Patients in septic shock can be tachycardic and hypotensive. They may have relatively warm extremities (i.e., warm shock or distributive shock), or they may be peripherally vasoconstricted, with mottled and cool extremities (i.e., cold shock). Warm shock is the predominant finding in most adult patients at the onset of septic shock, with evidence of diffuse vasodilation, bounding pulses, and a compensatory high cardiac output despite evidence of diminished myocardial performance. Increased cardiac output is accomplished primarily by increased heart rate in an attempt to maintain blood pressure and perfuse vital organs. If shock is not promptly corrected, myocardial dysfunction ensues and cold shock evolves over the next several hours. Older patients with limited cardiac reserves tolerate shock poorly and are more likely to develop cold shock. Evidence of septic shock at presentation that is refractory to early resuscitation portends a poor prognosis, with mortality rates exceeding 70%.

Besides hypotension, oliguria can represent developing AKI. It can arise from a combination of the disease process, infecting organism, and medications. Inflammatory cytokines, microbial toxins, systemic hypotension, and iatrogenic renal injury from medications can result in AKI. Other causes of renal injury include interstitial injury from infection or medications and immune complex–mediated injury, as seen in cases of endocarditis.

Besides tachypnea, pulmonary symptoms seen in septic patients include marked hypoxia due to interstitial edema, inflammation, or hemodynamic instability. ARDS is defined as an arterial partial pressure of oxygen less than 50 mm Hg despite fractional inspired oxygen of greater than 50%, together with diffuse alveolar infiltrates and a pulmonary capillary wedge pressure of less than 18 mm Hg. ARDS occurs in up to 40% of septic patients. The diffuse pulmonary inflammation in ARDS results in increased pulmonary vascular permeability, which complicates fluid resuscitation efforts because excessive fluid can exacerbate pulmonary edema and hypoxia. Altered mental status and sepsis-related myopathy also result in airway compromise and weak respiratory effort, necessitating invasive ventilatory support.

Patients with sepsis can have marked hematologic changes. They may have neutrophilic leukocytosis, which is often accompanied by increased immature cell counts, or they can be markedly leukopenic (particularly lymphopenic), often in cases of severe septic shock. Transient neutropenia is often seen in the early phase of septic shock and results from activation and adherence of neutrophils along endothelial surfaces in the microcirculation. This is rapidly followed by prolonged neutrophilia as sepsis-induced inflammatory cytokines stimulate bone marrow synthesis of new white blood cells.

Thrombocytopenia and coagulopathy can occur, and patients have petechiae or purpura at presentation. Severe derangements in coagulation can produce DIC, which can lead to thrombin deposition throughout the microcirculation. Excessive activation and degradation of clotting factors can deplete coagulation factors, resulting in diffuse hemorrhage. Excessive mucosal bleeding around airway tubes and prolonged bleeding from venipuncture sites presage internal bleeding events. Massive gastrointestinal hemorrhage can occur, which can cause or exacerbate hypotension and shock.

Derangements in glucose homeostasis can be seen at presentation. This can take the form of hyperglycemia in diabetics receiving glucose-containing fluids or acute metabolic derangement due to infection. Hypoglycemia is more common in patients with underlying liver disease. Increased anaerobic metabolism due to poor tissue oxygenation and coupled with mitochondrial dysfunction and impaired hepatic clearance of lactic acid may result in increased serum lactate levels and metabolic acidosis.

DIAGNOSIS

Accurate diagnosis of sepsis relies on the history, physical examination, and general laboratory investigation. Diagnostic criteria for sepsis in adults based on the Surviving Sepsis Campaign guidelines are listed in Table 89-1.

Accurate and timely identification of the underlying infectious cause is essential. For patients able to provide a history, an assessment of medical comorbidities, potential exposures, prior infections, and immune system abnormalities may help to guide empirical antimicrobial therapy and the laboratory investigation, particularly microbial cultures. Two sets of blood cultures drawn from a fresh venipuncture and from existing indwelling intravascular lines (before initiation of empirical antimicrobial therapy if possible) help to identify the causative organism in many cases. Symptomatic assessment and physical examination should suggest a location of focal infection that can help to guide radiologic studies and interventions to drain pus.

Beyond microbial cultures, several other laboratory studies can help to define the severity of illness and provide baseline data for monitoring the response to therapy. Basic laboratory testing, including a complete blood count with differential, chemistries, and creatinine and aminotransferase levels, can help to identify significant organ dysfunction. Oxygen saturation by pulse oximetry should be measured promptly to identify gas exchange capacity and the need for ventilatory support. Coagulation studies should be obtained, particularly for patients with evidence of DIC and those who are thrombocytopenic. For patients with altered mental status or marked respiratory difficulty, arterial blood gas sampling can help define the underlying derangement and physiologic compensation and can indirectly gauge the severity of illness.

Levels of inflammatory markers, including C-reactive protein and procalcitonin, usually are elevated. An elevated procalcitonin level can help to establish the diagnosis of severe sepsis and provide some prognostic data and a measure of response to therapy. In cases of sepsis due to pneumonia, serial measurement of procalcitonin can help to guide the duration of antibiotic therapy.

Other testing should be directed toward identifying the potential cause. Patients with severe diarrhea should undergo testing for antibiotic-associated *Clostridium difficile* infection. Imaging studies should focus on identifying infectious sources and facilitate drainage of fluid collections or abscesses. Computed tomography may be of use in such circumstances, although for the critically ill patient who is not stable for transport, bedside radiographic studies, especially ultrasound, should be considered.

Multiple tests of physiologic function and advanced microbiologic diagnostic tests are increasingly used in clinical practice. They include polymerase chain reaction (PCR)–based assays for