Sepsis
From EMS to ER to ICU
What we need to be doing

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ATHENS PULMONARY, CRITICAL CARE AND SLEEP
Objectives

1. Define the changes to the definition of Sepsis
2. Describe the assessment, interventions and strategies for the management of Sepsis.
3. Explain how effective transitions of care can impact patient outcomes.
"Except on few occasions, the patient appears to die from the body's response to infection rather than from it."

SIR WILLIAM OSLER – 1904
THE EVOLUTION OF MODERN MEDICINE

SURVIVING SEPSIS GUIDELINES - 2016

“Life-Threatening Organ Dysfunction caused by a Dysregulated Host Response to Infection.”
## Sepsis: Defining a Disease Continuum

<table>
<thead>
<tr>
<th>Infection/Trauma</th>
<th>SIRS</th>
<th>Sepsis</th>
<th>Severe Sepsis</th>
<th>Septic Shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated Mortality Rates</td>
<td>10%</td>
<td>35%</td>
<td>50%</td>
<td></td>
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</tbody>
</table>

### ≥2 of the following:
- Temp ≥38°C or ≤36°C
- HR ≥ 90
- RR ≥20/min
- WBC ≥12 or ≤4,000 or >10% Bands

**SIRS =** systemic inflammatory response syndrome.

**Bone et al. Chest. 1992;101:1644.**
Identifying Acute Organ Dysfunction as a Marker of Severe Sepsis

- **Hypotension** (SBP < 90, MAP < 65)
- **Tachycardia**
- **CVP**
- **PAOP**
- **Jaundice**
- **Enzymes**
- **Albumin**
- **PT/INR**
- **Bilirubin > 2 mg/dL**
- **Altered Consciousness** (Confusion, Psychosis)
- **Tachypnea**
  - PaO$_2$ < 70 mm Hg
  - SaO$_2$ < 90%
  - PaO$_2$/FiO$_2$ ≤ 300
- **Oliguria/Anuria**
  - Urine Output < 0.5 mL/kg X 2 hrs
  - Creatinine (> 2.0)
- **Platelets < 100K**
  - INR > 1.5
  - D-dimer
- **Lactate > 2.0**
Why do Septic Patients Die?

ANSWER: ORGAN FAILURE
Organ Failure in Sepsis

Pathophysiology of Severe Sepsis

Homeostasis

↑ INFLAMMATION

↑ COAGULATION

↓ FIBRINOLYSIS
Pathophysiology

An inflammatory stimulus

Production of proinflammatory mediators. Numerous cytokines.

Engulfing the Enemy
Neutral ph--endothelial cell adhesion

Activate the clotting mechanism

Microthrombi

Organ dysfunction and failure

Shunting + Capillary Obstruction (micro thrombi) = decreased delivery of O₂ and impaired removal of CO₂ and waste

Vasoactive mediators cause blood flow to bypass capillary exchange vessels (a distributive defect)

A Salvaging Attempt

Late Sign
Cardiac output increases Later decrease BP falls

arteries and arterioles dilate
decreasing peripheral arterial resistance

Opposed by anti-inflammatory mediators a negative feedback mechanism.
Sepsis: Who’s at Risk?

- Extremes of age (<1 year and >65 years)
- Malnutrition
- Hypothermia
- Use of central venous catheters
- Endotracheal intubation/mechanical ventilation
- Aspiration
- Chronic illness
- Diabetes
- Renal failure
- Hepatic failure
- Immunodeficiency
- AIDS
- Alcoholism
- Use of chemotherapeutic agents
- Use of surgery or invasive procedures
THE SHOCKING REALITY OF SEPSIS

- More common than a heart attack
- Claims more lives than cancer
- Largest killer of children and newborn infants in the world

Yet only 55% of American adults have heard of sepsis

Mortality from sepsis increases 8% every hour that treatment is delayed

Early detection is critical

As many as 80% of sepsis deaths could be prevented with rapid diagnosis and treatment
Management of Sepsis 2001-2016
Sepsis 6 Pack within 6 hours

1. Serum Lactate Level
2. Blood Cultures before Antibiotics
3. Antibiotics within 1 hour

For Hypotension and elevated Lactate

1. Fluids and Vasopressors (central line) to MAP > 65 mm Hg
2. CVP > 8 mm Hg
3. ScvO2 > 70%
INCLUSION = Sepsis AND [BP < 90 after fluid OR Lactate > 4]

<table>
<thead>
<tr>
<th>Control</th>
<th>Intervention</th>
<th>EGDT</th>
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<tbody>
<tr>
<td>CVP 8-12</td>
<td>Fluids</td>
<td>CVP 8-12</td>
</tr>
<tr>
<td>MAP &gt; 65</td>
<td>Vasopressors</td>
<td>MAP &gt; 65</td>
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<tr>
<td></td>
<td>Transfusions</td>
<td>ScvO2 &gt; 70%</td>
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<tr>
<td></td>
<td>Dobutamine</td>
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<tr>
<td>49% mortality</td>
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<td>33% mortality</td>
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<td>LOS 4 less days</td>
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<td>$13-16,000 savings</td>
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</tbody>
</table>

NNT to prevent 1 event (death) ~ 7
SBP <90 mmHg or MAP <65 mmHg after 20–30 cc/kg crystalloid IVF
-OR-
Lactate >4 mmol/L regardless of blood pressure

Supplemental oxygen ± endotracheal intubation and mechanical ventilation (if necessary)

Perform central venous catheterization while continuing crystalloid IVF resuscitation (250–1,000 mL boluses)

Critical care consultation

CVP

< 8 mmHg

Crystalloid IVF

8–12 mmHg

Vasopressor (s) (norepinephrine or dopamine preferred)

MAP

< 65 mmHg

≥ 65 mmHg

ScvO₂

< 70%

Transfusion of red cells to hematocrit ≥30%

≥ 70%

Inotropic agents (If PA catheter inserted, keep cardiac index ≥3.0 L/min/m²)

Goals achieved

No

Yes

Resuscitation completed

Establish reevaluation intervals
Hospital-wide impact of a standardized order set for the management of Severe Sepsis

SURVIVING SEPSIS GUIDELINES

COMPARISON OF RECOMMENDATIONS FROM 2012 TO 2016
The 2012 sepsis criteria maintained the model of “early goal-directed therapy” (EGDT) as a guiding principle which became the standard of care after the groundbreaking Emmanuel Rivers’ study in 2001.

The 2017 Surviving Sepsis Guidelines now reflect the results of the PROCESS, PROMISE, and ARISE trials; 3 large multi-center studies demonstrating no significant difference in the primary outcome of mortality between EGDT and usual care.

- Away from strict CVP and SVO2 monitoring
- Away from Dobutamine
- Away from Blood Transfusions

(ProCESS Investigators 2014, ARISE Investigators 2014, Mouncey 2015)
2016
Sepsis-3

**REDUNDANT**

**RETIRED**

Temp. >38°C or <36°C, HR >90, RR >20 or PaCO₂ <32, WBCs >12,000 or <4,000 or >10% bands
Let’s Replace SIRS with qSOFA

The new diagnostic tool for Sepsis = qSOFA

≥ 2 of the 3 indicators below:
- Altered Mental Status
- SBP of < 100
- Respiration rate > 22

Septic Shock Definitions
- Persisting hypotension requiring vasopressors to maintain MAP ≥ 65 mm Hg
- Blood lactate > 2 despite adequate volume resuscitation

So What is Sepsis Then?

**Sepsis** is Clinical Diagnosis now defined as: **Life-Threatening Organ Dysfunction caused by a Dysregulated Host Response to Infection.**

*Note that “Severe Sepsis” (previously used for sepsis with organ dysfunction) is no longer recognized since it would be redundant.*

**Septic Shock** is a Clinical Diagnosis now defined as: **A subset of Sepsis with circulatory and cellular/metabolic dysfunction associated with a higher risk of mortality.**

Sepsis and Septic Shock are Medical Emergencies and it is recommended that treatment and resuscitation begin Immediately.
Management of Sepsis 2017
Sepsis Bundle

Within 3 Hours:

1. Measure Lactate level
2. Obtain Blood Cultures before giving antibiotics
3. Administer broad spectrum Antibiotics
4. Administer 30ml/kg crystalloid for hypotension or lactate ≥ 4mmol/L
Severe Sepsis: Why Lactate?

As a marker of inadequate perfusion or inadequate consumption of O2.

As a marker of *resuscitation and restoration* of adequate cellular oxygen consumption.

As a predictor of patient outcome (mortality) and development of organ dysfunction.
Serum lactate level as a predictor of mortality in patients with sepsis (n = 1278). The 28-day in-hospital mortality was 8.2% (105 patients); death occurred within 3 days in 4.3% (55 patients).

Timing of Antimicrobial Therapy

- Data from 2,154 ICU patients with septic shock from 14 ICU’s in North America
- Median time to effective antibiotics: 6 hours
- Appropriate antibiotic use in the 1st hour was associated with 79.9% survival
- Survival ↓ by 7.6% per hour in the 1st six hours
- OR for death = 1.12 per hour of delay

Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival

Sepsis Bundle

Within 6 Hours:

5. Vasopressors (for fluid non-responders):
   maintain a mean arterial pressure (MAP) ≥ 65mmHg

6. If septic shock or initial lactate ≥ 4:
   Measure volume status and tissue perfusion
   CVP, ScVO2, Bedside US,
   Dynamic Assessment of fluid responsiveness to PLR or fluid bolus

7. Re-measure lactate (if initially elevated)
Sepsis: Source Control

A specific anatomic site of infection should be established as rapidly as possible and within the first 6 hours of presentation.

<table>
<thead>
<tr>
<th>Technique</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Drainage</td>
<td>Intra-abdominal abscess, Thoracic empyema</td>
</tr>
<tr>
<td>Debridement</td>
<td>Necrotizing fasciitis, Infected pancreatic necrosis</td>
</tr>
<tr>
<td>Device removal</td>
<td>Infected vascular catheter, Urinary catheter</td>
</tr>
<tr>
<td>Definitive control</td>
<td>Cholecystectomy, Sigmoid resection</td>
</tr>
</tbody>
</table>
Sepsis: Primary Source

- Pulmonary: 50%
- Abdomen/Pelvis: ~25%
- Primary bacteremia: ~15%
- Urosepsis: 10%
- Skin: 5%
- Vascular: 5%
- Other: ~15%

Martin GS, et al. NEJM 2003;348:1546
New Surviving Sepsis Guidelines
Fluid Resuscitation

• **Initial fluid resuscitation** - *Unchanged from 2012 guidelines*
  • 30ml/kg of IV crystalloid fluid (normal saline or balanced salt solution) within the first 3 hours of sepsis presentation.
  • Patients may require greater volumes of fluid as guided by frequent reassessment of volume responsiveness.
  • Consider 4% albumin in refractory hypotension.

• **Static fluid status measurements** (i.e. Central Venous Pressure)
  • No longer recommended as lone guiding principles as they carry limited value for measuring fluid responsiveness
  • 2017 - recommend the use of dynamic variables over static variables to predict fluid responsiveness
  • (i.e. passive leg raise, pulse pressure variation, stroke volume variation)

• **Weak suggestion to guide resuscitation to normal Lactate**
  • Use clinical judgement. For instance, if patient has adequate BP and urine output and is down-titrating vasopressors, but has a persistently elevated lactate, additional fluid carries the risk of over-resuscitation.
New Surviving Sepsis Guidelines

Antibiotics

• First priority is source control and obtaining cultures

• Cultures – Obtain prior to administration of antibiotics (when feasible)

• Give Antibiotics within 1 hour of identification of Septic Shock

• Antibiotic Regimen
  ◦ Begin with broad spectrum coverage when the potential pathogen is not immediately obvious
  ◦ Narrow once pathogen identification and sensitivities are established

• Consider using Procalcitonin to guide de-escalation of antibiotics
New Surviving Sepsis Guidelines
Vasopressors

- Useful in patients who remain hypotensive despite adequate fluid resuscitation
- Target MAP of 65mmHg
- First line vasopressor: **Norepinephrine**
  - Dose: start 2-12 mcg/min (no true maximum dose)
- Administer Vasopressin (up to 0.03) and Epinephrine as add-on therapies if not at target MAP
- Consider inotropes in low cardiac output states
  - i.e. septic cardiomyopathy, which can be common in these patients
New Surviving Sepsis Guidelines
Other

• **Steroids** - Indicated for patients with septic shock in which fluids and vasopressors fail to achieve hemodynamic stability

• **Transfusion** - indicated in majority of patients only when Hb <7.0

• **Target Glucose** <180mg/dL

• **Bicarbonate** - *not recommended* when pH > 7.15

• **Mechanical Ventilation** (unchanged from 2012)
  - Lung Protective Ventilation Strategy Target a TV of 6mL/kg of IBW
  - Plateau pressure of <30cm H20
  - PEEP: increase with FiO2 as per ARDSnet protocol
  - Recommend **prone** over supine position
    - in patients with sepsis-induced ARDS and Pa/Fio2 ratio<150
  - Recommendation **against** high frequency oscillatory ventilation
SEPSIS KILLS

RECOGNIZE - RESUSCITATE - REFER

EMS - ER - ICU
EMS and Sepsis
Likely encountered more often than suspected...
9 year experience in Seattle, WA reviewed 407,176 runs
- Severe Sepsis = 3.3 per 100 EMS encounters
- AMI = 2.3 per 100
- Stroke = 2.2 per 100

Severe Sepsis in Pre-Hospital Emergency Care
Analysis of Incidence, Care, and Outcome

Christopher W. Seymour1,2, Thomas D. Rea3,4, Jeremy M. Kahn2,5, Allan J. Walkey6, Donald M. Yealy7, and Derek C. Angus2,8

EMS Sepsis Trend

Also increasing

- Sepsis
- AMI
- Stroke
EMS and Sepsis

Wang et al, 2010
- 1/3 ED patients with severe sepsis & septic shock received initial care from prehospital providers
- 2/3 of sepsis deaths were transported by EMS

Studnek et al, 2012
- 51.4% transported by EMS
  - EMS patients had more organ failure
  - 41 minute reduction to Early Goal Directed Therapy (EGDT) (119 vs 160)
  - 35 minute reduction to administration of antibiotics (111 vs 146)
    - If EMS documented sepsis in report
  - 62 minute reduction to EGDT (69 vs 131)
  - 50 minute reduction to administration of antibiotics (70 vs 120)
Sepsis: RECOGNIZE

- **SIRS**
  - Temp > 38 or < 36
  - HR > 90
  - RR > 20
  - WBC > 12 or < 4 or > 10% Bands

- **qSOFA**
  - AMS
  - SBP < 100
  - RR > 22

- **100 Rule**
  - SBP < 100
  - HR > 100
  - Temp > 100

Remember:
This is used for a patient with known or suspected infection.
Ie. UTI, Pneumonia, visible wound/cellulitis
SEPSIS PATHWAY

Does your patient have risk factors, signs or symptoms of infection?
- Immunocompromised
- Indwelling medical device
- Recent surgery/invasive procedure
- History of fever or rigors
- Red Flags in ambulance handover
- Skin: cellulitis, wound
- Urine: dysuria, frequency, odour
- Abdomen: pain, peritonism
- Chest: cough, shortness of breath
- Neuro: decreased mental alertness, neck stiffness, headache

AND

Does your patient have 2 or more yellow criteria?
- Respiration ≤ 10 or ≥ 25 per minute
- SpO₂ < 95%
- Systolic blood pressure ≤ 100 mmHg
- Pulse ≤ 50 OR ≥ 120 per minute
- Altered LOC or change in cognitive status
- Temp ≤ 35.5 or ≥ 38.5°C

Re-assess
- Treat and re-assess simultaneously: Sepsis may still be a concern

Yes
- Perform venous blood gas if available

Does your patient have any red criteria?
- SBP ≤ 90mmHg
- Lactate ≥ 4 mmol/L
- Base Excess < - 5.0
- Age > 65 years
- Immunocompromised
Initiation of Prehospital Sepsis Alert

1. Suspected Infection
2. Two or more of the Following
   - Temperature > 38 or < 36
   - Heart Rate > 90
   - Respiratory Rate > 20
3. ETCO2 < 25 (Capnography)

Decreased:

- Time to blood culture 27 vs 14 min
- Time to antibiotics 56 vs 40 min
- Time to fluids 34 vs 10 min
- Length of Stay 13 vs 9 min
- ICU Admission 53% vs 33%
- Mortality 14% vs 7%
Capnography

The "Other" Vital Sign

© 2011 – BreathSounds, LLC
Capnography – The "Other" Vital Sign – 4th Edition
Capnography

What does exhaled CO$_2$ tell us?

1. Ventilation
2. Perfusion
3. Metabolism

Helps Assess:

1. Accurate respiratory rate
2. Airway patency
   - Bronchospasm
   - Air trapping
   - Obstruction
3. Shock states
4. Response to treatment
Sudden loss of waveform
- ET tube disconnected, dislodged, kinked or obstructed
- Loss of circulatory function

Decreasing EtCO₂
- ET tube cuff leak
- ET tube in hypopharynx
- Partial obstruction

CPR Assessment
- Attempt to maintain minimum of 10mmHg

Sudden increase in EtCO₂
- Return of spontaneous circulation (ROSC)

Bronchospasm ("Shark-fin" appearance)
- Asthma
- COPD

Hypoventilation

Hyperventilation

Decreased EtCO₂
- Apnea
- Sedation
## Abnormal ETCO₂

<table>
<thead>
<tr>
<th></th>
<th>Increased ETCO₂</th>
<th>Decreased ETCO₂</th>
</tr>
</thead>
</table>
| **Ventilation** | • Hypoventilation  
• Bronchoconstriction  
• Drug overdose | • Hyperventilation  
• Dislodged ET-Tube |
| **Circulation**  | • Good CPR  
• Return of pulse (ROSC)  
• Increased cardiac output | • Apnea  
• Cardiac Arrest  
• Pulmonary Edema  
• Pulmonary Embolism |
| **Metabolism**   | • Fever/Hyperthermia  
• Seizure  
• Burns  
• Muscle use | • DKA  
• Sepsis  
• Hypothermia |
EtCO2 and Sepsis

EtCO2 reflects **Perfusion**
- $\downarrow$ cardiac output $= \downarrow$ EtCO$_2$

EtCO2 reflects **pH**
- CO$_2$ is transported in the blood as bicarbonate (HCO$_3$)
- $\downarrow$ HCO$_3$ $= \downarrow$ EtCO$_2$

EtCO2 reflects **Lactate & Mortality**
- Inverse, linear relationship
- $\downarrow$ EtCO$_2$ $= \uparrow$ lactate

- *Lactate requires blood testing - Capnography is instantaneous*
RECOGNIZE - RESUSCITATE - REFER

EMS - ER - ICU
Sepsis Bundle

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Summary

- Sepsis (Severe Sepsis) and Septic shock are common with mortality rates ranging from 35%-50%
- Evidenced-based recommendations are available and should be practiced in an effort to improve patient outcomes

✓ Identify patients early and identify the severity of sepsis
✓ Quickly administer appropriate antibiotics and source control
✓ Establish institutional goals for physiologic resuscitation
✓ Multidisciplinary protocol based chronic phase of care to ensure compliance
DR.
BP < 100
HR > 100
AMS
Temp > 100
Tachypnea > 20
Questions?