Clinical Practice Guideline for Sepsis Treatment - Hospital and Clinic Settings

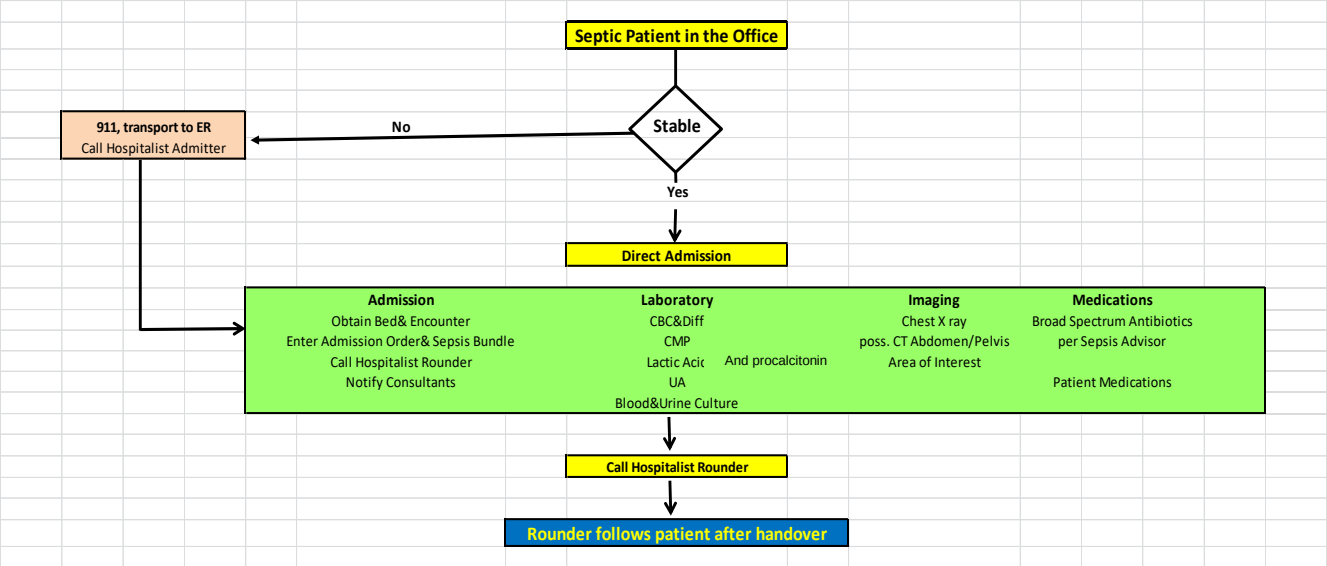
Sepsis is a serious, life-threatening rapidly progressive infection. The death rate can exceed 50% without rapid implementation of treatment protocols. The patient's outcome depends on the etiology of the infection and the swiftness with which medical interventions commence.

The guidelines set forth in this document outline the treatment protocol for patients in both the clinic and hospital setting. These guidelines are based upon the "Surviving Sepsis Campaign Guidelines" implemented as part of the Sepsis Initiative at Mercy One Hospital, Dubuque IA. The initiative incorporates elements of disease definition, intervention protocol, data collection, auditing all cases presenting with severe Sepsis and Septic Shock, feedback, and education.

Table 1: Defining Sepsis as a Disease Continuum

Infection/SIRS* →	**Sepsis** →	**Severe Sepsis**
Adult Criteria A clinical response arising from a non-specific insult, including ≥ two of the following: Temperature: > 38°C or < 36°C Cardiovascular, Heart Rate: > 90 beats/min Respiration: > 20/min WBC count: > 12,000/mm^3, or < 4,000/mm^3 or > 10% immature neutrophils	SIRS with a presumed or confirmed Infectious Process	Sepsis with ≥ 1 sign of organ dysfunction, hypo-perfusion, or hypotension. **Examples:** Renal, Respiratory Hepatic, CNS, Hematologic, unexplained Metabolic Acidosis

*SIRS = Systemic Inflammatory Response Syndrome
*Bone et al. Chest: 1992; 101:1644-1654*Figure 1 Workflow of Admission of septic patient from clinic



Sepsis Intervention for Clinic Setting:

1) Activate EMS (911).

2) Evaluate patient, address any immediate or life threatening issues.

3) Activate EMS again if necessary, especially for transport from West Campus to hospital.

4) Notify Mercy One Hospital house supervisor at #563-589-8300 to arrange for the encounter and a bed. (AKA Mercy Connect)

5) Re-evaluate patient, perform History and Physical.

6) Transport patient as soon as possible.

7) Enter orders (preferably in Cerner Powerchart), using Sepsis Bundle.

8) Notify hospital rounder of admission if the patient was admitted by their PCP in the clinic, and share pertinent clinical information. Notify the hospitalist admitter if rapid transport is required.

Sepsis Intervention for Hospital Setting : Goals

WITHIN 3 HOURS of Presentation:

1) Measure lactate level (order follow up, if lactic acid is elevated).

2) Obtain blood culture (aerobic and anaerobic) prior to administration of antibiotics.

3) Administer broad-spectrum antibiotics:

a. **Recommended as soon as possible** after recognition and within 1 hour:
b. **Empiric broad-spectrum therapy** with 1 or more antimicrobials to cover all likely pathogens (including bacterial, potentially fungal or viral) is recommended.
c. **Narrowing antimicrobial therapy** is recommended once pathogen is identified and sensitivities are established and/or adequate clinical improvement is noted.
d. **Empiric combination therapy** is suggested (using at least 2 antibiotics of different antimicrobial classes) aimed at the most likely bacterial pathogen(s) for the initial management of Septic Shock.
e. **If combination therapy is used for septic shock**, de-escalation is recommended with discontinuation of combination therapy within the first few days in response to clinical improvement and/or evidence of infection resolution. **This applies to both targeted** (for culture-positive infections) **and empiric** (for culture-negative infections) **combination therapy.**
f. **Antimicrobial treatment duration** of 7-10 days is suggested and adequate for most serious infections associated with Sepsis and Septic Shock.
g. **Longer courses are appropriate** and suggested in patients who have a slow clinical response, undrainable foci of infection, bacteremia with ***Staphylococcus aureus***, some fungal and viral infections, or immunologic deficiencies, including Neutropenia.
h. **Shorter courses are appropriate** and suggested in some patients, particularly those with rapid clinical resolution following effective source control of Intra-abdominal or Urinary Sepsis and those with anatomically uncomplicated Pyelonephritis.
i. **Daily assessment of de-escalation** is recommended of antimicrobial therapy.
j. **Measurement of Procalcitonin levels** is suggested to be used to support shortening the duration of antimicrobial therapy.
k. **Procalcitonin levels** is suggested to be used to support the discontinuation of empiric antibiotics in patients initially appeared to have sepsis, but subsequently have limited clinical evidence of infection.

NOT RECOMMENDED:

- **Sustained systemic antimicrobial prophylaxis** in patients with severe inflammatory states of noninfectious origin (e.g. severe Pancreatitis, Burn injury).
- **Combination therapy used for ongoing treatment** of most other serious infections, including Bacteremia and Sepsis without Shock. (This does not preclude the use of multidrug therapy to broaden antimicrobial activity.)

  Combination therapy for the routine treatment of Neutropenic Sepsis/Bacteremia. (This does not preclude the use of multidrug therapy to broaden antimicrobial activity.)

4) Administer bolus: 30 ml/kg Crystalloid for hypotension or a Lactate of > 4 mmol/L:

a. **Crystalloids are recommended and is the fluid of choice** for initial resuscitation and subsequent intravascular volume replacement.
b. **Balanced Crystalloids or Saline** for fluid resuscitation is suggested.
c. **Albumin in addition to Crystalloids** for initial resuscitation and subsequent intravascular volume replacement is suggested when patients require substantial amounts of Crystalloids.
d. **Crystalloids over gelatins** is suggested when resuscitating pts.

NOT RECOMMENDED:

- **Hydroxyethyl Starches** for intravascular volume replacement.

WITHIN 6 HOURS of Presentation:

5) Determine source of infection by imaging and laboratory (e.g., chest x-ray, CT abdomen/pelvis, urinalysis, blood culture (aerobic and anaerobic), etc).

6) Apply vasopressors (for hypotension that does not respond to fluid bolus) to maintain a mean arterial pressure (MAP) of 65 mm/Hg or greater. ***Norepinephrine is recommended and is first choice.***

a. Adding **Vasopressin (up to 0.03U/min)** or **Epinephrine** to **Norepinephrine** with the intent of raising MAP to target is suggested, or adding **Vasopressin** (up to 0.03U/min) to decrease **Norepinephrine** dosage.

b. Using **Dopamine** as an alternative vasopressor agent to **Norepinephrine** is suggested only in highly selected patients (e.g. pts with low risk of Tachyarrhythmias and absolute or relative Bradycardia).

c. Using **Dobutamine** is suggested in pts who show evidence of persistent Hypoperfusion despite adequate fld loading and the use of vasopressor agents. (If initiated, dosing should be titrated to an end point reflecting perfusion, and the agent reduced or discontinued in the face of worsening Hypotension or Arrhythmias.)

d. Patients requiring vasopressors is suggested to have an arterial catheter placed as soon as practical if resources are available.

NOT RECOMMENDED:

- Use of low dose **Dopamine** for renal protection.
- Use of **Sodium Bicarb** therapy to improve hemodynamics or to reduce vasopressor requirements in patients with hypoperfusion-induced Lactic Academia with pH $\geq$ 7.15.

7) Obtain central venous access (IJ catheter, subclavian catheter, or PICC line) in the event of persistent arterial Hypotension despite volume resuscitation (Septic Shock) or initial Lactate greater than 4 mmol/L.

- Measure **Central Venous Pressure (CVP)**
- Measure **Central Venous Oxygen saturation (ScVo2)-(more accurate than the CVP)**
- Prompt removal of intravascular access devices is recommended that are a possible source of Sepsis or Septic Shock after other vascular access has been established.

ONGOING MANAGEMENT:

8) If fluid resuscitation and vasopressors do not restore hemodynamic stability, use IV Hydrocortisone 200 mg/day.

9) Intubation/Ventilation recommended goals for tidal volume in adult patients with Sepsis-Induced Acute Respiratory Distress Syndrome (ARDS):

- **a. Using 6 ml/kg predicted body weight compared with 12ml/kg**.
- **b. Using an upper limit goal for plateau pressures of 30cm H_20 over higher plateau pressures.**
- **c.** Using **higher Positive End-Expiratory Pressure (PEEP)** is suggested over lower **PEEP**.
- **d.** Using recruitment maneuvers.
- **e.** Using prone over supine position and a **Pao_2/Fio_2 ratio < 150mm Hg**.
- **f. Using neuromuscular blocking agents is suggested for ≤ 48 hours and a Pao_2/Fio_2 ratio < 150mm Hg.**
- **g.** Conservative fld strategy on pts who don't have evidence of tissue perfusion.
- **h.** Using lower tidal volumes over higher tidal volumes is suggested in adult pts with Sepsis-Induced Respiratory Failure **without** ARDS.
- **i.** Mechanically ventilated Sepsis pts be maintained with the head of bed elevated between 30-45 degrees to limit aspiration risk and to prevent development of ventilator-associated pneumonia.
- **j.** Using spontaneous breathing trials in mechanically ventilated pts with Sepsis who are ready for weaning.
- **k.** Using a weaning protocol in mechanically ventilated pts who can tolerate weaning.
- **l.** Continuous or intermittent sedation be minimized in mechanically ventilated Sepsis pts, targeting specific titration endpoints.

NOT RECOMMENDED:

- High-frequency oscillatory ventilation.
- Use of **β-2 agonists** for the treatment of pts without bronchospasm.
- Routine use of the pulmonary artery catheter.

10) Target for glucose control is recommended with a protocolized approach:

- **a.** Commencing insulin dosing when 2 consecutive blood glucose levels are **> 180mg/dl**. This approach should target an upper blood glucose level **≤ 180mg/dl** rather than an upper target blood glucose level **≤ 110mg/dl**.
- **b.** Blood glucose values be monitored every 1-2 hours until glucose values and insulin infusion rates are stable, then every 4 hours thereafter in pts receiving insulin infusion.
- **c.** Glucose levels obtained with point-of-care testing in capillary blood be interpreted with caution because such measurements may not accurately estimate arterial blood or plasma glucose values.
- **d.** Use of arterial blood rather than capillary blood is suggested for point-of-care testing using glucose meters if pts have arterial catheters.

11. RBC transfusion is recommended to only occur when Hgb concentration decreased to <7.0g/dl in adults in the absence of extenuating circumstances such as Myocardial Ischemia, severe Hypoxemia, or acute Hemorrhage.

12. Prophylactic platelet transfusion is suggested when counts are <10,000/mm^3 (10x10^9/L) in the absence of apparent bleeding and when counts are <20,000/mm^3 (20x10^9/L) if the pt has significant risk of bleeding. Higher platelet counts (≥50,000/mm^3 [50x10^9/L] are advised for active bleeding, surgery, or invasive procedures.

NOT RECOMMENDED:

- Use of **Erythropoietin** for treatment of Anemia associated with Sepsis.
- Use of **fresh frozen plasma** to correct clotting abnormalities in the absence of bleeding or planned invasive procedures.
- Use of **IV Immunoglobulins.**
- Use of **Antithrombin.**

13. Continuous or intermittent renal replacement therapy (RRT) is suggested to be used in pts with Sepsis and Acute Kidney Injury (AKI):

a. Using continuous therapies to facilitate management of fld balance in hemodynamically unstable septic pts is suggested.

NOT RECOMMENDED:

- Use of RRT in pts with Sepsis and AKI for increase in Creatinine or Oliguria without other definitive indications for dialysis.

14. Venous Thromboembolism Prophylaxis recommendations:

a. Pharmacologic prophylaxis **(Unfractionated Heparin [UFH]** or **Low-Molecular-Weight Heparin [LMWH]** against **Venous Thromboembolism (VTE)** in the absence of contraindications to the use of these agents.

b. **LMWH** rather than **UFH** for **VTE** prophylaxis in the absence of contraindications to the use of **LMWH**.

c. Combination pharmacologic **VTE** prophylaxis and mechanical prophylaxis is suggested whenever possible.

d. Mechanical **VTE** prophylaxis is suggested when pharmacologic **VTE** is contraindicated.

15. Stress Ulcer Prophylaxis recommendations:

a. Be given to pts with Sepsis or Septic Shock who have risk factors for GI bleeding.
b. Use of **Proton Pump Inhibitors (PPIs)** or **Histamine-2 Receptor Antagonists** is suggested when stress ulcer prophylaxis is indicated.

NOT RECOMMENDED:

- Stress ulcer prophylaxis in pts without risk factors for GI bleeding.

16. Nutrition recommendations in critically ill pts with Sepsis or Septic Shock:

a. Early initiation of enteral feeding rather than a complete fast or only **IV Glucose** is suggested in pts who can be fed enterally.

b. Early trophic/hypocaloric or early full enteral feedings is suggested; if it is the initial strategy, then feeds should be advanced according to pt tolerance.

c. Measurement of gastric residuals in pts with feeding intolerance or who are considered to be at high risk of aspiration. (refers to nonsurgical critically ill pts with Sepsis or Septic Shock)

d. Use of **Prokinetic agents** in pts with a feeding intolerance.
e. Placement of post-pyloric feeding tubes in pts with feeding intolerances or who are considered to be at high risk of aspiration.

NOT RECOMMENDED:

- Administration of early parenteral nutrition alone or in combination with enteral feedings (but rather initiate early enteral nutrition) in pts who can be fed enterally.
- Administration of early parenteral nutrition alone or in combination with enteral feedings (but rather initiate **IV Glucose** and advance enteral feeds as tolerated) over the first 7 days in pts for whom early enteral feeding is not feasible.
- Use of **Omega-3 fatty acids** as an immune supplement.
- Routinely monitoring gastric residual volumes.
- Use of **IV Selenium** to treat sepsis and septic shock.
- Use of **Arginine** to treat sepsis and septic shock.
- Use of **Glutamine** to treat sepsis and septic shock.

17. Goals of care is suggested to be addressed as early as feasible, however no later than within 72 hours of ICU admission.

References:

http://www.nlm.nih.gov/medlineplus/ency/article/001355.htm, National Guideline Clearinghouse @ www.guideline.gov

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012 Critical Care Medicine 2013; 41: 580-637

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2016 Critical Care Medicine March 2017; Volume 45-Issue 3-pgs 381-385

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Chief Medical Officer — Date
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President, Board of Directors — Date
Medical Associates Clinic

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