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Shock: A Common Pathway For Life-Threatening Pediatric Illnesses And Injuries

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 monitors and then starts working to obtain intravenous access. The child has a pulse, and the monitor shows a heart rate of 190 beats per minute, which matches what you feel on examination. The blood pressure cuff inflates, deflates, and recycles 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 and — after a quick splash with Betadine® — punch the needle into the infant's anterior tibia. You ask the nurse to check the glucose on the aspirate from the intraosseous needle and start pushing normal saline into it. Realizing just how sick this kid is now, you ask the clerk to go ahead and call the tertiary children's hospital to arrange transfer. You obtain a little history from the mother. She tells you that her baby is usually healthy, but he has had a couple of episodes of vomiting overnight. He hasn't had any fever or diarrhea. 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 this 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?" "When is that transport team from the children's hospital going to call me back?

THERE may be nothing more anxiety-provoking for a physician than caring for a previously healthy infant or young child who presents in shock. 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

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CME Objectives

Upon completing this article, you should be able to:

1. Define shock;
2. Discuss the role of vasoactive agents in the management of pediatric shock; and
3. List etiologies of cardiogenic shock.

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life-threatening illnesses and injuries. As the child's condition worsens, the similarities among the clinical presentations of the divergent causes of shock overwhelm the differences. Fortunately, there are fundamental principles applicable to multiple causes of shock in children. In this issue of *Pediatric Emergency Medicine Practice*, we will present an approach to pediatric shock based, as far as possible, on the available evidence.

Abbreviations Used In This Article

APC — activated protein C
ARDS — adult respiratory distress syndrome
ATN — acute tubular necrosis
CVP — central venous pressure
DIC — disseminated intravascular coagulation
ECMO — extracorporeal membrane oxygenation
ED — emergency department
FDP — fibrin degradation product
FRC — functional residual capacity
GFR — glomerular filtration rate
IO — intraosseous
IVC — inferior vena cava
LPS — leukopolysaccharide
MODS — multiple organ dysfunction syndrome
MOSF — multiple organ system failure
PEEP — positive end-expiratory pressure
PIP — peak inspiratory failure
RSI — rapid sequence induction
SIRS — systemic inflammatory response syndrome
SVC — superior vena cava
VALI — ventilator-associated lung injury

Critical Appraisal Of The Literature

It is impossible to create a *purely* evidence-based approach to pediatric shock. The reasons for this are quite straightforward. First, "pediatric shock" is a heterogeneous clinical entity. Multiple etiologies lead to shock. It is impossible to compare treatments, for example, when a study population includes children with hemorrhagic shock from trauma, hypovolemic shock from a diarrheal illness, cardiogenic shock in chronically ill children with congenital heart disease, septic shock, and distributive shock from anaphylaxis. Second, individual cases of pediatric shock are not common. A single institution would have to study data spanning many years to have a reasonably sized study. Third, the cause of shock is often not immediately apparent on presentation to the ED or intensive care unit. Therefore, studies tend to be retrospective and rely on information that is only available as the case unfolds over time. This leads to studies that have limited applicability to ED care. Fourth, children in shock are often critically ill, and some clinicians consider interventional or experimental studies unethical.[1-3] Performing a study that substantially risks a child's death is unappealing, to say the least, to many researchers, patients, and families.[3] This leads to a paucity of relevant studies. Fifth, 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]

Given the difficulties associated with performing studies on pediatric shock, physicians are left to act on very incomplete information. This can lead to a continued use of ineffective or even harmful therapies, simply because evidence is not available to refute their use.[6,7] Reasons cited for using these ineffective therapies include: "love of [a] pathophysiological model (that is wrong)," "a need to do something," and "clinical experience."[7]

Another problem arises when the results of studies involving adults *only* are applied to the care of children. A recent example illustrates this point nicely. There have been studies and reports demonstrating that activated protein C (APC) is an effective therapy for adults in septic shock.[8-10] However, a recent multicenter study of APC for the treatment of *children* in septic shock was suspended due to excessive complications and a lack of demonstrated benefit over placebo.[11] In this case, there was an increase in intracranial bleeding, particularly in children younger than 2 months. Reliance on adult data to guide the care of children in this instance would have been harmful.

Finally, some of our most fundamental concepts are supported by very small studies. For example, any clinician who has been practicing for a few years knows that critically ill children are often found to be hypoglycemic on presentation. Studies that directly address this, however, are rare. Probably the best known is by Losek, who reported on 49 children undergoing "resuscitation," 9 of whom were discovered to be hypoglycemic.[12] Another example involves fluid resuscitation. Although nearly universally recommended, few studies have directly explored whether or not fluid resuscitation is beneficial. The most widely cited of these is probably the study by Carcillo et al, which included only 34 children.[13] Systematic reviews regarding fluid resuscitation seldom evaluate cherished, unproven "facts" and instead compare two similar therapies.[14,15]

Epidemiology, Etiology, Pathophysiology

Epidemiology

There are currently few data on the incidence of children presenting with shock to the ED. The evidence that does exist is predominantly related to septic shock. Based on data from children admitted to hospitals in 7 states, the national age-adjusted annual incidence of pediatric sepsis was found to be 0.56 cases per 1000 children, or 42,364 cases per year.[16]

The incidence of severe sepsis was found to be highest among infants, particularly low and very low birth weight babies. Boys were also found to have a significantly higher incidence compared to girls, approximating an additional 3300 boys per year nationally.[16] Hospital mortality was 10.3% — an estimated 4300 or more deaths nationally from severe sepsis. Half of those deaths were in patients with a chronic comorbidity.[17] Mortality in critically ill children is highly associated with multiple organ dysfunction syndrome (MODS) — it is common for multiple organs to fail

early, acutely, and simultaneously.[18] Data in children with septic shock and organ failure are limited, and most data analyze the incidence of sepsis, septic shock, and MODS in the pediatric intensive care unit rather than in the ED.[19]

Gram-negative septic shock comprises 50% of total cases of culture-proven bacterial sepsis, with approximately 115,000 deaths/year.[16,17] As a group, gram-negative bacteria cause most of the deaths due to sepsis. 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 longer lives of patients predisposed to sepsis. This rise in bacteremia and sepsis is also related to the increased use of invasive devices, such as surgical prostheses, home mechanical ventilatory equipment, and percutaneous intravenous catheters. The indiscriminate use of antibiotics — creating 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 the central nervous system.

Etiology

Definition of Shock

There are myriad ways to describe shock. While all these descriptions capture various features associated with shock, they do not directly define shock. Alterations in mental status, derangements of vital signs, abnormalities in laboratory results, and data from invasive monitoring can all be used to suggest shock. Technically, shock is defined by inadequate substrate for aerobic cellular respiration. Unfortunately, we can't measure this directly. When the cardiopulmonary system can no longer adequately supply the mitochondria with glucose and oxygen to create adenosine triphosphate (ATP), a shock state has developed. This shock state occurs when 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. 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, such that there is an appropriate hematocrit.

If substrate supplies continue to be 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 hypo- or hyperthermia, tachycardia, tachypnea, and abnormalities in white blood cell counts are seen. Further interruptions in substrate delivery are seen as the microcirculation becomes severely damaged. Eventually, as organs fail, the premorbid condition termed multiple organ system failure (MOSF) occurs.

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The cardiac and respiratory reserve available to compensate for shock is different in children than adults. The heart of a child has not been subject to the stresses of years of use, has not developed limitations to coronary blood flow due to atherosclerosis, and may therefore compensate for shock better than an adult heart. But the young heart has a limited ability to increase stroke volume, leaving an increase in heart rate as the predominant method of dealing with an inadequate cardiac output. The ability to deliver oxygen is also different. While the greater ratio of lung volume to body mass is a slight advantage in the child, this does not compensate for the increase in metabolic rate that children have relative to adults. Although the metabolic rate of a critically ill child is controversial, relative to the child's size, it is estimated that their metabolic rate can be as much as twice that of an adult's.[20] As a result of these factors, there can be a remarkably rapid rate of deterioration when the cardiopulmonary system is stressed or dysfunctional.

There are numerous causes of shock. (See **Table 1** on page 4.) Shock can be caused by inadequate intravascular volume (ie, hypovolemic shock). Vomiting and diarrhea are the most common causes of this type of shock in the pediatric population. Distributive shock, of which septic shock is the most common form, is also seen in children, usually as the result of an immunosuppressed state from chemotherapy. Children with congenital heart disease can present in cardiogenic shock or obstructive shock, depending on the anatomy of their lesion. And children who have been treated with steroids for various disease processes may present in endocrinologic shock, if there is a perturbation in the hypopituitary axis.

Yet despite this relatively common, life-threatening process, the data available to guide emergency practitioners who care for children with shock are practically nonexistent. Also, there are almost no pediatric-specific data with regard to types of fluid, rate of fluid replacement, optimal inotropes, or other cutting-edge therapies.

Fortunately, because the disease process is not radically different from what is seen in adults, the available data can be adapted, allowing for intelligent extrapolations to determine reasonable treatment for children. Many position papers and expert clinical guidelines have been created to assist physicians in the treatment of shock related to sepsis. Data suggest that the pathophysiology involved in septic shock is not radically different in cardiogenic or hemorrhagic shock. Therefore, goals and treatments have been extrapolated for the treatment of all shock in the ED.

Hypovolemic Shock

The most common cause of shock in children worldwide is hypovolemic, as seen with fluid losses caused by diarrhea and vomiting. These losses are often exacerbated by decreased oral intake, as well. This can occur from a variety of illnesses, including viral and bacterial gastroenteritis. Some viral causes of acute gastroenteritis include rotavirus and enterovirus, among others, while bacterial causes include *Escherichia coli*, *Salmonella* species, *Shigella* species, and globally, *Vibrio cholerae*. (See also *Pediatric Emergency Medicine Practice*, Volume 1, Number 5, Gastroenteritis: An Evidence-Based Approach To Typical Vomiting, Diarrhea, And Dehydration, December 2005.) Hypovolemic shock also occurs in the settings 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. 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 of the venous system, decreased vascular tone results in "pooling" of blood in the large veins. This decreases venous return to the right atrium, resulting in decreased preload and, eventually, 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 resulting in lack of substrate at the cellular

Table 1. Sepsis, Septic Shock, And Shock Syndromes: Definitions.

Infection	An inflammatory response to invasion of a normally sterile tissue by a microbial organism.
Bacteremia	Viable bacteria in the blood
Systemic inflammatory response syndrome (SIRS)	A systemic response to a variety of insults that results in at least 2 of the following: Temperature <36°C or >38°C Heart rate >90 bpm (adults) Respiratory rate >20 bpm (adults) or $PaCO_2$ <32 mm Hg White blood cell <4000 cells/cc^3, >12,000 cells/cc^3 or >10% bands
Sepsis	A systemic response to *infection* that results in at least 2 of the following: Temperature <36°C or >38°C Heart rate >90 bpm (adults) Respiratory rate >20 bpm (adults) or $PaCO_2$ <32 mm Hg White blood cell <4000 cells/cc^3, >12,000 cells/cc^3 or >10% bands
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 (MOSF)	Alterations in the function of multiple organs in a critically ill patient.
Cold shock	Decreased perfusion, including decreased mental status, capillary refill >2-3 seconds, diminished peripheral pulses, mottled, cool extremities, or decreased urine output (<1 cc/kg/h).
Warm shock	Decreased perfusion, including decreased mental status, flash capillary refill, bounding peripheral pulses, or decreased urine output (<1 cc/kg/h).
Fluid-refractory/dopamine-resistant shock	Shock persists despite 60 cc/kg fluid resuscitation in the first hour and dopamine infusion of 10 µg/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.

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.

Septic Shock

Though more complex in many ways, septic shock can be considered a form of distributive shock. In septic shock, the child has a combination of distributive, hypovolemic, cardiogenic, and possibly endocrinologic shock. Although it was once thought that the specific causative organism involved in a shock state made a large difference in treatment and outcome, now the actual host response to the insult is recognized as the key factor dictating the clinical course.[21,22] (**Table 1**)

Septic shock occurs when an infectious agent, the mediators that the infectious agent produces, and the response of the immune system to that infectious agent combine to create evidence of infection, cardiovascular instability, and organ dysfunction or failure. The myriad responses that occur in sepsis are predominantly the result of mediator release.[23] Some of the mediators involved include interleukin-1 (IL-1), tumor necrosis factor-alpha (TNF-α), 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, multiple organ system failure (MOSF) 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 intensive care unit.

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. In the normal child, the energy required to perform the work of breathing is relatively minor. As sepsis worsens, this work of breathing increases relative to energy production and becomes less effectual. In addition, SIRS develops, which increases parenchymal lung water, worsening the compliance of the lungs, making it more difficult for the child to breathe at his or her functional residual capacity (FRC). This results in increased atelectasis, increased intrapulmonary shunt, and eventually decreased oxygen saturation, all of which worsen the cellular hypoxic-ischemic state of the child.

As a result of decreased renal perfusion, there is a decrease in the glomerular filtration rate (GFR) of the kidneys, decreasing renal solute production, decreasing removal of filtered substances, increasing resorption of filtrate, and decreasing urine production. Initially, oliguria is seen in the patient with compensated sepsis, but as septic shock progresses, anuria is observed. Depending on the length and severity of renal hypoperfusion, acute tubular necrosis (ATN) and parenchymal renal damage with cortical necrosis may develop. Although uncommon, it is possible (depending on the length of time that a child has suffered from sepsis) for a child to develop the polyuric phase of ATN while still in the ED. This can lead to a false belief that intravascular volume has been restored, especially if other signs of volume status are not used in

Table 2. Etiologies Of Cardiogenic Shock.

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, post-cardiopulmonary bypass
	Connective tissue disorder	Systemic lupus erythematosus, juvenile rheumatoid arthritis, polyarteritis nodosa, Kawasaki syndrome
	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 (SVT), ventricular dysrhythmias, bradycardia
	Tachydysrhythmias	SVT, atrial flutter, ventricular tachycardia

combination when reassessing the patient.

Cardiogenic Shock

Cardiogenic shock is increasingly 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 2** on page 5.) 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 necessarily different. In making the diagnosis, modalities such as chest radiographs, electrocardiography, and 2-D echocardiogram are essential.

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.[24] Because of the intrinsic contractile dysfunction, this increased workload causes a further decrease in cardiac function, resulting in a vicious cycle that leads to congestive heart failure.

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 the increase in pressure around the heart. The pressure is transmitted to the right atrium, and this increased right atrial pressure 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 shock cannot be treated medically, it is paramount that they be recognized in order for proper, expeditious treatment to occur.

Endocrinologic Shock

Children who have either recently completed a prolonged course of steroid therapy or are on chronic steroid replacement therapy are at high risk for endocrinologic shock.[25,26] 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 those children who do not have a normal ability to produce ACTH and cortisol, the body will not respond to increased stress in a predictable manner. Seemingly inconsequential increases in metabolic demands, such as viral illnesses 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 inotropy and decreased venous tone, due to a decrease in the quantity 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 lab tests are obtained. In less emergent situations, a random cortisol level can help make the diagnosis of adrenal insufficiency.

Pathophysiology

Lack of substrate for cellular respiration is the final common pathway of shock. At cellular, microcirculatory, organ, and systemic levels, all manifestations of shock can be explained by a lack of oxygen or glucose utilization at the mitochondria and 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 death. The microcirculation, devastated by the loss of endothelial cell integrity, loses its ability to maintain homeostasis, which results in maldistribution of capillary blood flow. Individual organs, to which blood flow and pressure have fallen outside of the autoregulatory range, suffer dysfunction, necrosis, and apoptosis. Systems — including the cardiovascular, pulmonary, and nervous — that are protected by a lack of vasoconstrictive response to sympathetic signaling eventually become irreversibly damaged by the loss of cellular and component function, resulting in a disease state for which resuscitation is not possible.

Again, it is the disruption in supply of substrate at the cellular level that is basic to all forms of shock. When oxygen is not available, energy production switches from aerobic to anaerobic metabolism, and rather than 38 molecules of ATP being produced per molecule of glucose, only 2 molecules of ATP are created. This severe decrease in energy production is subsequently unable to sustain the ATP-dependent mechanism of cell membrane integrity, such as the ubiquitous Na^+-K^+-ATPase pump. Anaerobic metabolism also results in the production of organic acids, most notably lactic acid.

The decreased energy production and decreased activity of the Na^+-K^+-ATPase pump results in an efflux of potassium out of the cell and an influx of sodium into the cell. This, along with the acidosis, results in a movement of fluid into the cell, resulting in swelling and further disruption of cell activity. The loss of ion gradients eventually leads to an influx of Ca^{++} that ultimately causes cell death via both necrosis and apoptosis.

As energy production and cell integrity are failing,

marked damage and dysfunction are occurring at the microcirculatory level. The endothelium is increasingly being recognized as not just a component of a transport system throughout the body, but also as a complex system that maintains homeostasis. The loss of function that is seen at the cellular level results in mechanical obstruction of the microcirculation, as fluid shifts and cellular swelling cause a loss of lumen diameter and a greater osmotic concentration of intravascular material. The normal distortion of cell shape, which allows travel though capillaries, can no longer occur, and capillary beds become clogged. 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. Once again, there is a vicious cycle of damage that leads to worsening dysfunction.

Normally, organs autoregulate blood flow within a broad range of perfusion pressures. As pressure falls, there is dilation of the blood vessels that supply individual organs, such as the liver, kidneys, lungs, brain, intestinal tract, and skin. 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 those children being mechanically ventilated. Increased cardiac edema decreases contractility and increases the risk of dysrhythmias and cardiac conduction defects. In addition, a loss of kidney function can lead to electrolyte abnormalities and elevation in blood urea nitrogen (BUN). The hyperkalemia seen in renal failure can cause cardiac dysrhythmias and asystole, while elevated BUN causes decreased platelet function.

As previously stated, poor perfusion to the kidneys can result in worsening lung compliance and increased work of breathing. This leads to abnormalities in the matching of perfusion and ventilation (V/Q mismatch). A vicious cycle of worsening tissue hypoxia, worsening organ dysfunction, and increased inflammatory response occurs throughout the body. The lungs, having an extensive network of capillary endothelial cells, are particularly sensitive to damage and are a robust source of inflammatory mediators.

These individual organs, suffering the effects of energy depletion and anaerobic metabolism, trigger the release of biochemical mediators that further stimulate the development and worsening of shock. Cytokines with inflammatory properties from CD4+ type 1 helper T cells and anti-inflammatory cytokines from CD4+ type 2 helper T cells interact in an extremely complex fashion to provide protection against invasive pathogens while avoiding self-destruction. Vasoactive mediators are also released, including epinephrine, norepinephrine, arachidonic acid metabolites (leukotrienes, thromboxane A_2, prostaglandin F_2, and prostaglandin I_2), myocardial depressant factor, and inducible nitrous oxide. These vasoactives result in increased capillary permeability and maldistribution of blood flow.

Other systems involved include the complement system, in which endothelial damage and bacterial stimulation result in C3 and C5 fragments, causing release of histamine and other vasoactive mediators. This leads to vasodilation and increased capillary permeability, as well as the activation of granulocytes and platelets. Vasodilation and hypotension are worsened by the induction of nitric oxide synthetase (NOS), resulting in the generation of pathologic quantities of NO. Macrophages, cardiac myocytes, vascular endothelium, vascular myocytes, and hepatocytes all have the capacity to increase inducible NOS when stimulated by TNF-α and IL-1. Myocardial depressant factors, released when the pancreas and other organs are subject to ischemia, have been shown to have a negative inotropic effect on the heart. These small proteins are seen after stimulation by endotoxins, as well as in response to hemorrhagic pancreatitis and hypovolemic shock.

Septic shock involves not only endogenous inflammatory mediators, but also one of the most potent stimulators of the inflammatory cascade: endotoxin. This lipopolysaccharide (LPS) coat, which comprises the outer cell membrane of gram-negative bacteria, attaches to LPS-binding proteins, which stimulate CD14+ monocytes and macrophages. Stimulation of the CD12 receptor results in release of TNF-α and IL-1, triggering the inflammatory cascade.

Differential Diagnosis

In the ED, the specific etiology is less important than recognizing and responding to shock. Remember, it is the inability to provide substrate at the cellular level that unifies all types of shock, and a child's response may be subtle at first. In early or compensated shock, tachycardia, mild tachypnea, slightly delayed capillary refill (greater than 2-3 seconds), and mild irritability may be seen. (See **Table 3** on page 8.) Unfortunately, each of these can also be seen in a relatively well child presenting to a loud and busy ED, and the symptoms may easily be discounted or overlooked. Yet these early responses are evidence of the body's compensatory mechanisms at work to increase cardiac output and preserve blood flow to vital organs, such as the brain, heart, and kidneys.

In children, tachycardia must be recognized as an early sign of the relative inability to meet metabolic demands. Because immature myocardium has a decreased

proportion of contractile elements relative to structural elements, the primary mechanism of increasing cardiac output is increasing heart rate. Delay in capillary refill is the result of increased sympathetic tone in response to decreased baroreceptor stimulation. As a continuum, this may progress to cool and clammy extremities. This vasoconstrictive response has been termed "cold shock." In some instances, rather than vasoconstriction and delayed capillary refill, there is actually increased capillary blood flow. This vasodilatory response is caused by pathogenic bacteria and results in "warm shock." In this situation, cardiac output is actually increased, and systemic vascular resistance is low. Clinically, the skin is warm, and pulses are bounding with a widened pulse pressure. (See **Table 1** on page 4.)

If shock continues, early compensatory mechanisms become inadequate to meet the substrate demands of organs and tissues, and a state of uncompensated shock ensues. Cellular ischemia and the release of vasoactive metabolites and inflammatory mediators start to affect the microcirculation, and evidence of brain, heart, and kidney hypoperfusion is evident. There is further perturbation of vital signs, with increasing elevation of heart rate and respiratory rate. Skin changes seen in compensated shock are worsened, and the skin becomes mottled or extremely cool with decreased pulses. When hypotension is evident, decreased perfusion to the kidneys results in oliguria. The mental status is more severely altered; irritability may become agitation or confusion, and may progress to unconsciousness and coma if not treated. Increased oxygen demand and acidosis caused by anaerobic metabolism result in increased respiratory drive. This rapid presentation of respiratory distress, tachypnea, and hypoxia are the hallmarks of acute respiratory distress syndrome (ARDS). As many as 32% of children with septic shock have been shown to develop ARDS.[13]

Eventually, all organs can be affected if shock is not reversed. Once MOSF develops, heroic efforts are often required to reverse this level of shock. Altered mental status, respiratory failure, cardiac failure, hepatic failure, and renal failure are all witnessed at the end of uncompensated shock, as damage becomes irreversible and refractory shock is recognized.

Prehospital Care

Standard resuscitative measures are all that should be required for the prehospital care of children in shock. Mainstays of care, such as oxygen, fluid resuscitation, and ventilatory support, are all that is typically needed. The hospital of destination is determined by local protocols. Most localities divert critically ill children to specialized centers, provided the travel distance and time is not prohibitive.

ED Evaluation And Treatment

The treatment of shock is not related primarily to the specific etiology, but rather to the pathologic process occurring. This being the case, supporting cellular respiration by maximizing oxygen transport to cells becomes the focus of therapy. This is initially accomplished by providing oxygen as 100% FiO_2 by the most clinically appropriate route and attempting to optimize intravascular volume. 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 tissue and reversing anaerobic metabolism.

By understanding and preparing for children with shock, we have an opportunity to decrease morbidity and mortality. But this requires that we know what therapies are needed. Despite the lack of abundant research in children with shock, we still must apply the evidence

Table 3. Normal Vital Signs For Age Of Pediatric Patients.

Age	Heart Rate (bpm)	Respiratory Rate (bpm)	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
1 year	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

*Adapted from: Silverman BK. Practical Information. In: *Textbook of Pediatric Emergency Medicine*, ©2006. Also: Jorden RC. Multiple Trauma. In: *Emergency Medicine: Concepts and Clinical Practice*, ©1990. All rights reserved. See References 94 and 95, respectively.

that *is* available 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 shock must be undertaken.

Once the child enters the ED and shock is recognized, immediate therapy is indicated. (**Clinical Pathway**) Knowing that limitations of cellular respiration are causative to all forms of shock, basic therapies — providing a patent airway, determining the adequacy of ventilation, giving high-flow oxygen, and reversing circulatory compromise — are essential. Vascular access must be obtained. Initial attempts to place a peripheral intravenous (IV) catheter may not be successful in a patient with a depleted volume status and with vasoconstrictive compensatory mechanisms present. Once access has been established, aggressive fluid resuscitation with isotonic crystalloid, such as lactated Ringer's or 0.9% normal saline, is given rapidly in 20 cc/kg boluses. If fluid resuscitation in quantities greater than 80-100 cc/kg given rapidly is not adequate to reverse shock, vasoactives like dopamine, epinephrine, and norepinephrine must be considered to support the child. Simultaneously, if the shock state cannot be completely explained by noninfectious causes, it is paramount that timely administration of broad-spectrum antibiotics be initiated, either via an intravenous or intramuscular route.

The rare instances of cardiogenic shock must always be considered, since therapy in these situations is different from treatment in the patient with relative hypovolemia. 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 most other children with 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 capacitance 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.

Once therapy to reverse the process of shock has been initiated, additional efforts must be made to focus care. If possible, another physician 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 100% FiO_2 is not adequate to maintain an oxygen saturation of at least 92% and a pO_2 of at least 65 torr, mechanical support of breathing is indicated. If the child is responsive, rapid sequence intubation (RSI) is 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. 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. Modified RSI should employ a sedative, an analgesic, and a muscle relaxant. To prevent pain and anxiety in the child about to undergo intubation, use either the combination of a short-acting benzodiazepine, such as midazolam, in combination with a short-acting narcotic, such as fentanyl, or use a single, short-acting agent that provides deep sedation without significant cardiac depression, such as etomidate. These

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

Age	Uncuffed ETT ID*	Cuffed ETT ID*	Initial ETT†	Central Line Size‡
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

*Measured in mm.
†Depth measured at lips in cm.
‡Length is in cm, size is in French (Fr).

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 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 could be given immediately, if needed.

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** on page 9.) 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 ID), they can allow for the safe provision of the high pressures that may be needed in children with ARDS who have poorly compliant lungs and the need for relatively high inflating pressures. It is essential that placement be confirmed by monitoring of end-tidal CO_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. It is beyond the scope of this article to exhaustively describe the strategies used in treating children with shock and ARDS, but some mention is necessary. Increasingly, it is recognized that the use of relatively high positive end-expiratory pressures (PEEP) in the range of 8-16 mm Hg when conventionally ventilating children allows for decreased FiO_2, lower peak inspiratory pressures (PIP), and a decreased incidence of ventilator-associated lung injury (VALI). If bag-valve-mask ventilation 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.

Ventilatory status can be noninvasively monitored using pulse oximetry and end-tidal CO_2 monitoring. An arterial blood gas (ABG) should be obtained 10-15 minutes after stable respiratory support has been established, in order to more accurately measure pH, pO_2, and pCO_2. It may also be useful, if central venous access has been established, to measure a venous blood gas (VBG). Ideally, a central venous catheter, which can sample blood in the superior vena cava (SVC) or right atrium, will have an oxygen saturation of at least 70%. Blood sampled from the inferior vena cava (IVC) 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.

Vascular Access

In treating shock, it is essential that adequate vascular access be established. An experienced emergency practitioner can often place a peripheral intravenous catheter in the child with mild to moderate shock. If the extremities are cool and there is significant vasoconstriction, other means of vascular access may be required. Traditionally, intraosseous (IO) catheters were not recommended in children older than 5-8 years. In addition, some emergency physicians have found that it is difficult to infuse fluids as rapidly through an IO catheter as through an intravenous line. Nonetheless, there is literature to support the placement of IO catheters in older children (and even adults) when other forms of vascular access cannot be established, and IO catheters have proven to be just as effective as central venous lines for resuscitation.[27-33] The location used most often for placement of an IO catheter is on the proximal tibia, 2-3 cm below the tibial tuberosity. If placement is unsuccessful on 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 older children and adults, or in cases where placement is unsuccessful in the proximal tibia, placement can be attempted in the distal femur, 3-4 cm above the medial condyle. A properly placed IO line is considered equivalent to a central line, and through it all necessary medicines can be infused.

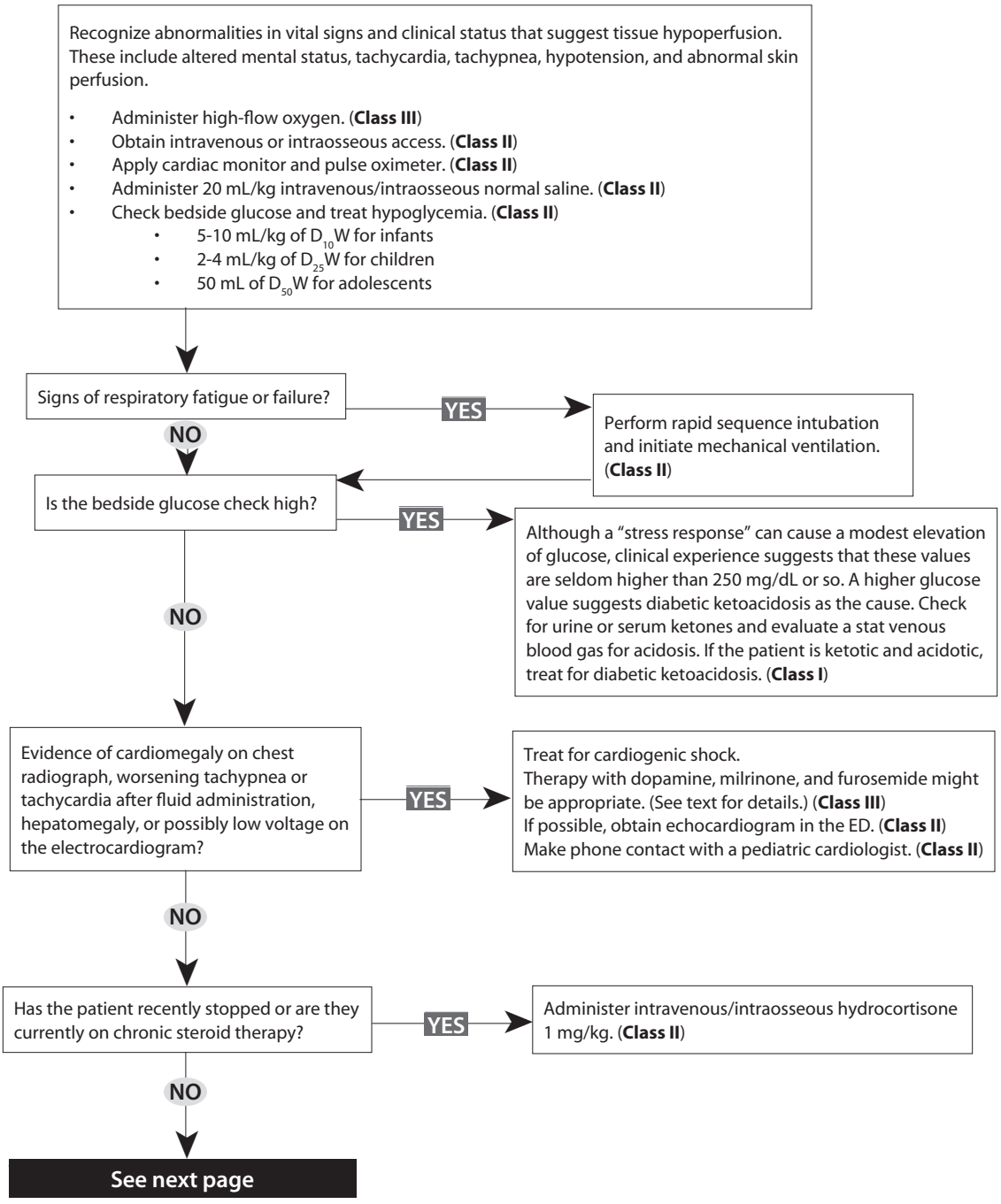
If personnel with adequate training are available and time permits, a central venous line should be placed. (**Table 4**) In younger children and infants, the femoral vein is the most easily accessed. Using the Seldinger technique, an appropriately sized single- or double-lumen central venous catheter can allow rapid volume replacement, medication administration, and safe continuous infusions of vasoactive agents, if needed. In older children, the internal jugular and subclavian vein can be cannulated — these 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 (femoral lines) are reasonably accurate, except in cases of abdominal compartment syndrome and high ventilation pressures.[34,35]

Fluid Resuscitation

Once an open airway, adequate breathing, and vascular access have been established, support of the circulatory system is the primary focus in treating shock. Rapid administration of either lactated Ringer's or 0.9% normal saline should be given.[36-41] An initial bolus of 20 cc/kg ideal body weight is considered the standard volume to administer.[42-45] The rate of infusion must be rapid enough to allow time for the infusion of at least 60 cc/kg fluid in 60 minutes. This means that each 20-cc/kg bolus is given over 10-15 minutes to allow for reassessment of the child's

Continued on page 13

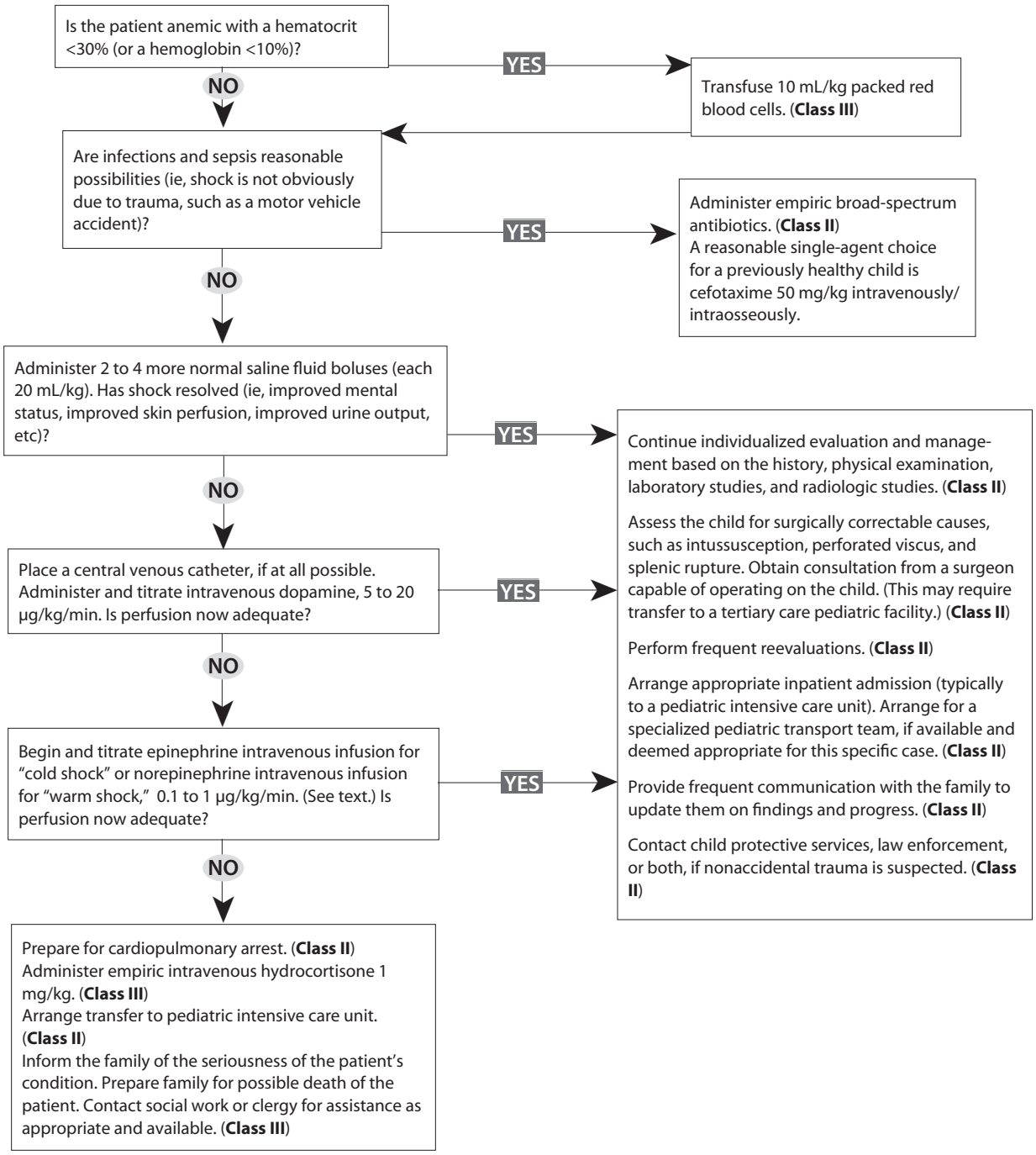
Clinical Pathway: Pediatric Shock



The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II:** Acceptable and useful. Good evidence provides support. **Class III:** May be acceptable, possibly useful. Fair-to-good evidence provides support. **Indeterminate:** Continuing area of research.

This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Clinical Pathway: Pediatric Shock



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This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Continued from page 10

volume and perfusion status, as well as preparation for repeated fluid administration. In cases of hemorrhagic shock, either type- and crossed-matched packed red blood cells or Type O/Rh– packed red blood cells should be administered, with the goal of attaining euvolemia. When red blood cell replacement starts to approach whole blood volume (75-80 cc/kg), replacement of clotting factors should be considered (such as fresh frozen plasma (FFP), platelets, and cryoprecipitate). In cases of cardiogenic shock, the administration of fluid must be approached with caution, and gentle diureses is in fact a more logical therapy. Unfortunately, this requires that an accurate diagnosis already be made, which is often not the case.

Resuscitation by means of fluids other than isotonic crystalloid and blood products is controversial. Many of these alternative fluids have been shown to decrease the time to euvolemia and to decrease the total amount of fluid required to reach adequate volume status, but none of these have been shown to change overall mortality.[46,47]

Determination of volume status can be extremely difficult. The return of normal mental processing, blood pressure, peripheral perfusion, and urine output may not occur in a child who is suffering from severe shock. Many adult studies have shown the effectiveness of goal-directed therapy for septic shock,[48-53] but these often require monitoring modalities that are not reasonably used in the ED (such as pulmonary artery catheters). Therefore, the best indicators of volume status are heart rate (controlling for temperature), respiratory rate, skin perfusion, and urine output. If a central venous line has been placed and pressure transduction is possible, this can be an effective device for monitoring volume status. Volume administration may or may not result in an increase in blood pressure in situations of fluid-refractory shock, but should increase central venous pressure. Administration of volume that does not result in at least a 5-mm Hg rise in central venous pressure (CVP) is suggestive of severe hypovolemia. As the large capacitance vessels in the venous system fill, a more robust increase in CVP 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 CVP and, ideally, an increase in arterial pressure.

Since urine output can be a useful tool in assessing volume resuscitation, accurate measurement of urine production is necessary. This requires placement of an appropriately sized bladder catheter, once resuscitation has been initiated. Bladder catheterization also allows for the sterile collection of urine, which is important in the investigation of shock not already explained by noninfectious causes. Once the bladder is accessed and urine production is being monitored, a reasonable goal for resuscitation in children is urine output of more than 1 cc/kg/hour. In rare cases of long-standing shock prior to medical attention, the child may quickly enter a polyuric phase of ATN 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 be used 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 greater than 40 cc/kg in the first hour was associated with improved outcome, with no increase in pulmonary edema or ARDS.[13] More recently, Han and Carcillo 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.[54] In fact, regardless of the duration of shock, both survivors and nonsurvivors received approximately 20 cc/kg of fluid resuscitation. The authors concluded that this indicates a failure by clinicians to continue fluid resuscitation after an initial bolus. Unfortunately, the data also demonstrated that prolonged shock was associated with a more than 9-fold increase in mortality.

Inotropic and Vasoactive Agents

In situations where volume resuscitation is inadequate to restore tissue perfusion, catecholamines are the next line of therapy employed in the treatment of shock. 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 (α), beta (β), and dopaminergic (DA).[55] Those agents that stimulate α-receptors cause smooth muscle contraction in arterioles and bronchiole muscles. This leads to vasoconstriction, which raises blood pressure and cardiac afterload. β-receptors have 2 important subtypes: β_1 and β_2. β_1-receptors mediate contractility (inotropy) and heart rate (chronotropy). This occurs through an increase in intracellular calcium. β_2-receptor activation, on the other hand, causes smooth muscle relaxation, resulting in arteriole vasodilation and bronchiole relaxation. The DA receptors are found predominantly on the kidneys and 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). Dopamine is well established as the first-line agent in pediatric shock.[50,51,56] The initial rate of infusion is 5 μg/kg/min. At this dose, the effect is predominantly β-adrenergic, causing an increase in heart rate and contractility. As the rate of infusion is increased to a maximum of 20 μg/kg/min, the inotropic effects also increase; however, there is an even larger increase in the α-adrenergic effects, which leads to an increase in peripheral vasoconstriction. In combination, dopamine improves blood pressure, cardiac output, urine production, and extremity perfusion.

In cases of severe shock, or if there has been inadequate clinical improvement with doses of dopamine ap-

proaching 20 μg/kg/min, epinephrine should be used.[51,56-58] The starting dose of epinephrine is 0.05 μg/kg/min. This produces predominantly β-adrenergic effects (increased inotropy and chronotropy). At doses beyond 0.2-0.3 μg/kg/min, there are increasing α-adrenergic effects, causing increased vasoconstriction. Although there is no true limit to the rate of epinephrine infusion, rates greater than 1 μg/kg/min are thought to cause severe peripheral vasoconstriction and tissue ischemia. A resuscitation that requires the prolonged use of epinephrine at these rates is seldom successful.

In patients with cardiogenic shock, dobutamine and milrinone, a phosphodiesterase-inhibitor, should be considered.[59-61] Dobutamine is a synthetic β-adrenergic agent that increases inotropy with no effect on alpha-receptors.[62] There is potential for a decrease in afterload and blood pressure, due to unopposed β_2-receptor stimulation. Often dopamine and dobutamine are used in combination at doses of 2.5-5 μg/kg/min, each to initiate support in conditions of cardiogenic shock.

Some practitioners prefer to use milrinone instead of dobutamine when caring for children with myocarditis or cardiomyopathy. Milrinone, via phosphodiesterase inhibition, increases inotropy as well as lusitropy (diastolic relaxation) and peripheral vasodilation.[63,64] 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 μg/kg/min, with a maximum of 1.0 μg/kg/min. (**Table 5**)

Norepinephrine and vasopressin are 2 vasoactive agents that preferentially cause vasoconstriction. In the case of norepinephrine, there is both α- and β-receptor stimulation, but because there is relatively greater α-receptor stimulation at lower doses, vasoconstriction is seen predominantly. In the case of vasopressin, only vasoconstriction is seen, because receptors are located only within the vasculature. Both 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.[50,51] 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

For circumstances in which the etiology of shock cannot be completely explained by noninfectious causes, antibiotics must be given as soon as possible.[17,50,65] It is often possible to obtain blood cultures when intravenous access is obtained and urine cultures when a bladder catheter is placed. This allows for the most accurate diagnosis in the case of septic shock. The choice of antibiotics depends on the age of the child and any particulars in their presentation or current and past medical history. In children under 1 month of age, it is reasonable to start ampicillin for coverage of *Listeria monocytogenes* and cefotaxime for coverage of group B streptococcus, *E Coli*, *Streptococcus pneumoniae*,

Table 5. Inotropes, Mechanism, Doses, And Clinical Indications In Patients With Shock.

Inotrope	Mechanism	Effects	Clinical Usage	Dosing Range
Dopamine	DA at lower dosing range $\beta_{1\&2}$ at increasing doses α at the higher end of dosing	Increased cardiac output; vasoconstriction at higher doses	**Septic shock** (low cardiac output shock)	**5-20 μg/kg/min**
Epinephrine	$\beta_{1\&2}$ at increasing doses α at the higher end of dosing	Increased cardiac output; vasoconstriction at higher doses	**Moderate to severe septic shock** (low cardiac output shock)	**0.05-5 μg/kg/min** (doses greater than 1 μg/kg/min indicate extremely severe dysfunction)
Norepinephrine	Predominance of α, even at lower doses $\beta_{1\&2}$ at increasing doses	Increased vasoconstriction and some increased cardiac output	**Moderate to severe "warm" septic shock** (high cardiac output with vasodilation)	**0.05-5 μg/kg/min** (doses greater than 1 μg/kg/min indicate extremely severe dysfunction)
Dobutamine	$\beta_{1\&2}$ at increasing doses	Increased cardiac output	**Septic shock** (low cardiac output shock) ***or*** **myocarditis/cardiomyopathy** (often with dopamine)	**2.5-20 μg/kg/min**
Milrinone	Increases cAMP via inhibition of phosphodiesterase, modulating intracellular Ca^{++}	Increased diastolic relaxation, increased cardiac output and vasodilation	**Myocarditis/cardiomyopathy** (often with dopamine)	**2.5-1.0 μg/kg/min**
Vasopressin	Increases levels of IP_3 and DAG, which in turn increase intracellular Ca^{++}	Increased peripheral vasoconstriction	**Moderate to severe "warm" septic shock** (high cardiac output with vasodilation)	**0.04-0.1 U/min** (adult) or **0.0005-0.001 U/kg/min**

and other coliform bacteria. Some practitioners would use a combination of ampicillin and gentamicin. Between 4 and 12 weeks of age, *Listeria* is unlikely; therefore, ampicillin is probably not necessary, *unless* there is evidence of meningitis. In children with severe, overwhelming sepsis infectious disease specialists may suggest coverage with vancomycin for methicillin-resistant *Staphylococcus aureus*. If an intraabdominal process seems to be at work, 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/cefotaxime or ceftriaxone and tobramycin/piperacillin/tazobactam.

In children with an underlying immunodeficiency (eg, oncologic patients, transplant patients, AIDS patients) the choice of antibiotic should be guided by their high-risk status. Many institutions also have "management pathways" for children who may have surgically placed central venous catheters. 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 the situation of a child who may be particularly susceptible or one who has been on broad-spectrum antibiotics for a prolonged period.

Steroids

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).[43,66,67] In a prospective, randomized, double-blind, placebo-controlled study of high-dose methylprednisolone in septic shock, no reduction in mortality was observed.[68] In fact, in a subset of these patients, there was actually an increase in mortality from secondary infections.

More recent studies in adults and children have shown that adrenal replacement therapy may improve outcomes in shock.[36,69-71] Physiologic doses of hydrocortisone are indicated in children with fluid- and vasoactive-refractory shock who have suspected or proven adrenal insufficiency. Note that the current definition of adrenal insufficiency in pediatric shock has yet to be completely resolved. Most practitioners would consider a cortisol level of 18 mg/dL or less, in a patient with shock, as an indication of adrenal insufficiency and would administer hydrocortisone in a dose of 1 mg/kg every 6 hours.[43,52]

Diagnostic Studies

Shock is a clinical diagnosis that does not require definitive studies for diagnosis. Still, depending on the presentation, there are studies that can help determine the *reason* for shock. More often than not, these studies are done after treatment has been initiated, and in no way should therapy be delayed in order to perform any diagnostic studies. In hypovolemic shock, since the most common etiology is related to vomiting and diarrhea, 2 types of studies may be useful. The first type can help determine the cause of symptoms. In children, the most common cause will be a viral infection, in which case 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 can be given for shigella and salmonella infections. Because a urinary tract infection can also cause vomiting and diarrhea in young children, and may even progress to urosepsis, a urinalysis and urine culture are helpful in patients with historical features or risk factors. Secondarily, studies assessing for abnormalities caused by persistent vomiting and stool losses in a severely dehydrated child will help guide and augment fluid 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 (BUN) and creatinine can help to determine volume status and give an indication of renal perfusion and function.

With any type of shock, various labs can assist in establishing the extent of end-organ hypoperfusion. Metabolic acidosis can be determined by low bicarbonate on a serum electrolyte panel or on a blood gas in which acidosis is not fully explained by respiratory insufficiency (since the bicarbonate value on a blood gas is a calculated value). This acidosis suggests that there is some degree of anaerobic metabolism. Although lactic acid is a nonspecific lab test, many practitioners 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.[72] Further trending of lactate may also be helpful in directing therapy.[74-75] Increased end-tidal CO_2 has also been shown to be associated with improved cardiopulmonary function.[76-79] This increase occurs as tissue perfusion increases and a larger CO_2 load is delivered to the lungs and exhaled.

In presumed septic shock, studies are primarily geared to assessing and diagnosing an infectious etiology. An elevated white blood cell count with left shift or polymorphonuclear cell predominance on complete blood cell count (CBC) with differential can help to determine whether there is an infectious etiology for the current clinical state. Although not usually of great value in the ED, a blood culture can help to confirm a diagnosis and guide antibiotic therapy in the future. The same is true of a urinalysis and urine culture in assessing for urinary tract infection and urosepsis. Gram's 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 intraabdominal process is suspected, an abdominal and pelvic computed tomography (CT) scan may be useful. Because disseminated intravascular coagulopathy (DIC) or consumptive

coagulopathy is associated with septic shock (as well as other forms of shock), it is reasonable to obtain a prothrombin time (PT), international normalized ration (INR), partial thromboplastin time (PTT), and some indicator of clot formation and breakdown, such as fibrin degradation products (FDPs) and platelets.

If either cardiogenic or obstructive shock is being considered in the differential, a chest radiograph (CXR) and an electrocardiograph (ECG) should be attained immediately. If there is cardiomegaly on the CXR or an abnormality on the ECG, a cardiac cause of the shock must be a strong consideration. A 2-dimensional echocardiogram with color Doppler should be performed as soon as possible and evaluated by a pediatric cardiologist, who can check for function, dilation, and valve competency.[80]

In cases of suspected endocrinologic shock, the diagnosis is again made clinically, and lab tests should not delay treatment. A serum cortisol level, serum electrolytes, and performance of a corticotrophin stimulation test may be supportive in making the diagnosis of adrenal insufficiency or failure. Two methods are routinely used to diagnose acute adrenal insufficiency in severely ill patients: a single, random cortisol level, and a change in cortisol level after an exogenous adrenocorticotropic hormone (ACTH) is administered. Traditionally, adrenal insufficiency is identified in patients with sepsis by a single, random cortisol level of less than 15-20 μg/dL. This may be particularly valid, since the median cortisol level in adult patients with

Ten Pitfalls To Avoid

1. "He wasn't hypotensive, so I figured he wasn't in shock."
In children, the only signs of compensated shock may be tachycardia and irritability, which are common findings in a loud, busy ED.

2. "The pulse ox reading was normal. Why would I have given oxygen?"
The primary deficiency in shock is failure of 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 didn't want to fluid overload the kid!"
Children with symptoms of shock can have fluid deficits that are far greater than may initially be estimated. An initial fluid bolus of 20 cc/kg of isotonic crystalloid over 15 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 60 mL/kg of normal saline. How could that possibly not be enough?"
Especially in cases of ongoing losses due to vomiting and diarrhea, both the fluid deficit and the ongoing losses need to be replaced.

5. "What do you mean, she decompensated in the CT scanner? She looked fine 2 hours ago!"
Resuscitation of a child in shock requires that a therapy not only be implemented, but that the results of that therapy then be evaluated. The reevaluation of the child allows for additional appropriate therapy.

6. "I didn't give antibiotics because I couldn't find a source of infection."
Although it can be impossible to make a *definitive* diagnosis of shock caused by a bacterial infection, if other causes cannot be excluded with some confidence, the timely administration of antibiotics may be life-saving.

7. "The chest x-ray was normal. There weren't any infiltrates or effusions. But I guess, now that I look at it, the heart does look big."
Although dilated cardiomyopathy is not a common cause of shock, an enlarged heart can be seen on chest radiograph; therefore, it should be considered in the differential. 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 administration of 60-100 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, this must be provided through whatever venous access is available, including a peripheral venous line or an intraosseous line.

9. "Hydrocortisone? No, I didn't give any. Why should I have given hydrocortisone?"
Children who are on chronic steroids or who are steroid-dependent have increased steroid needs during even minor acute illnesses. Increased doses of steroids, given in consultation with an endocrinologist, can successfully reverse shock.

10. "I wanted to make sure I knew what was going on before I called for transfer."
Whether the child needs to go to the operating room, the PICU, or the medical ward, detailed communication with those who will be providing care for the child after they leave the ED is essential. ▲

shock is 50 μg/dL, compared with a normal range of 10-20 μg/dL. The second method is a corticotrophin stimulation test with administration of tetracosactrin 250 μg. A resulting change in cortisol level of 9 μg/dL or less is considered relative adrenal insufficiency.[26]

Controversies/Cutting Edge

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 maddeningly difficult, because of the complex interaction between components of the immune system and other systems that regulate inflammation. The response to both infectious agents (in the case of septic shock) and 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.

Activated protein C (APC) is another agent that has been studied in septic shock. Because of the propensity for DIC in septic shock, and the capillary bed ischemia obstruction that occurs due to thrombus formation when the endothelium is injured, an agent such as APC, which promotes fibrinolysis and inhibits thrombus formation, may improve tissue perfusion. And it has been observed that, in adults, there is an increased risk of death from septic shock when levels of APC are reduced.[81] In adult trials, treatment with APC was associated with improved survival, although there was also an increased risk of complications.[82] Recently, a prospective trial of APC in children was suspended, due to a higher than expected rate of complications. At this point, APC is not recommended for use in children with shock.

Key Points For Pediatric Shock

- Although certainly present in cases of decompensated shock, hypotension is not required to diagnose shock. In fact, most children in shock are not hypotensive on presentation.
- Obtaining vascular access may be time-consuming and difficult. Be aware that vascular access can be attained via an intraosseous line, a peripheral IV, or a central venous line.
- 20 mL/kg of normal saline is the *starting point* for fluid resuscitation.
- A child who has worsening tachycardia, worsening respirations, and hepatomegaly after the administration of intravenous fluids is probably in cardiogenic shock.
- A child being evaluated and treated for shock should be closely monitored with pulse oximetry, a cardiorespiratory monitor, frequent checks of central temperature, and monitoring of urine output. ▲

Full cardiopulmonary mechanical support in shock continues to have variable acceptance.[80,83-88] The use of extracorporeal mechanical oxygenation (ECMO) via a centrifugal pump and membrane oxygenator has been employed during the acute and severe phases of shock, with anecdotal success in many institutions. There has not yet been a prospective, randomized trial in children to determine whether this high-risk therapeutic modality affects outcome. ECMO has been used to provide pulmonary support via venovenous (VV) cannulation — in which blood is removed from either the SVC, IVC, or both, and then returned to the right atrium — and venoarterial (VA) ECMO, in which blood is again removed from the venous side, but returned to the arterial side through the carotid artery. Because of the myriad risks ECMO carries — including potential carotid artery ligation in VA ECMO, hemorrhage (most notably intracranial) due to the necessity for anticoagulation, and secondary infections — it is not yet considered a standard therapy in severe shock with MOSF.

Disposition

Decisions regarding the most appropriate site for further management and observation of children who have been treated for shock in the ED can be difficult. It is not uncommon for a child who has had prolonged diarrheal illness to present to the ED in compensated shock, then respond well to 60 cc/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 PICU or another unit that can monitor vital signs closely, provide invasive physiologic monitoring, and continue resuscitation.

The disposition of the child who appears better, still has some abnormalities after reasonable fluid resuscitation, but clinically does not require inotropic support is often difficult. This is the child who is not uncommonly the sickest in the ED, but healthier than other children in a busy PICU. 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 stepdown 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 concert among emergency and critical care physicians.

In some situations involving surgically correctable causes of shock, such as hemorrhage due to intraabdominal organ rupture or septic shock due to ischemic bowel, the most appropriate disposition is directly to the operating room. Again, this requires that physicians from the ED, anesthesia, and surgical teams, as well as nurses in

both locations, act in concert to continue any resuscitative management that the child requires and to facilitate rapid transfer with the child in the best pathophysiologic state possible. Immaculate documentation and thorough verbal communication are paramount in the transfer and appropriate care of children moving quickly between various parts of a busy hospital.

Special Circumstances

Given the heterogeneity of the etiologies of pediatric shock, most children in shock can be said to represent "special circumstances." Nonetheless, a few specific conditions are worth mentioning here. One situation is when cellular respiration is disrupted by toxins. A good example of this is carbon monoxide poisoning.[89,90] Typically, however, toxicologic exposures are suspected based on the history. Another special circumstance is when a child has a known, terminal illness, such as cancer.[91,92] The difficult decisions regarding aggressiveness of care must be individualized for each child. Other, rare situations exist, such as splenic rupture, either spontaneously or following minor trauma. These cases are often seen following missed diagnoses of mononucleosis.[93] Many such scenarios can be envisioned, and it is best to keep a sharp eye out for the unusual.

Summary

Increasing knowledge about and preparedness for shock in children can potentially decrease the anxiety and wasted energy that sometimes occurs when a very sick child enters the ED. Because of the multiple etiologies of shock, but the common pathophysiology of the clinical results, a resuscitative approach to shock based on well-established strategies can help us continue to improve morbidity and mortality. With the understanding that, basic to all forms of shock, is an inability to supply oxygen and glucose at the cellular level, we can aim our initial resuscitation at reversing these abnormalities.

If we are to apply rational therapy to children with shock, it is essential that we first *recognize* it. 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 recognized, treatment and monitoring become paramount. A patent airway, appropriate breathing of 100% inspired oxygen, and rapid volume expansion with isotonic crystalloid will improve the pathophysiologic status of the child. Further therapies, if needed, can then be tailored to improve tissue perfusion.

We must bear in mind that our current understanding of shock is of its basic pathophysiology *only*, and evidence for therapies beyond providing an airway, oxygen, and adequate cardiac output does not exist now. The data that we need to further improve outcome must be increased. Without pediatric trials in shock, we will have no choice but to continue applying either 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. There is clearly both an ample population and a clinical need to continue research into pediatric shock. ▲

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 reference, where available. In addition, the most informative references cited in the paper, as determined by the authors, will be noted by an asterisk (*) next to the number of the reference.

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Physician CME Questions

49. Shock is the pathophysiologic state in which:
a. There is no blood pressure.
b. Oxygen saturations are less than 70%.
c. There is inadequate substrate for cellular respiration.
d. No pulse is palpable.

50. The most common cause of shock in children worldwide is:
a. Septic shock related to oncologic disease.
b. Hypovolemic shock caused by vomiting and/or diarrhea.
c. Ductal-dependent congenital heart disease.
d. Hemorrhagic shock caused by trauma.

51. For a pediatric patient in shock, which of the following most strongly influences the choice of an empiric antibiotic?
a. Age
b. Blood pressure
c. Gender
d. Temperature

52. When compensating for shock, children increase cardiac output by:
a. Increasing heart rate.
b. Increasing stroke volume.
c. Autotransfusion via splenic contraction.
d. Vasodilating the peripheral vasculature.

53. The specific type of shock must be known, since each type of shock requires a unique approach to resuscitation.
a. True
b. False

54. The incidence of septic shock in children in the United States is greatest in:
a. Infants
b. School-age children
c. Preteens
d. Teenagers

55. Hypotension, a recent viral illness, and cardiomegaly on CXR:
a. Suggest hypovolemic shock.
b. Are consistent with cardiogenic shock.
c. Require immediate surgical evaluation.
d. Should be treated with antibiotics immediately.

56. Sepsis results in anaerobic metabolism, which causes:
a. A decrease in lactic acid production per mole glucose utilized.
b. A decrease in ATP production per mole glucose utilized.
c. An increase in ATP production per mole glucose utilized.
d. An increase in oxygen production.

57. In children with shock, tachycardia:
a. Is one of the first indications of hypovolemia.
b. Should never be concerning to an experienced emergency physician.
c. Can always be explained by fever.
d. Requires treatment with ß-antagonists.

58. Because of the risk of causing pulmonary edema in children being appropriately fluid resuscitated:
a. No more than two 5-cc/kg boluses should be given each hour.
b. Diuretics can be given simultaneously, to encourage compensatory diuresis.
c. It is better to give 1 fluid bolus and observe for at least 2 hours.
d. There is almost no risk of causing pulmonary edema with appropriately aggressive fluid resuscitation.

59. The following is an acceptable route of intravenous fluid resuscitation in a hypotensive child:
a. Femoral central intravenous line
b. Antecubital peripheral venous line
c. Tibial intraosseous line
d. All of the above

60. The amount of fluid required to resuscitate a child in hypovolemic shock can be estimated by:
a. Measuring the body surface area.
b. The state of the child's health prior to this illness.
c. The response to resuscitation, including improvement in heart rate, blood pressure, urine output, and central venous pressure.
d. The degree of lactic acidosis.

61. Epinephrine, norepinephrine, and dopamine all:
a. Have both α- and ß-adrenergic effects on the heart.
b. Must be given after an initial test dose is administered.
c. Do not require continuous monitoring.
d. Cause fever in the child with septic shock.

62. The most accurate method of assessing the need for adrenal replacement therapy:
a. Is by determining the specific cause of shock.
b. Requires the performance of the corticotrophin

Physician CME questions conclude on back page

stimulation test.
c. Necessitates urgent endocrinologic consultation.
d. Is dependent on the degree of hypotension.

63. Venoarterial ECMO requires cannulation of:
a. Both a major artery and a major vein.
b. The heart directly.
c. Both carotid arteries.
d. The superior and inferior vena cava exclusively.

64. Any child who receives more than 20 cc/kg IV fluid resuscitation:
a. Must be admitted to an intensive care unit.
b. Should be started on inotropic support.
c. Cannot be given antibiotics.
d. Requires reassessment to direct further resuscitation.

Coming in Future Issues:

Fever In The Returning Child Traveler • Airway Management

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
- Non-randomized or retrospective studies: historic, cohort, or case-
- control studies
- Less robust RCTs
- 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

Significantly modified from: The Emergency Cardiovascular Care Committees of the American Heart Association and representatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. *JAMA* 1992;268(16):2289-2295.

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Target Audience: This enduring material is designed for emergency medicine physicians.

Needs Assessment: The need for this educational activity was determined by a survey of medical staff, including the editorial board of this publication; review of morbidity and mortality data from the CDC, AHA, NCHS, and ACEP; and evaluation of prior activities for emergency physicians.

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