The basics of an ICU admission for **SEVERE SEPSIS** and **SEPTIC SHOCK**

ICU admission for **SEVERE SEPSIS** and **SEPTIC SHOCK**

- Sepsis is likely when the patient exhibits signs of the systemic inflammatory response and has a likely infectious source.
  - Fever **or** hypothermia usually present
  - ICU evaluation usually prompted by unstable vital signs

- Initial bedside evaluation should focus on the stability of the patient.
  - Vital signs including your own measurement of respiratory rate
  - Assessment of mental status
  - Assessment of respiratory status. Is the patient “working hard”?
  - An ABG is usually obtained promptly to assess acid-base status.

TABLE 1. Diagnostic Criteria for Sepsis

Infection, documented or suspected, and some of the following:
General variables
Fever (> 38.3°C)
Hypothermia (core temperature < 36°C)
Heart rate > 90/min^{-1} or more than two SD above the normal value for age
Tachypnea
Altered mental status
Significant edema or positive fluid balance (> 20 mL/kg over 24 hr)
Hyperglycemia (plasma glucose > 140 mg/dL or 7.7 mmol/L) in the absence of diabetes
Inflammatory variables
Leukocytosis (WBC count > 12,000 μL^{-1})
Leukopenia (WBC count < 4000 μL^{-1})
Normal WBC count with greater than 10% immature forms
Plasma C-reactive protein more than two SD above the normal value
Plasma procalcitonin more than two SD above the normal value
Hemodynamic variables
Arterial hypotension (SBP < 90 mm Hg, MAP < 70 mm Hg, or an SBP decrease > 40 mm Hg in adults or less than two SD below normal for age)
Organ dysfunction variables
Arterial hypoxemia (Pao_2/Fio_2 < 300)
Acute oliguria (urine output < 0.5 mL/kg/hr for at least 2 hrs despite adequate fluid resuscitation)
Creatinine increase > 0.5 mg/dL or 44.2 μmol/L
Coagulation abnormalities (INR > 1.5 or aPTT > 60 s)
Ileus (absent bowel sounds)
Thrombocytopenia (platelet count < 100,000 μL^{-1})
Hyperbilirubinemia (plasma total bilirubin > 4 mg/dL or 70 μmol/L)
Tissue perfusion variables
Hyperlactatemia (> 1 mmol/L)
Decreased capillary refill or mottling

Sources of Infection

- The first question: Is this patient a community dweller or a frequent flyer?
  - Hospitalized patients at higher risk for the following:
    - Line infections or other iatrogenic infections
    - Resistant organisms
    - Multiple comorbid conditions that make them more prone to decompensation
  - Community dwellers more likely to have typical pathogens in typical infectious sources

Community-Acquired Infectious Sources

- The usual suspects
  - CAP (with or without pleural effusion)
  - Urinary source
  - Intra-abdominal
  - Primary bacteremia
- The next tier
  - Meningitis
  - Skin/soft tissue
  - Endocarditis
- Less common (both in frequency and cause of sepsis)
  - Peridontal/pharyngeal abscess
  - Septic joint
  - Osteomyelitis

Hospital-Acquired Infectious Sources

- The usual suspects
  - Health-care associated pneumonia
  - Urinary source
  - Line infection
  - Other iatrogenic infection (instrumentation, surgery)
- The next tier
  - Skin/soft tissue
  - Endocarditis
- Less common
  - Any other infection in the community

Stabilizing the patient in the ICU

- Step 1: **The ABC's of unstable patients**
  - Does the patient need to be intubated?
  - Does the patient require urgent blood pressure support?
  - Give at least 1 to 2 Liters of 0.9NS stat
- Step 2: **Antibiotics**
  - Get the antibiotics ordered and given STAT

Transfer to the ICU
SEVERE SEPSIS and **SEPTIC SHOCK**

- Step 3: **Get data**
  - Get the necessary data and imaging ASAP
    - CBC with diff, CMP, ABG, lactic acid, INR, PTT
    - Blood cultures, CXR, urine culture
    - Urine antigens for pneumococcus and Legionella if pneumonia supsected
    - Consideration of LP if meningitis suspected
    - CT abdomen/pelvis and surgical consult if intraabdominal source considered

Transfer to the ICU
SEVERE SEPSIS and **SEPTIC SHOCK**

- Step 4: **Get more data**
  - Consider placement of central line and arterial line and stabilize the BP
    - Get the Mean BP > 65
    - Measure SVO2
- Step 5: **Continue to stabilize patient**
  - Start a pressor if indicated
    - Usual order: norepinephrine, then vasopressin, then debated

Early goal-directed therapy (EGDT) of **SEVERE SEPSIS** and **SEPTIC SHOCK**

The three most critical values of EGDT

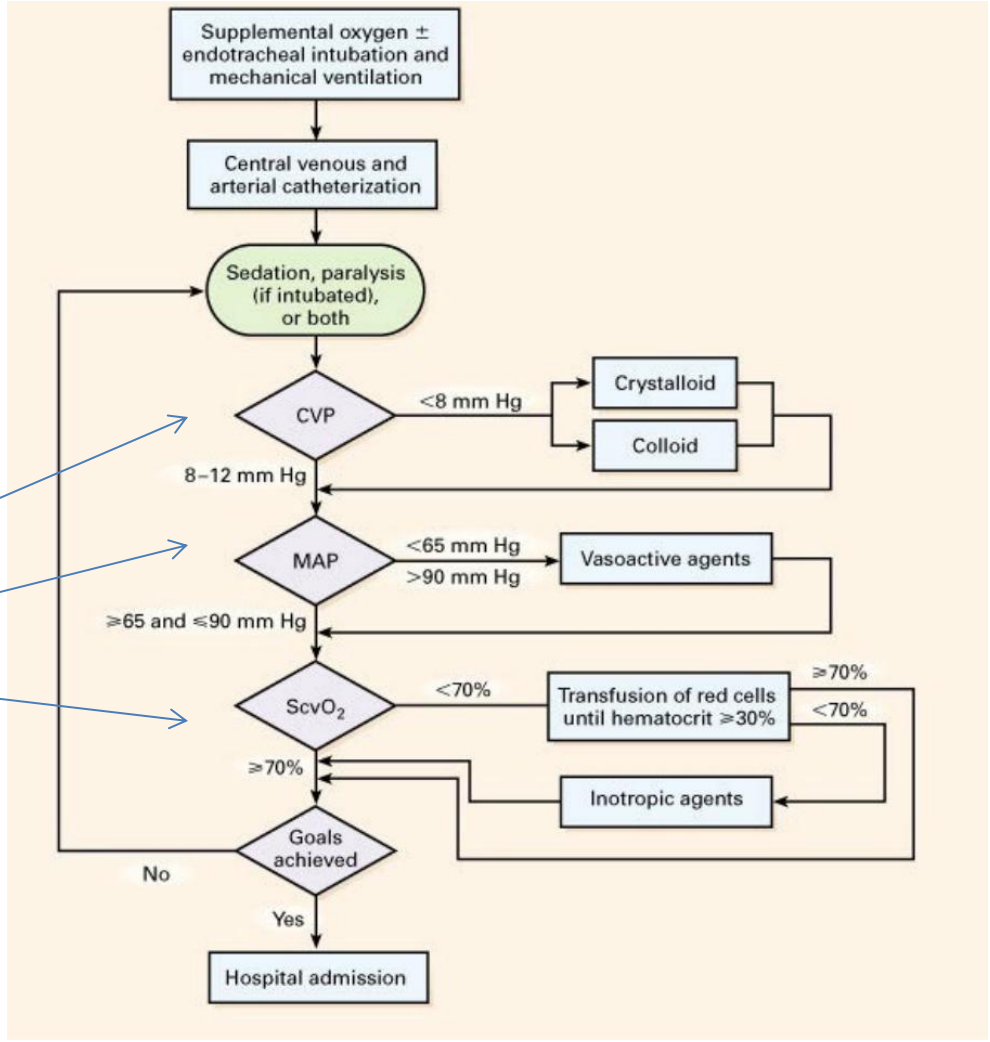

TABLE 5. Recommendations: Initial Resuscitation and Infection Issues

A. Initial Resuscitation

1. Protocolized, quantitative resuscitation of patients with sepsis- induced tissue hypoperfusion (defined in this document as hypotension persisting after initial fluid challenge or blood lactate concentration ≥ 4 mmol/L). Goals during the first 6 hrs of resuscitation:
   a) Central venous pressure 8–12 mm Hg
   b) Mean arterial pressure (MAP) ≥ 65 mm Hg
   c) Urine output ≥ 0.5 mL/kg/hr
   d) Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively (grade 1C).
2. In patients with elevated lactate levels targeting resuscitation to normalize lactate (grade 2C).

B. Screening for Sepsis and Performance Improvement

1. Routine screening of potentially infected seriously ill patients for severe sepsis to allow earlier implementation of therapy (grade 1C).
2. Hospital–based performance improvement efforts in severe sepsis (UG).

C. Diagnosis

1. Cultures as clinically appropriate before antimicrobial therapy if no significant delay (> 45 mins) in the start of antimicrobial(s) (grade 1C). At least 2 sets of blood cultures (both aerobic and anaerobic bottles) be obtained before antimicrobial therapy with at least 1 drawn percutaneously and 1 drawn through each vascular access device, unless the device was recently (<48 hrs) inserted (grade 1C).
2. Use of the 1,3 beta-D-glucan assay (grade 2B), mannan and anti-mannan antibody assays (2C), if available and invasive candidiasis is in differential diagnosis of cause of infection.
3. Imaging studies performed promptly to confirm a potential source of infection (UG).

D. Antimicrobial Therapy

1. Administration of effective intravenous antimicrobials within the first hour of recognition of septic shock (grade 1B) and severe sepsis without septic shock (grade 1C) as the goal of therapy.

2a. Initial empiric anti-infective therapy of one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into tissues presumed to be the source of sepsis (grade 1B).

2b. Antimicrobial regimen should be reassessed daily for potential deescalation (grade 1B).

3. Use of low procalcitonin levels or similar biomarkers to assist the clinician in the discontinuation of empiric antibiotics in patients who initially appeared septic, but have no subsequent evidence of infection (grade 2C).

4a. Combination empirical therapy for neutropenic patients with severe sepsis (grade 2B) and for patients with difficult-to-treat, multidrug-resistant bacterial pathogens such as *Acinetobacter* and *Pseudomonas* spp. (grade 2B). For patients with severe infections associated with respiratory failure and septic shock, combination therapy with an extended spectrum beta-lactam and either an aminoglycoside or a fluoroquinolone is for *P. aeruginosa* bacteremia (grade 2B). A combination of beta-lactam and macrolide for patients with septic shock from bacteremic *Streptococcus pneumoniae* infections (grade 2B).

TABLE 5. (*Continued*) Recommendations: Initial Resuscitation and Infection Issues

4b. Empiric combination therapy should not be administered for more than 3–5 days. De-escalation to the most appropriate single therapy should be performed as soon as the susceptibility profile is known (grade 2B).

5. Duration of therapy typically 7–10 days; longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteremia with *S. aureus;* some fungal and viral infections or immunologic deficiencies, including neutropenia (grade 2C).

6. Antiviral therapy initiated as early as possible in patients with severe sepsis or septic shock of viral origin (grade 2C).

7. Antimicrobial agents should not be used in patients with severe inflammatory states determined to be of noninfectious cause (UG).

E. Source Control

1. A specific anatomical diagnosis of infection requiring consideration for emergent source control be sought and diagnosed or excluded as rapidly as possible, and intervention be undertaken for source control within the first 12 hr after the diagnosis is made, if feasible (grade 1C).

2. When infected peripancreatic necrosis is identified as a potential source of infection, definitive intervention is best delayed until adequate demarcation of viable and nonviable tissues has occurred (grade 2B).

3. When source control in a severely septic patient is required, the effective intervention associated with the least physiologic insult should be used (eg, percutaneous rather than surgical drainage of an abscess) (UG).

4. If intravascular access devices are a possible source of severe sepsis or septic shock, they should be removed promptly after other vascular access has been established (UG).

TABLE 6. Recommendations: Hemodynamic Support and Adjunctive Therapy

G. Fluid Therapy of Severe Sepsis

1. Crystalloids as the initial fluid of choice in the resuscitation of severe sepsis and septic shock (grade 1B).
2. Against the use of hydroxyethyl starches for fluid resuscitation of severe sepsis and septic shock (grade 1B).
3. Albumin in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids (grade 2C).
4. Initial fluid challenge in patients with sepsis-induced tissue hypoperfusion with suspicion of hypovolemia to achieve a minimum of 30 mL/kg of crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid may be needed in some patients (grade 1C).
5. Fluid challenge technique be applied wherein fluid administration is continued as long as there is hemodynamic improvement either based on dynamic (eg, change in pulse pressure, stroke volume variation) or static (eg, arterial pressure, heart rate) variables (UG).

H. Vasopressors

1. Vasopressor therapy initially to target a mean arterial pressure (MAP) of 65 mm Hg (grade 1C).
2. Norepinephrine as the first choice vasopressor (grade 1B).
3. Epinephrine (added to and potentially substituted for norepinephrine) when an additional agent is needed to maintain adequate blood pressure (grade 2B).
4. Vasopressin 0.03 units/minute can be added to norepinephrine (NE) with intent of either raising MAP or decreasing NE dosage (UG).
5. Low dose vasopressin is not recommended as the single initial vasopressor for treatment of sepsis-induced hypotension and vasopressin doses higher than 0.03-0.04 units/minute should be reserved for salvage therapy (failure to achieve adequate MAP with other vasopressor agents) (UG).
6. Dopamine as an alternative vasopressor agent to norepinephrine only in highly selected patients (eg, patients with low risk of tachyarrhythmias and absolute or relative bradycardia) (grade 2C).
7. Phenylephrine is not recommended in the treatment of septic shock except in circumstances where (a) norepinephrine is associated with serious arrhythmias, (b) cardiac output is known to be high and blood pressure persistently low or (c) as salvage therapy when combined inotrope/vasopressor drugs and low dose vasopressin have failed to achieve MAP target (grade 1C).
8. Low-dose dopamine should not be used for renal protection (grade 1A).
9. All patients requiring vasopressors have an arterial catheter placed as soon as practical if resources are available (UG).

I. Inotropic Therapy

1. A trial of dobutamine infusion up to 20 micrograms/kg/min be administered or added to vasopressor (if in use) in the presence of (a) myocardial dysfunction as suggested by elevated cardiac filling pressures and low cardiac output, or (b) ongoing signs of hypoperfusion, despite achieving adequate intravascular volume and adequate MAP (grade 1C).
2. Not using a strategy to increase cardiac index to predetermined supranormal levels (grade 1B).

J. Corticosteroids

1. Not using intravenous hydrocortisone to treat adult septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (see goals for Initial Resuscitation). In case this is not achievable, we suggest intravenous hydrocortisone alone at a dose of 200 mg per day (grade 2C).
2. Not using the ACTH stimulation test to identify adults with septic shock who should receive hydrocortisone (grade 2B).
3. In treated patients hydrocortisone tapered when vasopressors are no longer required (grade 2D).
4. Corticosteroids not be administered for the treatment of sepsis in the absence of shock (grade 1D).
5. When hydrocortisone is given, use continuous flow (grade 2D).

Transfer to the ICU
SEVERE SEPSIS and **SEPTIC SHOCK**

- Step 6: **Take time to reconsider antibiotic coverage**
  - Have you identified a likely source?
  - Does the patient have an indwelling line?
  - Is there a history of resistant organisms?
- Step 7: **Continue to stabilize patient**
  - Start a pressor if indicated
    - Usual order: norepinephrine, then vasopressin, then debated

Basics of antibiotic selection
COMMUNITY-ACQUIRED

- CAP
  - Ceftriaxone with azithromycin +/- vancomycin +/- oseltamavir
    - Ceftriaxone for pneumococcus
    - Azithromycin for Legionella
    - Vancomycin a consideration if staphylococcal pneumonia possible
    - Oseltamavir during influenza season
- Urinary
  - Ceftriaxone
    - Ceftriaxone is effective against most enteric Gram-negatives and Gram-positives
- Meningitis
  - Ceftriaxone + vancomycin + acyclovir +/- ampicillin
    - Ampicillin added for *Listeria* coverage in elderly patients, alcoholics, etc.
- Abdominal
  - Ciprofloxacin + metronidazole *or*
  - Cefepime + vancomycin + metronidazole
    - Likely organisms include enteric Gram-negative rods, enteric Gram-positive cocci, anaerobic Gram-positive rods
- Soft tissue
  - Vancomycin +/- cefepime +/- clindamycin

Basics of antibiotic selection
HOSPITAL-ACQUIRED

- HCAP
  - Cefepime + vancomycin + metronidazole
    - Cefepime for *Pseudomonas* and other nosocomial Gram-negative infections
    - Vancomycin for MRSA
- Urinary
  - Cefepime + vancomycin
- Line
  - Cefepime + vancomycin

Other considerations in **HOSPITAL-ACQUIRED**

- History of recent VRE?
  - Consider linezolid or daptomycin (depending on source)
- Neutropenic?
  - Cefepime + tobramycin + vancomycin
- History of resistant Gram-negative?
  - Cefepime + tobramycin + vancomycin
- Risk factor for *Candida*?
  - Add micafungin to antibacterial coverage

Commonly affected organ systems in **SEPSIS**

- **CNS** – Altered mental status from confusion to coma
- **CV** – Sepsis-induced myocardial dysfunction and CHF
- **Respiratory** – ARDS, pulmonary edema
- **Liver** – Cholestasis of sepsis, ischemic hepatitis (so-called “shock liver”)
- **GI** – Ileus
- **Endo** – Hyperglycemia, relative adrenal insufficiency
- **Heme** – Thrombocytopenia, anemia

Resources / Reading

- Surviving Sepsis Guidelines: http://www.sccm.org/Documents/SSC-Guidelines.pdf
- The “Rivers” trial of early goal-directed therapy: http://www.nejm.org/doi/full/10.1056/NEJMoa010307
- UpToDate article about sepsis written by former UChicago faculty: http://www.uptodate.com/contents/evaluation-and-management-of-severe-sepsis-and-septic-shock-in-adults?detectedLanguage=en&source=search_result&search=sepsis&selectedTitle=2~150&provider=noProvider