identifying bacteria and viruses and various assays of inflammatory cytokines and other biomarkers alone and in combination as potential diagnostic and prognostic aids.

TREATMENT

Septic shock is a medical emergency. Immediate attempts to reestablish physiologic hemodynamics, vital organ support, and oxygen delivery to tissues should accompany early diagnosis and treatment of infection. Patients should be transferred to the intensive care unit as soon as possible to receive optimal monitoring, hemodynamic support, and expert supportive care.

Early recognition, prompt resuscitation, and early institution of appropriate antimicrobial agents are the most important determinants of a successful outcome. If appropriate, draining infectious foci (i.e., source control) should be done as soon as possible. Key elements of the 2012 Surviving Sepsis Champaign guidelines are summarized in Table 89-3.

An essential element in the treatment of sepsis is early administration of antibiotics active against the causative pathogen. Treatment is best given within 1 hour of the onset of septic shock, and an empirical, broad-spectrum antimicrobial regimen is usually employed until the results of cultures of blood and the site of infection become available. A suggested initial treatment regimen is provided in Table 89-4. Failing to treat the causative pathogen until its identity and susceptibility profile become available days later is associated with adverse outcomes. After the pathogen is identified, de-escalation to the simplest monotherapy to which it is susceptible is important.

PROGNOSIS

Despite advances in clinical practice and treatment, sepsis mortality rates remain high, ranging from 20% to 30% among relatively healthy adults to more than 80% among the elderly, immunocompromised, and those with significant chronic medical comorbidities. Patients may experience significant weakness, wasting, and debilitation due to severe catabolism, poor

TABLE 89-3 RECOMMENDED INITIAL MANAGEMENT OF SEPSIS IN ADULTS

- Start resuscitation immediately in patients with hypotension or serum lactate level >4 mmol/L.
- Obtain appropriate cultures before starting antibiotics if doing so does not significantly delay therapy.
- Evaluate for a focus of infection amenable to source control (e.g., abscess drainage).
- Remove intravascular catheters if potentially infected.
- Begin broad-spectrum antibiotics within the first hour of severe sepsis and septic shock. Initial antibiotic regimen is based on likely source of sepsis, likely pathogens, and local antibiotic susceptibility patterns of common pathogens.
- Begin fluid resuscitation using crystalloids as the first choice. If colloids are used, avoid starches and consider albumin in selected patients who have hypoalbuminemia or require large-volume fluid resuscitation.
- Give fluid challenge of up to 30 mL/kg of crystalloids over 15-30 min in septic patients with suspected volume depletion; larger volumes of fluids may be needed in some patients. The goals for resuscitation should be a central venous pressure of 8-12 mm Hg, a mean arterial pressure (MAP) ≥65 mm Hg, and a superior vena cava oxygen saturation ≥70% or mixed venous oxygen saturation ≥65%.
- Maintain targeted MAP of ≥65 mm Hg; if fluids are not effective in reestablishing adequate blood pressure, begin vasopressors. After hemodynamic parameters are stabilized, limit fluid therapy to prevent pulmonary fluid accumulation and exacerbation of hypoxemia.
- Use norepinephrine, centrally administered, as the vasopressor of choice. Epinephrine is the second choice, followed by vasopressin as salvage therapy. Dobutamine may be useful if an inotrope is needed. Avoid dopamine except for special situations (i.e., low risk of tachyarrhythmia and persistent bradycardia).
- Give red blood cells when the hemoglobin concentration decreases to <7 g/dL; target hemoglobin level is 7-9 g/dL.
- Target a tidal volume of 6 mL/kg in patients with acute respiratory distress syndrome.
- Give low-molecular-weight heparin or unfractionated heparin for deep vein thrombosis prophylaxis; use graduated pressure stockings or intermittent compression devices if heparin therapy is contraindicated.
- Provide stress ulcer prophylaxis using histamine H_2-blockers or a proton pump inhibitor.
- Provide expert supportive care; provide low-dose nutrition for the first week; consider stress-dose steroids if refractory septic shock occurs; maintain blood glucose in the 110-180 mg/dL range.

Data from Dellinger RP, Levy MM, et al: Surviving Sepsis Campaign: international guidelines for the management of severe sepsis and septic shock, 2012, Crit Care Med 41:580–637, 2013.

TABLE 89-4 INITIAL ANTIBIOTIC RECOMMENDATIONS FOR ADULT PATIENTS WITH SEPSIS

INDICATION	RECOMMENDED DOSAGES*
Empirical coverage (source unknown)	Vancomycin 15 mg/kg q12h plus piperacillin-tazobactam† 3.375 g IV q6h or imipenem 0.5 g IV q6h or meropenem 1.0 g IV q8h with or without an aminoglycoside (e.g., tobramycin 5 mg/kg IV q24).‡
Community-acquired pneumonia (CAP)	Ceftriaxone 1 g IV q24h plus azithromycin 500 mg IV q24h or a fluoroquinolone (e.g., moxifloxacin 400 mg IV q24h or levofloxacin 750 mg IV q24h).§
Community-acquired urosepsis	Piperacillin-tazobactam 3.375 g IV q6h or ciprofloxacin 400 mg. IV q12h
Meningitis	Vancomycin 15 mg/kg IV q6h plus ceftriaxone 2 g IV q12h plus dexamethasone 0.15 mg/kg IV q6h × 2-4 days, preferably before antibiotics; add ampicillin 2 g IV q4h if *Listeria* is suspected.
Nosocomial pneumonia	Vancomycin 15 mg/kg q12h plus piperacillin-tazobactam 4.5 g IV q6h or imipenem 0.5 g IV q6h or meropenem 1 g IV q8h or cefepime 2 g IV q8h plus an aminoglycoside (e.g., amikacin 15 mg/kg IV q24h or tobramycin 5-7 mg/kg IV q24h) or levofloxacin 750 mg IV q24h. Some authorities substitute linezolid 600 mg IV q12h for vancomycin if MRSA is a significant concern or known to be the cause.
Neutropenia	Cefepime 2 g IV q8h; add vancomycin 15 mg/kg IV q12h if a central line is present and infection is a concern. Add antifungal coverage with caspofungin 70 mg IV × 1, then 50 mg IV q24h if fever persists ≥5 days. For suspected or proven invasive aspergillosis, voriconazole 6 mg/kg IV q12h × 2, then 4 mg/kg IV q12h should be used.
Cellulitis and skin infections	Vancomycin 15 mg/kg IV q12h. Add piperacillin-tazobactam 3.375 g IV q6h in diabetics and immunocompromised patients. If necrotizing fasciitis is suspected, add clindamycin 900 mg. IV; surgical débridement is crucial.

IV, Intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*.

*Assumes normal renal function; dose adjustments are required with impaired creatinine clearance.

†Substitute aztreonam 2 g IV q8h if patient is allergic to penicillin.

‡Monitor drug levels of aminoglycosides (i.e., peak and trough).

§Substitute Cefepime or a carbapenem and azithromycin ± an aminoglycoside if the patient has severe CAP or health care–associated pneumonia.