintenance of metabolic (glucose and calcium) and hormonal (thyroid and hydrocortisone) homeostasis

Abbreviations: bpm, beats per minute; HR, heart rate; RR, respiratory rate; SIRS, systemic inflammatory response syndrome.

Adapted from Silverman A, Wang V, Shock: A Common Pathway For Life-Threatening Pediatric Illnesses And Injuries, *Pediatric Emergency Medicine Practice,* 2005, Volume 2(10), page 4.

The diastolic component of the blood pressure may be the most noticeably decreased.

Distributive Shock

Distributive shock occurs when there is a maldistribution of intravascular volume. There may not be an absolute decrease in the circulating volume (as seen in hypovolemic shock); rather, there is an increase in the capacity of the entire vascular system. Because of this large potential capacity in the venous system, decreased vascular tone results in pooling of blood in the large veins. This decreases venous return to the right atrium, results in decreased preload, and, eventually, causes a fall in cardiac output. In cases of spinal cord transection with loss of vascular innervation, the hypotension that is seen is at least partially related to this loss in venous tone. The end result, though, is not significantly different from other forms of shock: tissue hypoperfusion results in lack of substrate at the cellular level. Distributive shock is most often seen in the context of an abnormality in vascular tone. When treating patients with possible anaphylaxis or potential spinal cord injuries, this must be included in the differential of hypotension.

Cardiogenic Shock

Cardiogenic shock is increasingly being recognized as a cause of shock in children. Cardiogenic shock occurs when an intrinsic dysfunction of the heart causes decreased cardiac output, limiting substrate supply to the tissues and cells. The cause of this cardiac dysfunction and decreased myocardial contractility can be difficult to deduce in the ED due to the large number of potential etiologies. **(See Table 3.)**

In addition, because many of the therapeutic modalities used to treat other kinds of shock, including volume expansion and inotropic agents, can increase the work of the heart and worsen cardiac function, the treatment of cardiogenic shock is different. Tests such as chest radiographs, electrocardiograms, and 2-D echocardiograms are essential in making the diagnosis.

It is critical to recognize that the normal systemic responses that are compensatory in hypovolemic and hemorrhagic shock are detrimental to the disease state seen in cardiogenic shock. These mechanisms, which result in an increase in intravascular volume and an increase in systemic vascular resistance, increase the afterload on the heart, which increases the work that the heart must perform.[27] Because of the intrinsic contractile dysfunction, this increased workload causes a further decrease in cardiac function, resulting in a vicious cycle that can lead to congestive heart failure. This may lead to dilation of the cardiac silhouette by chest radiograph as well as increasing tachycardia or worsening respiratory distress coinciding with the administration of intravenous fluids.

Obstructive Shock

Obstructive shock occurs when blood is unable to enter or leave the heart, despite normal intravascular volume and cardiac function. Both cardiac and pulmonary causes exist for obstructive shock, such as cardiac tamponade, tension pneumothorax, pulmonary hypertension, and coarctation of the aorta. Cardiac tamponade, in which fluid accumulates in the potential space between the heart and the pericardium, results from an increase in pressure around the heart. The pressure is transmitted to the right atrium, which causes a decrease in blood return to the heart. As blood return decreases, there is decreased ventricular filling, resulting in a decrease in stroke volume and cardiac output. The end result is cardiac output that is insufficient to support cellular metabolism. Because most causes of obstructive

Table 3. Etiologies Of Cardiogenic Shock

Type	Subtype	Specific Etiology
Myocarditis/cardiomyopathy	Infectious	Viral, bacterial, fungal, protozoal, rickettsial, sepsis
	Metabolic	Hypothyroid, glycogen storage disease, hypoglycemia, carnitine deficiency, fatty acid metabolism, acidosis, hypothermia, hypocalcemia
	Hypoxic-ischemic damage	Cardiac arrest, traumatic brain injury, anomalous coronary artery, prolonged shock, postcardiopulmonary bypass
	Connective tissue disorder	Systemic lupus erythematosus, juvenile rheumatoid arthritis, polyarteritis nodosa, Kawasaki disease
	Neuromuscular disease	Duchenne muscular dystrophy, myotonic dystrophy, spinal muscular atrophy
	Toxins	Sulfonamides, penicillins, anthracyclines
	Other	Idiopathic dilated cardiomyopathy, familial dilated cardiomyopathy
Trauma	Cardiac injury	Cardiac contusion, ventricular rupture, coronary laceration
Dysrhythmias	Abnormalities of rate	Supraventricular tachycardia, ventricular dysrhythmias, bradycardia
	Tachydysrhythmias	Supraventricular tachycardia, atrial flutter, ventricular tachycardia

Reprinted from Silverman A, Wang V, Shock: A Common Pathway For Life-Threatening Pediatric Illnesses And Injuries, *Pediatric Emergency Medicine Practice,* 2005, Volume 2(10), page 5.

shock cannot be treated medically, it is paramount that they are recognized so that proper, expeditious surgical or invasive treatment can occur (eg, placement of a chest tube, placement of a pericardial drain, or removal of a mass from the mediastinum).

Adrenal Insufficiency (Endocrinologic Shock)

Children who have either recently completed a prolonged course of steroid therapy or who are on chronic steroid replacement therapy are at high risk for the development of adrenal insufficiency.[28,29] Because of the potential suppression of the endogenous production of both glucocorticoids and mineralocorticoids during treatment with exogenous steroids, the abrupt withdrawal of steroids can result in an abrupt deficiency. Additionally, in children who do not have a normal ability to produce adrenocorticotropic hormone and cortisol, the body will not respond to increased stress in a predictable manner. Seemingly inconsequential increases in metabolic demands, such as a viral illness and minor surgery, can result in adrenal crisis and shock in the individual who is not able to compensate.

Adrenal insufficiency causes a decrease in cardiac contractility and a decrease in venous tone, possibly due to a decrease in the density of available adrenergic receptors. This loss of receptors to both endogenous and exogenous epinephrine and norepinephrine results in a relatively inotropic-refractory shock that must be diagnosed and treated, if the shock is to be reversed. If clinical suspicion is high and shock is severe, treatment can be initiated before laboratory tests are obtained. In less-emergent situations, a random cortisol level can aid in making the diagnosis of adrenal insufficiency.

Prehospital Care

Standard resuscitative measures are all that should be required for the prehospital care of children in shock. The crux of initiating care is timely recognition by prehospital providers. Most prehospital providers have vastly greater experience caring for adults. Pediatric emergency medicine clinicians should consider working with local transport services to ensure that adequate training is available to increase the recognition and appreciation of septic shock in children. Once septic shock has been recognized, the mainstays of care, such as administration of oxygen, rapid intravenous or intraosseous access, initiation of fluid resuscitation, and ventilatory support (if indicated), are all that is typically needed. The hospital of destination is determined by local protocols. Most localities divert critically ill children to specialized centers, if the travel distance and time is not prohibitive.

Emergency Department Evaluation

Initial Evaluation And Resuscitation

The treatment of septic shock is based primarily on addressing the pathologic process occurring, not the specific etiology. This being the case, supporting cellular respiration by maximizing oxygen transport to cells becomes the focus of therapy.

Goal-directed therapy has become the primary approach when caring for adults with septic shock. In many EDs, the basic treatments of early goal-directed therapy can be ordered and implemented in clinical bundles. There is evidence that goal-directed therapy improves outcomes in adults,[30] although recent studies failed to show an improvement in protocoled treatment of septic shock incorporating goal-directed interventions.[31] This likely reflects the reality that the goal-directed approach to treating septic shock has become so ubiquitous that protocols provide little improvement of standard care. Therefore, the initial treatment is focused on optimizing intravascular volume and providing a high percentage of inspired oxygen by facemask or high-flow nasal cannula, if available, along with the early administration of antibiotics. If these interventions are not adequate to restore aerobic metabolism at the cellular level, further steps will be necessary. Increasing cardiac output using inotropic agents and optimizing oxygen-carrying capacity via red blood cell transfusions can have a dramatic effect on the delivery of oxygen to tissues and on reversing anaerobic metabolism.

Understanding and preparing for management of children with shock can achieve significant decreases in morbidity and mortality. But this requires knowledge of what therapies are needed. Despite the lack of abundant research in management of children with septic shock, the evidence that is available must be applied to the treatment of this pathophysiologic condition. By recognizing the signs and symptoms of both compensated and uncompensated shock, the process can be treated. To accomplish this, though, a methodical and thorough approach to septic shock must be undertaken.

Obtain A Focused History

When a child enters the ED and septic shock is suspected or recognized, immediate therapy is indicated. A brief history should be obtained to assess for specific causes of infection, which may require specific treatments to decrease the infectious burden. Recent surgeries (especially abdominal) could increase the risk of gram-negative and anaerobic bacteria as the source of infection. A history of recent or recurrent skin infections could indicate gram-positive bacteria and methicillin-resistant *Staphylococcus aureus* (MRSA). Headaches and altered mental status would suggest possible central nervous system

infections as the cause of septic shock. The risk of sepsis being the cause of shock is increased by a history of risk factors such as immunodeficiency from malignancy, chemotherapies, the presence of an indwelling catheter, the use of steroids, or diseases such as sickle cell disease.

Provide Ventilation And Oxygen
Knowing that limitations of cellular respiration are causative to all forms of shock, basic therapies such as providing a patent airway, determining the adequacy of ventilation, giving high-flow oxygen, and reversing circulatory compromise are essential.

Obtain Vascular Access And Begin Fluid Resuscitation
Vascular access must be obtained as well. Initial attempts to place a peripheral intravenous catheter may not be successful in a patient with a depleted volume status and with vasoconstrictive compensatory mechanisms present. Thus, obtaining intraosseous access must be considered expeditiously. Once vascular access has been established, aggressive fluid resuscitation with isotonic crystalloid, such as lactated Ringer's or 0.9% normal saline, should be given rapidly in 20 mL/kg boluses. If rapid fluid resuscitation in quantities > 80 to 100 mL/kg is not adequate to reverse shock, vasoactive agents such as dopamine, epinephrine, and norepinephrine must be considered to support the child.

Administer Antibiotics Early
Simultaneously, unless there are obvious reasons to eliminate septic shock from the differential in children presenting in a shock state, it is paramount that administration of broad-spectrum antibiotics are initiated quickly, either via an intravenous or intramuscular route. While instances of cardiogenic shock are rare, it must always be considered, since therapy in these situations differs from treatment in the patient with relative hypovolemia.

Cautions In Patients With Decreased Cardiac Function
Patients with decreased cardiac function, whether in the initial stages of myocarditis or in the more advanced stages of dilated cardiomyopathy, will not respond to rapid volume expansion in the same way that children with septic shock will. Because volume expansion occurs when there is cardiac pump failure, further increasing volume acutely can increase the afterload to a vascular system that has no capacity to hold that fluid. This increased fluid becomes increased pressure that markedly increases afterload to the failing heart. When a patient presents in extremis, there is little time to check a chest radiograph for cardiomegaly or to get a complete cardiac history. But if time permits, this information can drastically change the approach to the child. Consider early radiographs to evaluate for cardiomegaly, and perform frequent reevaluation of the child for signs and symptoms of cardiac insufficiency (worsening hemodynamics despite appropriate fluid resuscitation, decreased oxygen saturations, crackles in the lungs, or developing hepatomegaly).

Focus Care And Obtain Additional History
Once therapy to reverse the process of shock has been initiated, additional efforts must be made to focus care. If possible, a member of the team should attempt to obtain relevant historical information from the caregivers. Pertinent questions include those related to vomiting and diarrhea, fever, trauma, medical history (assessing for issues which could cause immunocompromise or heart disease), medications, and allergies.

Respiratory Support

If spontaneous breathing with a high percentage of inspired oxygen by face mask or high-flow nasal cannula is not adequate to maintain an oxygen saturation of at least 92% and a partial pressure of oxygen (pO_2) of at least 65 mm Hg, mechanical support of breathing is indicated. If the child is in respiratory failure, rapid sequence intubation (RSI) should be used to initiate mechanical ventilation. Great care must be taken when there is concern for decreased cardiac function. Since all sedatives can decrease vascular tone and potentially have negative inotropic effects, they should be used cautiously during RSI. In addition, since muscle relaxants (ie, paralytics) can decrease muscle tone, which affects the preload of the heart, intubation may cause acute and fatal cardiac deterioration.

Medications For Rapid Sequence Intubation
Ketamine And Etomidate
Ketamine can cause analgesia and amnesia at a dose of 1 to 4 mg/kg administered intravenously. Its onset of action is < 2 minutes, and the duration of action is up to 30 minutes. Ketamine has advantages as an induction agent: (1) It does not inhibit spontaneous respiration (making useful for a sedative-only intubation) (2) It causes a catecholamine release, which increases blood pressure and heart rate. Ketamine is considered to be especially useful in critically ill patients.[32] Side effects may include tachycardia, hypertension, emergence phenomenon in older patients, laryngospasm, and excessive salivation. Etomidate, dosed at 0.2-0.4 mg/kg IV, has a rapid onset within 30-60 seconds and has a short duration of action of 5 to 15 minutes. The main advantage of this induction agent is that there are few cardiovascular and respiratory effects.

Modified Rapid Sequence Intubation Technique
If the use of ketamine is contraindicated, then a

modified RSI technique can be utilized, which employs a sedative, an analgesic, and a muscle relaxant. A single, short-acting agent that provides deep sedation may be desirable, but propofol, and potentially ketamine, can have significant drawbacks. As hemodynamics are preserved by a compensatory release of noradrenalin, the patient's noradrenalin stores may be depleted by the prolonged stress state, and the use of ketamine may result in hypotension.[33] Etomidate is commonly avoided in the management of septic shock because of the concerns regarding adrenal suppression,[34-37] and propofol is known to cause hypotension due to vasodilation and direct cardiac depressant effects. Therefore, in order to prevent pain and anxiety in the child about to undergo intubation, it is reasonable to use the combination of a short-acting benzodiazepine (such as midazolam) and a short-acting opioid (such as fentanyl). These agents, used in conjunction with a nondepolarizing muscle relaxant (such as rocuronium), facilitate the relatively rapid attainment of a state in which endotracheal intubation is possible.

Atropine

Atropine may be used to prevent the vagal reflex caused by stimulation of the posterior oropharynx, trachea, and carina, although some practitioners believe that, in the setting of extreme tachycardia due to shock, this is not necessary. Since bradycardia would be poorly tolerated in the heart-rate–dependent child with decreased cardiac output, if atropine is not used, an adequate dose should still be drawn up and kept on a 3-way stopcock through which the other drugs for intubation are given, so that it can be given immediately, if needed.

Endotracheal Tubes

Once sedation and muscle relaxation have been provided, or if they are unnecessary due to the comatose state of the child, orotracheal intubation can be performed with an appropriately sized endotracheal tube. **(See Table 4.)** The choice to use a cuffed endotracheal tube in children has evolved over recent years. It is now recognized that, when modern tubes with high-volume, low-pressure cuffs are correctly sized (by decreasing the traditionally sized tube by 0.5 cm internal diameter), they can allow for the safe provision of the high pressures that may be needed in children with acute respiratory distress syndrome (ARDS) who have poorly compliant lungs and the need for relatively high inflating pressures.

It is essential that placement of the tube is confirmed by monitoring of end-tidal CO_2 ($ETCO_2$), auscultation of breath sounds over both lung fields and the stomach, increase or maintenance of oxygen saturations, and a chest radiograph. Once the endotracheal tube is appropriately placed, either bag-valve-mask ventilation or mechanical support with a ventilator can be provided.

Airway Pressures

Increasingly, it is recognized that the use of relatively high positive end-expiratory pressure (PEEP) in the range of 8 to 16 mm Hg when conventionally ventilating children allows for decreased fraction of inspired oxygen (FiO_2), lower peak inspiratory pressures (PIP), and a decreased incidence of ventilator-associated lung injury. But caution must be exercised when using high ventilatory pressures in the setting of septic shock. High ventilatory pressures will increase intrathoracic pressure, which potentially decreases venous return. If bag-valve-mask ventila-

Table 4. Approximate Size And Depth For Placement Of Endotracheal Tubes And Central Venous Lines

Age	Uncuffed ETT ID (mm)	Cuffed ETT ID (mm)	Initial ETT depth[a]	Central Line Size[b]
Newborn	3.0-3.5	3.0	9-10	5-8 cm/4 Fr
1-5 months	3.5	3.0-3.5	10	5-8 cm/4 Fr
6-11 months	3.5-4.0	3.5	11	8-12 cm/4-5 Fr
1 year	4.0-4.5	4.0	12	8-12 cm/4-5 Fr
2-3 years	4.5-5.0	4.0-4.5	12-13	8-12 cm/4-5 Fr
4-5 years	5.0-5.5	4.5-5.0	13-15	8-12 cm/5.5-6.0 Fr
6-9 years	5.5-6.0	5.0-5.5	15	8-12 cm/5.5-6.0 Fr
10-12 years	6.5-7.0	6.0-6.5	17	12-15 cm/6.0+ Fr
13+ years	7.0-7.5	6.5-7.0	19	12-15 cm/6.0+ Fr

Abbreviations: ETT, endotracheal tube; ID, internal diameter.

[a]Depth measured at lips in cm

[b]Length is in cm, size in French (Fr)

Reprinted from Silverman A, Wang V, Shock: A Common Pathway For Life-Threatening Pediatric Illnesses And Injuries, *Pediatric Emergency Medicine Practice*, 2005, Volume 2(10), page 9.

tion is to be used for a prolonged period of time, this increased end-expiratory pressure can be provided by the use of a PEEP valve on most bags.

Measuring Ventilatory Status

Ventilatory status can be noninvasively monitored using pulse oximetry and $ETCO_2$ monitoring. An arterial blood gas should be obtained 10 to 15 minutes after stable respiratory support has been established, in order to more accurately measure pH, partial pressure of oxygen (pO_2), and partial pressure of carbon dioxide (pCO_2). It may also be useful, if central venous access has been established, to measure a venous blood gas. Ideally, blood drawn from a central venous catheter, which can sample blood in the superior vena cava or right atrium, will have an oxygen saturation of at least 70%. Blood sampled from the inferior vena cava is not considered adequate for true prognostication with regard to saturation level, but it is often found to be useful when determining the success of resuscitation.

For additional information on the pediatric airway, see the *Pediatric Emergency Medicine Practice* issue titled "Evidence-Based Emergency Management Of The Pediatric Airway," at: www.ebmedicine.net/pediatricairway and listen to the *Pediatric Emergency Medicine Practice* Audio Series Vol. II at: www.ebmedicine.net/PEMPAUD14.

Vascular Access

In treating shock, it is essential that adequate vascular access is established in a timely manner. Delaying peripheral access to obtain a central venous line is seldom indicated when starting the resuscitation for septic shock, as normal saline, antibiotics (if needed), and inotropic agents can all be administered peripherally. An experienced emergency clinician can often place a peripheral intravenous catheter in a child with mild to moderate shock. If the extremities are cool and there is significant vasoconstriction, other means of vascular access may be required. Although the use of ultrasound can decrease the number of attempts and time needed for peripheral intravenous line placement,[38] there is no evidence currently available regarding its use in pediatric patients in shock.

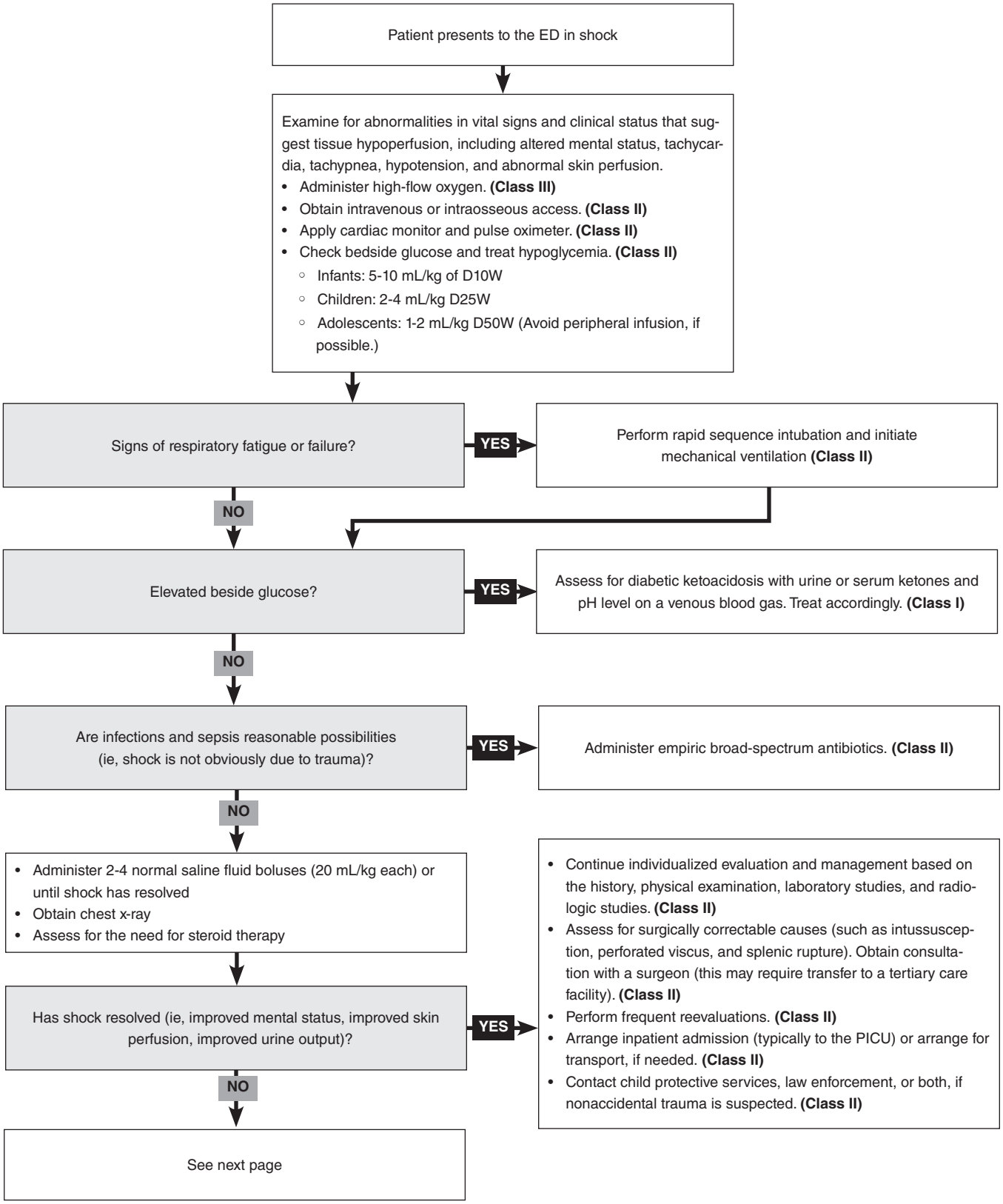
An intraosseous catheter can be placed in children when other forms of vascular access cannot be established, as intraosseous catheters have proven to be just as effective as central venous lines for resuscitation.[39-43] The location used most often for placement of an intraosseous catheter is on the proximal tibia, 2 to 3 cm below the tibial tuberosity. If placement is unsuccessful in one limb, the contralateral tibia can be attempted. After failure in any single bone, further attempts on that bone are contraindicated, since there may be cortical disruption. In both children and adults, when placement is unsuccessful in the proximal tibia, it can be attempted in the distal femur, 3 to 4 cm above the medial condyle. A properly placed intraosseous line is considered equivalent to a central line, and all necessary medicines can be infused through it. If personnel with adequate training are available and attempts at peripheral venous and intraosseous access have been unsuccessful, a central venous line should be placed. **(See Table 4, page 10.)**

In younger children and infants, the femoral vein is the most easily accessed. Using the Seldinger technique, an appropriately sized single- or double-lumen central venous catheter can allow volume replacement, medication administration, and safe continuous infusions of vasoactive agents, if needed. The use of ultrasound for guidance in central venous line placement has been shown to decrease the number of attempts and improve the overall likelihood of successful cannulation.[44,45] In older children, the internal jugular and subclavian vein can be cannulated. These upper lines have the added advantage of allowing for blood sampling and pressure monitoring of blood in close proximity to the right atrium. In most cases, pressure transduction of a venous line will not occur in the ED, but, in some situations, having this information can be extremely helpful. Pressure monitoring of low-lying central venous catheters (eg, femoral lines) is reasonably accurate, except in cases of abdominal compartment syndrome and high ventilation pressures.[46,47]

Fluid Resuscitation

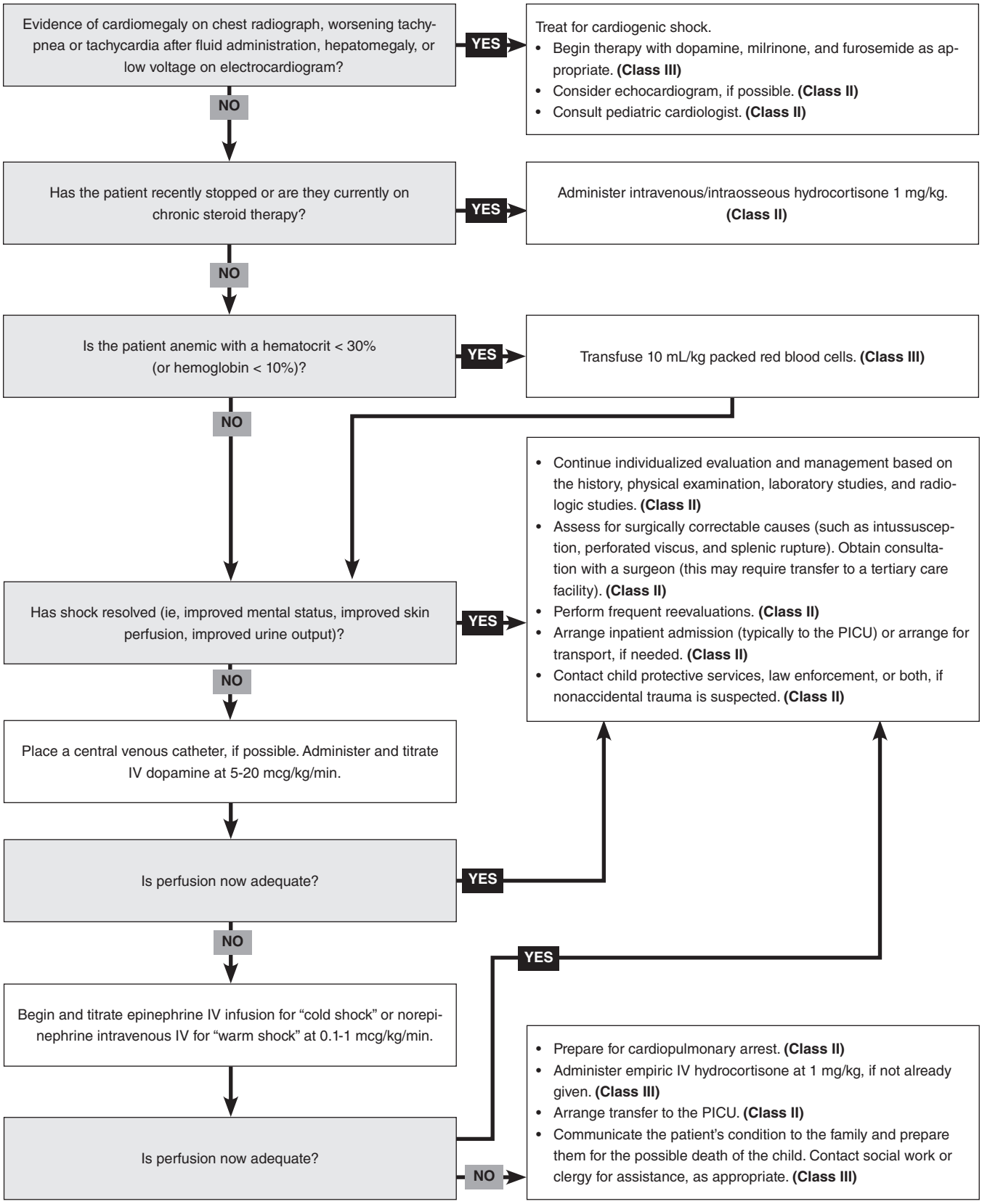
Once the airway is considered patent or secured, oxygen is given, and vascular access has been obtained, support of the circulatory system is the primary focus in treating shock. Either lactated Ringer's or 0.9% normal saline should be rapidly administered.[48-53] An initial bolus of 20 mL/kg ideal body weight is considered the standard volume to administer.[54-57] The rate of infusion must be rapid enough to allow time for infusion of at least 60 mL/kg fluid in < 60 minutes. This means that each 20 mL/kg bolus is given over 5 to 10 minutes to allow for reassessment of the child's volume and perfusion status as well as preparation for repeated fluid administration. In a 2008 study, no difference was shown with this method (20 mL/kg of isotonic fluid in repeated boluses up to 60 mL/kg/hr) when compared to giving 40 mL/kg of fluid followed by dopamine and further goal-directed titration of therapies.[58] During resuscitation for septic shock, fluids should be administered either with the "push-pull" method using a syringe, a 3-way stopcock, and a bag of intravenous fluids or by using multiple syringes that have been filled with the chosen resuscitation fluid. Fluids should not be administered via a standard electric pump during resuscitation because of limitation in infusion rate. Most electric pumps can only provide rates of 999 mL/h. However, a number

Clinical Pathway For Emergency Department Management Of Septic Shock In Pediatric Patients



Abbreviation: D10W, 10% dextrose in water; D25W, 25% dextrose in water; D50W, 50% dextrose in water; ED, emergency department.
See page 14 for the Class of Evidence definitions.

Clinical Pathway For Emergency Department Management Of Septic Shock In Pediatric Patients (continued)



Abbreviations: IV, intravenous; PICU, pediatric intensive care unit.

See page 14 for the Class of Evidence definitions.

of different techniques can be used to provide rapid fluid resuscitation: (1) the use of multiple normal saline-filled syringes; (2) the use of a single syringe connected to a 3-way stopcock which can "pull" fluid from a normal saline bag and, when the stopcock is turned, "push" fluid to the patient; or (3) in larger children or adults, a rapid infuser or pressure bag can be used. In cases where cardiogenic shock is a strong consideration, the administration of fluid must be approached with caution; if the diagnosis of cardiogenic shock is established, gentle diureses is a more logical therapy. Unfortunately, this requires that an accurate diagnosis has already been made, which is often not the case in the ED.

Alternative Fluids For Resuscitation

Resuscitation by means of fluids other than isotonic crystalloid and blood products is controversial. Many of these alternative fluids, such as albumin and hetastarch, have been shown to decrease the time to euvolemia and decrease the total amount of fluid required to reach adequate volume status, but none of these have been shown to change overall mortality when compared to normal saline or lactated Ringer's solution.[59,60]

Determining Volume Status

Determining volume status can be extremely difficult. The return of normal mental processing, blood pressure, peripheral perfusion, and urine output may not occur rapidly in a child who is suffering from severe shock. Many adult studies have shown the effectiveness of goal-directed therapy for septic shock,[6,30,61-64] but these often require monitoring modalities that are not reasonably used in the ED (such as pulmonary artery catheters). Therefore, the recommended indicators of volume status are capillary refill time ≤ 2 seconds, normal blood pressure for age, normal pulses with no difference between peripheral and central pulses, warm extremities, urine output > 1 mL/kg/hr, and normal mental status.[6]

Volume administration may or may not result in an increase in blood pressure in situations of fluid-refractory shock, but it should increase central venous pressure. Administration of volume that does not result in at least a 5-mm Hg rise in central venous pressure is suggestive of severe hypovolemia. As the large capacitance vessels in the venous system fill, a more robust increase in central venous pressure will be seen, albeit briefly in cases where there is still hypovolemia. As euvolemia is approached, the response to volume administration will be a prolonged increase in central venous pressure and, ideally, an increase in arterial pressure.

Urine output can be a useful tool in assessing volume resuscitation. This requires placement of an appropriately sized bladder catheter once resuscitation has been initiated. Bladder catheterization also allows for the sterile collection of urine as part of the workup for shock. A reasonable urine output goal during resuscitation in children is a minimum of 1 mL/kg/h. In rare cases of long-standing shock prior to medical attention, the child may quickly enter a polyuric phase of acute tubular necrosis once resuscitation begins. This can make the assessment of urine output misleading, and other indicators of volume status must then be relied upon.

The amount of fluid to use in resuscitation is clinically directed, but there are some limited data addressing the effectiveness of aggressive volume replacement. In a 1991 study of 34 patients with septic shock, Carcillo et al showed that giving > 40 mL/kg in the first hour was associated with improved outcome, with no increase in pulmonary edema or incidence of ARDS.[14]

More recently, Han et al showed that, in children with septic shock, fluid resuscitation was inadequate a majority of the time, and this was associated with a prolonged period of shock.[65] In fact, regardless of the duration of shock, both survivors and nonsurvivors received approximately 20 mL/kg of fluid resuscitation. The authors concluded that this indicates a failure by clinicians to continue fluid resuscitation after an initial bolus. Unfortunately, the

Class Of Evidence Definitions

Each action in the clinical pathways section of *Pediatric Emergency Medicine Practice* receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Nonrandomized or retrospective studies: historic, cohort, or case control studies
- Less robust randomized controlled trials
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

data also demonstrated that prolonged shock was associated with a > 9-fold increase in mortality.

Inotropic And Vasoactive Agents

In situations where volume resuscitation is inadequate to reverse signs of shock (such as tachycardia, hypotension, and altered mental status), catecholamines are the next line of therapy employed. These agents work on various receptors with different effects. Dopamine, dobutamine, epinephrine, and norepinephrine each have unique properties with regard to their interaction with these receptors and the degree of signaling. The receptors are categorized as alpha, beta, and dopaminergic.[66] The agents that stimulate alpha-receptors cause smooth muscle contraction in arterioles and bronchiole muscles. This leads to vasoconstriction, which raises blood pressure and cardiac afterload. Beta-receptors have 2 important subtypes: beta-1 and beta-2. Beta-1 receptors mediate contractility (inotropy) and heart rate (chronotropy). This occurs through an increase in intracellular calcium. Beta-2–receptor activation, on the other hand, causes smooth muscle relaxation, resulting in arteriole dilation and bronchiole relaxation. Dopaminergic receptors are found predominantly on the kidneys, and they increase renal blood flow. In most situations, if rapid fluid resuscitation does not restore perfusion, the continuous infusion of one of these agents is indicated. They all have short half-lives, so their pharmacologic effects are seen within minutes (although clinical effects may be delayed or blunted due to other clinical circumstances).

Table 5 provides a summary of inotropes, including mechanisms, doses, and clinical indications in patients with shock.

Dopamine

In pediatric shock, peripherally administered dopamine (ie, via a peripheral intravenous line) is a well-established choice for a first-line agent.[6,62,67] The initial rate of infusion is 5 to 10 mcg/kg/min. At this dose, the effect is predominantly beta-adrenergic, causing an increase in heart rate and contractility. As the rate of infusion is increased to a maximum of 20 mcg/kg/min, the inotropic effects also increase. However, there is an even larger increase in the alpha-adrenergic effects, which leads to an increase in peripheral vasoconstriction. The combination of these alpha-adrenergic and beta-adrenergic effects improves blood pressure, cardiac output, urine production, and extremity perfusion.

Epinephrine

In cases of severe shock, or if there has been inadequate clinical improvement with doses of dopamine approaching 20 mcg/kg/min, epinephrine is the next agent that should be used.[62,67-72] The starting dose of epinephrine is 0.05 mcg/kg/min. This produces predominantly beta-adrenergic effects (increased inotropy and chronotropy). At doses beyond 0.2 to 0.3 mcg/kg/min, there are increasing alpha-adrenergic effects, causing increased vasoconstriction. Although there is no true limit to the rate of epinephrine infusion, rates > 1 mcg/kg/min are thought to cause severe peripheral vasoconstriction

Table 5. Inotropes: Mechanism, Doses, And Clinical Indications In Patients With Shock[62,73,74]

Inotrope	Mechanism	Effects	Clinical Usage	Dosing Range
Dopamine	Dopaminergic at lower dosing range Beta-1 and beta-2 at increasing doses Alpha at the higher end of dosing	Increased cardiac output Vasoconstriction at higher doses	Septic shock (low–cardiac-output shock)	5-20 mcg/kg/min
Epinephrine	Beta-1 and beta-2 at increasing doses Alpha at the higher end of dosing	Increased cardiac output Vasoconstriction at higher doses	Moderate to severe septic shock (low -cardiac-output shock)	0.05-1 mcg/kg/min (doses > 1 mcg/kg/min indicate extremely severe cardiac dysfunction)
Norepinephrine	Predominance of alpha even at lower doses Beta-1 and beta-2 at increasing doses	Increased vasoconstriction Some increased cardiac output	Moderate to severe “warm” septic shock (high cardiac output with vasodilation)	0.05-1 mcg/kg/min (doses > 1 mcg/kg/min indicate extremely severe cardiac dysfunction)
Milrinone	Increases cAMP via inhibition of phosphodiesterase, modulates intracellular calcium	Increased diastolic relaxation; increased cardiac output and vasodilation	Myocarditis/cardiomyopathy (often with dopamine)	0.25-0.75 mcg/kg/min
Vasopressin	Increases levels of inositol triphosphate and diacylglycerol, which, in turn, increase intracellular calcium	Increased peripheral vasoconstriction	Moderate to severe “warm” septic shock (high cardiac output with vasodilation)	0.04-0.1 units/min (adult) or 0.0005-0.001 units/kg/min (pediatric)

Abbreviation: cAMP, cyclic adenosine monophosphate.

Adapted from Silverman A, Wang V, Shock: A Common Pathway For Life-Threatening Pediatric Illnesses And Injuries, *Pediatric Emergency Medicine Practice*, 2005, Volume 2(10), page 14.

and tissue ischemia. A resuscitation that requires the prolonged use of epinephrine at these rates is seldom successful.

Milrinone

In patients who have a demonstrable low cardiac output state by echocardiography and clinical signs of elevated systemic vascular resistance (extremely delayed capillary refill, nonpalpable peripheral pulses) with normal blood pressure, consider using vasodilators. Many emergency clinicians use milrinone in this situation. Milrinone increases inotropy as well as lusitropy (diastolic relaxation) and peripheral vasodilation, via phosphodiesterase inhibition.[70-72,75] Depending on the patient's fluid status and cardiac function, the balance between increased contractility and vasodilation may result in increased, decreased, or stable blood pressure. Dosing of milrinone starts at 0.25 mcg/kg/min, with a maximum of up to 0.75 mcg/kg/min.[73] Milrinone is not traditionally a first-line therapy for classic septic shock, and its use should be undertaken with caution, typically in consultation with physicians in the intensive care unit at the receiving facility or in pediatric cardiology.

Norepinephrine And Vasopressin

Norepinephrine and vasopressin are vasoactive agents that preferentially cause vasoconstriction. With the use of norepinephrine, there is both alpha- and beta-receptor stimulation, but, because there is relatively greater alpha-receptor stimulation at lower doses, vasoconstriction is predominantly seen. With vasopressin, only vasoconstriction is seen, because receptors are located only within the vasculature. Both of these drugs are indicated in cases of "warm shock," in which it appears that the child is in a state of hypotension due to peripheral vasodilation, with either normal or increased cardiac output.[6,62] This may be difficult to discern in the ED and often requires the use of invasive arterial blood pressure monitoring, central venous blood pressure monitoring, and even pulmonary artery catheters to determine cardiac output and vascular resistance.

Antibiotics

Antibiotics should be administered within the first hour of treatment in cases of septic shock.[6,20] It is often possible to obtain blood cultures when intravenous access has been obtained and urine cultures when a bladder catheter is placed. This may aid in determining the etiology of the septic shock. In addition to the use of antibiotics, removing infected tissue is an important aspect of the treatment of septic shock. Infected tissue (fasciitis, necrotizing pneumonia) or other infection sources (perforated appendicitis or other perforated bowel) should be debrided, drained, or repaired, once hemodynamic stability has been established.[6]

The choice of antibiotics depends on the age of the child and the clinical presentation or current and past medical history. In children aged < 1 month, it is reasonable to start ampicillin for coverage of *Listeria monocytogenes* and cefotaxime for coverage of group B *streptococcus*, *E coli, Streptococcus pneumoniae,* and other coliform bacteria. Initiation of acyclovir in newborns presenting in shock should be considered, as delays in the administration of acyclovir are associated with increased inhospital death.[76] Some clinicians use a combination of ampicillin and gentamicin, if there are concerns for resistance to ampicillin and cefotaxime. Between 4 and 12 weeks of age, *Listeria* is unlikely; therefore, ampicillin is probably not necessary, unless there is evidence of meningitis, in which case the addition of vancomycin (rather than ampicillin) is recommended.

In children with severe, overwhelming sepsis, infectious disease specialists suggest coverage with vancomycin for MRSA as well as gram-negative coverage with cefotaxime or ceftriaxone. If an intra-abdominal process seems to be present, coverage for anaerobic bacteria is required. Piperacillin/tazobactam is a reasonable choice in this situation. Combinations of antibiotics that are currently in use for severe sepsis include vancomycin and cefotaxime or ceftriaxone, and vancomycin and piperacillin/tazobactam. Consensus recommendations suggest the use of clindamycin and the administration of intravenous immunoglobulin (IVIG) in cases of toxic shock syndrome, septic shock, and erythroderma when hypotension is refractory.[6]

In children with an underlying immunodeficiency (eg, oncologic patients, transplant patients, autoimmune deficiency syndrome patients), the choice of antibiotic should be guided by their high-risk status. Many institutions have management pathways for children who may have surgically placed central venous catheters that include the presumptive use of vancomycin to cover for potential MRSA infection. Discussing the choice of antibiotics with the subspecialty service involved in the care of these children or with an infectious disease specialist is beneficial.

Other considerations include the use of antifungal agents, especially in a child who may be particularly susceptible, or in one who has been taking broad-spectrum antibiotics for a prolonged period of time.

A summary of antibiotics commonly used in the treatment of septic shock is presented in **Table 6.** **(See page 17.)**

Corticosteroids

As many as 25% of children with septic shock have relative or absolute adrenal insufficiency.[29] The use of steroids in the treatment of shock (usually septic shock) has been studied with many compounds that have varying mineralocorticoid and glucocorticoid properties (including methylprednisolone, hydrocortisone, and dexamethasone).[57,77] Many studies

in adults and children have shown that adrenal replacement therapy, namely hydrocortisone, may improve outcomes in shock.[48,78-80] Additionally, the early administration of adrenal replacement therapy is associated with improved survival.[81]

It is recommended that, in children with fluid- and catecholamine-refractory shock, stress-dose hydrocortisone should be initiated immediately after sending blood for a random serum cortisol level. A cortisol level of ≤ 18 mg/dL in a patient with shock should be considered as an indication of adrenal insufficiency, and hydrocortisone 1 mg/kg every 6 hours or 50 mg/m^2/24h as a continuous infusion or in divided doses should be administered.[6,78,80] Once cortisol levels are obtained, decisions can be made regarding the continuation of adrenal replacement therapy. The current definition of adrenal insufficiency in pediatric shock has yet to be completely determined.

Monitoring Response To Therapy

The importance of early recognition of septic shock and timely initiation of therapies cannot be understated, but the initiation of therapies is often insufficient. It is essential that the interventions are goal-directed and that there is ongoing monitoring of the response to those interventions. Clinical signs and symptoms are an important component in determining if therapeutic interventions have normalized cellular respiration. As stated previously, the recommended clinical indicators of volume status are capillary refill time ≤ 2 seconds, normal blood pressure for age, normal pulses with no difference between peripheral and central pulses, warm extremities, urine output > 1 mL/kg/hr, and normal mental status. **(See Table 7, page 18.)**

In the ED, clinical indicators may be the only information available to make an assessment, but in some situations, there may be the opportunity for obtaining additional information. Bedside calculations of severity of shock are appealing in that they are immediate and objective. Calculations such as the Shock Index (the ratio of heart rate to systolic blood pressure) have been shown to be different in survivors versus nonsurvivors of septic shock, although the differences may be too clinically similar to determine endpoints of therapy.[82] In children with septic shock who have had central lines placed in which the line ends in the right atrium (usually, upper lines placed in the internal jugular or subclavian vein), using the saturation of blood in the right atrium (mixed venous saturations [$ScvO_2$]) has been shown to improve outcome in children with septic shock.[83] $ScvO_2$ is an indicator of the effectiveness of the body in providing oxygen to the large tissue beds of the body. When the $ScvO_2$ is < 70%, interventions such as transfusing packed red blood cells or increasing cardiac output with inotropes can improve cellular respiration.

With any type of shock, various laboratory tests can assist in establishing the extent of end-organ hypoperfusion. Metabolic acidosis can be determined by low bicarbonate levels on a serum electrolyte panel or on a blood gas level, in which acidosis is not fully explained by respiratory insufficiency (since the bicarbonate value on a blood gas level is a calculated value). This acidosis would suggest that there is some degree of anaerobic metabolism. Although lactic acid is a nonspecific test, many emergency clinicians will use the removal or clearance of lactate as an indicator of improved tissue perfusion. A 5% decrease in lactic acid in the first hour of resuscitation has been shown to be a good prognostic indicator in shock.[84] Measuring and targeting lactate clearance in patients with severe sepsis and septic shock has also been shown to be effective in reducing mortality in adults.[85] Further trending of lactate may also be helpful in directing therapy.[86,87] Increased end-tidal CO_2 has also been shown to be associated with improved cardiopulmonary function.[88-91] This increase occurs as tissue perfusion improves and a larger CO_2 load is delivered to the lungs and exhaled.

Recent studies have looked at the use of bedside ultrasonography to guide resuscitation in septic shock in children. In an observational study, it was shown that it is possible, and potentially beneficial, to employ echocardiography to monitor volume status as well as biventricular function in patients with septic shock as a way to guide therapy.[92] But another study failed to show that ultrasonographic measurements of the inferior vena cava and aorta could reliably provide meaningful information about central

Table 6. Antibiotics Commonly Used In The Treatment Of Septic Shock

	Ampicillin	Vancomycin	Cefotaxime (or Ceftriaxone if Age > 4 weeks)	Acyclovir	Piperacillin/Tazobactam	Clindamycin
Age < 1 month	X		X	X		
Age > 4 weeks		X	X			
Concerns for intra-abdominal source		X			X	
Concerns for toxic shock syndrome		X	X			X

venous pressure and intravascular volume status or the need for further fluid resuscitation.[93]

Diagnostic Studies

Shock is a clinical diagnosis that does not require diagnostic studies for definitive diagnosis. Still, depending on the presentation, there are studies that can help determine the cause of shock. More often than not, these studies are done after treatment has been initiated, and therapy should not be delayed in order to perform any diagnostic studies.

In hypovolemic shock, since the most common etiology is related to vomiting and diarrhea, some studies may be useful. In children, the most common cause will be a viral infection, and studies to determine an etiology are not appreciably helpful. Depending on the clinical situation, such as prolonged diarrhea, bloody diarrhea, or diarrhea in infants, a stool culture may be useful, since antibiotics would be given for *Shigella*, *Salmonella*, and other enteric infections that result in shock.

Because a urinary tract infection can also cause vomiting in young children, and may even progress to urosepsis, a urinalysis and urine culture are helpful in patients with corresponding historical features or risk factors. Studies assessing for abnormalities caused by persistent vomiting and stool losses in a severely dehydrated child will help guide and augment fluid and electrolyte therapy. Hypovolemia caused by vomiting and diarrhea can result in profound electrolyte abnormalities and hypoglycemia in the small child.

Some would advocate obtaining a serum glucose level in any young child with a significant history of poor oral intake. In addition, blood urea nitrogen and creatinine can help determine volume status and give an indication of renal perfusion and function.

In presumed septic shock, studies are primarily aimed at assessing and diagnosing an infectious etiology. An elevated white blood cell count with left shift or polymorphonuclear cell predominance on complete blood cell count with differential can help to determine whether or not there is an infectious etiology for the current clinical state.

Although not usually of great value in the ED, a blood culture can help in confirming a diagnosis and guiding antibiotic therapy in the future. The same is true of a urinalysis and urine culture in assessing for urinary tract infection and urosepsis. Gram stain of urine, cerebrospinal fluid, and occasionally blood specimens may help determine the infectious etiology.

If there is a history of respiratory distress, a chest radiograph should be obtained, and if an intra-abdominal process is suspected, an abdominal and pelvic computed tomography scan may be useful. Because disseminated intravascular coagulopathy or consumptive coagulopathy is associated with septic shock (as well as other forms of shock), it is reasonable to obtain a prothrombin time, international normalized ratio, partial thromboplastin time, and some indicator of clot formation and breakdown, such as fibrin degradation products and platelets.

If either cardiogenic or obstructive shock is being considered in the differential, a chest radiograph and an electrocardiogram should be obtained immediately. If cardiomegaly is seen on the chest x-ray or an abnormality is noted on the electrocardiogram (eg, low voltage), a cardiac cause of the shock must be strongly considered. A 2-dimensional echocardiogram with color Doppler should be performed as soon as possible and evaluated by a pediatric cardiologist, who can assess for function, dilation, and valve competency.[92,93]

In cases of suspected adrenal insufficiency, the diagnosis is again made clinically (recent steroid use, hyperpigmented skin, vomiting, muscle wasting), and laboratory tests should not delay treatment. A serum cortisol level and serum electrolytes may help determine the diagnosis of adrenal insufficiency or failure. Two methods are routinely used to diagnose acute adrenal insufficiency in severely ill patients: (1) a single, random cortisol level, or (2) a change in cortisol level after an exogenous adrenocorticotropic hormone is administered. Traditionally, adrenal

Table 7. Normal Vital Signs For Pediatric Patients

Age	Heart Rate (beats/min)	Respiratory Rate (breaths/min)	Systolic Blood Pressure (mm Hg)	Diastolic Blood Pressure (mm Hg)
Newborn	90-180	30-50	60 ± 10	37 ± 10
1-5 months	100-180	30-40	80 ± 10	45 ± 15
6-11 months	100-150	25-35	90 ± 30	60 ± 10
12-23 months	100-150	20-30	95 ± 30	65 ± 25
2-3 years	65-150	15-25	100 ± 25	65 ± 25
4-5 years	65-140	15-25	100 ± 20	65 ± 15
6-9 years	65-120	12-20	100 ± 20	65 ± 15
10-12 years	65-120	12-20	110 ± 20	70 ± 15
13+ years	55-110	12-18	120 ± 20	75 ± 15

insufficiency is identified in patients with sepsis by a single, random cortisol level of < 15 to 20 mcg/dL. This may be particularly valid, since the median cortisol level in adult patients with shock is 50 mcg/dL, compared to a normal range of 10 to 20 mcg/dL.[29]

Table 8 provides a summary of diagnostic studies and their utility in the management of septic shock.

Special Circumstances

Given the heterogeneity of the etiologies of pediatric shock, most children in shock can be said to represent a special circumstance. Nonetheless, a few specific conditions are worth mentioning. Given the increase in intercontinental travel, infectious diseases that were not formally considered in the differential of septic shock in the United States must now be considered. Infectious agents such as dengue fever, complicated malaria, and Ebola virus are now increasingly plausible in the differential diagnosis. The initial steps of recognition, diagnosis, and administration of empiric therapy are not different in these situations. Because of the highly infectious nature of Ebola virus, many institutions have specific guidelines for the isolation, management, and possible transfer of patients with suspected or confirmed disease.

Controversies And Cutting Edge

As goal-directed therapy has become more widely accepted for management of septic shock, the ability to assess if these goals have been obtained has become increasingly important. Near-infrared spectroscopy is a noninvasive technology that allows for the determination of changes in the oxygen saturation of tissue beds. Animal and human studies have shown that improvement in near-infrared spectroscopy values follows improved microcirculatory blood flow in animal models of endotoxin shock, and oxygen tissue saturations are higher in survivors versus nonsurvivors undergoing goal-directed therapy for septic shock.[94]

The use of immune system and inflammatory modulators has received much attention in recent years. The ability to demonstrate improved outcomes in therapeutic trials using these agents is difficult because of the complex interaction between the components of the immune system and other systems that regulate inflammation. The response to both infectious agents (in the case of septic shock) as well as endothelial and tissue damage due to ischemia (which occurs in all types of shock) creates a situation in which the effect of a single therapeutic agent is difficult to use and study. At this time, there are no immune modulators that are routinely employed in cases of shock.

Other therapies, such as full cardiopulmonary mechanical support in shock, continue to have variable acceptance.[95-100] The use of extracorporeal mechanical oxygenation (ECMO) via a centrifugal pump and membrane oxygenator has been employed in many institutions during the acute and severe phases of shock, with anecdotal success. There has not yet been a prospective randomized trial in children to determine whether this high-risk theramodality affects outcome. ECMO has been used to provide pulmonary support via venovenous cannulation (in which blood is removed from either the superior vena cava, inferior vena cava, or both and then returned to the right atrium) and venoarterial ECMO (in which blood is again removed from the venous side but returned to the arterial side

Table 8. Diagnostic Studies And Utility Of Each Test In The Management Of Septic Shock

Diagnostic Study	Utility of Test
Complete blood cell count with differential	Likelihood of infection based on presence of elevated white blood cell count with left shift or polymorphonuclear cell predominance
Blood culture	Confirm diagnosis and guide antibiotic therapy
Urinalysis	Suggest diagnosis of urinary tract infection and urosepsis
Urine culture	Confirm diagnosis and guide antibiotic therapy
Electrolytes	Determine severe electrolyte abnormality
Blood urea nitrogen and creatinine	Determine presence and degree of dehydration and renal failure
Blood gas	Determine presence of metabolic acidosis
Lactate	Determine presence of lactic acidosis
Blood glucose	Determine presence of hypoglycemia
Chest radiograph	Assess likelihood of pneumonia
Abdominal and pelvic computed tomography	Assess likelihood of intra-abdominal source of infection
Prothrombin time, international normalized ratio, partial thromboplastin time	Determine presence of coagulopathy such as disseminated intravascular coagulopathy
Serum cortisol	Assess presence and degree of adrenal insufficiency or failure

Risk Management Pitfalls For Pediatric Septic Shock

1. **"He wasn't hypotensive, so I didn't think he was in shock."**
   In children, sometimes the only signs of compensated shock may be tachycardia and irritability, which are common findings. Although formal definitions of shock stress the presence of hypotension, it is important to note that it is not required to be present in children for the diagnosis of septic shock to be made.

2. **"The pulse oximetry reading was normal, so I didn't give oxygen."**
   The primary deficiency in shock is insufficient substrate for cellular respiration. The most essential substrate is oxygen. In all cases of presumed shock, supplemental oxygen should be provided at the onset of therapy.

3. **"I waited to give a second bolus because I didn't want to fluid overload this child."**
   Children with symptoms of shock can have fluid deficits that are far greater than may initially be estimated. An initial fluid bolus of 20 mL/kg of isotonic crystalloid over 5 to 10 minutes is only the start of resuscitation. Continuous reassessment is essential. Except for children in cardiogenic shock, those with underlying congenital cardiac disorders, and possibly those with diabetic ketoacidosis, most children in shock benefit from the administration of relatively large fluid volumes.

4. **"I gave the girl 60 mL/kg of normal saline, but it didn't seem to help. How could that not be enough?"**
   Especially in cases of ongoing fluid losses due to vomiting and diarrhea, both the fluid deficit and the ongoing losses need to be replaced.

5. **"I don't understand how she decompensated in the CT scanner. She looked fine 2 hours ago."**
   Resuscitation of a child in shock requires that a therapy is not only implemented, but also that the results of that therapy are evaluated. Ongoing reevaluation of the child allows for additional appropriate therapy, as children who have been in shock can quickly decompensate.

6. **"I didn't give antibiotics for this child who was in shock because I couldn't find a source of infection."**
   Although it can be difficult to make a definitive diagnosis of shock caused by a bacterial infection, if other causes cannot be excluded with some confidence, timely administration of antibiotics may be lifesaving.

7. **"The chest x-ray was normal, and there weren't any infiltrates or effusions indicating a problem with the boy's heart. But I guess now that I take another look, the heart does seem big."**
   Although dilated cardiomyopathy is not a common cause of shock, an enlarged heart can be seen on chest radiographs. Therefore, it should be considered in the differential, as the treatment for dilated cardiomyopathy is different from treatment for other causes of shock.

8. **"I've never given dopamine to a child, so I just kept giving fluids."**
   If, after the administration of 60 to 100 mL/kg of fluid, there is insufficient improvement in tissue perfusion, inotropic support should be initiated. Ideally, this is provided through a central venous line, but in some situations, it must be provided through whatever venous access is available, including a peripheral venous line or an intraosseous line.

9. **"I thought fluids would be enough to treat the shock. Why should I have given hydrocortisone to this child?"**
   Children who are on chronic steroids or who are steroid-dependent have increased steroid needs during even minor acute illnesses. Appropriate doses of steroids can successfully reverse shock.

10. **"The little girl didn't have a fever, so I was not concerned about septic shock."**
    Although fever often accompanies infection, it is not required in order to make the diagnosis of SIRS, sepsis, or septic shock. The use of nonsteroidal anti-inflammatory drugs, the use of immunosuppressive agents, or innate patient features can alter the expected febrile response to infection.

through the carotid artery). Because of the myriad risks (including potential carotid artery ligation in venoarterial ECMO, hemorrhage [most notably intracranial] due to the necessity for anticoagulation, and secondary infections) ECMO carries, it is not yet considered a standard therapy in severe shock with multi-organ system failure.

Increasingly, EDs are using screening tools to identify patients who are at risk for septic shock.[101-103] Many of these screening techniques are based on adult signs and symptoms of septic shock. There are concerns that the currently recommended tools are neither specific enough nor sensitive enough to accurately guide clinicians and allow for the appropriate use of resources in pediatric patients. Current research collaborations are underway to develop evidence-based tools appropriate for use in pediatric patients presenting to the ED in shock.

Disposition

Decisions regarding the most appropriate location for further management and observation of children who have been treated for septic shock in the ED can sometimes be difficult. It is not uncommon for a child who has had prolonged diarrheal illness to present to the ED in compensated shock and then respond well to 60 mL/kg of isotonic crystalloid and return to a near-normal pathophysiologic state. This patient will most likely continue to have ongoing losses and may need intravenous therapy for many hours, and in some instances, even days. The child who does not respond to reasonable quantities of fluid replacement and requires the initiation of inotropic support in the ED should be transferred to a pediatric intensive care unit (PICU) or another unit that can monitor vital signs closely, provide invasive physiologic monitoring, and continue resuscitation.

The disposition of the child who appears to have improved, still has some abnormalities after reasonable fluid resuscitation, but clinically does not require inotropic support, is often difficult. This is the child who is relatively stable but remains the sickest in the ED. In many instances, the most appropriate disposition would be to a PICU, since they would be best able to care for this child if there were either further deterioration or other complications. In some instances, when immediate transfer to a PICU is not possible, transfer to a unit that provides an intermediate level of care, such as a step-down unit, may be reasonable. A last alternative may be to provide ongoing critical care in the ED until a PICU bed becomes available.

These decisions are best made in conjunction with all of the caregivers involved, which, in different circumstances, may include emergency clinicians, critical care physicians, surgeons, anesthesiologists, and nurses from various disciplines. Comprehensive documentation and thorough verbal communication are paramount in the transfer and appropriate care of children moving quickly between various parts of a busy hospital.

Time- And Cost-Effective Strategies

- The most effective way to save time and cost when treating children with septic shock is to be complete and thorough during the initial evaluation and therapy. Unfortunately, the initial signs and symptoms of septic shock can be subtle and insidious. This leads to an underappreciation of the potential severity of disease and an approach in which 1 laboratory test or imaging study is ordered at a time, the results evaluated, and then another test ordered. This leads to long ED stays, high use of nursing resources, and the potential for further decline in patient status before definitive therapy is initiated. This may ultimately lead to further uses of resources in the PICU as well as an unnecessary extended stay in the hospital.
- Strategies that have been successfully employed to treat patients with septic shock rely on order sets and care bundles. If signs of shock persist after initial fluids, aggressive fluid resuscitation with 20 mL/kg boluses of isotonic fluid can reverse the deranged pathophysiology and possibly prevent the need for PICU resources. Ordering a CBC, blood culture, electrolytes (including calcium), blood gas, coagulations studies, and a cortisol level when septic shock is first suspected can reduce the time and resources needed.

Summary

Increasing knowledge about and preparedness for septic shock in children can potentially decrease the anxiety and delays in therapy that sometimes occur when a very sick child enters the ED. Because septic shock and the differential diagnosis of shock have common pathophysiology (despite different etiologies), a resuscitative approach to shock, based on well-established goal-directed strategies, can aid in reducing morbidity and mortality. Basic to all forms of shock is an inability to supply oxygen and glucose at the cellular level; thus, the initial resuscitation should be aimed at reversing these abnormalities. Vital signs that are abnormal for age, changes in mental status, decreased urine output, and increased respiratory effort must all be flagged as potential harbingers of shock. The longer that shock persists in an uncorrected state, the greater the chance of complications and death.

Once shock is recognized, treatment and monitoring become paramount. A patent airway, adequate breathing of 100% inspired oxygen, and rapid volume expansion with isotonic crystalloid will improve the pathophysiologic status of the child. Ongoing monitoring of the results of goal-directed therapies can allow treatment to be tailored to improve tissue perfusion. The current understanding of septic shock is of its basic pathophysiology only, and the data needed to further improve outcomes must be increased. Without trials of pediatric patients in septic shock, the small number of studies that are limited in their power and sample size or results from adult studies that may or may not be applicable to the pediatric population must be used. As ongoing studies move forward, a larger body of evidence will be obtained to allow improvement of diagnosis and management of pediatric patients with septic shock.

Case Conclusions

The first fluid bolus given to the adolescent girl was provided rapidly using a liter of normal saline, a 60-ml syringe, and a 3-way stopcock. You ordered a dose of vancomycin, ceftriaxone, and clindamycin because of your concern for tampon-related toxic-shock syndrome. A brief gynecologic examination revealed a retained tampon, which was removed. A second and third normal saline bolus was given. You asked the nurse to prepare dopamine to be given peripherally if the patient continued to demonstrate signs of shock. Her blood pressure improved, but she still had signs of poor peripheral perfusion, such as delayed capillary refill, so you started her on a dopamine infusion. She was then transferred to the PICU for further management.

Despite receiving oxygen by face mask, the infant's oxygen saturation hovered around 87% to 88%. You asked for a second normal saline bolus to be given rapidly through the intraosseous line, and the respiratory therapist began assisted ventilation with a self-inflating bag-valve mask. You were informed that the transport team was en route to your facility. You asked a nurse to prepare medicine for RSI (atropine, ketamine, and rocuronium), and you prepared the necessary equipment for orotracheal intubation. The infant tolerated intubation but remained hypotensive, and, while the third bolus was being given, the transport team arrived from the tertiary children's hospital. You asked the team to prepare the dopamine and assist with additional IV access. As the dopamine infusion was running, the patient's blood pressure and perfusion began to normalize, and the child was transferred to the transport gurney.

When you returned to the 3-year-old boy, you realized that the "flash" cap refill was an indication that his rapid decline had progressed to "warm shock," which is best treated with an inotropic agent with vasoactive features, such as norepinephrine. You instructed the nurse to increase the dopamine to 15 mcg/kg/min to take advantage of the alpha-adrenergic properties of the higher-dose dopamine and asked for a norepinephrine infusion to be prepared. You also recalled that the patient had been on dexamethasone for treatment of leukemia and concluded that he likely had adrenal insufficiency. You informed the nurse that you were ordering a dose of hydrocortisone and called the PICU to start the transition of care.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study will be included in bold type following the references cited in this paper, as determined by the author, will be noted by an asterisk (*) next to the number of the reference.

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CME Questions

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An 11-year-old boy is carried into the ED by his father. He was found unarousable this morning. He had returned the evening before from 1 week at sleep-away camp. He has no significant past medical history. In the ED, his vital signs are: temperature, 39.0°C; heart rate, 150 beats/min; respiratory rate, 35 breaths/min; blood pressure, 70/40 mm Hg; and oxygen saturation, 94%. On examination, he is responsive only to noxious stimuli and is otherwise nonpurposeful. His pupils are 6 mm bilaterally and react sluggishly to light. He has clear breath sounds but shallow respirations. He is tachycardic, without a murmur, and he has a capillary refill time of > 4 seconds. His abdomen is soft, and he has a purpuric rash on his shins and thighs.

1. **The most appropriate first step in the management of this patient would be:**
   a. Lumbar puncture
   b. Administer vancomycin
   c. Rapid bolus of isotonic crystalloid
   d. Obtain an infectious disease consultation
   e. Computed tomography scan of the brain

2. **During this patient's initial treatment, he develops rales and increasing tachypnea, and you can now palpate his liver below the right costal margin. There has not been a significant improvement his blood pressure. The most appropriate response is to:**
   a. Arrange for transfer to the PICU
   b. Insert a Foley catheter
   c. Insert a second intravenous catheter
   d. Administer an inotrope
   e. Administer furosemide

3. **While the nurse is making preparations, the patient's oxygen saturation falls to 82%. It is clear that this patient will require intubation. You perform RSI, place an endotracheal tube, and begin bag-valve-mask ventilation. The next blood pressure measurement is 50/30 mm Hg. What is the most likely reason for the fall in blood pressure?**
   a. Lowering of the CO_2
   b. Lower intrathoracic pressure
   c. Cardiotoxic effects of vecuronium
   d. Improved oxygen-carrying capacity
   e. Decreased venous return

4. **If this patient recently had a moderate asthma exacerbation for which he had seen his pediatrician for therapy, it would be prudent to give an empiric dose of what medication at this point?**
   a. Atropine
   b. Hydrocortisone
   c. Ranitidine
   d. Albuterol
   e. Activated protein C

5. **The nurse hands you the following capillary blood gas report: pH 7.01, pCO_2 55 torr, pO_2 150 torr, HCO_3 14, Base Deficit -9. You ask the respiratory therapist and the nurse to:**
   a. Increase ventilation rate and administer 20 mL/kg of normal saline
   b. Increase ventilation rate and administer magnesium
   c. Decrease ventilation rate and administer sodium chloride
   d. Decrease ventilation rate and administer furosemide
   e. Continue present management

A 2-year-old boy presents to the ED with a history of persistent vomiting and watery diarrhea for the last 2 days. His parents describe intermittent fever and foul-smelling watery diarrhea after almost every feeding. His emesis is nonbloody and non-bilious. In the ED, he appears lethargic with the following vital signs: temperature, 40°C; heart rate, 190 beats/min; respiratory rate, 44 breaths/min; and blood pressure, 65/38 mm Hg. You administer an isotonic saline bolus of 20 mL/kg. Serum electrolytes are: sodium, 132 mEq/L; potassium, 4 mEq/L; chloride, 92 mEq/L, bicarbonate, 8 mEq/L; and glucose, 68 mg/dL. There is no significant change in his examination at this point in his evaluation.

6. **The most appropriate next step in management is:**
   a. Repeat IV normal saline bolus
   b. Administer IV D25W 2 to 4 mL/kg
   c. Vasopressin infusion
   d. 3% hypertonic saline bolus
   e. Stool culture

7. **The best way to measure the adequacy of rehydration is to:**
   a. Monitor blood pressure and heart rate every 3 minutes
   b. Check serum electrolytes hourly
   c. Check serum lactate levels
   d. Check capillary refill time
   e. Measure urine output

A 3-week-old infant girl who was born at home is rushed to the ED by her parents with complaints of persistent vomiting and lethargy. Upon her arrival to the ED, you note that she looks pale and is barely responsive. Immediate vital signs upon arrival are: temperature, 37°C; heart rate, 210 beats/min; respiratory rate, 70 breaths/min; blood pressure, 58/palp mm Hg; and oxygen saturation, of 95% on room air. Bedside point-of-care testing reveals: pH, 7.0; bicarbonate, 8 mEq/L; sodium, 123 mEq/L; potassium, 7.2 mEq/L; and glucose, 68 mg/dL. Sinus tachycardia is noted on the monitor.

8. **Fluid resuscitation is initiated. Definitive management that will improve the clinical status is:**
   a. Administration of IV lidocaine
   b. Administration of IV dextrose and insulin
   c. Administration of IV ceftriaxone
   d. Administration of IV prostaglandin E1
   e. Administration of IV hydrocortisone

A 4-year-old girl with sickle cell anemia is brought to the ED with fever. She has been lethargic at home. On arrival, she appears tired but responds to your voice and is cooperative. Her vital signs are as follows: temperature, 39.5°C; heart rate, 175 beats/min; respiratory rate, 36 breaths/min; blood pressure, 72/36 mm Hg; and oxygen saturation, 93% on room air. She has a capillary refill time of 3 to 4 seconds. She has a III/VI systolic ejection murmur on cardiac auscultation, and her spleen is palpable, but the rest of her examination is normal. Intravenous access is established.

9. **Which of the following should be done next?**
   a. Administer IV isotonic crystalloid 20 mL/kg
   b. Administer 2 units type-specific blood
   c. Cardiac ultrasound
   d. Endotracheal intubation
   e. Await complete blood count and reticulocyte count results

10. **What is the recommended initial inotropic agent for "warm" septic shock?**
    a. Epinephrine
    b. Norepinephrine
    c. Milrinone
    d. Dobutamine
    e. Dopamine

Coming to *Pediatric Emergency Medicine Practice* next month!

Burn Management: Accurately Classify And Treat Burn Injuries In Pediatric Patients

Thermal burns are a frequent injury seen in the emergency department, with greater than 120,000 pediatric emergency department visits annually in the United States. Burns ranks as the third most common cause of death in pediatric patients. When managing a burn victim, emergency clinicians must be able to accurately classify the type of burn and the anatomy involved in order to appropriately treat the patient. This review addresses the management of different types of burns, from initial stabilization and pain control to wound management and discharge care. Additionally, this review will assess the identification of comorbidities, ways to control infection, and techniques for improving healing and cosmetic outcomes.

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