Severe Sepsis and Septic Shock

A question and answer outline to facilitate early recognition and effective care of your patients

How can I identify a patient with severe sepsis with or without septic shock (“severe sepsis” in remainder of text)?

The patient should meet the following criteria:

- Have 2 or more criteria of the Systemic Inflammatory Response Syndrome (SIRS) within the last 24 hours (the criteria do not have to be present simultaneously):
  - Pulse rate > 90 beats/min
  - Respiratory rate > 20 breaths/min OR PaCO₂ < 32 mm Hg
  - Temperature > 38°C (100.4°F) OR < 36°C (96.8°F)
  - WBC > 12,000 OR < 4,000 OR > 10% bands

- AND

- SIRS has to be due to suspected OR confirmed infection (NOTE: your suspicion is enough at the early stage. You should not wait for culture results for a diagnosis to be made)

- AND 1 or more of the following
  - SBP < 90 mm Hg OR SBP drop > 40 mm Hg below patient’s usual value AND / OR blood lactate ≥ 4.0 mmol/l AND / OR new organ failure or dysfunction thought to be due sepsis (examples: worsening oxygenation or increasing oxygen needs; decreasing GCS; decreasing U/O or increasing serum Cr; dropping platelet count; increasing bilirubin)

What are the key priorities in the care of patients with severe sepsis?

1) Recognize that the patient has severe sepsis (make the diagnosis)
2) Identify as early as possible patients with overt shock or with occult hypoperfusion (those with the highest risk of death)
3) Provide emergent support of failing/dysfunctional organs (i.e., resuscitation of shock or of occult hypoperfusion; support of other organs)
4) Start appropriate antibiotics within 60 minutes of making a diagnosis of severe sepsis (with or without shock)
5) Provide timely source control of infection (e.g., debridement surgery for necrotizing fasciitis; laparotomy for bowel perforation)

What is occult hypoperfusion?

This term refers to presence of inadequate supply of oxygenated blood to meet the needs of body organs. The term “occult shock” has also been used occasionally to describe these patients. Patients with uncorrected occult hypoperfusion face very high risk of death. As the term implies, these patients may be more difficult to recognize based on physical exam alone (see more detail below).

Why are timely recognition and timely use of effective interventions so important in patients with severe sepsis?

1) Severe sepsis (with or without shock or occult hypoperfusion) is one the deadliest clinical conditions. It is estimated that 500 to 1000 patients die every day in the US due to severe sepsis and septic shock
2) Each 60 minutes of delay in the administration of appropriate antibiotics in these patients drops their survival by 7.6% (absolute rate) [1]
3) Giving patients with severe sepsis inappropriate antibiotics leads to about 10-fold increase in their odds of death [2] (thus, by the time you get microbiology test results, it may be too late for many of these patients)
4) Failure to achieve early successful correction of overt shock and/or occult hypoperfusion is associated with very high risk of death. For example, the death rate of patients with severe sepsis who remained in occult hypoperfusion after the first 6 hours of resuscitation was 56% in one of the landmark studies of this population [3]

Note: instituting timely and effective diagnostic and therapeutic interventions in patients with severe sepsis and/or septic shock is now part of the core measures monitored at Medical Center Hospital

What are the key barriers and challenges in assuring both timely and effective care of patients with severe sepsis?

Barriers due to knowledge gaps about severe sepsis

In a recent survey of physicians [4] it was found that: a) Only 17% agreed on any definition of sepsis b) Two thirds were concerned that a common definition is lacking and c) 83% felt that sepsis is likely to be missed frequently

Barriers due lack of timely recognition that a patient has severe sepsis (general)
In severe sepsis there are no signs, symptoms or diagnostic tests that are specific for this condition.

What are some of the barriers to timely recognition of systemic inflammation in patients with severe sepsis?

Absence of fever: patients can present with normal or reduced temperature

Absence of leucocytosis or “left shift”: patients can have normal WBC and no bandemia

Absence of tachycardia: patients may have normal pulse rate (e.g., use of beta blockers, pacemakers, intrinsic heart disease)

Thus, looking only for the typical “septic” patient may leave many other unrecognized and lead to delay of effective care and worse outcomes.

What are the barriers to timely recognition of occult hypoperfusion in severe sepsis and how they can be overcome?

Clinicians commonly rely on physical exam findings to judge about presence or absence of occult hypoperfusion. These findings usually include one or more of the following: low blood pressure, skin mottling, cold extremities or reduced capillary refill. Any of these signs may be associated with occult hypoperfusion as well as overt shock. However, these signs are not sensitive for presence of occult hypoperfusion. This means that the patient may “look good”, with none of these signs but still have significant occult hypoperfusion.[5, 6]. The bottom line: clinicians cannot accurately estimate who does or does not have occult hypoperfusion without actually testing for it. Even following resuscitation, patients may have persistent occult hypoperfusion while showing normal BP, CVP, and adequate urine output.

**Approach:** Checking blood lactate is the fastest and least invasive way to test patients for presence of occult hypoperfusion. In addition, knowing patient’s lactate is helpful for both prognosis and therapy: a) increased blood lactate above the upper limit of normal is associated with increased risk of death in direct relationship to lactate level [5] b) specific rates of decrease in blood lactate may serve as indicators of effective early resuscitation in patients with severe sepsis [7].

What are the barriers to effective circulatory resuscitation of patients with severe sepsis who have overt shock or occult hypoperfusion and how they can be overcome?

**Overreliance on past history (i.e., heart failure, ESRD) – concerns about causing pulmonary edema.** However, these patients can develop profound intravascular volume depletion during severe sepsis or septic shock (related in part to fluid leak from the microcirculation and profound vasodilation). Although some patients may develop pulmonary edema, ongoing hypoperfusion is by far more lethal [3].

**Approach:** Non-sepsis illness is an important consideration, but cannot reliably predict the circulatory state of patients with severe sepsis.

**Overreliance on nonspecific lab markers (e.g., BNP)** – these markers are not reliable indicators of intravascular volume state and ability to tolerate volume resuscitation in patients with severe sepsis.

**Approach:** Patients with elevated BNP, while having severe sepsis or septic shock can still have profoundly reduced effective circulating volume

**Use of ineffective methods for IV volume resuscitation** – a) use of hypotonic crystalloids (e.g., half NS) b) use of low rates of infusion: the maximal hourly rates of commonly used volumetric pumps (999 mL/h) are too slow; free flow of “wide open” IV bag may also be too slow with commonly used peripheral IV lines. c) utilizing one line/port at a time. **Approach:** a) use isotonic crystalloids (e.g., NS, LR) b) the initial fluid bolus should be 20-30 mL/kg – that would mean about 1500-2000 mL for a 70 kg patient c) use a dedicated resuscitation pump or in its absence a pressure bag (it takes only 6 minutes to complete 1 liter of normal saline via an 18 ga angiocath, with properly inflated pressure bag). In the absence of a pressure bag, you can improvise by directly squeezing the bag or wrapping a BP cuff around it. You should closely observe the patient to prevent air embolism when the fluid bag empties d) use more than one IV line/port to administer fluid resuscitation.

**Awaiting too long for initiation of vasopressors in patients with overt shock (or awaiting for the patient to be transferred from the ward to ICU to start pressors).** Slow titration of pressors once initiated. Capping pressors at dose rates not sufficient for patients with septic shock.

**Approach:** a) If the patient is persistently hypotensive (i.e., MAP < 65 mm Hg) start pressors while continuing IV volume resuscitation; it is usually clear within the first 10-15 minutes or less of properly administered IV fluid bolus, whether the blood pressure is properly increasing (although a central line is preferable for such drips, delay in start of carefully administered IV pressors can be lethal) b) levophed is more effective than dopamine and may be associated with better patient outcome [8] c) levophed and dopamine are very short-acting, thus can be titrated every 2-3 minutes if target BP has not been achieved promptly. Note: the duration of hypotension in septic shock is directly associated with mortality d) for ward patients, calling the Rapid Response Team can facilitate both timely start of pre-mixed levophed and facilitate timely transfer to the ICU e) the average dose of levophed reported in trials of patients with septic shock has been around 1 mcg/kg/min (i.e., 70 mcg/min in a 70 kg patient). Some patients require even higher doses; capping levophed at 30 mcg/min is not appropriate for these patients.

**Delays in placement of or lack of use of proper IV access.** **Approach:** Patients with overt septic shock or occult hypoperfusion can be managed more effectively with the use a central venous catheter. This is in part due to need to frequently assess the status of systemic perfusion (e.g., ScvO2, point-of-care lactates). Coagulopathy or thrombocytopenia do not require routine correction prior to placement of an ultrasound-guided central venous catheter.
Reliance only on vital signs and urine output (+/- CVP) to decide whether shock or occult hypoperfusion were resolved with resuscitation (see above). **Approach:** In addition to the resuscitation end-points just mentioned, patients with overt shock or occult hypoperfusion must have more direct evidence that hypoperfusion has resolved. The indicators commonly used at present include central venous oxygen saturation [3, 9] (or mixed venous oxygen saturation in patients with a pulmonary artery catheter in place) and blood lactate [7]. As noted above, the death rate of patients with severe sepsis who achieved MAP $\geq$ 65 mm Hg, CVP 8-12 mm Hg, and urine output $\geq$ 0.5 ml/kg/hour after the first 6 hours of resuscitation, but remained in occult hypoperfusion, was 56% [3].

What are the barriers to timely and effective antimicrobial therapy in patients with severe sepsis and how they can be overcome?

The barriers to timely administration of appropriate antibiotics are multi-factorial, involving most often the following: a) delays due to failure to recognize that the patient has severe sepsis b) delays due to ordering inappropriate antibiotics c) delays due to slow turnaround time from order writing to having the antibiotics at the bedside d) delays due to long intervals between antibiotics [10]. **Approach:** a) ongoing vigilance to identify patients with severe sepsis as early as possible (see above) b) use appropriate broad spectrum empiric antibiotics (see below) c) assuring effective communication with pharmacy, beyond submission of orders (for example, call personally right away) OR use appropriate antibiotics already stocked in your unit (e.g., in ED) c) use all available IV ports to administer more than one antibiotic at the same time. Initiate the next antibiotic right after the first was completed.

The barriers to use of appropriate antibiotics in patients with severe sepsis are commonly due to the following: a) failure to recognize that the patient has severe sepsis (as opposed to milder infection) b) lack of recognition that (specific) combination therapy reduces risk of death in severe sepsis, as opposed to monotherapy [10, 11] c) use of too narrow initial antibiotics d) lack of consideration of healthcare-associated infection (a different population than those with hospital-acquired infections) e) lack of consideration of possibility of non-bacterial pathogens in selected patients (e.g., fungi, viruses) d) lack of familiarity with local patterns of causative pathogens and their resistance trends. **Approach:** a) use combination empiric therapy in patients diagnosed with severe sepsis b) use available, infection site-specific, pathways of empiric antimicrobial therapy developed by local clinicians and pharmacy that adopt available clinical trial data and guidelines c) consider whether the patient may have risk factors for a healthcare-associated infection.

**References**

7. Jones AE, et al. JAMA 2010;303:739-746