

In the persistently hemodynamically unstable patient, dexamethasone sodium phosphate, 4 mg, should be given intravenously. This agent is preferred if empiric therapy is required because, unlike hydrocortisone, it does not interfere with the ACTH stimulation test. If the diagnosis of absolute or relative adrenal insufficiency is established as shown by nonresponse to corticotropin stimulation (cortisol  $\leq 9$   $\mu\text{g/dL}$  change after stimulation), the patient has a reduced risk of death if treated with hydrocortisone, 100 mg every 6–8 h, and tapered as the patient achieves hemodynamic stability. Simultaneous volume resuscitation and pressor support are required. The need for simultaneous mineralocoid is unclear.

### ADJUNCTIVE THERAPIES

The sympathomimetic amines dobutamine, dopamine, and norepinephrine are widely used in the treatment of all forms of shock. Dobutamine is inotropic with simultaneous afterload reduction, thus minimizing cardiac-oxygen consumption increases as cardiac output increases. Dopamine is an inotropic and chronotropic agent that also supports vascular resistance in those whose blood pressure will not tolerate peripheral vascular dilation. Norepinephrine primarily supports blood pressure through vasoconstriction and increases myocardial oxygen consumption while placing marginally perfused tissues, such as extremities and splanchnic organs, at risk for ischemia or necrosis, but it is also inotropic without significant chronotropy. Arginine-vasopressin (antidiuretic hormone) is being used increasingly to increase afterload and may better protect vital organ blood flow and prevent pathologic vasodilation.

### REWARMING

Hypothermia is a frequent adverse consequence of massive volume resuscitation (Chap. 478e). The infusion of large volumes of refrigerated blood products and room temperature crystalloid solutions can rapidly drop core temperatures if fluid is not run through warming devices. Hypothermia may depress cardiac contractility and thereby further impair cardiac output and oxygen delivery/utilization. Hypothermia, particularly temperatures  $<35^{\circ}\text{C}$  ( $<95^{\circ}\text{F}$ ), directly impairs the coagulation pathway, sometimes causing a significant coagulopathy. Rapid rewarming to  $>35^{\circ}\text{C}$  ( $>95^{\circ}\text{F}$ ) significantly decreases the requirement for blood products and produces an improvement in cardiac function. The most effective method for rewarming is endovascular countercurrent warmers through femoral vein cannulation. This process does not require a pump and can rewarm a patient from  $30^{\circ}$  to  $35^{\circ}\text{C}$  ( $86^{\circ}$  to  $95^{\circ}\text{F}$ ) in 30–60 min.

## 325 Severe Sepsis and Septic Shock

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### DEFINITIONS


(Table 325-1) Animals mount both local and systemic responses to microbes that traverse their epithelial barriers and enter underlying tissues. Fever or hypothermia, leukocytosis or leukopenia, tachypnea, and tachycardia are cardinal signs of the systemic response. To date, attempts to devise precise definitions for the harmful systemic reaction to infection (“sepsis”) have not resulted in a clinically useful level of specificity, in part because the systemic responses to infection, trauma, and other major stresses can be so similar. In general, when an infectious etiology is proven or strongly suspected and the response results in hypofunction of uninfected organs, the term *sepsis* (or *severe sepsis*) should be used. *Septic shock* refers to sepsis accompanied by hypotension that cannot be corrected by the infusion of fluids.

**TABLE 325-1** DEFINITIONS USED TO DESCRIBE THE CONDITION OF SEPTIC PATIENTS

Bacteremia	Presence of bacteria in blood, as evidenced by positive blood cultures
Signs of possibly harmful systemic response	Two or more of the following conditions: (1) fever (oral temperature $>38^{\circ}\text{C}$ [ $>100.4^{\circ}\text{F}$ ]) or hypothermia ( $<36^{\circ}\text{C}$ [ $<96.8^{\circ}\text{F}$ ]); (2) tachypnea ( $>24$ breaths/min); (3) tachycardia (heart rate $>90$ beats/min); (4) leukocytosis ( $>12,000/\mu\text{L}$ ), leukopenia ( $<4000/\mu\text{L}$ ), or $>10\%$ bands
Sepsis (or severe sepsis)	The harmful host response to infection; systemic response to proven or suspected infection plus some degree of organ hypofunction, i.e.: <ol style="list-style-type: none"> <li><b>Cardiovascular:</b> Arterial systolic blood pressure <math>\leq 90</math> mmHg or mean arterial pressure <math>\leq 70</math> mmHg that responds to administration of IV fluid</li> <li><b>Renal:</b> Urine output <math>&lt;0.5</math> mL/kg per hour for 1 h despite adequate fluid resuscitation</li> <li><b>Respiratory:</b> <math>\text{Pao}_2/\text{Fio}_2 \leq 250</math> or, if the lung is the only dysfunctional organ, <math>\leq 200</math></li> <li><b>Hematologic:</b> Platelet count <math>&lt;80,000/\mu\text{L}</math> or 50% decrease in platelet count from highest value recorded over previous 3 days</li> <li><b>Unexplained metabolic acidosis:</b> A pH <math>\leq 7.30</math> or a base deficit <math>\geq 5.0</math> mEq/L and a plasma lactate level <math>&gt;1.5</math> times upper limit of normal for reporting lab</li> </ol>
Septic shock	Sepsis with hypotension (arterial blood pressure $<90$ mmHg systolic, or 40 mmHg less than patient’s normal blood pressure) for at least 1 h despite adequate fluid resuscitation <sup>a</sup> or Need for vasopressors to maintain systolic blood pressure $\geq 90$ mmHg or mean arterial pressure $\geq 70$ mmHg
Refractory septic shock	Septic shock that lasts for $>1$ h and does not respond to fluid or pressor administration

<sup>a</sup>Fluid resuscitation is considered adequate when the pulmonary artery wedge pressure is  $\geq 12$  mmHg or the central venous pressure is  $\geq 8$  mmHg.

### ETIOLOGY

 The systemic response to any class of microorganism can be harmful. Microbial invasion of the bloodstream is not essential because local inflammation can also elicit distant organ dysfunction and hypotension. In fact, blood cultures yield bacteria or fungi in only ~20–40% of cases of severe sepsis and 40–70% of cases of septic shock. In a prevalence study of 14,414 patients in intensive care units (ICUs) from 75 countries in 2007, 51% of patients were considered infected. Respiratory infection was most common (64%). Microbiologic results were positive in 70% of individuals considered infected; of the isolates, 62% were gram-negative bacteria (*Pseudomonas* species and *Escherichia coli* were most common), 47% were gram-positive bacteria (*Staphylococcus aureus* was most common), and 19% were fungi (*Candida* species). This distribution is similar to that reported a decade earlier from eight academic centers in the United States (Table 325-2). In patients whose blood cultures are negative, the etiologic agent is often established by culture or microscopic examination of infected material from a local site; specific identification of microbial DNA or RNA in blood or tissue samples is also used. In some case series, a majority of patients with a clinical picture of severe sepsis or septic shock have had negative microbiologic data.