Content Description

Sepsis continues to be a primary cause of death in our ICUs, yet opportunities to improve patient outcomes abound. This session provides an overview of the inflammatory response and pathophysiologic events in sepsis as the basis for early identification, use of new biomarkers, and early goal directed therapy. The Surviving Sepsis Campaign (SSC), initiated in 2002 has resulted in decreased mortality and in 2013 released updated guidelines. In addition, the Joint Commission has awarded their first sepsis disease specific certification, and recently the National Quality Forum has endorsed the sepsis bundles. This session will review the key principles of the SSC, protocols for sepsis prevention with an emphasis on the role of the critical care nurse.

Objectives:

1. Relate the pathophysiology of sepsis to the components of protocol driven, early goal directed management of sepsis.
2. Identify new updates to current recommendations in the SSC
3. Describe the impact of Joint Commission and National Quality Forum standards and other initiatives on sepsis diagnosis and management.

Pathophysiology of Sepsis: A Disease of The Microcirculation

“Lethal Traid” Systemic inflammation ↔ Coagulation ↔ Impaired fibrinolysis

Activation of the inflammatory response - Protection vs Destruction

Result:
→ Hypoperfusion, global tissue hypoxia
→ Organ dysfunction

Inflammatory Mediators and Biomarkers associated with SIRS, Sepsis and Septic Shock

- Tumor Necrosis Factor alpha (TNFa)
- Interleukins (IL-1, IL-6, IL-10)
- C-Reactive Protein
- Procalcitonin
The Continuum: SIRS to Septic Shock

SIRS – CARS – MODS - PICS

Definitions and Classification

**SIRS** (≥ 2 criteria)
- T ≥ 38.3°C or ≤ 36°C
- HR > 90bpm
- RR > 20 breaths/min
- WBC > 12K or < 4K

**Sepsis**
- ≥ 2 SIRS criteria
- Plus confirmed or suspected infection

**Severe Sepsis**
- Sepsis plus ≥ 1 organ dysfunction

**Septic Shock**
- Sepsis plus hypotension despite fluid
- Plus perfusion abnormalities
- Plus MODS (>1 organ failure, inability to maintain homeostasis w/o tx)

Clinical Manifestations and Organ Response to Sepsis

Early Phase/SIRS

Progressive Phase

Late Phase

Protocols To Manage And Prevent Sepsis/Septic Shock

Where it all started: Early Goal Directed Therapy (EGDT™) Rivers, et al. 2001 NEJM 345:1368-1377
Objective: Assure Adequate Perfusion & Oxygenation

Updated Surviving Sepsis Guidelines (2013)

http://www.survivingsepsis.org/Bundles/Pages/default.aspx, accessed 1-7-13
Initial Resuscitation
Protocolized, quantitative resuscitation of patients with sepsis-induced tissue hypoperfusion (defined as hypotension persisting after initial fluid challenge or blood lactate concentration ≥ 4 mmol/L)

Resuscitation Bundle

- Serum lactate on admission and serial evaluation
- 2 blood cultures (1 percutaneous) within 45 mins & prior to antibiotics (1C)
- Antibiotics within the 1st hour of recognition (1B)
- Hypotension/Lactate >4
  - Keep MAP >65 mmHg
    - Fluid Therapy
      - Crystalloids ≥ 1L, administer as boluses;
        - achieve ≥ 30 ml/kg in 4-6 hrs
        - use goals as end points (1B)
      - Continue fluid boluses based on improvement in dynamic hemodynamic parameters:
        - PPV, SVV, MAP, HR (1C)
    - Norepinephrine, 1st choice of pressors (1B)
    - Dobutamine for high cardiac filling pressures or low cardiac output (1C)
- PRBC to maintain Hgb ≥ 7.0 (1B)

Goals during the first 6 hrs of resuscitation (grade 1C):
  a) CVP 8–12 mm Hg
  b) MAP ≥ 65 mm Hg
  c) Urine output ≥ 0.5 mL/kg/hr
  d) ScvO2 70%

- SCCM 2010 Abstract (Maxwell, et al): achievement of continuous venous oximetry ≥70% in sepsis bundle associated with reduced cost, LOS and mortality in 111 septic patients.

- ScvO2 as a predictor of mortality in patients with sepsis:
  Hypoxia = ScvO2 < 70% Mortality 40%
  Hyperoxia = ScvO2 >90% Mortality 34%

Discuss goals of care, and prognosis for achieving the goal with family (1B)
  – As early as possible, not later than 72 hrs after admission. (2C)

Performance improvement efforts should be employed to improve outcomes (1C)
Impact of interdisciplinary protocol driven sepsis management and EGDT on patient outcomes

  Odds Ratio of Survival: 1.91, p<0.0001 favors use of sepsis bundles

- Surviving Sepsis Campaign results (SCCM 2012)
  4 year follow up Final n= 28,150
  > 250 sites, >18 countries contributed data
  Overall bundle compliance = 30%
  Morality reductions:
  12 % Absolute Risk Reduction 38% → 26.1%  p<.001
  25 % Relative Risk Reduction  p<.005
  Potential: If 10,000 Hospitals participate, we will save 400,000 lives

SSC: Phase IV

- Collaboration with IHI, NQF, & CDC
- New data collection tool and database
- New website *www.survingsepsis.org*

National Quality Forum Endorses SSC Bundle: SCCM/IDSA support adoption

*NQF, National Voluntary Consensus Standards: Infectious Disease Endorsement Maintenance 2012, Addendum Report  October 22, 2012*

“This measure will focus on patients aged 18 years and older who present with symptoms of severe sepsis or septic shock. These patients will be eligible for the 3 hour (severe sepsis) and/or 6 hour (septic shock) early management bundle. “

NQF Proposed Measures
1. Measure lactate level
2. Obtain blood cultures prior to antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30 ml/kg crystalloid for hypotension or lactate >=4 mmol/L
5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation
6. to maintain a mean arterial pressure >= 65)
7. In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate >=4 mmol/L (36 mg/dl) measure CVP and ScvO2
9. Remeasure lactate if initial lactate is elevated

Sean Thompson, MD, SSC-SSG Committee, SCCM 1/13 paraphrased, “There is interest at HHS/CMS re: the NQF measures. CMS is sponsoring conversion of “0500” (the code for SSG measure set) into EHR Standards.”

"Rory's Regulations,"
New York State is the first state to require all hospitals to adopt best practices for the early identification and treatment of sepsis. January 29, 2013
PREVENTION, PREVENTION, PREVENTION

The Joint Commission Standards:

NPSG: Comply with either the current CDC hand hygiene guidelines.

NPSG: Implement evidence-based practices to prevent health care–associated infections due to multidrug-resistant organisms.

NPSG: Implement evidence-based practices to prevent central line–associated bloodstream infections.
  - Use a catheter checklist and a standardized protocol for central venous catheter insertion.
  - For adult patients, do not insert catheters into the femoral vein unless other sites are unavailable.
  - Use a standardized supply cart or kit that contains all necessary components for the insertion
  - Use a standardized protocol for sterile barrier precautions, to disinfect catheter hubs and injection ports

CLABSI Prevention Protocols (CDC, 4-11)

NPSG: Implement evidence-based practices for preventing surgical site infections.

NPSG: Implement evidence-based practices to prevent indwelling catheter-associated urinary tract infections (CAUTI).

UTI-Prevention Bundle (CDC, 1-09)
Urinary Catheter Removal Protocol

SUMMARY
References

1. AACN Sepsis Practice Alert 4-10, aacn.org
Self Assessment Questions

Which of the following describes the role of endothelial cells in the pathogenesis of septic shock?
   A. Release of nitric oxide producing vasodilation
   B. Disruption of endothelial cell junctions resulting in increased vascular permeability
   C. Disruption of endothelial cells resulting in the activation of the coagulation cascade
   D. All of the above.

Use of early goal directed therapy sepsis bundles help to assure:
   A. Antibiotic administration within an hour of detection
   B. ScvO2 monitoring initiated to evaluate global tissue oxygenation
   C. Intravascular volume is optimized prior to vasopressor administration
   D. All of the above.

A primary focus of The Joint Commission National Patient Safety goals is to:
   A. Improve patient outcomes
   B. Reduce hospital acquired infections
   C. Improve use of evidence-based practices
   D. All of the above
APPENDIX: Surviving Sepsis Guidelines 2012


Diagnosis
1. Cultures before antimicrobial therapy (> 45 mins) (grade 1C).
   At least 2 sets of blood cultures (both aerobic and anaerobic bottles) 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).

Antimicrobial Therapy
1. Administration of effective IV antimicrobials within the first hour of recognition of septic shock (grade 1B) and severe sepsis without septic shock (grade 1C)
2a. Initial empiric anti-infective therapy of one or more drugs that have activity against all likely and that penetrate into tissues presumed to be the source of sepsis (grade 1B).
2b. Antimicrobial regimen should be reassessed daily for potential de-escalation (grade 1B).
3. Use of low procalcitonin levels or similar biomarkers to assist in the discontinuation of empiric antibiotics in patients who initially appeared septic, but have no subsequent evidence of infection (grade 2C).

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 (grade 1B).
3. Albumin in the fluid resuscitation when patients require substantial amounts of crystalloids (grade 2C).
4. Initial fluid challenge in patients with sepsis-induced tissue hypoperfusion to achieve a minimum of 30 mL/kg of crystalloids (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 PPV, SVV) or static (eg, MAP, HR) variables (UG).

Vasopressors
1. Vasopressor therapy initially to target a MAP 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 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 except in circumstances where (a) norepinephrine is associated with serious arrhythmias, (b) CO is known to be high and BP 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 (UG).

Inotropic Therapy
1. A trial of dobutamine up to 20 micrograms/kg/min be administered in the presence of (a) myocardial dysfunction as suggested by elevated cardiac filling pressures and low CO, 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).

Corticosteroids
1. Not using IV hydrocortisone if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (see goals for Initial Resuscitation). In case this is not achievable, suggest IV hydrocortisone alone at a dose of 200 mg per day (grade 2C).
2. Not using the ACTH stimulation test to identify who should receive hydrocortisone (grade 2B).

Blood Product Administration
1. Once tissue hypoperfusion has resolved and in the absence of extenuating circumstances, such as MI, ischemia, severe hypoxemia, acute hemorrhage, or ischemic heart disease, 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 (grade 1B).

Mechanical Ventilation of Sepsis-Induced Acute Respiratory Distress Syndrome (ARDS)
1. Target a tidal volume of 6 mL/kg predicted body weight in patients with sepsis-induced ARDS (grade 1A vs. 12 mL/kg).
2. Plateau pressures be measured in patients with ARDS and initial upper limit goal for plateau pressures in a passively inflated lung be ≤30 cm H2O (grade 1B).
Sedation, Analgesia, and Neuromuscular Blockade in Sepsis
1. Continuous or intermittent sedation be minimized in mechanically ventilated sepsis patients, targeting specific titration endpoints (grade 1B).
2. NMBAs be avoided if possible in the septic patient without ARDS. (grade 1C).

Glucose Control
1. A protocolized approach to blood glucose management in ICU patients commencing insulin dosing when 2 consecutive blood glucose levels are >180 mg/dL. This target an upper blood glucose ≤180 mg/dL rather than an upper target blood glucose ≤110 mg/dL (grade 1A).
2. Blood glucose values be monitored every 1–2 hrs until glucose values and insulin infusion rates are stable and then every 4 hrs thereafter (grade 1C).
3. Glucose levels obtained with point-of-care testing of capillary blood be interpreted with caution, as such measurements may not accurately estimate arterial blood or plasma glucose values (UG).

Renal Replacement Therapy
1. CRRT and intermittent hemodialysis are equivalent with severe sepsis and acute renal failure (grade 2B).
2. Use CRRT to facilitate management of fluid balance in hemodynamically unstable septic patients (grade 2D).

Bicarbonate Therapy
1. Not using sodium bicarbonate therapy for the purpose of improving hemodynamics or reducing vasopressor requirements in patients with hypoperfusion-induced lactic acidemia with pH ≥7.15 (grade 2B).

Deep Vein Thrombosis Prophylaxis
1. Patients with severe sepsis receive daily pharmacoprophylaxis against venous thromboembolism (VTE) (grade 1B). This should be accomplished with LMWH (grade 1B).
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 receive mechanical prophylactic treatment, such as graduated compression stockings or intermittent compression devices (grade 2C), unless contraindicated

Stress Ulcer Prophylaxis
1. Stress ulcer prophylaxis using H2 blocker or proton pump inhibitor be given to patients with severe sepsis/septic shock who have bleeding risk factors (grade 1B).
2. When stress ulcer prophylaxis is used, proton pump inhibitors rather than H2RA (grade 2D)
3. Patients without risk factors do not receive prophylaxis (grade 2B).

Nutrition
1. Administer oral or enteral (if necessary) feedings, as tolerated, rather than either complete fasting or provision of only intravenous glucose within the first 48 hours after a diagnosis of severe sepsis/septic shock (grade 2C).
2. Avoid mandatory full caloric feeding in the first week but rather suggest low dose feeding (eg, up to 500 calories