Patients with a diagnosis of severe sepsis or septic shock suffer from a high rate of organ failure which often leads to death. Multiple studies have demonstrated that following the guidelines identified in the *Surviving Sepsis Campaign* improves patient chance of recovery.

A 2011 study by Coba et al. demonstrated a 14% reduction in mortality when the compliance with the bundle occurs.

Encouraged by the decrease in organ failure, mortality, length of stay and cost of care, CMS has included the sepsis bundle into its CQI (Continuous Quality Improvement) program.
Data collection for this measure will be required by CMS starting with the October 1, 2015 discharges.

For the severe sepsis project, determining presentation time is either the triage time for patients entering through the ED or the date and time that there is documentation in the progress notes that support the diagnosis of severe sepsis.
Objectives

1. Define SIRS, Sepsis, Severe Sepsis
2. To identify the symptoms of severe sepsis and septic shock syndrome.
3. To list the bundle recommendations for treating severe sepsis.
What is Sepsis?

- A clinical syndrome that complicates severe infection.
- It is characterized by signs of inflammation occurring in tissues that are remote from the infection.
  - Vasodilation
  - Leukocyte accumulation
  - Increased microvascular permeability
- Definitions of systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis, and septic shock were initially defined in 1991 by ACCP and SCCM.
What is SIRS?
Systemic Inflammatory Response Syndrome (SIRS)

- A clinical syndrome that results from a dysregulated inflammatory response to a noninfectious insult.
  - Autoimmune disorder, pancreatitis, vasculitis, burns, surgery, or thromboembolism.

- Requires two or more of the following:
  - Temperature above 100.4°F or below 96.8°F
  - Heart rate above 90 beats per minute
  - RR above 20 per minute or PaCO2 below 32 mm Hg
  - WBC >12,000 cells/mm³, <4000 cells/mm³, or >10% bands
Definitions

- Sepsis – SIRS plus a culture-proven or visually identified infection.
- Severe sepsis = Sepsis-induced tissue hyperfusion or organ dysfunction.

- Areas of mottled skin
- Urine output <0.5 mL/kg
- Lactate >2 mmol/L
- AMS
- <100,000 platelets/mL
- DIC
- ARDS
- Cardiac dysfunction
Definitions cont.

- Septic shock – when there is severe sepsis plus one or both of the following:
  - MAP <60 mmHg despite adequate fluid resuscitation
  - Maintaining a MAP >65 mmHg requires a vasopressor

- Multiple Organ Dysfunction Syndrome (MODS) – a progressive dysfunction in two or more organs of the body after the onset of sepsis
Relationship Between Sepsis and SIRS

- BACTEREMIA
- TRAUMA
- BURNS
- PANCREATITIS

INFECTION
SEPSIS
SIRS

In the late 1970s, it was estimated that 164,000 cases of sepsis occurred in the United States each year.

Recent estimates indicate more than 650,000 cases of sepsis are diagnosed in the United States annually

- Advancing age
- Immunosuppression
- Multidrug-resistant infections
Clinical Presentation

- Fever
- Leukocytosis or bandemia
- Tachypnea
- Tachycardia
- Hypotension
- Organ Dysfunction
Organ System Involvement

- Circulation
  - Hypotension (microvascular permeability)
- Lung
  - Pulmonary edema, hypoxemia
- GI tract
  - Translocation of bacteria, Liver Failure
Organ System Involvement cont.

- Nervous System
  - Encephalopathy, Critical Illness Polyneuropathy
- Hematologic
  - DIC, coagulopathy
- Kidney
  - Acute Tubular Necrosis, renal failure
Severe Sepsis Symptoms

Let’s review the symptoms that lead to the diagnosis of severe sepsis.

**Sepsis**
- Body Temp. above 101F (38.3C) or below 96.8F (36C)
- Heart rate > 90 beats per minute
- Respiratory rate > 20 breaths per minute
- Probable or confirmed infection

**Severe sepsis = all signs of sepsis + at least one of the following**
- Significantly decreased urine output (≥0.5 mL/kg/h)
- Abnormal heart pumping function
- Difficulty breathing
- Decrease in platelet count
- Abrupt change in mental status
- Abdominal pain
Septic Shock Symptoms

- The diagnosis of septic shock is made when a patient has the symptoms of severe sepsis plus extreme hypotension that does not respond to fluid replacement.
- Other symptoms may include reddish patches in the skin or adult respiratory distress syndrome which may lead to ventilatory failure.
Goals

- Distinguishing Sepsis from SIRS
  - Appropriate antibiotics**
- Early initiation of supportive care to correct physiologic abnormalities
  - Optimize organ perfusion
- Early Goal Directed Therapy
SURVIVING SEPSIS CAMPAIGN BUNDLES

TO BE COMPLETED WITHIN 3 HOURS OF TIME OF PRESENTATION:
1. Measure lactate level
2. Obtain blood cultures prior to administration of antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30ml/kg crystalloid for hypotension or lactate ≥4mmol/L

TO BE COMPLETED WITHIN 6 HOURS OF TIME OF PRESENTATION:
5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65mmHg
6. In the event of persistent hypotension after initial fluid administration (MAP <65 mmHg) or if initial lactate was ≥4 mmol/L, re-assess volume status and tissue perfusion and document findings.
7. Re-measure lactate if initial lactate elevated.
The Sepsis Bundle

- Timeliness of the interventions is key to improving patient outcomes:
- Within **three hours** of presentation of **severe sepsis**.
  - An initial lactate level measurement must be obtained. If the results are $\geq 4$mmol/L, resuscitation with 30ml/kg crystalloid fluids should be started.
  - Blood cultures drawn prior to antibiotic administration.
  - Broad spectrum or other antibiotics must be administered.
Blood Cultures

- 30 to 50% of patients presenting with severe sepsis or shock have positive blood cultures.
- Blood should be obtained for culture in any critically ill septic patient (prior to antibiotics).
- Two or more blood cultures need to be obtained.
  - If there is a suspected catheter-related infection, one culture needs to come from the catheter and the other from a peripheral site.
Blood cultures MUST be drawn PRIOR to antibiotic therapy initiated!

- 2 sets drawn – from two different sites simultaneously
- If Central Line in place – one from central line and one peripheral stick.
- If factors preventing 2 peripheral sticks - then 2 sticks same site no less than 30 minutes apart.
Appropriate and timely antibiotic administration has been shown to decrease mortality
- Goal is with 1 hour of recognition of septic shock

Once the causative agent and antibiotic susceptibilities are known, antimicrobial therapy needs to be de-escalated.
Patients with severe sepsis may experience ineffective arterial circulation due to the vasodilatation associated with infection or impaired cardiac output.

Poorly perfused tissue results in hypoxia and is often associated with elevated serum lactate levels.

Lactic acid is increased secondary to anaerobic metabolism due to hypoperfusion.

- Cellular metabolic failure in sepsis
Hypotension and Lactate Levels cont.

- A serum lactate value equal to or greater than 4 mmol/L is correlated with increased severity of illness and poorer outcomes even if hypotension is not yet present.

- Those with hypotension or lactates equal to or greater than 4 mmol/L require intravenous fluids (30 mL/kg of crystalloid) given as fluid challenges within 3 hours of time of presentation.
Fluid Challenge Definition…

- Term used to describe the initial volume expansion period during which the response to fluid administration is evaluated.

- During this process, large amounts of fluids are administered over a short period of time to evaluate the patient’s response to the fluids.
  - Crystalloids are given
  - 500–1000 mL over 30 mins
Next steps:

- Within six hours of presentation, patients with **severe sepsis** should have a repeat lactate level measurement done if the initial lactate measurement was elevated (> 2 mmol/L).
Patients with Septic Shock

- Along with the bundle elements listed for severe sepsis, patient with a diagnosis of septic shock have additional needs.
- Within three hours of presentation start resuscitation with 30ml/kg crystalloid fluids.
Septic Shock cont.

- Within six hours of presentation, if hypotension (systolic blood pressure (SBP) <90 mmHg or mean arterial pressure (MAP) <65 mmHg) or initial lactate is ≥ 4 mmol/L persist after fluid administration, the following treatments must be initiated:
The table below lists the Vasopressors approved for Septic Shock.

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine</td>
<td>Levophed</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>Adrenalin</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>Neosynephrine Vazculep</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Intropin</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>Pitressin</td>
</tr>
</tbody>
</table>

- Specifications Manual for National Hospital Inpatient Quality Measures Discharges 10-01-15 (4Q15) through 6-30-16 (2Q16)
Repeat volume status and tissue perfusion assessment consisting of either a focused physical exam including:

1. Vital signs
2. Cardiopulmonary exam
3. Capillary refill evaluation
4. Peripheral pulse evaluation
5. Skin examination

OR

- BP 90/65
- Pulse 60/min
- SpO₂ 99% on air
- Temp 36°C
Two of the following:

1. Central venous pressure measurement
2. Central venous oxygen measurement
3. Bedside cardiovascular ultrasound
4. Passive leg raise or fluid challenge
For Refractory Hypotension and to be completed within 6 hours of time of presentation:
Vasopressors

- Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation).
- When appropriate fluid challenge fails to restore an adequate blood pressures, vasopressor agents are initiated.
  - Norepinephrine as first choice with goal MAP greater than or equal to 65 mm Hg
  - Vasopressor therapy may be required transiently in cases of life-threatening hypotension, even when hypovolemia has not been resolved or when a fluid challenge is in progress.
CVP and $S_{CV}O_2$

- Early goal-directed therapy defines resuscitation end points to help clinicians resuscitate patients in septic shock.

- Two essential features of early goal-directed therapy include:
  1. Maintaining an adequate central venous pressure (CVP)
  2. Maximizing mixed or central venous oxygen saturation ($S_{CV}O_2$)
Central Venous Pressure

- If the lactate is $> 4$ mmol/L or the hypotension is refractive to initial fluid challenges, patients should then have their CVP maintained $> 8$ mm Hg
  - In ventilated patients, the target CVP should be 12-15 mmHg (account for PEEP and increases in intrathoracic pressure)
- The appropriate CVP value is obtained by delivering repeated fluid challenges until the target value is achieved.
  - Does this mean fluid challenges or maintenance fluids?
Central Venous Oxygen Saturation ($S_{CV}O_2$)

- If the lactate is $>4 \text{ mmol/L}$ or the hypotension is refractive to initial fluid challenges, patients should then have their CVP maintained $>8 \text{ mm Hg}$ and $S_{CV}O_2$ should be $>70\%$.

- There are two principal strategies.

  1. After the patient has been adequately resuscitated and the CVP is $>8 \text{ mm Hg}$, dobutamine infusion can be used as...

     - Cardiac output may remain insufficient to meet metabolic needs
     - Cardiac output itself may be low (sepsis-induced cardiac dysfunction)
Transfusing PRBCs and \( S_{CV}O_2 \)

2. If a patient is hypovolemic and the HCT < 30 %, PRBCs can be transfused after adequate fluid resuscitation (CVP > 8 mm Hg) **
   - 2012 guidelines ~ 7.0 to 9.0 g/dL in adults

** Supportive Therapy of Severe Sepsis (Table 8)

K. Blood Product Administration

1. Once tissue hypoperfusion has resolved and in the absence of extenuating circumstances, such as myocardial ischemia, severe hypoxemia, acute hemorrhage, or ischemic coronary artery disease, we recommend that red blood cell transfusion occur when the hemoglobin concentration decreases to < 7.0 g/dL to target a hemoglobin concentration of 7.0 to 9.0 g/dL in adults (grade 1B).
Adrenal Insufficiency

**J. Corticosteroids**

1. We suggest not using intravenous hydrocortisone as a treatment of adult septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (see goals for Initial Resuscitation). If this is not achievable, we suggest intravenous hydrocortisone alone at a dose of 200 mg per day (grade 2C).
Maintaining Adequate Glycemic Control

- Effective glucose control in the ICU has been shown to decrease morbidity across a large range of conditions and also to decrease mortality.

Q. Glucose Control

1. A protocolized approach to blood glucose management in ICU patients with severe sepsis commencing insulin dosing when 2 consecutive blood glucose levels are $>180 \text{mg/dL}$. This protocolized approach should target an upper blood glucose $\leq 180 \text{mg/dL}$ rather than an upper target blood glucose $\leq 110 \text{mg/dL}$ (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).
Fluid Resuscitation

- Favor use of crystalloids as the initial fluid resuscitation
- 30 mL/kg of crystalloid (2.1 L in a 70 kg or 154-pound person) in the first 4-6 hours.

Vasopressors and Inotropes

- Strongly recommend norepinephrine (Levophed) as the first choice for vasopressor therapy.
- When a second agent is needed, epinephrine is their weakly-recommended vasopressor choice.
Corticosteroids

- For those with vasopressor-refractory septic shock, they recommend IV hydrocortisone in a continuous infusion totaling 200 mg/24 hrs

Lactate Levels

- Re-measure lactate if initial lactate elevated.
1. For patients with severe sepsis, which of these treatments should be started within 3 hours of presentation?

A. An initial lactate level measurement must be obtained.
B. Blood cultures drawn prior to antibiotic administration.
C. Broad spectrum or other antibiotics must be administered.
D. All of the above
2. Along with the bundle elements listed for severe sepsis, patient with a diagnosis of septic shock must have resuscitation with 30ml/kg crystalloid fluids started within 3 hours of presentation.

A. True

B. False
3. If severe hypotension does not respond within 6 hours to fluid administration ____________ should be administered.

A. Different antibiotics

B. Vasopressors
80 year old female admitted to the medical unit with complaints of a sore throat, persistent cough x 3-4 days. She also has chest pains when she takes deep breaths.

Temp - 101.2 F
HR - 110 beats per minute
RR – 40 breaths per minute
BP – 110/60mmHg

WBC 15,000 (no Bands)
PLT 300,000
Review of Case Study 1

- Is this just pneumonia?
- Is this considered SIRS or Sepsis?
Review of Case Study 1 cont.

**SIRS = 2 or more of . . .**

- Temperature above 100.4°F or below 96.8°F
- Heart rate above 90 beats per minute
- Respiratory rate above 20 per minute or PaCO2 below 32 mm Hg
- WBC above 12,000uL-1 or below 4,000uL-1

**Patient has . . .**

- Temp – 101.2°F
- Heart rate – 110
- Respiratory Rate – 40
- WBC – 15,000uL-1
- CXR shows infiltrates

**This is Sepsis!!**
Case Study 2

80 year old male came to the ED with abdominal pain. His wife says he’s an alcoholic.

Temp 99.0°F
HR 125 beats per minute
RR 26 breaths per minute
BP 125/80 mmHg
WBC 11,000
CT Abd – Acute pancreatitis without necrosis
Review of Case Study 2

SIRS = 2 or more of . . .

- Temperature above 100.4°F or below 96.8°F
- Heart rate above 90 beats per minute
- Respiratory rate above 20 per minute or PaCO2 below 32 mm Hg
- WBC above 12,000uL-1 or below 4,000uL-1

Patient has . . .

- Temp – 99.0°F
- Heart Rate - 125
- Respiratory Rate – 26
- Acute Pancreatitis is an inflammatory condition (no necrosis on CT scan).
- Infection Process or Inflammatory Process

This is SIRS - Order Sepsis Panel to rule out Sepsis
Sepsis is a clinical syndrome characterized by systemic inflammation and widespread tissue injury due to infection.

Severe sepsis has a very high mortality rate and the incidence of it is said to double in the next 20-30 years.

There needs to be prompt recognition.

Early goal directed therapy must be initiated as it is life saving.
Surviving Sepsis "Care Bundles"

SURVIVING SEPSIS CAMPAIGN BUNDLES

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Surviving Sepsis Campaign
References

