POLICY AND PROCEDURE
ADULT SEVERE SEPSIS AND SEPTIC SHOCK MANAGEMENT

SUBJECT:

Guidelines for the management of Severe Sepsis and Septic Shock at Shands UF

PURPOSE:

Sepsis is recognized as a challenging disease to overcome. The progression of sepsis to severe sepsis and septic shock is devastating yielding a mortality of 30-80%.[1]
In an effort to reduce the morbidity and mortality from sepsis, Shands University of Florida Hospital has committed to identify and implement "bundles." Bundles are a series of maneuvers that when applied concurrently have been shown to impact on outcome. The sepsis bundles are developed from evidence based therapies shown to improve patient outcomes.[2 3 4] The following bundles are designed to cater to the specific needs of our patient population.
As you manage these patients, and implement these bundles, it is important that communication occur amongst all members of the patient care team in order to ensure patient safety.

Sepsis exists as a continuum which progresses from signs of inflammation to fulminant shock. These guidelines serve as evidence and rationale for treatment bundles described on the Sepsis order sets.

KEY REFERENCES: (see end of document):

Rivers E, Nguyen B, Havstad S et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001 345: pp 1368-1377.
Dellinger RP. Cardiovascular management of septic shock. *Crit Care Med*. 2003;31(3):946-955.
Dellinger RP, Levy MM, Carlet JM, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med. 2008;36:296-327.
Dellinger RP, Carlet JM, Masur H, et al. Surviving sepsis campaign guidelines for management of severe sepsis and septic shock. *Crit Care Med*. 2004;32(3):858-873.
Trzeciak S, Dellinger R, Abate N et al. Translating Research into Clinical Practice. Chest 2006;129:225-232.
Shapiro N, Howell M, Talmor D. A Blueprint for a Sepsis Protocol. Academic Emergency Medicine 2005; 12:332-359.

RESPONSIBILITY:

The Directors for Patient Care Services are responsible to ensure compliance with the policy.

The Directors of Patient Care Services, Patient Care Coordinators and Nurse Manager/designee are responsible for monitoring and evaluating compliance with this policy. The Nurse Educators are responsible for educating staff in the use of the order sets and guidelines. The Registered Nurse is responsible to comply with this policy and procedure.

DEFINITIONS:

Sepsis: The existence of 2 or more Systemic Inflammatory Response Syndrome **SIRS** criteria:

1. Heart Rate >90 beats/minute
   NOTE patients on beta blockers may not present with tachycardia
2. Respiratory Rate >24 breaths/minute or pCO2<32 mmHg
3. WBC >12,000 cells/mm^3, < 4,000 cells/mm^3, or bands >10%
4. Temperature >38°C/100.9°F or <36°C/96.8°F

PLUS

A known or suspected source of infection [5 6 7]

Severe Sepsis: Sepsis state with one of the following

- Lactate >4
- Acute Sign of at least one end organ damage (the following are examples)
  - Neurological
    - altered mental status
    - Coma
    - Agitation
    - Lethargy
    - Stupor
  - Respiratory
    - hypoxia O2 Sat <92% on room air
    - bilateral diffuse infiltrates consistent with ARDS
  - Cardiac
    - poor capillary refill exhibited by mottling
    - Acute ischemic changes on EKG
    - Pulmonary edema
    - Elevated troponin
  - Hepatobiliary
    - acute elevations in liver enzymes
    - Skin changes consistent with DIC
    - Elevated coagulation tests

- Elevated lactate
- Renal
  - decreased urine output <0.5 ml/kg/hour
  - Acute elevations in creatinine by >0.5 from baseline

Septic Shock: Sepsis state with an SBP $\leq$ 90mmHg refractory to a 20ml/kg fluid bolus challenge[8]

Patients targeted by the bundles are those in severe sepsis or septic shock

Please review the following exclusion criteria in your patient before initiating the protocol as they may be placed at increased risk. Seek appropriate consultation to ensure patient safety.

EXCLUSION CRITERIA:

Absolute

Age less than 18
Pregnancy
Advanced directives restricting implementation of the protocol

Relative

Presence of an acute cerebrovascular event
Acute coronary syndrome
Acute pulmonary edema
Status asthmaticus
Cardiac dysrhythmia (primary diagnosis)
Contraindication to central venous catheterization
Active gastrointestinal hemorrhage
Seizure
Drug overdose
Burn injury
Trauma
Requirement for immediate surgery
History of recent organ Transplantation
In order to identify these patients early, all patients requiring blood cultures, should have a lactate level drawn[9]. Once identified maneuvers should be implemented as follows:

6 HOUR BUNDLE

Diagnostic Workup

1. Within 1 hour:
   a. Obtain the following lab work: CBCD, BMP, LFTs, CK, CK-MB, troponin I, PT/PTT/INR, urine analysis, type and screen, arterial/venous blood gas with electrolytes and lactate level. CXR, EKG

b. Blood culture (two sets from sterile site) and from indwelling vascular access, urine culture, sputum culture (if intubated)
c. ScvO2 . This level is obtained by drawing a venous blood gas from the central venous line (subclavian or internal jugular vein) if an oximetric catheter is not used

2. Drawn every 3 hours:
    a. ScvO2 drawn from the central venous line (subclavian or internal jugular vein) if an oximetric catheter is not used
3. Drawn every 6 hours:
    a. CBC, BMP, lactate, and arterial blood gas
    b. consider repeating troponin, PT/PTT if the clinical scenario suggests progressive hypoperfusion or persistent shock

<u>Hemodynamic Monitoring within 2 hours</u>

1. Cardiac Monitoring
2. Central Venous Pressure Monitoring- CVP measurements should be obtained from the subclavian or internal jugular vein . *Placement of the central line should be performed by an experienced clinician)*
    a. Ultrasound guided placement is recommended when available
    b. Radiographic confirmation is required prior to use of the line.

3. ScvO2- Central venous oxygen saturation monitoring
    a. ScvO2 continuous monitoring utilizing the central venous oximetric catheter OR
    b. Intermittent measurements via blood gas draws from CVP line

4. Intra-arterial catheterization

5. Foley catheter placement with temperature sensor if available

DIAGNOSIS of INFECTION and SOURCE CONTROL:

1. In the event of an unknown source in the acute or chronically altered patient, consider performing a head CT and lumbar puncture.
2. If the clinical assessment or physical exam is unreliable perform a CT of the chest, abdomen and pelvis to expedite the identification of an infectious source. [10]
3. A diligent and global skin exam, inclusive of the digits and perineal area, is compulsory as the presence of cellulitis, fascitis, bullae, or ulcerative lesions may be diagnostic.

THERAPEUTIC GOALS

<u>Therapeutic Goals within 1 Hour</u>

Initiate broad spectrum antibiotic administration[11] [12] [13] (Refer to empiric antibiotic recommendations attached)

Therapeutic Goals within 6 Hours

Central Venous Pressure (preload)
GOAL: CVP should be maintained >8 mmHg[14] [15] [16]

1. CVP < 8mmHg:
    a. administer 1000ml crystalloid or 300-500 ml colloid bolus over 15- 30 minutes every 15-30 minutes until CVP 8-12 mmHg achieved
    b. maintenance fluids may be administered at 125 ml/hr once goal CVP achieved
2. CVP <4 mmHg and patient has a hemoglobin <8 mmHg.
    a. Consider transfusing packed red blood cells
    b. Refer to item 1

Special Considerations

- Patients that are intubated and/or require PEEP may have artificially elevated CVP. Target a higher CVP in these patients of 12-15 mmHg.
- If CVP >8mmHg. Proceed to Mean Arterial Pressure Goal

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Mean arterial pressure (afterload)
GOAL: MAP should be maintained >65mm Hg or systolic blood pressure SBP >90mmHg[14]

1. MAP<65mmHg or SBP <90mmHg despite fluid challenge of 20ml/kg or 2L crystalloid OR CVP >8mmHg
    a. Initiate vasopressor therapy[17]
        i. The preferred route of administration is via central venous access
        ii. Begin with one vasopressor and titrate until goal has been achieved.
    b. Administer additional vasopressors in the following order if initial vasopressor is ineffective in achieving goal:
        i. Norepinephrine 2-20 mcg/min (preferred first line in sepsis)[18]
        ii. Dopamine 5-20mcg/kg/min
        iii. Phenylephrine 40-200 mcg/min (preferred for HR>120)
        iv. Vasopressin 0.01U-0.03U/min (must be administered in conjunction with at least one other vasopressor)[19] [20] [21]
        v. Epinephrine 2-10 mcg/min

2. Treat for presumed adrenal insufficiency in the event of pressor resistant hypotension[22] [23] [24] [25] [26] [27] [28] [29] [30]
    a. Administer Hydrocortisone 50 mg IV
3. Patients previously on chronic steroids should remain on steroid therapy

Central venous oxygen saturation – contractility and oxygen content
GOAL- maintain ScvO2 >70% [14] (if PA catheter used GOAL SVO2>65%)

1. ScvO2<70% after above therapies AND Hb <10gm/dl [10 31]
    a. Transfuse packed red blood cells to a Hb ≥10gm/dl or an ScvO2 >70%
2. ScvO2<70% after above therapies AND Hb ≥10 gm/dl
    a. Administer Dobutamine 2.5-20mcg/kg/min titrated to an ScvO2≥70%[32]
        i. Caution when administering to a patient with MAP <70mmHg or SBP <100mmHg; dobutamine is associated with hypotension
        ii. Caution when administering to a patient with HR > 120; dobutamine is associated with tachycardia
    b. Airway protection/respiratory distress
        i. consider intubation to reduce work of breathing
    c. Agitation/Pain[33]
        i. consider sedation utilize short acting agents such as versed
        ii. consider analgesia; utilize short acting agents such as fentanyl
    d. Hyperthermia/Fever
        i. consider antipyretic agents
        ii. consider cooling blanket

Return to each of the above steps and ensure all goals have been met
Goals are

1. **CVP 8-12 mmHg (target higher in intubated patients)**
2. **MAP >65 mmHg or SBP >90mmHg**
3. **ScvO2>70%**

Obtain intensive care consult for transfer to the ICU

ADDITIONAL CONSIDERATIONS

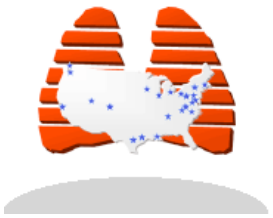
1. Hemodynamic Optimization
    a. Goal Directed Therapy should be maintained keeping
        i. CVP >8mmHg
        ii. MAP > 65mmHg or SBP > 90mmHg
        iii. ScvO2 ≥ 70% (or SVO2≥65% when a PA catheter is used)
2. Glycemic Control[34 35 36]
    a. Maintain normoglycemia with dextrosticks 80-150 mg/dl
    b. initiate insulin by intravenous route or continous drip for glucose >180 mg/dl[37]
3. Relative Adrenal Insufficiency
        i. Suspected adrenal insufficiency should be treated with hydrocortisone 50mg IV q6

4. APACHE score calculation
    a. APACHE score ≥25
        i. Xigris is recommended in severe sepsis or septic shock patients in whom contraindications do not exist with a score ≥ 25[38 39 40 41 4243 44]
    b. If score <25 re-calculate APACHE score in 24 hours
5. GI prophylaxis
    a. GI Prophylaxis should be administered to all patients in severe sepsis or septic shock
        i. Administer one of the following:
            1. H2 Blocker (ie zantac) OR
            2. PPI (ie nexxium) OR
            3. Sucralfate
6. DVT prophylaxis
    a. DVT prophylaxis should be administered to all patients in severe sepsis or septic shock.
        i. Administer one of the following:
            1. Low molecular weight heparin (ie Lovenox) (use unfractionated heparin in renal failure) OR
            2. Compression boots
7. Screen for ALI/ARDS Criteria
    a. PaO2/FiO2 ≤ 300
    b. Bilateral patchy, diffuse, or homogeneous infiltrates on Chest radiograph
    c. No clinical evidence of left atrial hypertension

8. Patients with evidence of acute lung injury or acute respiratory distress syndrome ALI/ARDS should have the following initiated (log on to www.ardsnet.org for details or see addendum):[45 46 47]
    a. Mechanical ventilation
    b. Low tidal volume (6 cc/kg of predicted body weight)
    c. Judicious use of PEEP/FiO2 to maintain SaO2 88-95% or PaO2 55-80 mmHg
    d. Head of bed >30 degrees
9. Laboratory tests should be drawn q6 hours including CBC, BMP, ABG, lactate [48]
10. Cultures[49]
    a. Additional
    b. sputum culture via BAL or combocath performed by respiratory

therapy[50]

11. Administer appropriate antibiotics once the infectious etiology has been identified
    a. Refer to the suggested empiric antibiotic guideline
    b. Narrow the selection of antibiotics to sensitivity once the organism is identified
12. Consultations
    a. Obtain prompt consultations from surgery and/or interventional radiology for the purpose of source control (ie intra-abdominal abscess)
    b. Consider consultation by infectious disease
        i. If source is unknown after 24 hours
        ii. If non-surgical septic patient requires >1 dose of imipinem
        iii. If patient does not improve after 24-48 hours of therapy
13. HIV testing: if the patient is able to consent, the HIV team should be consulted for a rapid HIV test



ARDSNET

NIH NHLBI ARDS Clinical Network
Mechanical Ventilation Protocol Summary
www.ardsnet.org

INCLUSION CRITERIA: Acute onset of
1. PaO2/FiO2 ≤ 300 (corrected for altitude)
2. Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
3. No clinical evidence of left atrial hypertension

PART I: VENTILATOR SETUP AND ADJUSTMENT
1. Calculate predicted body weight (PBW)
Males = 50 + 2.3 [height (inches) - 60]
Females = 45.5 + 2.3 [height (inches) -60]
2. Select Assist Control Mode
3. Set initial TV to 8 ml/kg PBW
4. Reduce TV by 1 ml/kg at intervals ≤ 2 hours until TV = 6ml/kg PBW.
5. Set initial rate to approximate baseline VE (not > 35 bpm).
6. Adjust TV and RR to achieve pH and plateau pressure goals below.
7. Set inspiratory flow rate above patient demand (usually > 80L/min)

OXYGENATION GOAL: PaO2 55-80 mmHg or SpO2 88-95%
Use incremental FiO2/PEEP combinations below to achieve goal

FiO2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO2	0.7	0.8	0.9	0.9	0.9	1.0	1.0	1.0
PEEP	14	14	14	16	18	20	22	24

PLATEAU PRESSURE GOAL: ≤ 30 cm H2O
Check Pplat (0.5 second inspiratory pause), SpO2, Total RR, TV and pH (if available) at least q 4h and after each change in PEEP or TV.

If Pplat > 30 cm H2O: decrease TV by 1 ml/kg steps (minimum = 4 ml/kg).
If Pplat < 25 cm H2O: TV < 6 ml/kg, increase TV by 1 ml/kg until Pplat > 25 cm H2O or TV = 6 ml/kg.
If Pplat < 30 and breath stacking occurs: may increase TV in 1 ml/kg increments (maximum = 8 ml/kg).

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pH GOAL: 7.30-7.45
Acidosis Management: (pH < 7.30)
If pH 7.15-7.30: Increase RR until pH > 7.30 or PaCO2 < 25 (Maximum RR = 35).
If RR = 35 and PaCO2 < 25, may give NaHCO3.
If pH < 7.15: Increase RR to 35.

If pH remains < 7.15 and NaHCO3 considered or infused, TV may be increased in 1 ml/kg steps until pH > 7.15 (Pplat target may be exceeded).
Alkalosis Management: (pH > 7.45) Decrease vent rate if possible.

I:E RATIO GOAL: 1:1.0 - 1:3 Adjust flow rate to achieve goal.
If FiO2 = 1.0 and PEEP = 24 cm H2O, may adjust I:E to 1:1.

PART II: WEANING

A. Conduct a CPAP Trial daily when:
1. FiO2 ≤ 0.50 and PEEP ≤ 8.
2. PEEP and FiO2 ≤ values of previous day.
3. Patient has acceptable spontaneous breathing efforts. (May decrease vent rate by 50% for 5 minutes to detect effort.)
4. Systolic BP ≥ 90 mmHg without vasopressor support.

CONDUCTING THE TRIAL:
Set CPAP = 5 cm H2O, FiO2 = 0.50
If RR ≤ 35 for 5 min.: advance to Pressure Support Weaning below:
If RR > 35 in < 5 min.: may repeat trial after appropriate intervention (e.g., suctioning, analgesia, anxiolysis)
If CPAP trial not tolerated: return to previous A/C settings

B. PRESSURE SUPPORT (PS) WEANING PROCEDURE
1. Set PEEP = 5, and FiO2 = 0.50
2. Set initial PS based on RR during CPAP trial:
a. **If CPAP RR < 25:** set PS = 5 cm H2O and go to step 3d.
b. **If CPAP RR = 25-35:** set PS =20 cm H2O then reduce by 5 cm H2O at ≤ 5 min. intervals until RR = 26-35 then go to step 3a.
c. **If initial PS not tolerated:** return to previous A/C settings.
3. **REDUCING PS:** (No reductions made after 1700 hors)
a. Reduce PS by 5 cm H2O q1-3 hr.
b. If PS ≥ 10 cm H2O not tolerated, return to previous A/C settings (Reinitiate last tolerated PS level next AM and go to step 3a)
c. If PS = 5 cm H2O not tolerated, return to PS = 10 cm H2O. If tolerated, 5 or 10 cm H2O may be used overnight with further attempts at weaning the next morning
d. If PS = 5 cm H2O tolerated for ≥ 2 hours assess for ability to sustain unassisted breathing below.

C. UNASSISTED BREATHING TRIAL:
1. Place on T-piece, trach collar, or CPAP ≤ 5 cm H2O
2. Assess for tolerance as below for two hours.
a. SpO2 ≥ 90: and/or PaO2 ≥ 60 mmHg
b. Spontaneous TV ≥ 4 ml/kg PBW
c. RR ≤ 35/min
d. pH ≥ 7.3
e. No respiratory distress (distress= 2 or more)
   - HR > 120% of baseline
   - Marked accessory muscle use
   - Abdominal paradox
   - Diaphoresis
   - Marked dyspnea
3. If tolerated consider extubation.
4. If not tolerated resume PS 5 cm H2O.

COMPLETE PROTOCOL ONLINE: www.ardsnet.org

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