Sepsis Early Management Protocol

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I. PURPOSE AND SCOPE

A. Purpose

This protocol establishes a standardized, evidence-based approach for the rapid recognition and treatment of sepsis and septic shock in adult patients. The goals are to:

1. Enable early identification of patients with sepsis or at risk for sepsis
2. Implement time-sensitive interventions ("sepsis bundles") to improve survival
3. Reduce sepsis-related mortality and morbidity through rapid, coordinated care
4. Ensure compliance with national quality measures (SEP-1 Core Measure)
5. Provide clear roles and responsibilities for the multidisciplinary sepsis response team
6. Achieve door-to-antibiotic times of <1 hour for septic shock and <3 hours for sepsis

B. Scope

Applies to:

- All adult patients (≥18 years) presenting to the Emergency Department, inpatient units, or ICU with suspected or confirmed sepsis
- All clinical staff (physicians, nurses, respiratory therapists, pharmacists) involved in acute care

Does NOT apply to:

- Pediatric patients (<18 years) – separate pediatric sepsis protocol
- Patients with "Do Not Resuscitate" (DNR) or comfort-care-only status (goals of care discussions should occur, but comfort measures may still include antibiotics and symptom management per patient/family wishes)

C. Definitions

Sepsis: Life-threatening organ dysfunction caused by a dysregulated host response to infection.

Clinically:

- Suspected or confirmed infection
- PLUS acute organ dysfunction (increase in Sequential Organ Failure Assessment [SOFA] score ≥2 points from baseline)

Septic Shock: Subset of sepsis with profound circulatory, cellular, and metabolic abnormalities.

Clinically:

- Sepsis (as defined above)
- PLUS persistent hypotension requiring vasopressors to maintain mean arterial pressure (MAP) ≥65 mmHg
- AND serum lactate >2 mmol/L despite adequate fluid resuscitation

Septic shock has ~40% mortality risk; early recognition and treatment are critical.

SIRS (Systemic Inflammatory Response Syndrome): Older term, less specific than sepsis-3 definition, but still useful for screening.

SIRS Criteria (≥2 of the following):

1. Temperature >38.3°C (101°F) or <36°C (96.8°F)
2. Heart rate >90 bpm
3. Respiratory rate >20 breaths/min or $PaCO_2$ <32 mmHg
4. WBC >12,000/mm^3 or <4,000/mm^3, or >10% immature bands

qSOFA (Quick SOFA): Bedside screen for patients at risk of poor outcomes; less sensitive than SIRS for early sepsis detection.

qSOFA Criteria (≥2 of the following):

1. Respiratory rate ≥22/min
2. Altered mentation (GCS <15)
3. Systolic BP ≤100 mmHg

Note: In our protocol, we use SIRS or clinical suspicion to trigger early sepsis alert; qSOFA is used for risk stratification, but we do NOT rely solely on qSOFA for screening (as it may miss early sepsis).

II. RECOGNITION AND SCREENING

A. Nurse-Driven Sepsis Screening

All patients presenting to the ED or being admitted to inpatient units should be screened for sepsis.

Screening Tools:

1. **SIRS Criteria + Suspected Infection:** If patient meets ≥2 SIRS criteria AND has a suspected or confirmed source of infection, proceed to assess for organ dysfunction.
2. **Modified Early Warning Score (MEWS):** Automated early warning score based on vital signs (used in some EHR systems). A high MEWS score triggers nursing assessment for sepsis.

Screening Frequency:

- **ED:** At triage and reassessment (every 1-2 hours for high-acuity patients)
- **Inpatient units:** On admission and with any change in condition (new fever, hypotension, tachycardia, altered mental status, etc.)
- **ICU:** Continuous monitoring (sepsis often develops in ICU patients post-operatively or from nosocomial infections)

B. Red Flags for Sepsis (Organ Dysfunction Indicators)

If infection is suspected, look for signs of organ dysfunction:

Cardiovascular:

- Hypotension (SBP <90 mmHg, or MAP <65 mmHg, or SBP drop ≥40 mmHg from baseline)
- Requiring vasopressors to maintain MAP ≥65

Respiratory:

- Hypoxia (SpO_2 <90% on room air, or PaO_2/FiO_2 ratio <300)
- Tachypnea (RR >22) or need for mechanical ventilation

Renal:

- Oliguria (urine output <0.5 mL/kg/hr for ≥2 hours)
- Acute rise in creatinine (≥0.5 mg/dL increase)

Hepatic:

- Elevated bilirubin (>2 mg/dL)

Hematologic:

- Thrombocytopenia (platelets <100,000/mm³)
- Coagulopathy (INR >1.5)

Metabolic:

- Elevated lactate (>2 mmol/L, especially >4 mmol/L)

Neurologic:

- Altered mental status (confusion, decreased Glasgow Coma Scale)

Presence of ANY of these in the context of suspected infection should prompt a sepsis alert.

C. Lactate as a Key Marker

Serum lactate is a critical marker:

- Lactate ≥2 mmol/L indicates tissue hypoperfusion (even if BP is normal – "cryptic shock")
- Lactate ≥4 mmol/L is associated with high mortality and defines septic shock (along with hypotension requiring vasopressors)

Action: Measure serum lactate immediately in all patients with suspected sepsis.

III. SEPSIS ALERT ACTIVATION

A. When to Activate a Sepsis Alert

Criteria:

- Suspected or confirmed infection
- PLUS ≥2 SIRS criteria or elevated MEWS
- PLUS ≥1 sign of organ dysfunction (see Section II.B) OR lactate ≥2 mmol/L

OR

- Any patient with suspected infection and septic shock (hypotension + lactate ≥2)

Who Can Activate:

- Any RN, physician, or advanced practice provider (APP)

How to Activate:

- Call overhead page: "Sepsis Alert, [Location/Room Number]"
- Or use EHR-based sepsis alert button (alerts the sepsis response team via pager/text)

B. Time Zero

"Time Zero" is defined as the time when sepsis is first recognized (when sepsis alert is called or documented in the chart).

All subsequent time-based interventions (e.g., antibiotics within 1 hour) are measured from Time Zero.

Accurate documentation of Time Zero is essential for quality reporting (SEP-1 measure).

C. Sepsis Response Team

Upon sepsis alert activation, the following team members respond (or are notified):

- **ED Attending Physician or Hospitalist** (team leader)
- **Primary Nurse** caring for the patient
- **Charge Nurse** (to allocate resources)
- **Respiratory Therapist** (for airway/oxygen support)
- **Pharmacist** (to facilitate rapid antibiotic delivery)
- **Lab/Phlebotomy** (priority labs)
- **Critical Care Physician/ICU Team** (if patient in septic shock or requires ICU-level care)

Team Leader Role:

- Assess the patient
- Confirm sepsis diagnosis and severity
- Direct implementation of sepsis bundle interventions
- Communicate with patient/family

- Decide on ICU vs. floor admission

IV. SEPSIS BUNDLE: HOUR-1 INTERVENTIONS

The "**Hour-1 Bundle**" refers to interventions that should be initiated immediately upon recognition of sepsis or septic shock. The goal is to complete these within **1 hour** for septic shock and ideally within **3 hours** for sepsis without shock (per Surviving Sepsis Campaign 2021 guidelines).

The 5 components of the bundle are:

1. **Measure lactate level**
2. **Obtain blood cultures (before antibiotics)**
3. **Administer broad-spectrum antibiotics**
4. **Begin rapid IV fluid resuscitation (30 mL/kg crystalloid for hypotension or lactate ≥4)**
5. **Apply vasopressors if hypotensive during or after fluid resuscitation to maintain MAP ≥65 mmHg**

Each is detailed below.

A. Measure Lactate Level

Action: Draw a serum lactate level immediately (within minutes of sepsis recognition).

Rationale: Lactate is a marker of tissue hypoperfusion and predicts mortality. Elevated lactate (≥2 mmol/L) indicates sepsis severity; ≥4 mmol/L is part of septic shock definition.

Follow-Up:

- If initial lactate is >2 mmol/L, **repeat lactate in 2-4 hours** to assess response to resuscitation.
- Goal: Decreasing lactate ("lactate clearance") suggests improving perfusion and is associated with better outcomes.

Laboratory Priority: Lactate should be resulted as STAT (within 15-30 minutes). Our lab processes sepsis lactates on priority.

B. Obtain Blood Cultures (Before Antibiotics)

Action: Obtain at least **two sets of blood cultures** (aerobic and anaerobic bottles from two different sites, e.g., two separate peripheral venipunctures, or one peripheral and one from a central line if present).

Additional Cultures: Also obtain cultures from other suspected sources:

- **Urine culture** if urinary source suspected (UTI, pyelonephritis, urosepsis)
- **Sputum culture** if pneumonia suspected (if patient can produce sputum; not necessary if delays care)
- **Wound culture** if soft tissue infection (abscess, cellulitis, necrotizing fasciitis)
- **CSF culture** if meningitis suspected (after ensuring no contraindication to lumbar puncture)

Timing:

- Blood cultures should be obtained **before administering antibiotics** whenever possible (ideally within 45 minutes of sepsis recognition).
- **However:** Do NOT significantly delay antibiotics to obtain cultures. If obtaining cultures will take >45 minutes or the patient is in extremis (septic shock, very unstable), give antibiotics first and obtain cultures immediately after (or attempt cultures while antibiotics are being prepared).
- Preferred: Two team members work simultaneously—one drawing cultures, another preparing antibiotics.

Technique:

- Use aseptic technique to avoid contamination (false positives)
- At least 10 mL of blood per bottle (aerobic and anaerobic)
- Label with time, site, and "sepsis alert" to ensure priority processing

Lab Processing: Blood cultures are processed as STAT; preliminary results (Gram stain of positive cultures) often available within 24-48 hours, final culture and sensitivities in 3-5 days. Early communication of results to the clinical team is critical for antibiotic de-escalation.

C. Administer Broad-Spectrum Antibiotics

This is the single most important time-sensitive intervention. Early antibiotics save lives.

Timing Goals:

- **Septic Shock (hypotension or lactate ≥4):** Antibiotics within **1 hour** of recognition (Time Zero)
- **Sepsis without shock:** Antibiotics within **3 hours** (ideally <1 hour)

Evidence: Each hour of delay in antibiotic administration in septic shock is associated with increased mortality (~7-8% increased risk per hour delayed).

Antibiotic Selection:

Empiric broad-spectrum antibiotics must cover the most likely pathogens based on the suspected source of infection and patient-specific factors (local resistance patterns, recent antibiotic use, immunosuppression, healthcare exposure).

General Principles:

- **Cover Gram-positive, Gram-negative, and anaerobes** as appropriate
- **Consider MRSA coverage** if risk factors present (prior MRSA, IV drug use, hemodialysis, recent hospitalization, skin/soft tissue infection)
- **Consider Pseudomonas coverage** if risk factors present (structural lung disease, neutropenia, recent antibiotics, healthcare-associated infection)
- **Consider fungal coverage (Candida)** in immunocompromised or high-risk patients (prolonged ICU stay, TPN, broad-spectrum antibiotics, high Candida score)

Empiric Antibiotic Regimens by Suspected Source:

1. Community-Acquired Pneumonia (CAP):

- **Regimen:** Ceftriaxone 1-2 g IV + Azithromycin 500 mg IV (or Doxycycline if azithro unavailable)
- **Alternative (severe or risk of Pseudomonas):** Piperacillin-Tazobactam 4.5 g IV (or Cefepime 2 g IV) + Azithromycin
- **If MRSA risk:** Add Vancomycin 15-20 mg/kg IV (load dose ~2 g for typical adult)

2. Healthcare-Associated Pneumonia (HCAP) or Hospital-Acquired/Ventilator-Associated Pneumonia (HAP/VAP):

- **Regimen:** Piperacillin-Tazobactam 4.5 g IV Q6H (or Cefepime 2 g IV Q8H, or Meropenem 1 g IV Q8H if very high risk)
- **PLUS** Vancomycin 15-20 mg/kg IV load
- **Consider adding** Ciprofloxacin or Amikacin if high risk for resistant Pseudomonas

3. Intra-Abdominal Infection (e.g., perforated appendix, diverticulitis, cholangitis):

- **Regimen:** Piperacillin-Tazobactam 4.5 g IV Q6H (covers Gram-negatives and anaerobes)
- **Alternative:** Ceftriaxone 2 g IV + Metronidazole 500 mg IV (or Cefepime + Metronidazole)

- **If severe or healthcare-associated:** Meropenem 1 g IV Q8H (broader coverage)

4. Urinary Tract Infection/Urosepsis:

- **Regimen:** Ceftriaxone 1-2 g IV
- **If recent fluoroquinolone use or high local resistance:** Piperacillin-Tazobactam 4.5 g IV
- **If concern for resistant organisms (prior ESBL, recent hospitalization):** Meropenem 1 g IV

5. Skin and Soft Tissue Infection (cellulitis, abscess, necrotizing fasciitis):

- **Regimen:** Vancomycin 15-20 mg/kg IV (for MRSA) + Piperacillin-Tazobactam 4.5 g IV (for Gram-negatives and anaerobes, especially if necrotizing infection suspected)
- **If necrotizing fasciitis suspected:** ADD Clindamycin 900 mg IV Q8H (toxin suppression) and consider early surgical consultation

6. Meningitis:

- **Regimen:** Ceftriaxone 2 g IV Q12H + Vancomycin 15-20 mg/kg IV load (to cover S. pneumoniae, including resistant strains)
- **If age >50 or immunocompromised:** ADD Ampicillin 2 g IV Q4H (for Listeria coverage)
- **PLUS** Dexamethasone 10 mg IV (give before or with first antibiotic dose, improves outcomes in bacterial meningitis)

7. Unknown Source (undifferentiated sepsis):

- **Regimen:** Piperacillin-Tazobactam 4.5 g IV + Vancomycin 15-20 mg/kg IV (broad coverage)
- **OR** Meropenem 1 g IV + Vancomycin (if very high risk or recent broad-spectrum antibiotic exposure)

Special Populations:

- **Neutropenic fever/Immunocompromised:** Use antipseudomonal beta-lactam (Cefepime, Piperacillin-Tazobactam, or Meropenem); consider adding Vancomycin if skin/line infection or MRSA risk. Consult infectious disease (ID) or oncology early.
- **Post-splenectomy or functional asplenia:** Cover encapsulated organisms (Streptococcus pneumoniae, Haemophilus, Neisseria) – Ceftriaxone is appropriate.
- **Recent travel or specific exposures:** Consider atypical infections (malaria, rickettsial diseases, etc.) – consult ID if unclear.

Antibiotic Administration:

- **First dose should be a loading dose** (higher dose for some agents, e.g., vancomycin 25-30 mg/kg load if septic shock)
- Ensure antibiotics are **administered IV** (not PO in septic patients due to poor absorption)
- Use IV push or rapid infusion when possible (e.g., give vancomycin over 1 hour, pip-tazo over

30 min) to expedite administration
- **Pharmacy should prepare sepsis antibiotics STAT** (within 15-30 minutes of order)
- **Nurse administers immediately** upon receipt from pharmacy

Documentation:

- Document **time of antibiotic order** and **time of administration** (for quality measure compliance)
- Time of administration is when the infusion is started (not when it finishes)

De-escalation and Antibiotic Stewardship:

- Once culture results and sensitivities are available (typically 48-72 hours), **narrow antibiotic spectrum** to target the identified organism(s) (de-escalation)
- Stop unnecessary antibiotics (e.g., stop vancomycin if MRSA not isolated, stop antifungals if no Candida)
- **Duration of therapy:** Typically 7-10 days for most infections; longer for complicated infections (endocarditis, osteomyelitis, etc.)
- Consult Infectious Disease or Antimicrobial Stewardship Team for complex cases

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D. Rapid Intravenous Fluid Resuscitation

Indication: Administer IV fluids if the patient has:

- Hypotension (MAP <65 mmHg, or SBP <90 mmHg)
- OR Lactate ≥4 mmol/L (even if BP currently normal – indicates "cryptic shock")

Fluid Bolus:

30 mL/kg of IV crystalloid fluid given rapidly (within the first 3 hours, ideally within the first hour)

For an average 70-kg adult: ~2-3 liters

Fluid Type:

- **Balanced crystalloids preferred:**
  Lactated Ringer's (LR) or Plasma-Lyte
  - Evidence: Balanced crystalloids associated with lower mortality and less acute kidney injury compared to normal saline (0.9% NaCl) in some studies

- **Normal saline (0.9% NaCl):** Acceptable alternative (widely available), but large volumes may

cause hyperchloremic metabolic acidosis
- **Avoid colloids (albumin, starches) for initial resuscitation** (no proven benefit over crystalloids, more expensive; albumin may be used later in specific circumstances)

Administration:

- Use large-bore IV access (at least 18-gauge, ideally 16-gauge or larger) x 2 if possible
- Give fluid as rapidly as possible ("wide open"): Use pressure bags or rapid infusers if available
- **Reassess frequently**
  during and after fluid bolus:
  - Monitor vitals (BP, heart rate), urine output, mental status
  - Listen to lung sounds (watch for signs of fluid overload: rales, increased work of breathing)
  - If patient has known heart failure or end-stage renal disease, give fluid more cautiously in smaller increments (e.g., 500 mL boluses) and reassess; consider early use of vasopressors

Goals of Fluid Resuscitation:

- **MAP ≥65 mmHg**
- Improved urine output (≥0.5 mL/kg/hr)
- Improved mentation
- Decreasing lactate on repeat measurement

Fluid Responsiveness Assessment:

After initial 30 mL/kg:

- If hypotension persists Start vasopressors (see below) and give additional fluids guided by hemodynamic assessment
- **Tools to assess fluid responsiveness:**

  - **Passive leg raise test** (if MAP increases by ≥10 mmHg with legs elevated 45°, patient is likely fluid-responsive)
  - **Bedside ultrasound** (assess IVC collapsibility, cardiac function, lung B-lines for pulmonary edema)
  - **Pulse pressure variation or stroke volume variation** (if patient is on mechanical ventilation and has arterial line)

- **Avoid excessive fluid administration** (>4-5 liters) without evidence of benefit; excessive fluids can lead to pulmonary edema, abdominal compartment syndrome, and worse outcomes

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E. Vasopressors for Persistent Hypotension

Indication: If MAP remains <65 mmHg **despite** fluid resuscitation (or during fluid resuscitation if patient is severely hypotensive), initiate vasopressors.

Do NOT delay vasopressors waiting for full 30 mL/kg fluid bolus if patient is profoundly hypotensive or in extremis.

First-Line Vasopressor: Norepinephrine

Norepinephrine (Levophed):

- Alpha-1 adrenergic agonist (vasoconstriction) with some beta-1 activity (inotropy)
- **Starting dose:** 0.05-0.1 mcg/kg/min (typically start 5-10 mcg/min in an average adult) via IV infusion
- **Titrate** to achieve MAP ≥65 mmHg (increase by 2-5 mcg/min every 5-10 minutes as needed)
- **Usual dose range:** 2-40 mcg/min (higher doses indicate severe shock)

Route of Administration:

- **Ideally via central venous catheter** (subclavian, internal jugular, or femoral central line) to avoid extravasation and tissue necrosis
- **However:** In emergency, may start via peripheral IV if central access not immediately available (use large peripheral IV, monitor site closely, and obtain central access ASAP)
- **Never delay vasopressors** for central line placement if the patient is crashing; start peripherally and convert to central when feasible

Monitoring:

- Continuous vital signs (ideally with arterial line for continuous BP monitoring in ICU)
- Watch for signs of inadequate perfusion (mental status, urine output, skin mottling/ temperature)
- Monitor for vasopressor side effects: arrhythmias, extremity ischemia

Add-On or Alternative Vasopressors:

Vasopressin:

- **Dose:** 0.03-0.04 units/min (fixed dose, not titrated)
- **Use:** Add to norepinephrine if MAP not achieved with norepi alone, or as second-line agent
- **Advantage:** Vasopressin levels are often depleted in septic shock; supplementation may help reduce catecholamine requirements
- **Note:** Do not use as sole vasopressor (use in combination with norepinephrine)

Epinephrine:

- **Dose:** 0.05-0.5 mcg/kg/min IV
- **Use:** If refractory hypotension despite norepinephrine + vasopressin, or if patient has bradycardia and low cardiac output
- **Mechanism:** Alpha and beta agonist (vasoconstriction + inotropy + chronotropy)
- **Side effects:** Tachycardia, arrhythmias, hyperglycemia, lactic acidosis (can make lactate clearance harder to interpret)

Phenylephrine:

- Pure alpha agonist (vasoconstrictor)
- Generally **avoided in septic shock** (can cause reflex bradycardia and decrease cardiac output)
- May be used if norepinephrine not available, or if patient has tachyarrhythmia exacerbated by norepi

Dopamine:

- Older vasopressor; **generally not recommended** as first-line (higher risk of arrhythmias than norepinephrine)
- May be considered in select patients with bradycardia and low cardiac output

Dobutamine:

- Inotrope (increases cardiac contractility)
- **Use:** If patient has persistent hypoperfusion (low cardiac output) despite adequate MAP on vasopressors; typically in patients with septic cardiomyopathy
- **Not a vasopressor** (may actually lower BP due to vasodilation); use in combination with vasopressors

Goal:

Target MAP ≥65 mmHg (higher targets, e.g., 75-80 mmHg, may be considered in patients with chronic hypertension, but generally 65 is adequate)

V. ADDITIONAL MANAGEMENT (WITHIN 6 HOURS)

After the Hour-1 Bundle is initiated, the following interventions should be completed within the first 6 hours of sepsis recognition.

A. Reassess Volume Status and Tissue Perfusion

Perform a reassessment within 2-4 hours of initial resuscitation:

- **Vital signs:** Is MAP ≥65? Heart rate improving?
- **Physical exam:**
  - Mental status (is confusion resolving?)
  - Skin (warm and dry, or still cold/clammy/mottled?)
  - Capillary refill time (should be <3 seconds)
  - Urine output (Foley catheter in place, goal ≥0.5 mL/kg/hr)
- **Repeat lactate:** If initial lactate was >2, recheck; goal is clearance (decreasing lactate)
- **Labs:** Repeat CBC, BMP to assess response and guide further therapy

If goals NOT met (persistent hypotension, elevated lactate, poor urine output):

- Ensure adequate fluid resuscitation (consider additional fluid boluses guided by fluid responsiveness assessment)
- Ensure vasopressors optimized (adequate dose, appropriate agent)
- Consider other causes or complications (see Section VII)

B. Source Control

Identify and address the source of infection as soon as possible (ideally within 12 hours, but urgently if indicated).

Examples of Source Control:

- **Abscess:** Drainage (percutaneous or surgical)
- **Infected catheter or device:** Remove (e.g., remove infected central line, Foley catheter, prosthetic device if source)
- **Necrotizing soft tissue infection:** Urgent surgical debridement
- **Cholangitis/obstructed biliary system:** ERCP for biliary drainage
- **Bowel perforation, ischemic bowel:** Surgical exploration and resection
- **Empyema:** Chest tube drainage
- **Infected joint (septic arthritis):** Arthrocentesis and washout

Consultation:

- Obtain **surgical consultation** early if any surgical source is suspected or if patient has an acute abdomen, suspected necrotizing fasciitis, or perforated viscus
- Involve **interventional radiology** for image-guided drainage of abscesses if amenable

Delay in source control is associated with increased mortality. In some cases (e.g., necrotizing fasciitis), emergency surgery is life-saving and should not be delayed even for full resuscitation.

C. Oxygen and Respiratory Support

Goal: Maintain adequate oxygenation (SpO_2 ≥94%, or ≥90% in patients with COPD).

Interventions:

- **Supplemental oxygen** via nasal cannula, face mask, or high-flow nasal cannula (HFNC) as needed
- **High-Flow Nasal Cannula (HFNC):** For patients with hypoxemic respiratory failure (SpO_2 <90% on standard O_2), HFNC can deliver up to 100% FiO_2 and provide PEEP-like effect; may avoid intubation in some patients
- **Non-invasive positive pressure ventilation (NIPPV/BiPAP):** Use cautiously in sepsis (risk of aspiration, delay in intubation); generally reserved for patients with COPD exacerbation or cardiogenic pulmonary edema superimposed on sepsis
- **Intubation and Mechanical Ventilation:**
    - Indications: Severe hypoxemia refractory to HFNC, respiratory distress, inability to protect airway (altered mental status, GCS <8), respiratory fatigue
    - Use **lung-protective ventilation** strategy (see below)

Lung-Protective Ventilation (for ARDS):

Many septic patients develop acute respiratory distress syndrome (ARDS). If patient is intubated:

- **Tidal volume:** 6 mL/kg ideal body weight (IBW) (lower tidal volumes reduce ventilator-induced lung injury)
- **Plateau pressure:** Keep ≤30 cm H_2O
- **PEEP:** Use moderate to high PEEP per ARDSNet PEEP/FiO_2 table to optimize oxygenation
- **FiO_2:** Target SpO_2 88-95% (avoid excessive oxygen, as hyperoxia may be harmful)
- **Prone positioning:** For severe ARDS (PaO_2/FiO_2 <150), consider proning (improves oxygenation and mortality)

D. Urine Output Monitoring

Insert Foley catheter to monitor urine output closely.

Goal: ≥0.5 mL/kg/hr

Rationale: Urine output is a marker of renal perfusion and adequacy of resuscitation.

Oliguria (<0.5 mL/kg/hr) suggests:

- Inadequate fluid resuscitation (give more fluids if patient is fluid-responsive)
- Inadequate MAP (increase vasopressors)
- Acute kidney injury (intrinsic renal damage from sepsis) – manage supportively, may require renal replacement therapy if severe

E. Central Venous Access and Arterial Line

Central Venous Catheter (CVC):

- Indicated for administration of vasopressors (preferred route), large-volume fluid resuscitation, CVP monitoring (optional), blood draws
- Placement sites: Internal jugular, subclavian, or femoral vein
- Use ultrasound guidance to reduce complications

Arterial Line:

- Indicated for continuous blood pressure monitoring in patients on vasopressors (more accurate than cuff BP)
- Also facilitates frequent blood gas and lab draws
- Placement sites: Radial artery (most common), femoral artery

Timing:

- These should be placed as soon as feasible in septic shock patients, but should NOT delay initial resuscitation (start peripheral IV pressors and manual BP monitoring if needed initially)

F. Laboratory and Imaging Studies

Labs to Obtain (STAT):

- **CBC with differential** (WBC, hemoglobin, platelets)
- **Comprehensive metabolic panel** (electrolytes, BUN, creatinine, glucose, liver enzymes, bilirubin)
- **Lactate** (initial and repeat)
- **Coagulation studies** (PT/INR, PTT) – if concern for DIC or need for procedures
- **Arterial blood gas (ABG)** or venous blood gas (VBG) – assess acid-base status, oxygenation, lactate
- **Blood cultures** (as above)
- **Urinalysis and urine culture**
- **Procalcitonin** (optional; elevated in bacterial infection, can help with antibiotic stewardship decisions)

Imaging:

- **Chest X-ray:** For suspected pneumonia, to assess for pulmonary edema, line/tube placement
- **CT scan (chest, abdomen/pelvis, etc.):**
  If source of infection is unclear or if concern for abscess, perforation, etc.
  - **CT Abdomen/Pelvis with IV contrast** is often obtained in undifferentiated sepsis to look for intra-abdominal source

- **Ultrasound:** Bedside ultrasound (POCUS) for volume status assessment, cardiac function (ejection fraction, tamponade), pleural effusions, or to guide procedures

Do NOT delay treatment (antibiotics, fluids) to obtain imaging. Imaging can occur concurrently or after initial stabilization.

VI. CRITICAL CARE AND ICU MANAGEMENT

A. ICU Admission Criteria

All patients with septic shock should be admitted to the ICU.

Also consider ICU for:

- Severe sepsis requiring close monitoring or potential for decompensation
- Need for mechanical ventilation
- Need for continuous vasopressor infusions
- Multi-organ dysfunction
- Hemodynamic instability

Transfer to ICU should occur as soon as possible (delays in ICU admission >6 hours are associated with worse outcomes).

B. Hemodynamic Monitoring

In ICU, use advanced monitoring:

- Arterial line for continuous BP
- Frequent reassessment of perfusion (mentation, skin, urine output, lactate)
- Consider echocardiography to assess cardiac function (ejection fraction, fluid responsiveness, valvular abnormalities)
- Some centers use advanced hemodynamic monitoring (e.g., pulmonary artery catheter, PiCCO) in refractory shock, though routine use is not required

C. Adjunctive Therapies

Corticosteroids:

- **Indication:** Septic shock refractory to adequate fluid and vasopressor therapy (i.e., patient still requiring significant vasopressor support despite resuscitation)
- **Regimen:** Hydrocortisone 200 mg/day IV (either as continuous infusion or divided Q6H, e.g., 50 mg IV Q6H)
- **Evidence:** Modest benefit in refractory septic shock (faster shock reversal, possibly reduced mortality in some studies); minimal harm
- **Duration:** Continue until shock resolves (vasopressors discontinued), typically 3-5 days, then taper or stop
- **Do NOT delay treatment to perform cosyntropin (ACTH) stimulation test** (relative adrenal insufficiency is assumed in refractory shock)

Contraindications to steroids: None specific in septic shock (use with caution in uncontrolled infection, but antibiotics should be on board)

Blood Transfusion:

- **Transfusion threshold:** Hemoglobin <7 g/dL (restrictive strategy)
- **Target:** Hemoglobin 7-9 g/dL (higher targets not beneficial in sepsis unless active bleeding or severe coronary disease)
- **Use packed red blood cells (PRBCs)** as needed

Albumin:

- **Use:** After substantial crystalloid resuscitation, some clinicians add albumin (4-5% or 20-25%) for additional volume expansion, especially if patient is hypoalbuminemic
- **Evidence:** SAFE trial showed albumin is safe (noninferior to saline); ALBIOS trial in sepsis showed no mortality benefit but faster shock reversal with albumin
- **Our practice:** Consider albumin if patient has received >4 liters of crystalloid and still needs volume, or if severe hypoalbuminemia

Stress Ulcer Prophylaxis:

- **Indication:** All ICU patients with sepsis (risk of stress gastritis and GI bleeding)
- **Regimen:** Proton pump inhibitor (e.g., pantoprazole 40 mg IV daily) or H2 blocker (e.g., famotidine 20 mg IV Q12H)

DVT Prophylaxis:

- **Indication:** All septic patients unless contraindication (active bleeding, severe thrombocytopenia <25k)
- **Regimen:** Subcutaneous heparin (5000 units Q8H or Q12H) or enoxaparin (40 mg daily)

- **Mechanical prophylaxis:** Sequential compression devices (SCDs) if pharmacologic contraindicated

Glycemic Control:

- **Target:** Blood glucose 140-180 mg/dL
- **Method:** IV insulin infusion in ICU (with frequent glucose monitoring)
- **Rationale:** Avoid hyperglycemia (>180) which is associated with worse outcomes; avoid hypoglycemia (<70) which is also harmful. Tight control (80-110) is NOT beneficial and increases hypoglycemia risk.

Renal Replacement Therapy (RRT):

- **Indication:**
  Acute kidney injury with:
  - Severe hyperkalemia refractory to medical management
  - Severe acidosis (pH <7.1)
  - Severe volume overload refractory to diuretics
  - Uremic complications (encephalopathy, pericarditis)
  - Anuria/severe oliguria with fluid overload

- **Modalities:** Intermittent hemodialysis (IHD) or continuous renal replacement therapy (CRRT) – choice depends on hemodynamic stability (CRRT is gentler for unstable patients)

VII. TROUBLESHOOTING AND SPECIAL CONSIDERATIONS

A. Persistent Hypotension Despite Resuscitation

If MAP <65 despite 30 mL/kg fluids and vasopressors:

Consider:

1. **Inadequate source control:** Undrained abscess, ongoing infection
2. **Incorrect diagnosis:**
   Not sepsis/septic shock; consider other causes of shock:
   - **Cardiogenic shock** (MI, acute heart failure) – check troponin, ECG, echo
   - **Hypovolemic shock** (GI bleed, hemorrhage) – check hemoglobin, look for bleeding
   - **Obstructive shock** (massive PE, tension pneumothorax, tamponade) – clinical exam, imaging, echo
3. **Adrenal insufficiency:** Give stress-dose steroids (hydrocortisone)

4. **Severe anemia or coagulopathy:** Transfuse blood products as needed
5. **Myocardial dysfunction (septic cardiomyopathy):** Consider adding inotrope (dobutamine)
6. **Inadequate vasopressor therapy:** Increase dose, add second agent (vasopressin, epinephrine)

Refractory Shock:

- Consult critical care
- Consider advanced hemodynamic monitoring (echo, PA catheter)
- Ensure no ongoing hemorrhage or other non-septic causes

B. Antibiotic Allergies

If patient reports antibiotic allergy:

- Clarify the type of reaction (true allergy vs. side effect)
- **Penicillin allergy:**
    - If history of anaphylaxis or severe reaction: Avoid all beta-lactams; use fluoroquinolone + metronidazole or aztreonam + vancomycin for Gram-negative coverage
    - If mild rash years ago: Risk of cross-reactivity with cephalosporins is low (~2%); can often use ceftriaxone or cefepime with monitoring

- **In life-threatening sepsis, do not withhold necessary antibiotics solely due to reported allergy** (especially if allergy history is vague); discuss risk/benefit and monitor closely; can consider desensitization or premedication if needed

C. Immunocompromised Patients

Patients on immunosuppression (chemotherapy, transplant, HIV, chronic steroids) are at high risk for severe sepsis and opportunistic infections.

Management:

- Broader empiric coverage (add antifungals, consider atypical pathogens)
- Early consultation with infectious disease and/or hematology-oncology
- Consider opportunistic infections: Pneumocystis jirovecii pneumonia (PCP), invasive fungal infections (Aspergillus, Candida), CMV, etc.

D. Sepsis in Pregnancy

Pregnant or postpartum women with sepsis require urgent obstetric involvement.

Source Control:

- Consider obstetric sources: chorioamnionitis, endometritis, septic abortion, pyelonephritis
- Delivery of fetus/placenta may be necessary for source control in some cases

Antibiotics:

- Most antibiotics safe in pregnancy (penicillins, cephalosporins, aztreonam, vancomycin)
- Avoid: Fluoroquinolones (cartilage risk), tetracyclines (teeth staining), aminoglycosides if possible (ototoxicity)

Resuscitation:

- Perform resuscitation as per sepsis protocol; if pregnant >20 weeks, position patient with left lateral tilt (or manually displace uterus) to relieve aorto-caval compression
- Fetal monitoring if viable pregnancy

VIII. DOCUMENTATION AND QUALITY MEASURES

A. Required Documentation

To meet SEP-1 core measure and internal quality standards, the following must be documented:

1. **Time Zero** (time sepsis recognized)
2. **Initial lactate level** (and result)
3. **Blood cultures obtained** (time drawn)
4. **Broad-spectrum antibiotics administered** (time of order and time of administration)
5. **Fluid resuscitation** (if hypotensive or lactate ≥4): volume given (30 mL/kg within 3 hours)
6. **Repeat lactate** (if initial lactate >2 mmol/L, within 2-6 hours)
7. **Vasopressors** (if indicated, time started)
8. **Reassessment** of volume status and tissue perfusion

EHR Sepsis Navigator: Our EHR has a "Sepsis Navigator" order set and documentation tool that auto-populates times and prompts for required elements. Use this tool for every sepsis patient.

B. Performance Metrics

Sepsis Committee reviews:

- **Door-to-antibiotic time** for sepsis/septic shock (goal: <1 hour for shock, <3 hours for sepsis)
- **Compliance with 3-hour bundle** (lactate, cultures, antibiotics, fluids)
- **Compliance with 6-hour bundle** (reassessment, repeat lactate, vasopressors if needed)

- **Sepsis mortality rate** (risk-adjusted)
- **ICU transfer time** for septic shock

Benchmarking: Compare to national sepsis data (CMS SEP-1, Surviving Sepsis Campaign registries).

C. Sepsis Code Debriefing

After each sepsis alert, the team conducts a brief debrief (within 24-48 hours):

- What went well?
- What could be improved? (delays, communication issues, missing equipment, etc.)
- Any system issues to address?

Lessons learned are discussed in monthly Sepsis Committee meetings and drive quality improvement initiatives.

IX. EDUCATION AND TRAINING

A. Mandatory Training

All clinical staff (RNs, MDs, APPs, RTs) must complete:

- **Initial sepsis recognition and management training** (2-hour module) within 30 days of hire or annually
- **Sepsis simulation drills** (quarterly in ED and ICU)

B. Sepsis Champions

Each unit (ED, ICU, Med-Surg floors) has designated **Sepsis Champions** (usually senior RNs or physicians) who:

- Serve as local experts
- Promote adherence to the sepsis protocol
- Participate in quality reviews and education

X. REFERENCES

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4. Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med.* 2006;34(6):1589-1596.
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6. Centers for Medicare & Medicaid Services (CMS). SEP-1 Severe Sepsis and Septic Shock: Management Bundle Core Measure.

XI. APPENDICES

Appendix A: Sepsis Alert Activation Card (pocket reference for nurses)

Appendix B: Empiric Antibiotic Quick Reference Table

Appendix C: Fluid Resuscitation and Vasopressor Dosing Guide

Appendix D: Sepsis Order Set (EHR Navigator)

Appendix E: Lactate Clearance Monitoring Form

Appendix F: Sepsis Debrief Template

END OF PROTOCOL

For urgent questions during sepsis resuscitation, contact:

- **ED Attending/Hospitalist on duty**
- **Critical Care Attending (ICU):** Pager (555) 7000

- **Sepsis Response Team:** Overhead page "Sepsis Alert [Location]"
- **Pharmacy (STAT antibiotics):** (555) 8000

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