

Surviving Sepsis

Recognition, Resuscitation and Rapid Interventions

Sara Levin, MD
April 30, 2010
(5 years later)



Epidemiology

- ◆ Sepsis: Accounts for 10% of deaths annually with a 30% mortality rate
 - ◆ More deaths from sepsis each year than Myocardial Infarction
 - ◆ Kills more than breast, colon, pancreatic & prostate cancer combined
- ◆ Number one cause of multiple-organ failure and death in patients with critical illness
- ◆ Increased incidence without any significant change in mortality over past 30 years

Angus DC, et al. Crit Care Med 2001;29:11303-10.

Dombrovskiy V, et al.. Crit Care Med. 2007;35:1244

Epidemiology - 2010

- ◆ Further analysis suggests regional & demographic variations in incidence & mortality that may be important
- ◆ Estimates range from 660,000 to 750,000 cases annually with mortality rates from 18% to 30%
- ◆ The highest regional incidence & mortality was in contiguous Southeastern & Midatlantic states
- ◆ Older age, male sex & Black race confer significantly increased risk for incidence, severity & mortality in sepsis

Martin GSN Engl J Med. 2003 Apr 17;348(16):1546-54.

Angus DC Crit Care Med. 2001 Jul;29(7):1303-10

Wang HE Int J Health Geogr. 2010 Feb 15;9:9

History of Clinical Sepsis

You would have to ask the gods for Help:



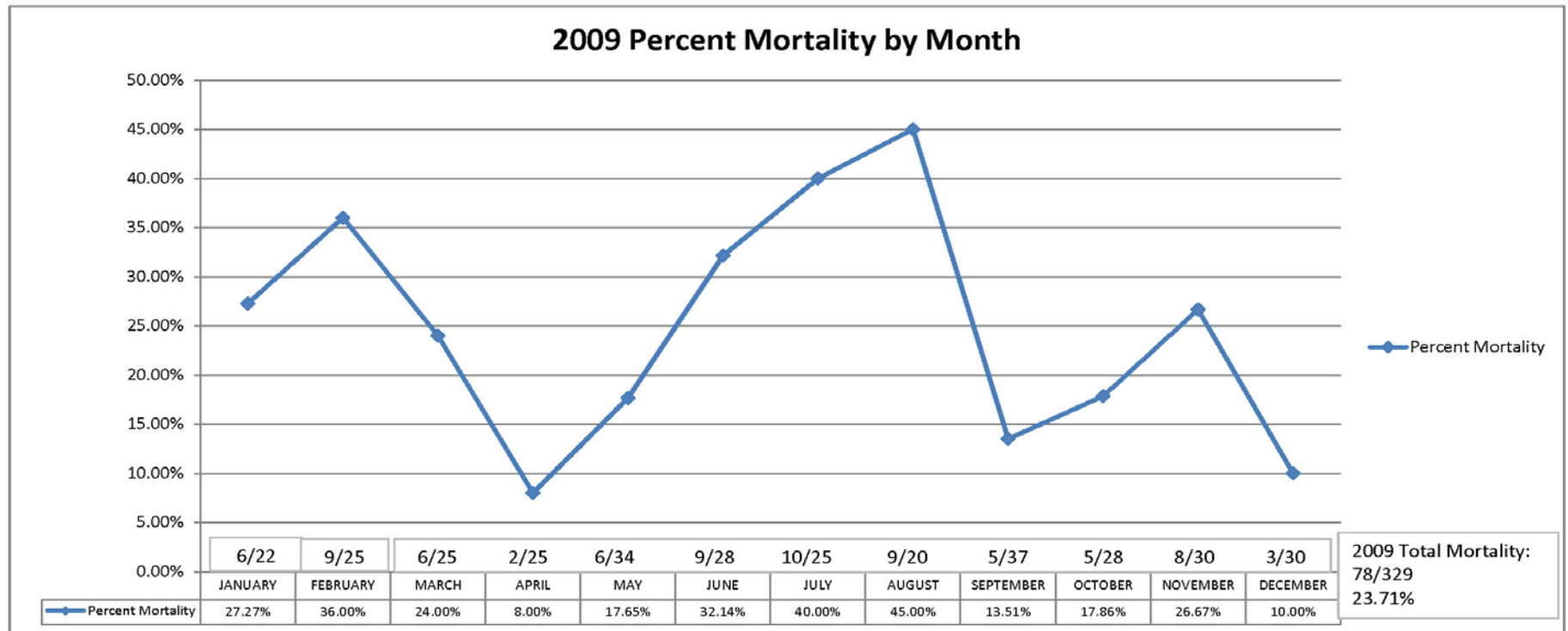
History of Clinical Sepsis:

Than Came Antibiotics:

The First Use of Penicillin in the United States Charles M. Grossman Ann Intern Med July 15, 2008 149:135136

33 yo woman with septicemia with beta-hemolytic streptococcus

Epidemiology of Sepsis CCRMC



YEAR

2009

2006-8

2004-5

CASES(ICD-9 D/C DX)

329

127 (ICD-9 limited)

115 (ICD-9 limited)

MORTALITIES (%)

78 (24%)

37 (29%)

23 (20%)

Today's Objectives

1. Understand the clinical features associated with Sepsis.
2. Understand the spectrum of disease in Sepsis and be able to define the criteria that distinguish Sepsis from Severe Sepsis and Septic Shock.
3. Be able to define the basic principles of "Early Goal-Directed Therapy" for Severe sepsis and septic shock.
4. Become familiar with the CCRMC sepsis screening tool; its utility and limitations.

CCRMC Case (2009)

- ♦ 62 yo man with DM2 & HTN presented with acute GI distress with vomiting, diarrhea, poor po intake weakness, and leukocytosis. Admitted for IV hydration and antibiotic treatment. HD#2 became hypotensive to SBPs 80s-90s and was given an IV fluid bolus with initial response. HD#3, at noon, he had recurrent hypotension but was not addressed until he was noted to have a change in level of consciousness at 7PM and he was then recognized to be in septic shock and multi-organ failure. Transferred to ICU, severe sepsis bundle initiated. He expired 2 days later.

CCRMC Case (4 weeks ago)

- ♦ 76 yo man with hypoxemia, LLL consolidation and leukocytosis. He received appropriate initial treatment in ED with antibiotics but did not get aggressive fluid resuscitation because of concern for his CHF. He developed worsening hypotension with SBPs decreased from his baseline of 130s-150s to 70s-90s. Hypotension started in the ED and continued in the IMCU for 14 hours with poor response to repeated fluid bolus. By the next day he had oliguric renal failure, acute cardiac ischemia & delirium. After 24 hrs. of hospitalization he was transferred to the ICU to receive Sepsis bundle/EGDT with aggressive fluid resuscitation & vasopressor support & CVP monitoring. Over the subsequent 48 hours he had resolution of his hypotension with improvement in his multi-organ failure. He slowly recovered to be discharged to a SNF.



State of Sepsis - 2010

- ◆ Successful Interventions:
- ◆ EGDT (Rivers, et al., NEJM 11/8/01):
 - ◆ Emergency Dept. Recognition of Severe Sepsis/Septic shock with EGDT. NNT=6
- ◆ Sepsis Screening Tools in SICU identified with a Sensitivity and PPV of 96.5% and 80.2%, respectively. A NPV of 99.5% (Moore LJ, et al. J trauma 2009;66:1539-47)
 - ◆ Mortality reduced from 35% to 23% (NNT=8)
- ◆ Clearly Early Recognition & Intervention is the KEY!!

CCRMC (INLP) Stomp Out Sepsis Campaign:

- ◆ Initiative of the Integrated Nurse Leadership Program funded by the Betty Moore Foundation
- ◆ Major #1 Goal: "To Reduce Mortality in Severe Sepsis by 15%"
- ◆ How: Improve the early recognition and early guidelines-based treatment interventions for patients with or at risk for severe sepsis or septic shock.
- ◆ How: "Develop sustaining plans, including policies, procedures, new processes, new tools, new orientation approach"
 - ◆ Use of sepsis screening tool 95% of the time in all units
 - ◆ Use of EGDT bundle in severe sepsis/shock 85% of the time

CCRMC SOS (Stomp Out Sepsis) Team:

- ◆ Joelle Kennedy, RN
- ◆ Jaspreet Benepal, RN
- ◆ Miles Kotchevar, RN
- ◆ Kathy Ferris, RN, ID
- ◆ Sue Batterton, Lab Dir.
- ◆ Sharon Sihota, Pharm.
- ◆ Jane Yimbo, Ed/Tr.
- ◆ Carol Lucido, RN, ED
- ◆ Donna Garro, RN, QM
- ◆ Gina Peters
- ◆ Mary Murphy, RN
- ◆ Baraka Peterson
- Akiko Rodriguez, RN, ED
- Neil Jaysekera, MD
- Kim Hauer, RN, 4B
- Myra Mellena, RN, 5D
- Kip Norwood, RN, ICU
- Erlyn Marmbett, RN, 5D
- Wayne Dixon, RN, 4A
- Teresita Inton, 5D
- Luz Baldoza
- Helena Martey, RN, ICU
- Denise Donnelly
- Sara Levin, MD



Definitions

The SIRS to Septic Shock

- ◆ Systemic Inflammatory Response Syndrome (SIRS):
 - ◆ Temperature >100.4 or <96.8
 - ◆ Heart Rate >90
 - ◆ Respiratory Rate >20 or $\text{PaCO}_2 < 32$
 - ◆ WBC $>12,000$ or <4000
- ◆ SIRS can be self limited or can progress to septic shock.



Definitions

The SIRS to Septic Shock

- ◆ Sepsis:
 - ◆ Suspected infection with at least 2 of 4 SIRS criteria
- ◆ Severe Sepsis:
 - ◆ Suspected infection with 2 of 4 SIRS criteria and evidence of organ dysfunction and/or global hypoperfusion (lactic acid $>4\text{mmol/L}$)
- ◆ Septic Shock:
 - ◆ Sepsis with acute circulatory failure marked by persistent hypotension after an adequate fluid resuscitation (20-30ml/kg over 30min)

Pathophysiology

- ◆ "The microorganisms that seem to have it in for us....turn out...to be rather more like bystanders...it is our response to their presence that makes the disease. Our arsenal for fighting off bacteria are so powerful...that we are more in danger from them than the invaders." -Lewis Thomas



Pathophysiology

- ◆ Sepsis - SIRS with suspected infection
 - ◆ Release of inflammatory mediators resulting in arterial vasodilatation
- ◆ Severe sepsis is marked by organ dysfunction because of tissue ischemia.
 - ◆ Mismatch of oxygen demand and supply
 - ◆ Tissue ischemia progresses to multiple organ failure.

Pathophysiology

- ◆ Septic Shock - the end stage of sepsis syndrome with circulatory collapse.
 - ◆ High mortality rate in sepsis is due to multiple organ failure and cardiovascular failure resulting in death.
- ◆ Identify where the patient is on the continuum and act appropriately.



Sepsis

Standard of Care Interventions

- ◆ Fluid Resuscitation
- ◆ Antimicrobial treatment
- ◆ Hemodynamic monitoring
- ◆ Vasopressor support for hypotension
- ◆ Ventilatory support for respiratory failure



What Has Changed?

- ◆ Previous studies were in the ICU starting 24-72 hours into the course of sepsis
- ◆ Rivers study started at hour 1 in the ER
- ◆ The identification of the "golden hour" of sepsis
- ◆ The understanding that "time is tissue"



What Has Changed?

- ◆ The urgency of the interventions
 - ◆ 6-hour time frame from identification to achievement of clinical goals
- ◆ The parameters we use to assess the severity of illness and the adequacy of our interventions
 - ◆ CVP, MAP, Urine Output, Lactic Acid, Hct, ScvO₂

Sepsis Screening Tool

**CONTRA COSTA HEALTH CENTERS
CONTRA COSTA REGIONAL MEDICAL CENTER
SEVERE SEPSIS SCREENING TOOL**

DRAFT 4/27/2010

Date: _____

Instructions: Screen patients ≥ 14 years of age for severe sepsis in the ED, on the floors, or in the CCU/IMCU.

MR362 (4-10) Page 1

SEVERE SEPSIS SCREENING TOOL

NOC SHIFT		DAY SHIFT		PM SHIFT	
TIME OF SCREENING: <input type="checkbox"/> 0000 <input type="checkbox"/> New Adm		TIME OF SCREENING: <input type="checkbox"/> 0800 <input type="checkbox"/> New Adm		TIME OF SCREENING: <input type="checkbox"/> 1600 <input type="checkbox"/> 2000 <input type="checkbox"/> New Adm	
I. <u>TWO</u> or more of the following NEW signs of SIRS: <input type="checkbox"/> T > 100.4° F (38° C) OR < 96.8° F (36° C) <input type="checkbox"/> HR > 90 <input type="checkbox"/> RR > 20 OR PaCO ₂ < 32 <input type="checkbox"/> WBC > 12K or < 4K		I. <u>TWO</u> or more of the following NEW signs of SIRS: <input type="checkbox"/> T > 100.4° F (38° C) OR < 96.8° F (36° C) <input type="checkbox"/> HR > 90 <input type="checkbox"/> RR > 20 OR PaCO ₂ < 32 <input type="checkbox"/> WBC > 12K or < 4K		I. <u>TWO</u> or more of the following NEW signs of SIRS: <input type="checkbox"/> T > 100.4° F (38° C) OR < 96.8° F (36° C) <input type="checkbox"/> HR > 90 <input type="checkbox"/> RR > 20 OR PaCO ₂ < 32 <input type="checkbox"/> WBC > 12K or < 4K	
<input type="checkbox"/> YES <input type="checkbox"/> NO		<input type="checkbox"/> YES <input type="checkbox"/> NO		<input type="checkbox"/> YES <input type="checkbox"/> NO	
II. Suspected or Confirmed Infection? <input type="checkbox"/> YES <input type="checkbox"/> NO		II. Suspected or Confirmed Infection? <input type="checkbox"/> YES <input type="checkbox"/> NO		II. Suspected or Confirmed Infection? <input type="checkbox"/> YES <input type="checkbox"/> NO	
If the answer is YES to both I AND II above , notify MD regarding patient's status and recommend use of Sepsis Screening Labs. Proceed to Step III.		If the answer is YES to both I AND II above , notify MD regarding patient's status and recommend use of Sepsis Screening Labs. Proceed to Step III.		If the answer is YES to both I AND II above , notify MD regarding patient's status and recommend use of Sepsis Screening Labs. Proceed to Step III.	
III. SBP < 90 or a drop to more than 40 below baseline (if known) <input type="checkbox"/> YES <input type="checkbox"/> NO		III. SBP < 90 or a drop to more than 40 below baseline (if known) <input type="checkbox"/> YES <input type="checkbox"/> NO		III. SBP < 90 or a drop to more than 40 below baseline (if known) <input type="checkbox"/> YES <input type="checkbox"/> NO	
IV. One or more NEW signs of organ failure: <input type="checkbox"/> Unexplained acute changes in mental status <input type="checkbox"/> New or increased need for oxygen		IV. One or more NEW signs of organ failure: <input type="checkbox"/> Unexplained acute changes in mental status <input type="checkbox"/> New or increased need for oxygen		IV. One or more NEW signs of organ failure: <input type="checkbox"/> Unexplained acute changes in mental status <input type="checkbox"/> New or increased need for oxygen	
<input type="checkbox"/> YES <input type="checkbox"/> NO		<input type="checkbox"/> YES <input type="checkbox"/> NO		<input type="checkbox"/> YES <input type="checkbox"/> NO	
If the answer is YES to either III OR IV AND pt has a suspected or confirmed infection, patient meets criteria for SEVERE SEPSIS. Begin Sepsis Screening Labs and Notify MD.		If the answer is YES to either III OR IV AND pt has a suspected or confirmed infection, patient meets criteria for SEVERE SEPSIS. Begin Sepsis Screening Labs and Notify MD.		If the answer is YES to either III OR IV AND pt has a suspected or confirmed infection, patient meets criteria for SEVERE SEPSIS. Begin Sepsis Screening Labs and Notify MD.	
<input type="checkbox"/> Patient does not meet criteria for possible SEPSIS. RN Signature: _____ Comments: _____		<input type="checkbox"/> Patient does not meet criteria for possible SEPSIS. RN Signature: _____ Comments: _____		<input type="checkbox"/> Patient does not meet criteria for possible SEPSIS. RN Signature: _____ Comments: _____	
<input type="checkbox"/> Patient meets criteria for possible SEPSIS. Name of MD notified: _____ Time MD notified: _____ RN Initials: _____ Comments: _____		<input type="checkbox"/> Patient meets criteria for possible SEPSIS. Name of MD notified: _____ Time MD notified: _____ RN Initials: _____ Comments: _____		<input type="checkbox"/> Patient meets criteria for possible SEPSIS. Name of MD notified: _____ Time MD notified: _____ RN Initials: _____ Comments: _____	



Target Population EGDT

- ◆ **Severe sepsis or septic shock**
 - ◆ Patient must have all 3 of the following to meet this definition:
 - ◆ Suspected infection
 - ◆ At least 2 of 4 SIRS criteria
 - ◆ Lactic Acid >4 **OR** hypotension (SBP <90 or MAP <65) after an adequate fluid bolus (20-30ml/kg or apx. 1-3L)
- ◆ Exclusion of patients with other suspected causes of hypotension (e.g. GI bleed, myocardial infarction, etc.)

Is This Septic Shock?

$$CO = (HR)(SV)$$
$$BP = (CO)(SVR)$$

Hypovolemic Shock

- ◆ Primary problem volume
- ◆ Decreased stroke volume
- ◆ Decreased cardiac output
- ◆ Increased SVR

Cardiogenic Shock

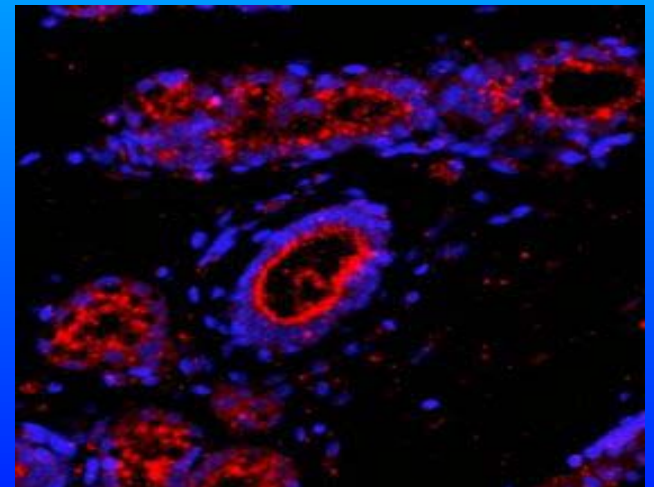
- ◆ Primary problem contractility
- ◆ Decreased stroke volume
- ◆ Decreased cardiac output
- ◆ Increased SVR


Both hypovolemic and cardiogenic shock are PUMP PROBLEMS. Body's homeostatic mechanisms are INTACT

Septic Shock

- ◆ Decreased SVR BAD HUMORS!!
- ◆ Endothelial/cellular dysfunction
- ◆ Multi-organ failure
 - ◆ Lung
 - ◆ Kidney
 - ◆ Liver
 - ◆ Heart
- ◆ Clotting derangements

Toxins!!





Early Goal Directed Therapy

Time is Tissue

- ◆ Rapid resuscitation with colloid or crystalloid
 - ◆ Initial NS bolus followed by q30 minute repeated bolus to goal of CVP 8-12
- ◆ Early Broad-Spectrum Antibiotics
 - ◆ Draw cultures and administer antibiotics within 1 hour of identified sepsis case




Early Goal Directed Therapy

Time is Tissue

Fluid Resuscitation

- ◆ Begin fluid resuscitation in ER/floor while patient is being moved to the ICU
- ◆ Initial NS bolus: 20-30ml/kg
- ◆ Repeat 500ml bolus every 30 minutes to achieve CVP of 8-12mm Hg
- ◆ In mechanically ventilated patients, target CVP is 12-15 mm Hg




Early Goal Directed Therapy

Time is Tissue

- ◆ **Cultures and Antibiotics**
- ◆ Antibiotics administered within 1 hour of identification
- ◆ Immediate cultures and work-up:
 - ◆ Blood (2 peripheral), Urine, Sputum (gram stain and culture), CXR.
 - ◆ If patient has an indwelling central line than this line should be removed or changed over a wire with the tip sent for culture

Early Goal-Directed Therapy

- ◆ Central line
- ◆ Titrate CVP 8-12
- ◆ Urine output 0.5 cc/kg/hr
- ◆ Titrate mean arterial pressure to ≥ 65
 - ◆ Dopamine or norepinephrine
- ◆ Titrate ScvO₂ > 70
 - ◆ Hgb
 - ◆ Dobutamine



Early Goal Directed Therapy

Time is Tissue

- ◆ **Establish Central Venous Access**
 - ◆ Objectives:
 - ◆ To provide vasopressor support safely without increasing risk for peripheral ischemia
 - ◆ To measure CVP
 - ◆ Goal: 8-12 mm Hg (12-15 mm Hg in mechanically ventilated patients)
 - ◆ To measure central venous O₂ saturation:
 - ◆ Goal: ScvO₂ > 70%

Vasopressors Smorgasboard

Medication	Receptors	Inotropy	Chronotropy	Dose
Dopamine	$\alpha = \beta$ $\alpha > \beta$	Yes Vasoconstriction effect	Yes	5-10 mcg/kg/min > 10 mcg/kg/min
Dobutamine	β_1 and β_2 Peripheral vasodilator	Yes	Yes	2.5 - 20 mcg/kg/min
Norepinephrine (Levophed)	$\alpha > \beta$	Yes	No	0.03 – 1.5 mcg/kg/min.
Phenylephrine (Neosynephrine)	α	Peripheral Vasoconstriction		0.5 - 8 mcg/kg/min.

Vasopressors and Inotropes

Pure α

Alpha=Beta

Pure β

Phenylephrine

Norepinephrine

Epinephrine

Dobutamine

High dose

Dopamine

Low dose
($<10\text{mcg/kg/min}$)

Adjunctive Therapy--Steroids


- ◆ Consider IV hydrocortisone if blood pressure responds poorly to fluid resuscitation and pressors.
- ◆ Hydrocortisone dose ≤ 300 mg/day
- ◆ ACTH stim test no longer recommended
- ◆ Wean steroids once pressors are off
- ◆ Do not use steroids in the absence of shock unless there are other medical indications.

Adjunctive Therapy—rhAPC

- ◆ Consider rhAPC in adult patients with sepsis-induced organ dysfunction with clinical assessment of high risk of death (typically APACHE II 25 or multiple organ failure) if there are no contraindications
- ◆ Adult patients with severe sepsis and low risk of death (typically, APACHE II 20 or one organ failure) should not receive rhAPC

Adjunctive Therapy--Blood


- ◆ Give red blood cells when hemoglobin decreases to 7.0 g/dL unless there is another medical indication (MI, severe hypoxia, EGDT goals, etc.)
- ◆ Do not use erythropoietin to treat sepsis-related anemia.
- ◆ Give FFP only if active bleeding or planned procedure
- ◆ Give platelets only if indicated



Early Goal Directed Therapy

Time is Tissue

- ◆ **Central Venous Oxygen Saturation (ScvO₂):**
 - ◆ Goal: ScvO₂ > 70%
 - ◆ ScvO₂ < 70% suggests maximal extraction and O₂ delivery may be insufficient
 - ◆ Optimization of O₂ delivery:
 - ◆ Transfusions to HCT > 30%
 - ◆ Dobutamine titrated to ScvO₂ > 70%



Early Goal Directed Therapy

Time is Tissue

◆ Other Goals

- ◆ Urine output: 0.5ml/kg/hour
- ◆ Lactate: <4mmol/L
- ◆ SaO₂: >92%
- ◆ Fluids, O₂ supplementation or other interventions may be used by the treating physician to achieve these goals.

Early Goal Directed Therapy

- ◆ Monitoring:
- ◆ Vital signs, laboratory data, cardiac monitoring, pulse oximetry, urinary catheterization, central venous catheterization, CVPs
- ◆ Laboratory data:
 - ◆ Basic Metabolic panels, Mg, PO₄, CBC, Lactic acid, ScvO₂, INR



Early Goal Directed Therapy Summary

- ◆ *Early recognition and resuscitation is the key to survival in sepsis.*
- ◆ *Time is Tissue* and we need to use the *golden hours* to achieve these goals:
- ◆ CVP > 8mm Hg
- ◆ MAP > 65 mm Hg or SBP > 90 mm Hg
- ◆ HCT > 30% or Hgb > 9.0
- ◆ ScvO₂ > 70%



A man & A bug

- ◆ A 72 year old man was admitted with ACS. He has no ECG changes and negative enzymes. On day #2, he has a fever to 102.5 and shaking chills. His BP is 100/60, HR 60, RR 34, Pox 92%. His left sided chest pain now has a pleuritic component. His medications are ASA, Enoxaparin, Atenolol, Lipitor, HCTZ.
- ◆ What do you want to do next?



A man & A bug

- ◆ He tells you that he feels short of breath. His BP is now 85/40. He does not feel well but he does not feel presyncopal or lightheaded. The primary MD arrives at the bedside and orders an ECG.
- ◆ What other interventions would you recommend at this moment?



A man & A bug

- ◆ He is 100 kg. So you give him 2L NS bolus over the next 45 minutes. His BP comes up to 110/50. Blood cultures, sputum gram stain and culture, U/A, urine culture and CXR are completed. You start the antibiotics. His labs return and his WBC count is 18.0 and his Lactic Acid is 4.2.
- ◆ Should he be started on the early goal directed therapy? Does he meet the criteria? What is the next step?



□ A man & A bug



- ◆ An IJ line is placed and his CVP is 5. The doctor orders a 500ml NS bolus and then LR at 100ml/hour. One hour later his CVP is 6 and his BP has been trending down and is now 88/46. His other labs are back which include a creatinine of 1.6, an anion gap of 15. His CXR shows a LLL consolidation.
- ◆ What should be done now?

A man & A bug



- ◆ You continue to give him repeated boluses as well as maintenance fluids but his ongoing hypotension requires vasopressor support. The Doctor orders Dopamine starting at 5mcg/kg/min. His heart rate increases to 108 but his pressure is still only 92/40
- ◆ What should be done now?

A man & A bug



- ◆ This dose of dopamine is likely having more beta effects than alpha effects resulting in increased heart rate and inotropy but not in increased SVR. You suggest that the dopamine be titrated to BP to meet the goal MAP of >65 . You titrate the dopamine up to 14mcg/kg/min . After 5 liters of fluid and titration of dopamine, his CVP is now 9 and his SBP is 100-110 with a MAP of 70. His pulse oximetry is 92% and his RR is 28. His CBC shows a WBC of 18 and a Hgb of 7.
- ◆ If you were to follow the algorithm, what is your next step?

A man & A bug



- ◆ You want to check his urine output and ScvO₂. His urine output during the last hour was 100ml. You send a blood sample from the central line in an ABG syringe and ask respiratory to run a central mixed venous oxygen saturation. The ScvO₂ is 74%.
- ◆ What should be done next?

A Man & A Bug

- ◆ Take a deep breath!
- ◆ Take a break!
- ◆ He is doing well, because you STOMPED OUT SEPSIS with Early Recognition and Early Goal-Directed Therapy

