Sepsis Guideline Updates
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Objectives

• Review the changes to the 2012 sepsis guidelines and the 2016 Sepsis Guidelines
• Discuss the literature impacting the sepsis guideline changes between 2012 and 2016
• Recognize the appropriate approach to treating a patient based on the updated sepsis guidelines

Definition of Sepsis

Guidelines 2012

Sepsis: Infection + 2 SIRS criteria:
  - Temp ≥38°C or ≤36°C
  - HR ≥90 bpm
  - RR ≥20/min or PaCO2 <32 mmHg
  - WBC ≥12k, ≤4k, or >10% bands

Severe Sepsis: Sepsis + organ dysfunction or tissue hypoperfusion

Septic Shock: Sepsis-induced hypotension persisting despite adequate fluid resuscitation

Guidelines 2016

• Sepsis: Life-threatening organ dysfunction ≥2 dysregulated responses to infection measured by ≥2 point increase in SOFA score
  - Quick SOFA for out of hospital, ED or ward, 2 or more of following:
    • RR ≥22/min
    • AMS
    • SBP ≤100 mmHg
• Septic Shock: subset of sepsis clinically identified by:
  - Vasopressor to maintain MAP ≥65 mmHg + lactate >2 mmol/L in absence of hypovolemia

Singer, M et al., Sepsis-3. JAMA 2016
Behind the Change

- 2012 definition:
  - Excessive focus on inflammation
  - Misdising sepsis continuum of severe sepsis to shock, severe sepsis redundant
  - Inadequate specificity and sensitivity of the SIRS criteria
  - Multiple definitions and terminologies for sepsis, septic shock and organ dysfunction lead to discrepancies in reported incidence and mortality


- Updated 2016 definition:
  - Should replace previous definition (CMS not yet updated)
  - Offer greater consistency for epidemiologic studies and trials
  - Facilitate earlier recognition and timely management of sepsis

Initial Resuscitation

Guidelines 2012

1. Protocolized, quantitative resuscitation of pt with sepsis induced tissue hypoperfusion persisting after initial fluid bolus or lactate ≥ 4 mmol/L.
   - Goals within 6 hrs:
     a) CVP 8-12 mm Hg
     b) MAP ≥ 65 mm Hg
     c) UOP ≥ 0.5 mL/kg/hr
     d) ScvO2 70% or Svo2 65% (grade 1c)
   - Target resuscitation to normalize lactate (grade 2c)

2. Target resuscitation to normalize lactate (grade 2c)

Guidelines 2016

1. Sepsis and septic shock are medical emergencies, treatment and resuscitation should begin immediately (BPS)
2. Resuscitation of sepsis-induced hypoperfusion with at least 30 mL/kg IV crystalloid within 3 hours (strong rec, low quality)
3. Following initial fluids, additional fluids guided by hemodynamic status (BPS)
4. Hemodynamic assessment to determine type of shock if exam doesn’t lead to clear diagnosis (BPS)
5. Dynamic over static variables be used to predict fluid responsiveness (weak rec, low quality)
6. Initial Target MAP of 65 mm Hg in septic shock requiring vasopressors (strong rec, moderate quality)
7. Target resuscitation to normalize lactate based on clinical judgment

Behind the Change

- Early effective fluid resuscitation is crucial for stabilization
- Early goal directed therapy using CVP and ScvO2 has not shown a mortality reduction, but is still safe and may be considered (B RTO)
- 30mL/kg average of crystalloid pre-randomization in PROCESS &ARISE trials
- Use of CVP or other static measurements alone no longer be justified. Dynamic measures have demonstrated better diagnostic accuracy
- Use of CVP, pulse pressure, and other static measurements alone no longer justified.
- No mortality benefit between initial MAP of 65 mm Hg vs 85 mm Hg
  - Previous studies of HTN higher MAP may reduce need for CRRT. Higher targets individualized after initial goal met
- A significant reduction in mortality was seen in lactate guided resuscitation of patients with septic shock. (B RTO)
Resuscitation Studies

- CVP and Svo2
- 30mL/Kg
  - PROCESS
  - ARISE
- Lactate Guided Resuscitation

Sepsis Screening & Performance Improvement

Guidelines 2012
1. Routine Screening of potentially infected, seriously ill patients for severe sepsis to allow early implementation of therapy (grade IC)
2. Hospital-based performance improvement efforts in severe sepsis (UG)

Guidelines 2016
1. We recommend that hospitals and hospital systems have a performance improvement program for sepsis, including screening for acutely ill, high-risk patients (BPS)

Behind the Change

- No tangible change between the guidelines
- Performance improvement efforts for sepsis are associated with improved patient outcomes
**Diagnosis**

**Guidelines 2012**

1. Cultures as clinically appropriate before antimicrobial therapy if no significant delay (>45min) in the start of antimicrobials (grade 1c). At least 2 sets of blood cultures (aerobic & anaerobic) be obtained with at least 1 drawn percutaneously and 1 through each vascular access device, unless device was recently inserted (<48hrs) (grade 1c).

2. Use of the 1,3-β-D-glucan assay (grade 2B), mannan and anti-mannan antibody assays (2c), if available, and invasive candidiasis in differential diagnosis of cause of infection.

3. Imaging studies performed promptly to confirm a potential source of infection.

**Guidelines 2016**

1. We recommend that appropriate routine microbiologic cultures (including blood) be obtained before starting antimicrobial therapy in patients with suspected sepsis or septic shock if doing so results in no substantial delay in the start of antimicrobials (BPS).

Remarks: Appropriate routine microbiologic cultures always include at least two sets of blood cultures (aerobic and anaerobic).

**Behind the Change**

- Sterilization of cultures can occur within minutes to hours after the first dose of an appropriate antimicrobial.
- “Pan culture” of all sites that could potentially be cultures should be discouraged (unless the source of sepsis is not clinically apparent), because this practice can lead to inappropriate antimicrobial use.
- Molecular diagnostic methods may offer the potential to diagnose infections more quickly and accurately. Clinical experience remains limited and requires additional validation.

**Antimicrobial Therapy**

**Guidelines 2012**

1. Administration of effective IV antibiotics within 1 hr of recognition of septic shock, if not contraindicated (grade 1).

2. 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).

3. Antimicrobial regimen should be reassessed daily for potential de-escalation (grade 1B).

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

**Guidelines 2016**

1. Administration of IV antibiotics initiated ASAP and within 1 hr of sepsis and septic shock (strong rec, mod quality).

2. Empiric broad-spectrum 1+ abx for pts with sepsis or septic shock to cover likely pathogens (bacterial + potential fungal/viral) (strong rec, mod quality).

6. Empiric combo tx (2+antibiotics of different classes) aimed at likely bacterial pathogen(s) for initial management of septic shock (weak rec, low quality).

3. Antimicrobial tx is narrowed once pathogen identification & sensitivities are established and/or adequate clinical improvement is noted (BPS).

7. Combo tx not be routinely used for ongoing tx of most other serious infections, including bacteremia & sepsis w/o shock (weak rec, low quality).

9. If combo therapy is used for septic shock, de-escalation w/ discontinuation of combination therapy within first few days in response to clinical improvement and/or evidence of infection resolution. Both targeted and empiric combination therapy (BPS).

Antimicrobial Therapy Cont...

Guidelines 2012

Procalcitonin

4. Use of low procalcitonin levels or similar biomarkers to support the decision to discontinue empiric antibiotics in patients who do not have evidence of infection (grade 2C).

Duration of treatment

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

Guidelines 2016

Procalcitonin

14. Measure of procalcitonin levels can be used to support shortened duration of antimicrobial therapy in sepsis patients (weak rec, low quality).

15. Procalcitonin levels can be used to support discontinuation of empiric antibiotics in patients who initially appeared septic, but subsequently have limited clinical evidence of infection (weak rec, low quality).

Duration of Treatment

10. Antimicrobial treatment duration of 7 to 10 days is adequate for most serious infections associated with sepsis & septic shock (weak rec, low quality).

11. Longer course appropriate in patients with slow clinical response, undrainable foci of infection, bacteremia with Staphylococcus aureus, some fungal & viral infections, or immune deficiencies, especially neutropenia (Weak rec, low quality).

12. Shorter courses appropriate in some, particularly those with rapid clinical resolution following effective source control of intra-abdominal or urinary sepsis and those with uncomplicated pyelonephritis (weak rec, low quality).

Antimicrobial Therapy Cont...

Guidelines 2012

Inflammatory States

9. Antimicrobial agents should not be used in patients with severe inflammatory states (grade 2B).

Neutropenia & MDR

5. 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 species (grade 2B). For patients with severe infections associated with respiratory failure and septic shock, combination therapy with an extended-spectrum β-lactam and either an aminoglycoside or a fluoroquinolone for Pseudomonas aeruginosa bacteremia (grade 2B). A combination of β-lactam and macrolide for patients with septic shock from bacteremic Staphylococcus pneumoniae infections (grade 2B).

Guidelines 2016

Inflammatory States

4. Against sustained systemic antimicrobial prophylaxis in patients with severe inflammatory states of noninfectious origin (e.g., severe pancreatitis, burn injury) (BPS).

Neutropenia & MDR

8. We recommend against combination therapy for the routine treatment of neutropenic sepsis/bacteremia (strong recommendation, moderate quality of evidence).

Dosing

5. We recommend that dosing strategies of antimicrobials be optimized based on accepted pharmacokinetic/pharmacodynamic principles and specific drug properties in patients with sepsis or septic shock (BPS).

Behind the Change

• Narrowing
  - Recent data suggest that some serious infection may be treated with shorter courses of antimicrobials if there is a need for good source control, prompt resolution of source control, and no prolonged fever.

• Dosing
  - Failure to achieve peak plasma targets on initial dosing has been associated with clinical failure in β-lactams.
  - Inadequate troughs in Vancomycin have been associated with clinical failure in MRSA.
  - β-Lactams have superior clinical and microbiologic cure with a longer duration of plasma concentration above pathogen MIC in ICU patients with sepsis or septic shock.

• Procalcitonin
  - More studies around use of procalcitonin in the ICU supporting its use for monitoring course of antimicrobials.


Source Control

Guidelines 2012
1. A specific anatomic diagnosis of infection requiring emergent source control should be identified or excluded as rapidly as possible, and intervention be undertaken for source control within the first 12 hours after the diagnosis is made, if feasible (grade 1C).

Guidelines 2016
1. Specific anatomic diagnosis of infection requiring emergent source control should be identified or excluded as rapidly as possible in patients with sepsis or septic shock, and that any required source control intervention should be implemented within 12 hours after the diagnosis is made (BPS).

2. Prompt removal of intravascular access devices that are a possible source of sepsis or septic shock after other vascular access has been established (BPS).

Fluid Therapy

Guidelines 2012
1. Crystalloids as the initial fluid of choice in the resuscitation of severe sepsis and septic shock (grade 1B).

Guidelines 2016
1. Crystalloids as the fluid of choice for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock (strong rec, moderate quality).

2. Balanced crystalloids or saline for fluid resuscitation of patients with sepsis or septic shock (weak rec, low quality).

3. Albumin in addition to crystalloids for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock, when patients require substantial amounts of crystalloids (weak rec, low quality).

4. Against using hydroxyethyl starches for intravascular volume replacement in patients with sepsis or septic shock (strong rec, high quality).

5. Using crystalloids over gelatins when resuscitating patients with sepsis or septic shock (weak rec, low quality).

Behind the Change

• Positive fluid balance: now evidence that sustained positive fluid balance is harmful.

• Chloride restrictive approach:
  - One before and after study on 31 ICU patients suggested increased rates of AKI and RIF in patients managed with chloride liberal strategy (AL) compared to chloride restrictive strategy (LR).

• Albumin:
  - SAFE study indicated that albumin administration was safe and equally effective as NS.
  - Several meta-analysis have shown conflicting evidence of benefit of albumin, thus making albumin a very weak recommendation for fluid resuscitation.
  - ALBIOS showed no mortality benefit of albumin in combo with crystalloids compared with crystalloids alone.

• HES:
  - No studies focusing on critically ill patients.
Vasoactive Medications

Guidelines 2012

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 with intent of either raising MAP or decreasing norepinephrine 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 (e.g., patients with low risk of tachyarrhythmias and absolute or relative bradycardia) (grade 2C).

Guidelines 2016

1. Norepinephrine as the first-choice vasopressor (strong rec, moderate quality).
2. Adding either vasopressin (up to 0.03 U/min) (weak rec, moderate quality) or epinephrine (weak rec, low quality) to norepinephrine with intent of raising MAP to target, or adding vasopressin (up to 0.03 U/min) to decrease norepinephrine dosage.
3. We suggest using dopamine as an alternative vasopressor agent to norepinephrine only in highly selected patients (e.g., patients with low risk of tachyarrhythmias and absolute or relative bradycardia) (weak rec, low quality).
4. We recommend against using low-dose dopamine for renal protection (strong recommendation, high quality of evidence).

Vasoactive Medications Cont...

Guidelines 2012

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).
10. A trial of dobutamine infusion up to 20 μg/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).
11. Not using a strategy to increase cardiac index to predetermined supranormal levels (grade 1B).

Guidelines 2016

5. Using dobutamine in patients who show evidence of persistent hypoperfusion despite adequate fluid loading and the use of vasopressor agents (weak rec, low quality). Remarks: 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.
6. We suggest that all patients requiring vasopressors have an arterial catheter placed as soon as practical if resources are available (weak recommendation, very low quality of evidence).

Behind the Change

- Vasopressin
  - Large studies lacking comparing vasopressin to other vasopressors in septic shock; most data in NE sparing effects; NE remains first line. Most robust study: VASST and those doses did not exceed 0.03U/min.
  - Advocates caution in doses greater than 0.03U/min.

- Dobutamine
  - First line inotrope for patients with measure or suspected low cardiac output in the presence of adequate left ventricular filling pressure. Monitor for decreasing lactate and improvement in ScvO2.

- Arterial Catheter
  - Arterial catheters more accurate and reproducible measurement and low risk of complication.
**Corticosteroids**

**Guidelines 2012**
1. Not using IV hydrocortisone to treat adult septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (goals for Initial Resuscitation). In case this is not achievable, we suggest IV hydrocortisone alone at a dose of 200 mg/day (grade 2C).
2. Not using the adrenocorticotropic hormone 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).

**Guidelines 2016**
1. We suggest against using IV hydrocortisone to treat septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability. If this is not achievable, we suggest IV hydrocortisone at a dose of 200 mg per day (weak recommendation, low quality of evidence).


**Blood Products**

**Guidelines 2012**
1. Once tissue hypoperfusion has resolved and in the absence of extenuating circumstances, such as myocardial ischemia, severe hypoxemia, acute hemorrhage, or ischemic heart disease, we recommend that RBC transfusion occur only when hemoglobin concentration decreases to < 7.0 g/dL to target a hemoglobin concentration of 7.0–9.0 g/dL in adults (grade 1B).
2. Not using erythropoietin as a specific treatment of anemia associated with severe sepsis (grade 1B).
3. Fresh frozen plasma not be used to correct laboratory clotting abnormalities in the absence of bleeding or planned invasive procedures (grade 2D).
5. In patients with severe sepsis, administer platelets prophylactically when counts are < 10,000/mm³ (10 × 10⁹/L) in the absence of apparent bleeding. We suggest prophylactic platelet transfusion when counts are < 20,000/mm³ (20 × 10⁹/L) if the patient has a significant risk of bleeding. Higher platelet counts (≥ 50,000/mm³ [50 × 10⁹/L]) are advised for active bleeding, surgery, or invasive procedures (grade 2D).

**Guidelines 2016**
1. We recommend that RBC transfusion occur only when hemoglobin concentration decreases to < 7.0 g/dL in adults in the absence of extenuating circumstances, such as myocardial ischemia, severe hypoxemia, or acute hemorrhage (strong recommendation, high quality of evidence).
3. Fresh frozen plasma not be used to correct clotting abnormalities in the absence of bleeding or planned invasive procedures (weak recommendation, very low quality).
4. We suggest prophylactic platelet transfusion when counts are < 10,000/mm³ (10 × 10⁹/L) in the absence of apparent bleeding and when counts are < 20,000/mm³ (20 × 10⁹/L) if the patient has a significant risk of bleeding. Higher platelet counts (≥ 50,000/mm³ [50 × 10⁹/L]) are advised for active bleeding, surgery, or invasive procedures (weak recommendation, very low quality of evidence).

*Antithrombin found in anticoagulant section—still not recommended*


**CRRT**

**Guidelines 2012**
1. Continuous renal replacement therapies and intermittent hemodialysis are equivalent in patients with severe sepsis and acute renal failure (grade 2B).
2. Use continuous therapies to facilitate management of fluid balance in hemodynamically unstable septic patients (grade 2D).

**Guidelines 2016**
1. We suggest that either continuous or intermittent CRRT be used in patients with severe sepsis and acute renal failure (weak recommendation, moderate quality of evidence).
2. We support the use of continuous therapies to facilitate management of fluid balance in hemodynamically unstable septic patients (grade 2D).

Stress Ulcer Prophylaxis

Guidelines 2012
1. Stress ulcer prophylaxis using histamine-2 blocker or proton pump inhibitor be given to patients with severe sepsis or septic shock who have bleeding risk factors (grade 1B).
2. When stress ulcer prophylaxis is used, proton pump inhibitors rather than histamine-2 receptor antagonists (grade 2D).
3. Patients without risk factors do not receive prophylaxis (grade 2B).

Guidelines 2016
1. We recommend that stress ulcer prophylaxis be given to patients with severe sepsis or septic shock who have risk factors for gastrointestinal (GI) bleeding (strong rec, low quality).
2. Use either proton pump inhibitors or histamine-2 receptor antagonists when stress ulcer prophylaxis is indicated (weak rec, low quality).
3. Do not use stress ulcer prophylaxis in patients without risk factors for GI bleeding (BPS).


Venous Thromboembolism Prophylaxis

Guidelines 2012
1. Patients with severe sepsis receive daily pharmacoprophylaxis against venous thromboembolism (VTE) (grade 1B). This should be accomplished with daily subcutaneous low-molecular-weight heparin (LMWH) (grade 1B versus twice daily unfractioned heparin [UFH], grade 2C versus three times daily UFH). If creatinine clearance is $< 30$ mL/min, use dalteparin (grade 1A) or another form of LMWH that has a low degree of renal metabolism (grade 2C) or UFH (grade 1A).
2. Patients with severe sepsis be treated with a combination of pharmacologic therapy and intermittent pneumatic compression devices whenever possible (grade 2C).
3. Septic patients who have a contraindication for heparin use (e.g., thrombocytopenia, severe coagulopathy, active bleeding, recent intracerebral hemorrhage) not receive pharmacoprophylaxis (grade 1B), but receive mechanical prophylactic treatment, such as graduated compression stockings or intermittent compression devices (grade 2C), unless contraindicated. When the risk decreases, start pharmacoprophylaxis (grade 2C).

Guidelines 2016
1. 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 (strong recommendation, moderate quality of evidence).
2. LMWH rather than UFH for VTE prophylaxis in the absence of contraindications to the use of LMWH (strong recommendation, moderate quality of evidence).
3. We suggest combination pharmacologic VTE prophylaxis and mechanical prophylaxis, whenever possible (weak recommendation, low quality of evidence).
4. We suggest mechanical VTE prophylaxis when pharmacologic VTE is contraindicated (weak recommendation, low quality of evidence).

Other Therapies

Guidelines 2012
IMMUNOGLOBULINS
• Not using IV immunoglobulins in adult pts w/ severe sepsis or septic shock (grade 2B).

BLOOD PURIFICATION
• Not applicable.

ANTICOAGULANTS
• Not applicable (found in Blood products section)

Guidelines 2016
IMMUNOGLOBULINS
• Not using IV immunoglobulins in adult pts w/ sepsis or septic shock (weak rec, low quality)

BLOOD PURIFICATION
• No recommendation regarding the use of blood purification techniques.

ANTICOAGULANTS
1. We recommend against the use of antithrombin for the treatment of sepsis and septic shock (strong recommendation, moderate quality of evidence).
2. We make no recommendation regarding the use of thrombomodulin or heparin for the treatment of sepsis or septic shock.
### Other Therapies

**Guidelines 2012**

**SEDATION**
- Aligns with the sedation and analgesia guidelines

**GLUCOSE**
- Aligns with the management of hyperglycemia guidelines in the ICU

**BICARBONATE**
- Not using sodium bicarbonate therapy for the purpose of improving hemodynamics or reducing vasopressor requirements in patients with hypoperfusion-induced lactic acidemia with pH $\geq 7.15$ (grade 2B).

**Guidelines 2016**

**SEDATION**
- Aligns with the sedation and analgesia guidelines

**GLUCOSE**
- We suggest the use of arterial blood rather than capillary blood for point-of-care testing using glucose meters if patients have arterial catheters (weak recommendation, low quality of evidence).

**BICARBONATE**
- Do not use sodium bicarbonate therapy to improve hemodynamics or to reduce vasopressor requirements in patients with hypoperfusion-induced lactic acidemia with pH $\geq 7.15$ (weak recommendation, moderate quality of evidence).

### Summary of Changes

- **Definition**
  - changed away from SIRS criteria to SOFA and QSOFA to allow for quick recognition and less focus on inflammatory response

- **Resuscitation strategies**
  - include more dynamic markers for end points
  - prevention of volume overload
  - lactate guided resuscitation
  - initial MAP goal of $\geq 65$ mmHg

- **Cultures**
  - guided cultures better than pan culture mentality
  - upcoming molecular diagnostics may impact guidance to therapy

### Nutrition

- Not addressed in this presentation.
Summary of Changes

- **Antimicrobials**
  - Emphasis on appropriate dosing strategies
  - Narrowing early to urgent specimens
  - Narrowing in setting of empiric coverage
  - Utilizing procalcitonin to guide duration of therapy

- **Fluid therapy**
  - Emphasis on balanced fluid vs chloride rich fluids to prevent AKI
  - HES not safe
  - Albumin no strong evidence for support
  - Positive fluid balance may be harmful

- **Vasopressors**
  - Vasopressin recommendation at 0.03u/min
  - Dobutamine and Scvo2
  - Arterial Catheter for BP monitoring

- **CRRT**
  - Risk outweigh benefit of using early in therapy without clear markers

- **SUP**
  - Infection risk from PPI allow for either H2RA or PPI use