Management of Sepsis

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Faces of Sepsis
A Call for Action

On April 1, 2012, Rory Staunton died from sepsis after falling on a gym floor and cutting his arm. After his fall, Rory developed a fever, vomiting, and leg pain. He was treated at a local ED for stomach pain/dehydration and was sent home. He died in an ICU 2 days later after seeking medical attention*.


NY Governor Cuomo announces state hospital requirements for:
• Sepsis screening
• Performance reporting
• Family/patient advocacy
The Problem

- Sepsis is the 10th leading cause of death in the United States (Zu et al., 2007)
- Sepsis mortality is high (27%) and sepsis incidence is increasing (Kumar et al., 2011)
- Nationally, sepsis kills more than 215,000 every year (500 per day) (Angus et al., CCM, 2001)
- Sepsis is the leading cause of death in non-coronary Intensive Care Units (Sands et al., 1997)
- Hospital cost for severe sepsis is $16.7B annually (Angus et al., CCM, 2001)
Sepsis: A disease continuum

- Body’s increasingly severe clinical responses to infection
  - Infection $\rightarrow$ sepsis $\rightarrow$ severe sepsis $\rightarrow$ septic shock $\rightarrow$ multiple organ dysfunction syndrome

- Multiple etiologies
  - Bacteria, fungi, viruses

- Variable clinical course
  - Type of infectious organism,
  - Site and size of infecting insult and
  - Genetic properties of host’s immune system

- Difficult to differentiate and recognize
Systemic Inflammatory Response Syndrome (SIRS)

- A clinical response arising from a non-specific insult (*burns, trauma, infection, pancreatitis, surgery, anesthesia*)
- 2 or more of the following criteria:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature</td>
<td>&gt; 38.3°C or &lt; 36°C</td>
</tr>
<tr>
<td>Heart rate</td>
<td>&gt; 90 beats/min</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>&gt; 20 breaths/min or PaCO2 &lt; 32mmHg</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>&gt; 12,000/mm³ or &lt; 4,000/mm³ or &gt; 10% bands</td>
</tr>
</tbody>
</table>
Sepsis

- Systemic inflammatory response to an infection
- Infection can be suspected or confirmed
  - Suspected: based on risk factors, signs, history, exposure
  - Confirmed: based on signs of infection, positive cultures, current treatment with antibiotics
Sepsis

- Other variables
  - *Altered mental status*
  - *Significant edema or positive fluid balance (>20 mL/kg over 24 h)*
  - *Glucose > 140 mg/dL (in the absence of diabetes)*
  - *Elevated plasma C-reactive protein*
  - *Elevated plasma procalcitonin*
  - *Mottled skin or ↓ capillary refill*
Severe Sepsis

- Sepsis with manifestations of ≥ 1 or more acute signs of organ dysfunction

**CNS:**
- Altered LOC
- Cerebral ischemia

**Respiratory:**
- Tachypnea
- \( \downarrow \) \( \text{PaO}_2 \), \( \downarrow \) \( \text{SpO}_2 \)
- \( \uparrow \) \( \text{O}_2 \) requirement
- \( \text{PaO}_2/\text{FiO}_2 \leq 300 \)

**Hepatic:**
- Jaundice
- \( \uparrow \) Liver Enzymes
- \( \downarrow \) Albumin

**Hematologic:**
- \( \downarrow \) Platelets
- \( \uparrow \) PT/INR/aPTT
- \( \downarrow \) Protein C, \( \uparrow \) D-dimer

**Cardiovascular:**
- Tachycardia
- Hypotension
- \( \downarrow \) \text{Capillary refill}
- Mottled skin
- \( \text{Altered CVP} \) & \( \text{PAOP} \)
- \( \downarrow \) \( \text{Capillary refill} \)
- Mottled skin

**Renal:**
- \( \downarrow \) Urinary Output
- (< 0.5 ml/kg/hr)
- \( \uparrow \) Creatinine

**Metabolic:**
- Metabolic Acidosis
- \( \uparrow \) Lactate Level
- \( \downarrow \) Lactate clearance

Severe Sepsis

INFECTION

SEVERE SEPSIS

SEPSIS

SIRS

Septic Shock

Pancreatitis

Trauma

Burns

Other
Septic Shock

- **Severe sepsis** plus hypotension despite adequate fluid resuscitation or lactate > 4 mmol/L
  - SBP < 90 or ↓ 40 mmHg from baseline
  - MAP < 70 mmHg
  - In the absence of other causes of hypotension
- Characterized by
  - Reduced EF - depressed myocardium
  - Reduced relaxation
  - High or normal CO – high LVEDV
Mortality

- Rate is 20-50%
- Denominator = patients with Dx
- Numerator = patients who die w/ Dx
- *What’s included in the denominator?*

Severe Sepsis
+ Septic Shock
+ Infection & Organ Dysfunction
Local Pathophysiology

• Normal localized inflammatory response
  – *Vessels dilate to bring WBCs to fight infection (redness and warmth)*
  – *Capillaries become permeable releasing fluid and immune mediators (swelling and pain)*

• Results in ↑ O₂, gluc, clotting factors, humoral and cellular immune factors
Systemic Pathophysiology

- **Infection** (Bacterial, viral, fungal, or parasitic infection/endotoxin)
- ↑ **Inflammation**
- ↑ **Coagulation**
- ↓ **Fibrinolysis**
- **Endothelial Dysfunction and Microvascular Thrombosis**
- **Hypoperfusion Ischemia**
- **Acute Organ Dysfunction**
Systemic Pathophysiology

*Macrophages* bind to and engulf foreign cells

*Monocytes* release pro and anti-inflammatory cytokines

*Neutrophils* release cytokines, binds to endothelium, migrates to interstitium
Thrombosis/ fibrinolysis

- Endothelium release of cytokines
- Platelet activation
- Extrinsic pathway activated
- Anticoagulant factors (antithrombin III, protein C, protein S, tissue pathway inhibitor)
Systemic Pathophysiology

- Endothelial damage from endotoxins/immune cells
- Release of nitric oxide → vasodilation
- Reduced sensitivity to catecholamines

- Rolling/adhesion of blood cells to endothelium
- Shunting
- Capillary edema
- Impaired RBC flexibility

- Microvascular plugging

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Inflammatory Response to Infection

Thrombotic Response to Infection

Fibrinolytic Response to Infection
Decreased Perfusion/Tissue Oxygen Delivery

- Endothelial activation
- Increased microvascular permeability
- Decreased RBC deformability
- Opening of AV shunts and pooling
- Altered vascular flow and resistance
- Viscosity alterations
- Abnormal RBC/WBC rheology
- Microvascular thrombi

Glycolysis
(2 ATP)

Oxidative Phosphorylation
(36 ATP)

Glucose → Pyruvate → Lactate

Glucose → Glycogen

Anaerobic Glycolysis
(2 ATP)

CO₂ + H₂O → Lactate

Glucose → Glycolysis
(2 ATP)
Shocks Associated with Sepsis

• Classic septic shock – distributive shock
  – Vasodilation
  – Maldistribution of blood flow
  – Myocardial depression

• Persistent hypotension without hypoperfusion
  – Hypotension with normal lactate

• Cryptic shock
  – Normal blood pressure with elevated lactate
Hypotension with Lactates

Dugas et al., 2012, *J Critical Care*
Lactate and Blood Pressure

28 Day Mortality

Systolic Blood Pressure (mmHg)

< 2.5
2.5-4
> 4

Howell, 2007, Intensive Care Med
Multi Organ Dysfunction/Failure

- **Diffuse cell injury/death**
  - *Cellular necrosis*
  - *Apoptosis*
  - *Leukocyte mediated tissue injury*
  - *Cytopathic hypoxia*

- **Ischemic organ injury**
  - *Cytokines* $\rightarrow$ *endogenous vasodilators*
  - *Endothelium damage* $\rightarrow$ *edema*
  - *Vascular bed plugging* $\rightarrow$ $\downarrow$ *perfusion*
  - *Organ specific vasoconstriction*
“Mottling”
• Cutaneous Dysfunction
  ▪ petechiae,
  ▪ purpura and
  ▪ necrosis
Clinical Manifestations

- Tachycardia, hypotension
- Tachypnea, hyperventilation, ↓ SpO2
- Body temperature alteration
- Metabolic acidosis, ↑ lactate level
- WBC/diff alteration, C-reactive protein, procalcitonin
- Altered coagulation
  - Plts, PT/INR, PTT, Fibrinogen, D-dimers
- Hyperglycemia, hypermetabolism > catabolism
- Edema
- Altered organ function
  - pulmonary, renal, GI/liver, CNS, coagulation, cardiovascular, cutaneous
Management: Screening (1C)

• Signs of infection
  – **Confirmed**
    • Current Rx for infection *(not prophylaxis)*
  – **Suspected**
    • Risks factors
    • Recent cultures
    • Talked about on rounds
    • Recent procedures
    • Signs/symptoms of potential infection

Grading System

**Recommendations:**
Grade 1 (high)
Grade 2 (weak)

**Evidence:**
A (high) – D (very low)

[www.survingsepsis.org](http://www.survingsepsis.org)
Management: Screening (1C)

- **Signs of SIRS**
  - temp > 38.3 < 36 C
  - heart rate > 90
  - respiratory rate > 20
  - WBC > 12 < 4; > 10% bands

- **Other variables**
  - glucose > 140 in non diabetics
  - significant edema or positive fluid balance
  - altered mental status
  - mottled skin or ↓ capillary refill
  - PaCO2 < 32mmHg
Management: Screening (1C)

- Signs of organ dysfunction
  - altered mental status
  - hypotension (SBP < 90; decrease of 40 mmHg from baseline; MAP < 70)
  - ↓ oxygenation or ↑ O₂ need
  - ↓ urinary output
  - ↓ capillary refill
  - cutaneous changes
  - abnormal organ specific labs
**Time of Presentation**

Example TOPs (not all-inclusive)

- Arrow starts at 1\textsuperscript{st} component present, ends with 3rd
- Color of arrow indicates time that should represent TOP (note: no white arrows)
- Exceptions may be determined upon clinical review
Case Study

- 77 yo male admitted through the ED from a nursing home with failure to thrive, poor PO intake and hypotension
- PMH: Dementia, tachycardia arrhythmias, PVD w/ BKA, sacral, perineal & left knee stump ulcers, chronic foley, 2 recent hospitalizations
- Ulcers have purulent drainage
- Assessment: T 35.6, HR 120, RR 21, 86/56, SpO2 97 (2L NC), A&O x 2
- Pertinent labs: WBCs 14,000mm$^3$, lactate 2.4
Case Study

- **ED Rx**
  - 1 liter NS IV bolus
  - 1 gram Vancomycin, 1 gram Meropenum
  - Blood, urine, wound culture
  - CXR, EKG
  - **Following fluid bolus and antibiotics**
  - VS: T 36.3, HR 122, RR 22, BP 105/58, lactate 2.1
  - Transferred to transitional care unit
## Case Study

<table>
<thead>
<tr>
<th>Time</th>
<th>T</th>
<th>HR</th>
<th>RR</th>
<th>WBC</th>
<th>BP</th>
<th>SpO2/ O2</th>
<th>LOC</th>
<th>LAC</th>
<th>Bili</th>
<th>U/O</th>
<th>Cr</th>
<th>Plt</th>
<th>PT/PTT</th>
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<tr>
<td>2100</td>
<td>36</td>
<td>116</td>
<td>20</td>
<td></td>
<td>94/56</td>
<td>100/2L NC</td>
<td>A&amp;O X 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>0030</td>
<td>35.8</td>
<td>118</td>
<td>22</td>
<td></td>
<td>102/63</td>
<td>100/2L NC</td>
<td>A &amp; O X 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>0815</td>
<td>37</td>
<td>122</td>
<td>16</td>
<td>12.6</td>
<td>90/51</td>
<td>96/2L NC</td>
<td>Lethargic</td>
<td></td>
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<td>.74</td>
<td>441</td>
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<tr>
<td>0930</td>
<td>36.2</td>
<td>117</td>
<td>18</td>
<td></td>
<td>88/50</td>
<td></td>
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<td>0</td>
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# UCSF Screening Tool

## 1. Infection

- **NEW SIGNS OF INFECTION (✓ = yes)**
  - NEW suspected infection?
  - NEW worsening current infection?

## 2. Sepsis

- **TWO OR MORE NEW SIGNS OF SIRS (✓ = yes)**
  - Temperature > 38°C or < 36°C
  - Heart rate > 90 beats/minute
  - Respiratory rate > 20 breaths/minute
  - WBC count over 12,000/mm³ or under 4,000/mm³

## 3. Severe Sepsis

- **NEW SIGNS OF ORGAN DYSFUNCTION (✓ = yes)**
  - Worsening mental status
  - SpO₂ < 90% on RA or requires more O₂ to maintain SpO₂ > 90%
  - Decrease in urine output
  - SBP < 90 mmHg or < 40 mmHg below baseline
  - MAP ≤ 65 mmHg

### SCREEN RESULTS

- **1 + 2 OR 1 + 3 = (+) ⋆ Complete (+) Screen Form ⋆**
  - Time/Initials: +
  - Time/Initials: +

- **Does not meet criteria for Sepsis Screen = (-)**
  - Time/Initials: -
  - Time/Initials: -

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MD called for (+) screen: ___________________________
Screening Studies

- **Giuliano, 2007, AJCC**
  - MAP, T, HR, RR evaluated
  - Sensitivity 79%; specificity 45%
  - MAP < 70 & T > 38°C most predictive
  - Hypothermia not predictive

- **Moore et al., 2009, J Trauma**
  - 3 part screening process: SIRS by RN, Inspection by APRN, escalation to attending
  - Sensitivity 97%; specificity 97%

- **Thiel et al., 2010, J Hosp Med**
  - $\text{PaO}_2$, SBP, absolute neutrophil count, BUN, pH, $\text{HCO}_3^-$, $\text{Cl}^-$ and albumin were significant predictors
  - Shock index, MAP, bilirubin, INR, WBC, absolute neutrophil count, albumin, Hgb, Na⁺
# Early Warning Scoring Tools

<table>
<thead>
<tr>
<th>Variable</th>
<th>Score Range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
</tr>
<tr>
<td><strong>SBP</strong></td>
<td>&lt; 70</td>
</tr>
<tr>
<td><strong>HR</strong></td>
<td>&lt; 40</td>
</tr>
<tr>
<td><strong>RR</strong></td>
<td>&lt; 9</td>
</tr>
<tr>
<td><strong>Temp °C</strong></td>
<td>&lt; 35</td>
</tr>
<tr>
<td><strong>AVPU</strong></td>
<td>A</td>
</tr>
</tbody>
</table>

- Low risk: score 0-2, Intermediate risk 3-4, High risk > 4 – MD must see patient within 60 minutes

Subbe et al., 2001, Quart J Med
This patient has 2 or more SIRS criteria. Notify provider immediately.

If the patient has a new or worsening infection, this patient has sepsis (SIRS + infection) and should be evaluated for the following:

- Severe sepsis (sepsis + new/worsening organ dysfunction (including lab abnormalities, increased O2 requirement, and AMS))
- Septic shock (sepsis + lactate \(\geq 4\) or hypotension not responsive to fluids)

Follow UCSF Lactate Policy:

1. May order lactate if new or suspected infection
2. Always notify provider

*Heart Rate: 120 *Resp: 25 *Temp: 39 °C (102.2 °F)

Last WBC: Not on file
Last LACT: Not on file

Open order: Blood Gas, Lactate (Parnassus only)
This patient has SEVERE SEPSIS criteria. Notify provider immediately.

If the patient has a new or worsening infection, this patient has sepsis (SIRS + infection) and should be evaluated for the following:

- Severe sepsis (sepsis + new/worsening organ dysfunction (including lab abnormalities, increased O2 requirement, and AMS))
- Septic shock (sepsis + lactate >/= 4 or hypotension not responsive to fluids)

Patients with severe sepsis or septic shock should receive the following within 1 hour of onset (time of hypotension, time lactate resulted, etc):

1. NS bolus (20ml/kg or at least 1000ml IV)
2. Blood cultures prior to antibiotic administration
3. Appropriate antibiotics

Filed Vitals:

<table>
<thead>
<tr>
<th>BP</th>
<th>Temp</th>
<th>Resp</th>
<th>SpO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>88/50</td>
<td>39 °C (102.2 °F)</td>
<td>40</td>
<td>88%</td>
</tr>
<tr>
<td>39 °C (102.2 °F)</td>
<td>25</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Last WBC: Not on file
Last LACT: Not on file

Provider Notified | Treatment Initiated
Management – Initial Resuscitation

- Measure lactate level
- Obtain blood cultures
- Administer broad spectrum antibiotics
- Administer 30 cc/kg fluid as a challenge for hypotension +/- or lactate > 4
  - Quantitative goals for fluid resuscitation to determine when hypoperfusion has been corrected (1C)
Measuring Lactates

• Mortality associated with higher lactates (Mikkelsen et al., 2009)
• Critical lab
• Nurse driven lactate protocols
• Lactates drawn using
  – Serum draw
    • Methods to ensure validity
  – Venous/arterial blood gas
  – Point of care
• Evaluating high lactates
• Lactate clearance, lactime
Obtaining Cultures

• 2 blood culture sets (anaerobic and aerobic)
  – one drawn peripherially
  – one drawn through each lumen of each central access device (unless device is < 48 hours old)

• Cultures should be drawn from other sites before antibiotics are administered if it doesn’t cause a delay (1C)

• 50% blood cultures are negative

Shafazand & Weinacker, 2002, Chest, 122;1727-1736
Blood Culture Algorithm

- MD writes order for BCx
- Is the BCx STAT?
- BCx in last 24 hrs?
- Does pt have a CVC?

- RN or Phlebotomy attempts to obtain BCx
- BCx not obtained
- RN gets help to obtain BCx
- BCx not obtained

- MD writes order for BCx
- Does pt have a CVC?
- Is the BCx STAT?

- RN or Phlebotomy attempts to obtain BCx
- BCx not obtained
- RN gets help to obtain BCx
- BCx not obtained

- Call primary service to ask about alternatives including starting Abx w/o cultures
- ICU RN
- ICU busy?
- Call ICU MD for assistance

- Time Zero
- 20 mins
- 40 mins
- 60 mins
Administering Broad Spectrum Antibiotics

• (+) BCx associated with severe sepsis (Cohen et al., 2004)
• Mortality increase with delay of antibiotics (Kumar et al., 2006)
• **Antibiogram**
• Stock common sepsis antibiotics on floor
• **Broad spectrum**
  – *cefepime, ceftriazone, piperacillin-tazobactam, meropenem, vancomycin, linezolid, aztreonam*
• **First dose antibiotic guidelines for code sepsis (UCSF)**
• Antibiotic stewardship
Management – Initial Resuscitation

- **Fluid resuscitation**
  - hypotension
  - lactate ≥ 4 mmol/L
  - *Administer 30 cc/kg fluid as a challenge*
  - Over 30 mins
  - *crystalloid first, albumin second, no hydroxyethyl starches*
How To Give A Fluid Bolus

What does the word IV bolus mean to you?

a. Give the fluid as fast as you can
b. Give the fluid in $\leq 60$ minutes
c. Give the fluid as fast as you think the patient’s condition allows
d. No answer here defines bolus for me.
How To Give A Fluid Bolus

You are asked to give 1000 cc of Normal Saline as a bolus to a patient who is considered septic.

When you get an order for an IV bolus do you ask for clarification of how fast the rate should be?

a. Yes
b. No
c. Only if I have a tenuous IV
d. Only if I have an opportunity to talk to the MD
How To Give A Fluid Bolus

You are asked to give 1000 cc of Normal Saline as a bolus to a patient who is considered septic.

How fast do you run the IV bolus?

a. Set the IV pump to 999
b. Free flow without a pump
c. Free flow with a pressure bag
d. Rate of 250 cc/hr
How To Give A Fluid Bolus

You are asked to give 1000 cc of Normal Saline as a bolus to a patient who is considered septic.

You have a 22 gauge IV, what do you consider?

a. If the IV site is positional but patent, give the bolus with this IV and start another IV.
b. If the IV site is reddened but functional, give the bolus with this IV and change it if it infiltrates.
c. Start another IV preferably large bore.
Management – Initial Resuscitation

- Quantitative goals for fluid resuscitation (1C)
  - CVP: 8–12 mmHg; 12-15 mmHg
  - MAP ≥ 65 mmHg
  - Urine output > 0.5 mL/kg/hr
  - ScvO2 ≥ 70% or SvO2 ≥ 65%
  - Normalize lactate (2C)
Quick Review of $\text{DO}_2$ and $\text{VO}_2$

- $\text{DO}_2 = \text{O}_2$ delivery
  - Increase $\text{CO}$
  - Increase contractility
  - Decrease peripheral vasoconstriction
  - Increase HR
  - Increase stroke volume

- $\text{VO}_2 = \text{O}_2$ consumption
  - Increased
    - Pain, fever, shivering, agitation, burns, hyperthyroidism
  - $\text{SV}_\text{O}_2 = \text{mixed venous O}_2$ saturation
    - Normal 60-80%
    - Decrease peripheral vasoconstriction
    - Increase $\text{O}_2$ delivery to tissues
    - Decrease tissue consumption

- $\text{Scv}_\text{O}_2 = \text{central venous O}_2$ saturation
  - Decrease $\text{O}_2$
    - Transfusion
    - Supplemental $\text{O}_2$
  - higher than $\text{SV}_\text{O}_2$
Other Therapeutic Endpoints

- Blood pressure increase
- Capillary refill < 2 secs
- Warm extremities
- Normal mental status
- HR normalized
- Adequate urinary output
Management – Initial Resuscitation

• Unresponsive to fluids (Rx options)
  
  – Dobutamine up to 20 mcg/kg/min
  
  – RBCs to ≥ Hct 30%
  
  – Vasopressors to achieve MAP ≥ 65 (1C)
    
    • Norepinephrine (1B)
    • Epinephrine (2B)
    • Vasopressin
    • Dopamine
    • Phenylephrine – not recommended

Survival increase with restored organ perfusion

(Beale et al., 2004; Vincent & Gerlach, 2004).
Adjunctive/Supportive Therapies

- Corticosteroids
- Blood product administration
- Glucose control (1A)
  - 2 consecutive levels > 180
- DVT prophylaxis
- Stress ulcer prophylaxis for at risk patients
- Nutrition
- Goals of care
- Quality of life issues
Not Recommended

- Immunoglobulins
- Selenium
- Erythropoietin
- Fresh frozen plasma
- Antithrombin
- Bicarbonate therapy
- No pharmacoprophylaxis for DVT when heparin contraindicated
Sepsis Programs

• Morality benefit w/ protocols
  (Rivers et al, 2001; Dellinger et al., 2008)

• Executive sponsorship

• Formulate a multidisciplinary team

• Develop detection processes

• Develop and publicize standards of care

• Develop mechanisms to facilitate standards

• Develop systems to evaluate care and provide feedback
Facilitating Standards

- Order sets
- Accessibility of antibiotics, fluids and supplies
- Narrowing choices
- Unit based phlebotomy
- Defining time of presentation

- Sepsis flowsheet
- Sepsis Handoff tool
- Checklist to assure bundle compliance
- Lactate critical lab
- RN lactate procedure
- RN protocols for initiating Rx
- Sepsis team
**Sepsis Alert/Code Sepsis**

**Patient screens positive on sepsis screening tool with new signs**

- **Positive screen with SIRS criteria only**
  - **Acute Care/Transitional Care**
    - Call RRT
    - Notify Primary Team
  - **ICU**
    - Order venous or arterial lactate
    - Draw using blood gas syringe
    - Send to blood gas lab.

- **Positive screen with organ dysfunction**
  - All Units
    - Call Primary or designated Team
    - Activate **Code Sepsis**
    - Order venous or arterial lactate
    - Draw using blood gas syringe & send to blood gas lab.
    - Assist with sepsis resuscitation.

**Lactate < 2**
- Call Primary or Designated Team & report lactate result w/in 30 mins.
- Inquire about further action.

**Lactate ≥ 2**
- Call Primary or Designated Team & report lactate result w/in 30 mins.
- Activate **Code Sepsis**
- Assist with sepsis resuscitation.
Evaluate Care and Feedback

• Data
• Dashboards
• Frequent reporting in multiple venues
• Feedback to clinicians
• Education
  – Pocket cards
  – Intranet site
  – Conference lectures
  – Sepsis simulations
  – Videos, posters, and internal newsletter articles
  – Orientation and ongoing competency training
References


References

• Kumar et al. (2006). Duration of hypotension prior to initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med*, 34, 1589-1596


Cryptic Shock – They look too good to be in septic shock!
Activated Protein C

- Inhibit the production of inflammatory cytokines
- Limits adhesion and rolling of neutrophils and monocytes
- Inactivates various components of the coagulation cascade
- Enhances the fibrinolytic system by reducing the production of thrombin and the actions of plasminogen activator inhibitor