sepsis

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- Sepsis is a clinical syndrome that complicates severe infection.
- Infection — Infection is the invasion of normally sterile tissue by organisms.

- Bacteremia — Bacteremia is the presence of viable bacteria in the blood

- Systemic inflammatory response syndrome — SIRS is the clinical syndrome that results from a dysregulated inflammatory response to a noninfectious insult, such as an autoimmune disorder, pancreatitis, vasculitis, thromboembolism, burns, or surgery

- Identification of early sepsis(SOFA)

SOFA: sepsis related organ failure assessment

NEWS:national early warning score

Guideline emphasis on the early identification of infected patients who may go on to develop sepsis as a way to decrease sepsis associated mortality.

qSOFA: RR>22, altered mentation, sBP< 100

SOFA score 2 or more= poor outcome.(organ disfunction)

NEWS: RR, O2 sat, sBP, PR, Temp, altered mentation

0-4 Low risk

5-6 medium risk

7 or more high risk

- ORGAN SYSTEM SCORE
  Respiration
  Pao2/Fio2, mm Hg (kPa)
  <400 (53.3) 1
  <300 (40) 2
  <200 (26.7) with respiratory support 3
  <100 (13.3) with respiratory support 4
  Central nervous system
  GCS score
  13–14 1
  10–12 2
  6–9 3
  <6 4
  Cardiovascular
  MAP or use vasopressors (µg/kg/min)
  MAP <70 mm Hg 1
  Dopamine <5 or dobutamine (any dose)a 2
  Dopamine 5.1–15 or epinephrine ≤0.1 or norepinephrine ≤0.1 3
  Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1 4
  Liver
  Bilirubin, mg/dL (µmol/L)
  1.2–1.9 (20–32) 1
  2.0–5.9 (33–101) 2
  6.0–11.9 (102–204) 3
  >12.0 (204) 4
  Coagulation
  Platelets, × 103/µL
  <150 1
  <100 2
  <50 3
  <20 4
  Renal
  Creatinine, mg/dL (µmol/L) or urine output, mL/day
  1.2–1.9 (110–170) 1
  2.0–3.4 (171–299) 2
  3.5–4.9 (300–440) or <500 3
  >5.0 (440) or <200

- Sepsis is defined as the presence (probable or documented) of infection together with systemic manifestations of infection. Diagnostic criteria:
- temperature >38.3 or <36ºC
- Heart rate >90 beats/min or more than two standard deviations above the normal value for age
- Tachypnea, respiratory rate >20 breaths/min
- Leukocytosis (WBC count >12,000 microL $^{-1}$) or leukopenia (WBC count <4000 micro or >10% bands

Sepsis: Infection + SIRS

Severe sepsis: Sepsis + acute organ dysfunction

Septic shock : Sepsis + persistent hypotension after fluid resuscitation

- Severe sepsis — Severe sepsis refers to sepsis-induced tissue hypoperfusion or organ dysfunction with any of the following thought to be due to the infection :
- Sepsis-induced hypotension: systolic blood pressure (SBP) <90 mmHg or mean arterial pressure (MAP) <70 mmHg or a SBP decrease >40 mmHg or less than two standard deviations below normal for age,
- Altered mental status
- Lactate above upper limits
- Urine output <0.5 mL/kg/hr for more than two hours despite adequate fluid resuscitation
- Acute lung injury with PaO_2/FIO_2 <250 in the absence of pneumonia as infection source
- Acute lung injury with PaO_2/FIO_2 <200 in the presence of pneumonia as infection source
- Creatinine >2 mg/dL (176.8 micromol/L)
- Bilirubin >2 mg/dL (34.2 micromol/L)
- Platelet count <100,000 $microL^{-1}$
- Coagulopathy (INR >1.5)

- *Septic shock:* Sepsis with hypotension for at least 1 h despite fluid resuscitation or need for vasopressors to maintain systolic bp ≥90 mmHg or mean arterial bp ≥70 mmHg with serum lactate >2 mmol/L

- **Refractory septic shock** is defined as persistently low mean arterial blood pressure despite volume resuscitation and titrated vasopressors/inotropes in patients with a proven or suspected infection and concomitant organ dysfunction.

- RISK FACTORS — approximately 50 percent of ICU patients have a nosocomial infection and, therefore, are at high risk for sepsis .
- Other risk factors include the following:
- Bacteremia –
- Advanced age (≥65 years) –Immunosuppression –
- Diabetes and cancer .
- Community acquired pneumonia –
- Genetic factors –susceptibility to infection have initially focused on defects of antibody production, or a lack of T cells, phagocytes, natural killer cells, or complement.
- indwelling catheters, and mechanical devices

- The incidence is also greatest during the winter, probably due to the increased likelihood of a respiratory source
- sepsis in the United States range from 300 to more than 1000 cases per 100,000 person-years depending on method of database abstraction .

- • ETIOLOGY
- • Blood cultures are positive in 20–40% of sepsis cases and in 40–70% of septic shock cases.
- • For infected pts in ICUs, respiratory infections have been most common (64%).
- Pneumonia is the most common source of sepsis in adults, followed by abdominal, urinary tract, and skin/soft tissue infections.
- However, in most series, no obvious source of infection can be found in one-sixth of patients.

- Microbiologic results have revealed that 62% of isolates are gram-negative bacteria (most commonly *Pseudomonas* spp. and *Escherichia coli*), 47% are gram-positive bacteria (most commonly *Staphylococcus aureus*), and 19% are fungi (most commonly *Candida* spp.), with some cultures being polymicrobial.

- Mortality — Sepsis has a high mortality rate, with estimates ranging from 20 to 50 percent. Mortality rates increase stepwise according to disease severity.
- PROGNOSTIC FACTORS
- Host response
- Site of infection :urosepsis generally being associated with the lowest mortality rates.
- Type of infection — Sepsis due to nosocomial pathogens has a higher mortality than sepsis due to community-acquired pathogens .
- Increased mortality is associated with bloodstream infections due to methicillin-resistant staphylococcus aureus or MDR
- Antimicrobial therapy —early institution of adequate antibiotic therapy was associated with a 50 percent reduction in the mortality rate, Progression from sepsis to septic shock increases by 8.0% per hour from presentation until administration of antimicrobial agents
- Restoration of perfusion — Failure to aggressively try to restore perfusion early may also be associated with mortality

- CLINICAL FEATURES
- • Hyperventilation that produces respiratory alkalosis
- • Encephalopathy (disorientation, confusion)
- • Acrocyanosis and ischemic necrosis of peripheral tissues (e.g., digits) due to hypotension and DIC
- • Skin: hemorrhagic lesions, bullae, cellulitis, pustules. Skin lesions may suggest specific pathogens; e.g., petechiae and purpura suggest *Neisseria meningitidis*, and ecthyma gangrenosum suggests *Pseudomonas aeruginosa*.
- • GI: nausea, vomiting, diarrhea, ileus, cholestatic jaundice
- Multiple organ dysfunction syndrome

- Major Complications
- • *Cardiopulmonary manifestations*
- – Ventilation-perfusion mismatch, increased alveolar capillary permeability, increased pulmonary water content, and decreased pulmonary compliance impede oxygen exchange and lead to ARDS (progressive diffuse pulmonary infiltrates and arterial hypoxemia) in ~50% of pts.
- – Hypotension: Normal or increased cardiac output and decreased systemic vascular resistance distinguish septic shock from cardiogenic and hypovolemic shock.
- • *Adrenal insufficiency:* may be difficult to diagnose in critically ill pts
- • *Renal manifestations*: oliguria or polyuria, azotemia, proteinuria, and renal failure due to acute tubular necrosis
- • *Neurologic manifestations*: delirium in the acute phase, polyneuropathy with distal motor weakness in prolonged sepsis. Survivors may have long-term cognitive impairment.
- • *Immunosuppression*: Pts may have reactivation of HSV, CMV, or VZV.

- Laboratory Findings
- • *CBC:* leukocytosis(leukopenia) with a left shift, thrombocytopenia

Coagulation: prolonged thrombin time, decreased fibrinogen, presence of d-dimers suggestive of DIC.(35%) With DIC, platelet counts usually fall below 50,000/µL.

- • *Chemistries:* metabolic acidosis, elevated anion gap, elevated lactate levels
- • *LFTs:* transaminitis, hyperbilirubinemia, azotemia, hypoalbuminemia

DIAGNOSIS

- Definitive diagnosis requires isolation of the microorganism from blood or a local site of infection. Culture of infected cutaneous lesions may help establish the diagnosis.

Key Recommendations of the Surviving Sepsis

- Sepsis and septic shock are medical emergencies, and treatment and resuscitation should begin immediately.

- Routine microbiologic cultures are obtained before starting antimicrobial therapy in patients with suspected sepsis. These always include at least two sets of blood cultures (aerobic and anaerobic).

- Patients with hypoperfusion should receive crystalloid within 3 hours and should be reassessed frequently.

- Intravenous antimicrobials should be initiated as soon as possible after recognition and within 1 hour for both sepsis and septic shock.

1 hour for septic shock and within 3 hour for both sepsis.

- It is suggested to use empirical combination therapy (using at least two antibiotics of different antimicrobial classes) aimed at the most likely bacterial pathogens for initial management of septic shock. (β-lactams or carbapenem + aminoglycoside or fluoroquinolone) + MRSA coverage.

- It is suggested that combination therapy is not routinely used for ongoing treatment of most other serious infections including bacteremia and sepsis without shock.
- Antimicrobial therapy should be narrowed once pathogen identification and sensitivities are established or adequate clinical improvement is noted

- The use of combination therapy for routine treatment of neutropenic sepsis/bacteremia is not recommended.

- Antimicrobial treatment duration of 7–10 days is adequate for most serious infections associated with sepsis and septic shock

- Daily assessment for deescalation of antimicrobial therapy in patients with sepsis and septic shock is recommended

- **Source Control** :removal of intravascular access devices that are a possible source of sepsis.

- The choice of empirical antibiotic treatment depends on the suspected source of infection, global geography, location where the infection was acquired (e.g., community, nursing home, or hospital), medical history, and local microbial susceptibility patterns

- TREATMENT SEPSIS AND SEPTIC SHOCK

Pts in whom sepsis is suspected must be managed expeditiously, if possible within 1 h of presentation.

- **1. Antibiotic treatment:**
- **2. Removal or drainage of a focal source of infection**
- **a. Remove indwelling intravascular catheters; replace Foley and other drainage catheters; drain local sources of infection.**
- **b. Rule out sinusitis in pts with nasal intubation.**
- **c. Image the chest, abdomen, and/or pelvis to evaluate for abscess.**
- **3. Hemodynamic, respiratory, and metabolic support: first**
- **a. Initiate treatment with 1–2 L of normal saline administered over 1–2 h, keeping the CVP at 8–12 cmH2O, urine output at >0.5 mL/kg per hour, and mean arterial bp at >65 mmHg. Add vasopressor therapy if needed.**
- **b. If hypotension does not respond to fluid replacement therapy, hydrocortisone**

(50 mg IV q6h) should be given. If clinical improvement results within 24–48 h, most experts would continue hydrocortisone treatment for 5–7 days.

- c. Maintain oxygenation with ventilator support as indicatedd.
- Erythrocyte transfusion is recommended when the blood Hb level decreases to ≤7 g/dL, with a target level of 9 g/dL.
- 4. General support: Nutritional supplementation should be given to pts with prolonged sepsis (i.e., that lasting >2–3 days), with available evidence suggesting an enteral delivery route. Prophylactic heparin should be administered to prevent deep-venous thrombosis if no active bleeding or coagulopathy is present.
- Insulin should be used only if it is needed to maintain the blood glucose concentration below ~180 mg/dL.

- Immunocompetent adult
- 1) piperacillin-tazobactam (3.375 g q4–6h); (2) imipenem-cilastatin(0.5 g q6h), ertapenem (1 g q24h), or meropenem (1 g q8h); or (3) cefepime (2 g q12h). If the pt is allergic to β-lactam agents, use ciprofloxacin(400 mg q12h) or levofloxacin (500–750 mg q12h)plus clindamycin (600 mg q8h). Vancomycin (15 mg/kg q12h) may be added to each of the above regimens.
- Splenectomy

Cefotaxime (2 g q6–8h) or ceftriaxone (2 g q12h) should be used. If the local prevalence of cephalosporin-resistant pneumococci is high, add vancomycin. If the pt is allergic to β-lactam drugs, vancomycin(15 mg/kg q12h) plus either moxifloxacin (400 mgq24h) or levofloxacin (750 mg q24h) should be used

- IV drug user Vancomycin (15 mg/kg q12h) is essential

- AIDS
- Cefepime alone (2 g q8h) or piperacillin-tazobactam(3.375 g q4h) plus tobramycin (5–7 mg/kg q24h)should be used. If the pt is allergic to β-lactam drugs,ciprofloxacin (400 mg q12h) or levofloxacin (750 mg

q12h) plus vancomycin (15 mg/kg q12h) plus tobramycin should be used.

- Neutropenia (<500neutrophils/µL)

(1) imipenem-cilastatin (0.5 g q6h)or meropenem (1 g q8h) or cefepime (2 g q8h) or (2) piperacillin-tazobactam (3.375 g q4h) plus tobramycin

(5–7 mg/kg q24h).

Vancomycin (15 mg/kg q12h) should be added if the pt has an indwelling vascular catheter, has received quinolone prophylaxis, or intensive chemotherapy that produces mucosal damage; if staphylococci are suspected; if the institution has a high incidence of MRSA infections.

Empirical antifungal therapy with an echinocandin (for caspofungin: a70-mg loading dose, then 50 mg daily), voriconazole (6 mg/kg q12h for 2 doses, then 3 mg/kg q12h), or a lipid formulation of amphotericin B should be added if the pt is hypotensive, has been receiving broadspectrum antibacterial drugs, or remains febrile 5 days after initiation of empirical antibacterial therapy.