TABLE 51. Selected Causes of Shock
Distributive
Anaphylaxis
Sepsis
Spinal injury (usually above T4 level)
Drugs (peripheral vasodilators, nitrates)
Hypovolemic
Acute blood loss (trauma, GI bleeding, surgery, uterine bleeding, obstetrical, retroperitoneal bleeding, aortic rupture)
Crush injury, metabolic rhabdomyolysis
Cutaneous losses (burns, toxic epidermal necrolysis, erythroderma, excessive sweating)
Drugs (diuretics, laxatives)
GI losses (vomiting/diarrhea)
Kidney losses (diabetic ketoacidosis, hyperglycemic hyperosmolar syndrome, adrenal insufficiency, post-ATN osmotic diuresis)
Cardiogenic (Including Noncardiac Causes of Decreased Cardiac Output)
Abdominal compartment syndrome
Arrhythmia (tachycardia, bradycardia)
Atrial myxoma
Heart failure
Left ventricular infarction, right ventricular infarction
Pericardial tamponade, constrictive pericarditis
Pulmonary embolism
Tension pneumothorax, severe dynamic hyperinflation (for example, excessive PEEP)
Valvular heart disease (severe insufficiency, valve or chordae rupture, critical stenosis)
Ventricular septal rupture, free ventricular wall rupture

ATN = acute tubular necrosis; GI = gastrointestinal; PEEP = positive end-expiratory pressure; T4 = fourth thoracic vertebra.

KEY POINT

HVC

- Several studies have compared the effectiveness of crystalloid versus colloid administration for treatment of distributive shock, with no clear evidence that one is better than the other; given the relative expense of colloids, crystalloid administration is generally preferred and recommended by guidelines.

Hypovolemic Shock

Hypovolemic shock occurs when decreased intravascular blood volume causes decreased preload, decreased ventricular filling, and diminished stroke volume. Initially, tachycardia and peripheral vasoconstriction help to preserve perfusion of vital organs but cannot compensate in the setting of severe hypovolemia. Treatment of hypovolemic shock includes aggressive volume or blood product replacement and, if possible, control of bleeding. Patients with hemorrhage may initially receive intravenous fluids to maintain hemodynamic stability, but ultimately need erythrocyte transfusion to prevent tissue ischemia. In stable ICU patients, hemoglobin levels should be maintained at about 7 g/dL (70 g/L); however, different thresholds and hemoglobin levels may trigger transfusion in actively bleeding patients who are in shock. Higher values may be necessary in patients with underlying cardiovascular disease. In patients with severe trauma, massive blood replacement requirements, and coagulopathy, evidence supports early resuscitation with a 1:1:1 ratio of erythrocytes, platelets, and fresh frozen plasma.

Cardiogenic Shock

Cardiogenic shock occurs when a primary cardiac insult causes decreased cardiac output. This can result from any combination of obstructed filling or emptying of the ventricles, high or low heart rates, and decreased ejection fraction. It is essential to promptly identify the cause of cardiogenic shock to ensure appropriate medical therapy, surgical therapy, or both. In addition to a physical examination, evaluation should include laboratory testing for myocardial ischemia and heart failure, chest radiograph, electrocardiogram, and echocardiogram. In patients presenting with severe cardiogenic shock, additional supportive measures may include short-term mechanical support to allow a bridge toward definitive therapy. These include ECMO, intraaortic balloon pump, temporary pacemaker, and left or right ventricular assist device. However, recent technological advances have allowed many of these devices to be used for longer durations and even as destination therapy.

Sepsis

Definition, Pathophysiology, and Clinical Presentation of Sepsis

The Third International Definitions for Sepsis and Septic Shock (Sepsis-3) were published in 2016 and reflect evolving understanding of sepsis. Sepsis-3 defines sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection. Septic shock is defined as a subset of sepsis in which profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. The previous definition, combining known or suspected infection and systemic inflammatory response syndrome criteria, which can be appropriate (not necessarily dysregulated) responses to infection, is neither sensitive nor specific enough to diagnose sepsis. The terms *severe sepsis* and *septicemia* should no longer be used.

Infections giving rise to sepsis can include any agent and involve any organ, and need not be disseminated. The pathophysiology of sepsis is complex and involves dysfunction at many levels, from subcellular mitochondrial dysfunction to failure of entire organ systems. Loss of regulation of the body's finely balanced proinflammatory and antiinflammatory

mediators and unregulated coagulation in the microvasculature are characteristic of the syndrome, although these features are difficult to assess clinically.

Operationally, sepsis can be identified whenever infection is known or suspected and clinical criteria defining organ dysfunction are met. The recommended criteria to assess organ dysfunction are included in the Sequential Organ Failure Assessment (SOFA) score, which assigns a value of 0-4 for each of six organ systems assessed: respiratory, coagulation, hepatic, cardiovascular, central nervous, and kidney, with increasing scores for more severe dysfunction (online SOFA score calculators are available: http://clincalc.com/IcuMortality/SOFA.aspx; https://www.mdcalc.com/sequential-organ-failure-assessment-sofa-score). An initial SOFA score of 2 or greater or an increase in SOFA score of 2 or more correlates with acute organ dysfunction and predicts hospital mortality of greater than 10%. The SOFA score should be used to assess patients in the ICU.

In the pre-ICU arena, Sepsis-3 guidelines recommend the use of the quick SOFA (qSOFA) score, a simplified clinical scoring system that includes only three criteria: respiration rate of 22/min or greater, altered mentation, and systolic blood pressure 100 mm Hg or less (**Table 52**). A qSOFA score of 2 or greater in the setting of known or suspected infection predicts increased mortality and should prompt evaluation for resuscitation and consideration of ICU admission. Failure to meet two or more qSOFA criteria should not be construed as ruling out sepsis, and investigation or treatment of infection should be pursued as deemed necessary by the responsible physicians. Although there is no definitive test for sepsis, the qSOFA score (specific but not sensitive) and the systemic inflammatory response syndrome (SIRS) criteria (sensitive but not specific) are complementary and can be used together to inform clinical judgment when diagnosing sepsis.

The criteria for diagnosing septic shock include hypotension requiring pressors to maintain a mean arterial pressure of greater than 65 mm Hg and serum lactate level of greater than 2 mEq/L (2 mmol/L) after adequate volume resuscitation. Patients who meet these criteria have a 40% or greater risk of in-hospital mortality. H

TABLE 52. qSOFA Score

Criterion	Value	qSOFA Points
Respiration rate	>22/min	1
Systolic blood pressure	<100 mm Hg	1
Mental status	Altered from baseline	1
qSOFA score	**Predicted mortality**	
0	**<1%**	
1	**2-3%**	
≥2	**≥10%**	

qSOFA = quick sequential organ failure assessment.

KEY POINTS

- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
- Septic shock is defined as a subset of sepsis in which profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone.

Epidemiology of Sepsis H

The epidemiology of sepsis is difficult to judge accurately because of its evolving definition, challenges with clinical recognition of the syndrome, and lack of standardized reporting. However, it is possible to estimate its incidence and clinical and economic effects. There are disparities in sepsis rates among different demographic groups. For example, sepsis is more common among black men than other racial groups or women. Sepsis is also more common among elderly patients, with incidence increasing with each year after the age of 65. Mortality from sepsis is high. A patient who is septic has a mortality rate 4 or more times greater for the same underlying condition and comorbidities without sepsis. Mortality increases by roughly 15% for each sepsis-related organ system failure.

Management of Sepsis

Early diagnosis and timely treatment of sepsis are important to improve survival. In settings where sepsis is suspected, cultures and other investigations to identify infection, as well as the use of diagnostic instruments like the SOFA and qSOFA scoring tools to identify organ dysfunction, are helpful. Once sepsis is diagnosed, the two main pillars of management are: 1) supporting organ perfusion and function; and 2) controlling the infection. Various other adjunctive therapies may also affect survival. H

KEY POINT

- The two main pillars of sepsis management are: 1) supporting organ perfusion and function; and 2) controlling the infection.

Initial Resuscitation H

Sepsis can have serious hemodynamics effects, with decreased preload (due to capillary leak), impaired cardiac contractility, and decreased vascular tone. Patients may present in shock, sometimes with profound hypotension requiring large volume resuscitation with intravenous fluids and often vasopressor therapy.

The fourth iteration of the Surviving Sepsis Guidelines, published in 2016, recommends early and aggressive fluid resuscitation for patients with hypoperfusion due to sepsis, with an initial bolus of 30 mL/kg of body weight. Additional fluids may be needed, and physiologic markers such as mean arterial pressure, pulse pressure variation, change in serum lactate level, bedside echocardiographic assessment of inferior

vena cava filling, or other techniques are used as indicators of adequate fluid resuscitation. Although experts agree that aggressive fluid resuscitation is essential, the adequacy of fluid resuscitation requires clinical judgment in conjunction with the available data.

Fluid resuscitation should be with crystalloid, using normal saline or a balanced crystalloid solution. A balanced crystalloid solution has an electrolyte composition similar to plasma with the addition of a buffer, such as lactate (for example, Ringer's lactate solution). Data are emerging that suggest a balanced crystalloid solution may be associated with improved outcomes compared to normal saline, particularly in patients receiving a large volume of fluid, but current guidelines recommend either. There is weak evidence suggesting benefit from the use of albumin in patients requiring large volume resuscitation; however, sepsis guidelines offer this as a consideration rather than a recommendation.

KEY POINT

- Early and aggressive fluid resuscitation for patients with hypoperfusion due to sepsis begins with an initial bolus of 30 mL/kg body weight of normal saline or a balanced crystalloid solution.

Antibiotic Therapy

Early administration of antibiotic therapy is crucial in treating sepsis. Broad spectrum antibiotics should be given within the first hour of suspected sepsis, and the regimen adjusted based on culture results. A delay in the first dose of antibiotic therapy increases sepsis mortality. The Surviving Sepsis Guidelines recommend empiric combination therapy for the initial management of septic shock, or when broad empiric coverage is needed for initial management of sepsis, bacteremia, or both. However, they recommend against combination therapy for the routine or ongoing treatment of sepsis and bacteremia without shock, even in the setting of neutropenia. The guidelines define combination therapy as the use of two different classes of antibiotics for a single putative pathogen expected to be sensitive to both, for purposes of accelerating pathogen clearance. The term is not used when the purpose of a multidrug strategy is to strictly broaden the range of antimicrobial activity. Antibiotic therapy should usually be continued for 7 to 10 days, depending on the clinical situation, and continually reassessed for efficacy and possible deescalation.

Procalcitonin, a serum marker for bacterial infection, should be measured when the probability of infection is estimated to be low. If the procalcitonin level is low, bacterial infection is unlikely and antibiotic therapy may not be warranted. There is no role for procalcitonin measurement in sepsis likely due to infection.

Prompt identification and control of any potential source of infection is essential in the management of sepsis. Examples include drainage of abscesses and removal of possibly infected intravenous catheters (once alternative intravenous access has been established). One exception is necrotizing pancreatitis, for which definitive resection should be delayed until the extent of necrosis is clear.

KEY POINTS

- Antibiotic therapy for patients with sepsis should usually be continued for 7 to 10 days, depending on the clinical situation, and continually reassessed for efficacy and for possible deescalation.
- Procalcitonin, a serum marker for infection, should be measured when the probability of infection is estimated to be low.
- There is no role for procalcitonin measurement in sepsis likely due to infection. **HVC**
- Prompt identification and control of any potential source of infection is essential in the management of sepsis.

Adjunctive Therapies

Norepinephrine is the vasopressor of choice for shock due to sepsis. Vasopressin at a fixed dose of 0.03 or 0.04 units per minute can be added to norepinephrine to further raise blood pressure or reduce the dose of norepinephrine. Vasopressin should generally not be used in cardiogenic or hypovolemic shock and is not recommended as a first pressor agent in septic shock (see Table 39). If possible, all patients receiving vasopressor therapy should have an arterial catheter for continuous blood pressure monitoring.

The use of glucocorticoids in the setting of sepsis is suggested to achieve hemodynamic stability when not achieved using intravenous fluids and vasopressor therapies. They have no role in sepsis without shock. If used, glucocorticoids can be added at a dose of not more than 200 mg daily of hydrocortisone (usually 50 mg intravenously every 6 hours). An adrenocorticotropic hormone stimulation test is not recommended.

KEY POINTS

- Norepinephrine is the vasopressor of choice in treatment of shock due to sepsis; vasopressin can be added to further raise the blood pressure or reduce the dose of norepinephrine.
- The use of glucocorticoids in the setting of sepsis is suggested if adequate fluid resuscitation and vasopressor therapy are unable to restore hemodynamic stability; there is no role for glucocorticoids in sepsis without shock. **HVC**

Specific Critical Care Topics

Anaphylaxis

Anaphylaxis is a severe reaction caused by acute mediator release into the circulation, usually triggered by IgE-linked