#### **Abstract:**

Septic shock is a significant source of morbidity and mortality in children. Adhering to evidence-based guidelines for treatment for children with septic shock can lead to better outcomes. Initiation of treatment should begin promptly after recognition of shock in the emergency department. Elements of best practices include rapid administration of intravenous fluid for resuscitation and antibiotics in the first hour. Fluid resuscitation should be titrated to clinical and biochemical end points. If fluid resuscitation is not sufficient to reverse shock, an ionotrope or vasopressor infusion should be initiated. Steroids should be administered in patents known to be at high risk for adrenal insufficiency. All of these interventions should be achieved in the emergency department, ideally within the first hour after recognition of shock.

#### **Keywords:**

pediatric septic shock; emergency department; systemic inflammatory response syndrome

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# Management of Pediatric Septic Shock in the Emergency Department

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n recent decades, there have been many advances in the treatment and prevention of septic shock in children. However, the burden of septic shock in children in the United States has been increasing. During the decade from 1995 to 2005, a study of severe pediatric sepsis in 7 US states noted an 81% increase in cases. 1 At the same time as the incidence has increased, mortality due to pediatric sepsis has decreased to less than 10%. 1-3 In the United States in 2005, the estimated health care costs associated with pediatric septic shock were nearly 5 billion dollars. 1

In the emergency department (ED), septic shock must first be recognized. Systemic inflammatory response syndrome (SIRS) is defined as fever or leukocytosis in addition to tachycardia or tachypnea, or both fever and leukocytosis. 4 Sepsis is defined as SIRS due to a proven or suspected infection. Finally, pediatric septic shock is defined as sepsis with cardiovascular dysfunction. Metabolic acidosis, hypotension, elevated lactate, oliguria, prolonged capillary refill (>5 seconds), or cool extremities (>3°C difference between core and peripheral temperature) qualify as cardiovascular dysfunction. <sup>4</sup> Hypotension may be a late manifestation of shock in children, so hypotension is confirmatory of shock but is not required to make the diagnosis. This is in contrast to the adult definition of septic shock, which requires hypotension. 5 Clinicians must have a high index of suspicion for shock in children and search for the signs of cardiovascular dysfunction in all patients who have SIRS.

The management of sepsis has evolved greatly over the past few decades. Early, goal-directed therapy (EGDT) and effective broad-spectrum antibiotics have greatly improved outcomes. Evidence-based guidelines have made it possible for providers to deliver a common standard of care. <sup>5,6</sup> This article will review the initial resuscitation of children with septic shock.

#### PHYSIOLOGY OF SEPTIC SHOCK

Septic shock is characterized by insufficient oxygen and substrate delivery to tissues to meet their metabolic demands. This deficit in oxygen delivery leads to shunting of energy containing compounds into the less efficient anaerobic pathway. Lactic acid is a by-product of anaerobic metabolic and therefore is often used as a marker for hypoperfusion. Eventually, cell death may occur from lack of adenosine triphosphate, if shock is not corrected.

Shock is the result of cardiovascular dysfunction leading to tissue hypoperfusion. The function of the cardiovascular system is described by the classic equation Q = P/R, where Q is flow, P is pressure, and R is resistance. When clinically applied to the patient in shock, the equation can be transformed to CO = (MAP - CVP)/SVR, where CO is cardiac output, MAP - CVP is mean arterial pressure minus central venous pressure, and SVR is systemic vascular resistance.

Septic shock can be classified as cold or warm shock based on clinical findings. 7-9 Children in cold septic shock have cool extremities, delayed capillary refill, and poor pulses. Children with cold septic shock have low CO with elevated SVR in an attempt to maintain perfusion pressure. Conversely, warm shock is due to vasodilation and low SVR. Patients with warm shock have an increased CO and clinically are characterized by flash capillary refill, warm extremities, and bounding pulses. Historically, it was thought that most children with septic shock present with low CO and high SVR shock or cold shock.<sup>8</sup> More recently, it has been shown that community-acquired septic shock usually does present as cold shock; however, hospital-acquired or central line-associated septic shock is most frequently warm shock. <sup>7,9</sup> Children's hemodynamics can progress over time; they may switch from one shock state to another. 7,8 Clinicians must follow examination findings closely to monitor for these changes. Septic shock in adults presents differently; most adults present with warm septic shock. 10

#### EARLY, GOAL-DIRECTED THERAPY

Early, goal-directed therapy consists of titration of therapies to clinical and biochemical end points. It is considered the standard of care for adults and children with septic shock and should be initiated immediately after diagnosis in the ED.

In a seminal 2001 study by Rivers et al,  $^{11}$  263 adults with septic shock were randomized to EGDT or current standard of care. Those in the EGDT arm had therapies titrated to CVP, MAP, and mixed venous saturation (SvO<sub>2</sub>) goals. Patients who were randomized to EGDT had a mortality of 30.5% compared with 46.5% for standard of care (P = .009). The benefits of EGDT protocols have been reproduced many times in adults with septic shock.  $^{12,13}$ 

Studies have also shown benefits from EGDT in children with septic shock. <sup>14–17</sup> Adherence to American College of Critical Care Medicine/Pediatric Advanced Life Support (ACCM/PALS) guidelines (Figure 1) has been shown to be associated with significant decreases in mortality. <sup>14,17</sup> Han et al <sup>14</sup> in a retrospective study showed that when resuscitation of septic children was consistent with ACCM/PALS guidelines for EGDT, there was a increase of greater than 6-fold in odds of survival, after adjusting for severity of illness, compared with patients whose management was not consistent with EGDT.

#### **FLUID RESUSCITATION**

The first intervention of EGDT, after recognition of shock, is immediate and aggressive fluid resuscitation. Early and aggressive fluid resuscitation involves multiple goals. Intravenous access must be obtained quickly, ideally within the first 5 minutes of recognition of shock. An initial fluid bolus of 20 mL/kg should given be as rapidly as possible. When the fluid bolus is complete, the patient should be immediately reassessed for clinical signs of reversal of the shock state. The clinical end points to target are normal mental status, age-appropriate heart rate and blood pressure, capillary refill less than 3 seconds, palpable distal pulses, and urine output greater than 1 mL/kg/hr.6 Adequate fluid resuscitation routinely requires 40 to 60 mL/kg in the first 15 to 60 minutes, but may require greater than 100 mL/kg for some children in septic shock. Patients should receive fluid boluses until the clinical markers of shock are corrected or the decision is made that the patient is fluid replete, and other forms of resuscitation are appropriate.

Children who receive aggressive fluid resuscitation in the first hour have significantly better

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