Sepsis

From EMS to ER to ICU

What we need to be doing

NEHAL BHATT, MD

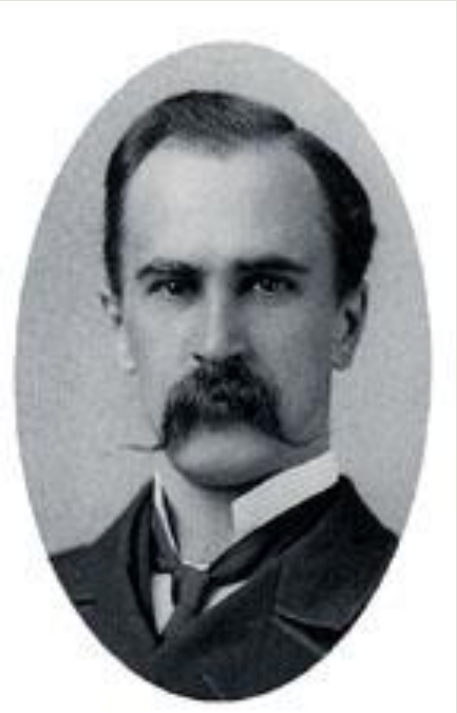
ATHENS PULMONARY, CRITICAL CARE AND SLEEP

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

Infection/ Trauma	SIRS	Sepsis	Severe Sepsis	Septic Shock
Associated Mortality Rates		**10%**	**35%**	**50%**
	≥2 of the following: ◦ Temp ≥38°C or ≤36°C ◦ HR ≥ 90 ◦ RR ≥20/min ◦ WBC ≥12 or ≤4,000 or >10% Bands	SIRS + Evidence of Infection	Sepsis + one or more organ dysfunction criteria (except shock) SBP < 90 or MAP < 65 Lactate > 2 INR > 1.5 BR > 2 UP < 0.5 ml/kg/hr x 2 hrs Cr > 2 Plts < 100 SpO2 < 90% on RA	Sepsis + Shock criteria Lactate > 4 at any point Hypotension persisting after 30 ml/kg of IVF

SIRS = systemic inflammatory response syndrome.

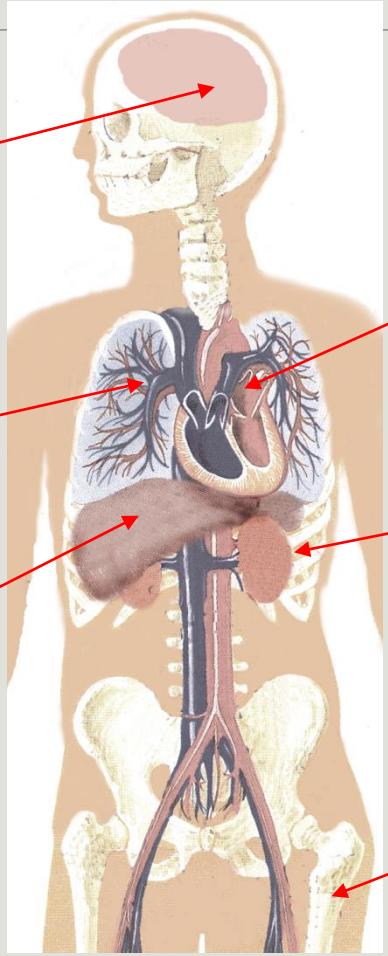
Bone et al. *Chest.* 1992;101:1644.

Identifying Acute Organ Dysfunction as a Marker of Severe Sepsis

Altered Consciousness
Confusion
Psychosis

Tachypnea
PaO_2 <70 mm Hg
SaO_2 <90%
PaO_2/FiO_2 ≤300

Jaundice
↑ Enzymes
↓ Albumin
–**PT/INR**
–**Bilirubin > 2 mg/dL**



Hypotension
(SBP < 90, MAP < 65)
Tachycardia
↑ CVP
↑ PAOP

Oliguria/Anuria
Urine Output < 0.5 mL/kg **X 2 hrs**
–**Creatinine (> 2.0)**

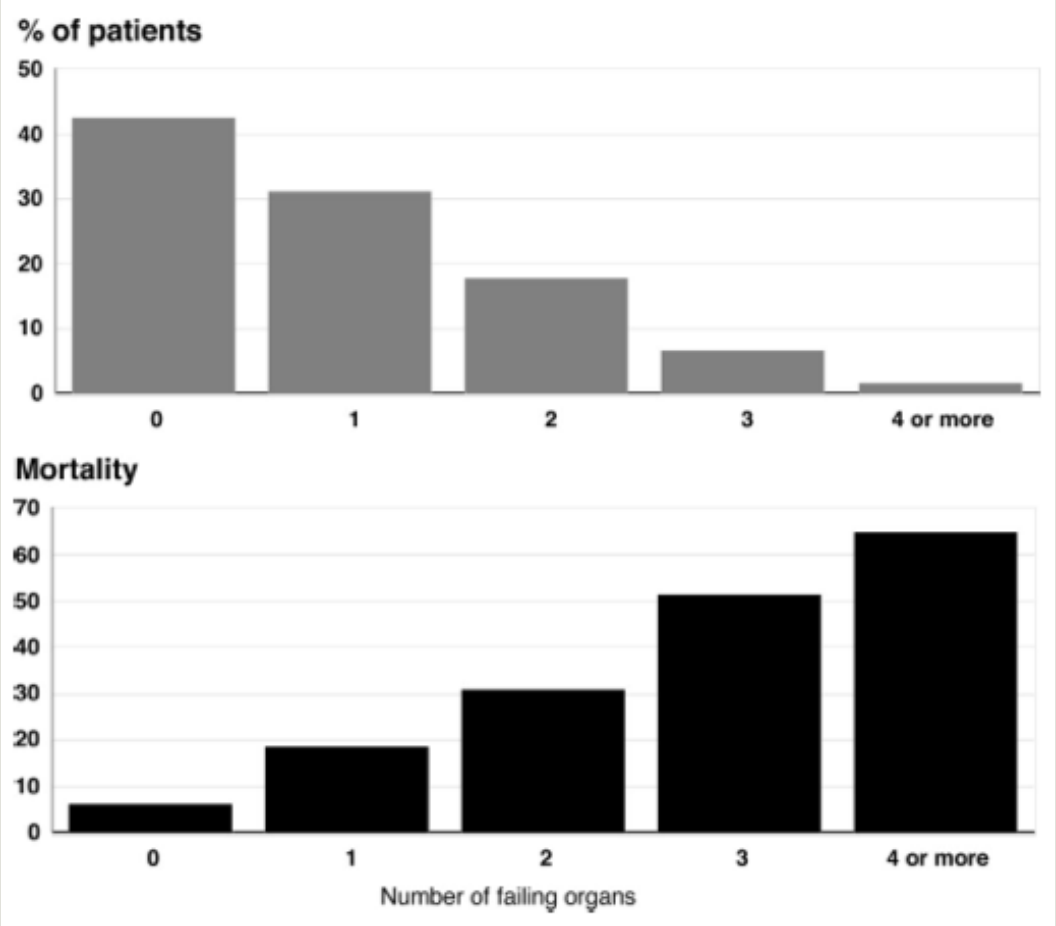
Platelets < 100K
INR > 1.5
–D-dimer

Lactate > 2.0

Why do Septic Patients Die?

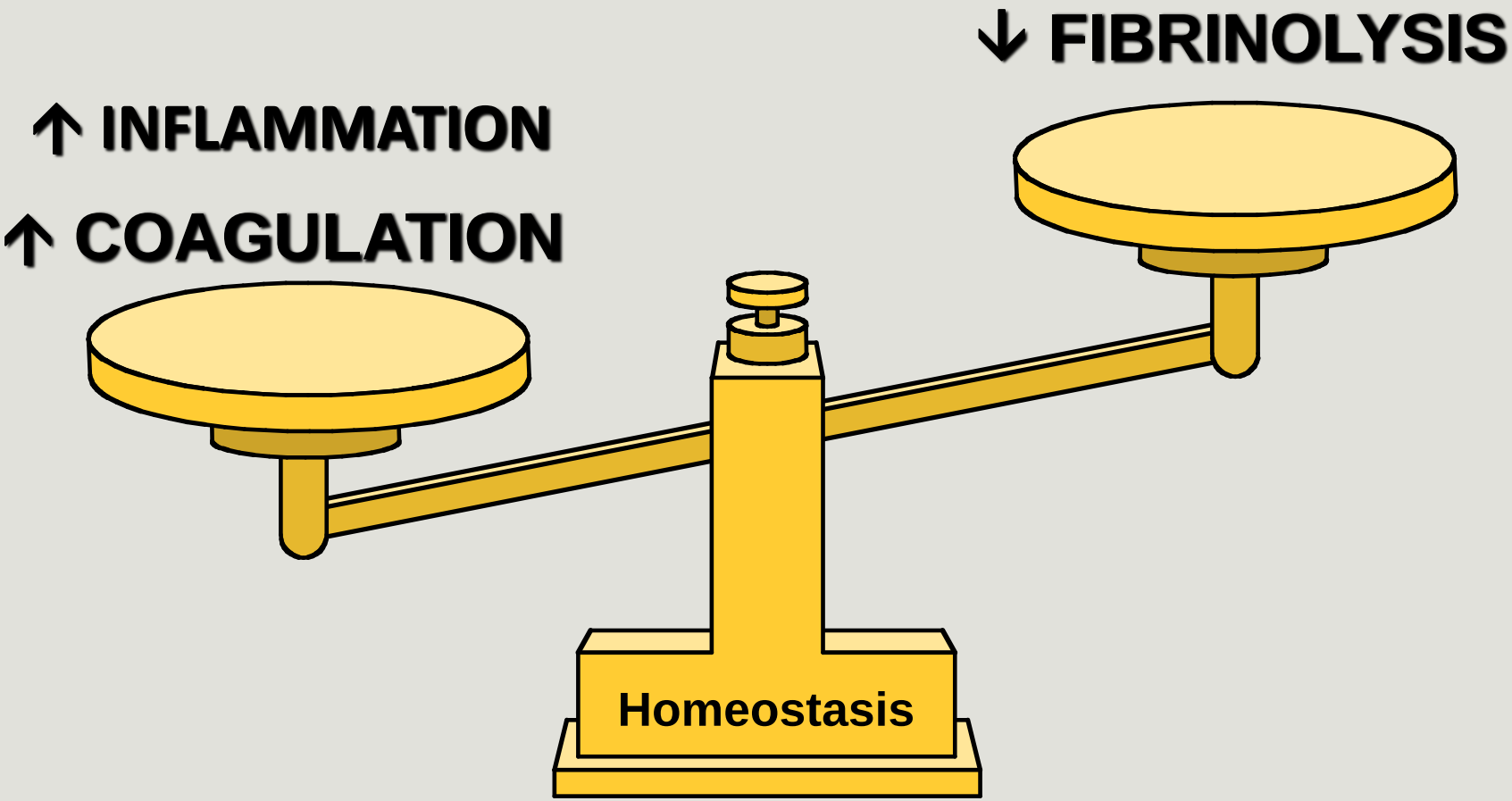
ANSWER: ORGAN FAILURE

Organ Failure in Sepsis



Vincent, J.-L., Sakr, Y., Sprung, C. L., Ranieri, V. M., Reinhart, K., Gerlach, H., Moreno, R., et al. (2006). Sepsis in European intensive care units: results of the SOAP study. *Critical Care Medicine*, *34*(2), 344–353.

Pathophysiology of Severe Sepsis



Carvalho AC, Freeman NJ. *J Crit Illness* 1994;9:51-75.
Kidokoro A, et al. *Shock* 1996;5:223-8.
Vervloet MG, et al. *Semin Thromb Hemost* 1998;24:33-44.

Pathophysiology

SEPSIS CASCADE

An inflammatory stimulus

Production of **proinflammatory** mediators. Numerous **cytokines.**

Engulfing the Enemy

Neutrophil–endothelial **cell adhesion**

Activate the **clotting** mechanism

Microthrombi

Opposed by **anti-inflammatory mediators**

a negative feedback mechanism.

arteries and arterioles **dilate**

decreasing peripheral arterial resistance

Late Sign

Cardiac output Increases Later decrease BP falls

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

A Salvaging Attempt

Shunting + Capillary Obstruction (micro thrombi) = **decreased delivery of O_2** and impaired removal of CO_2 and waste

Organ dysfunction and failure

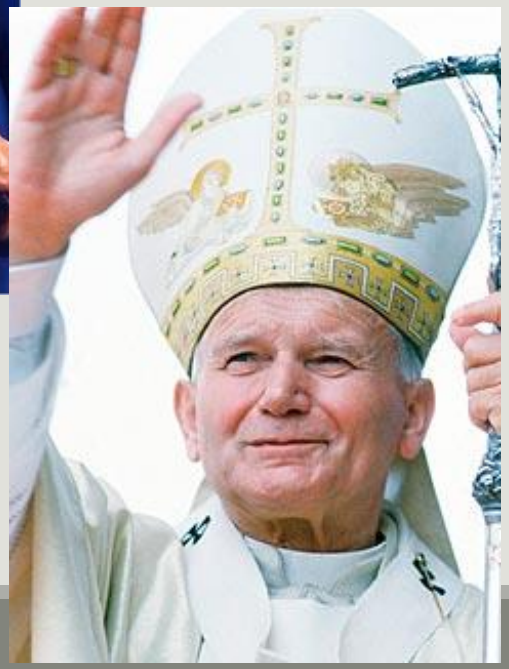
Sepsis

Severe Sepsis

Septic Shock

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[1]

Claims more lives than cancer[1]

Largest killer of children and newborn infants in the world[2]

YET ONLY **55%** OF AMERICAN ADULTS HAVE HEARD OF **SEPSIS**[3]

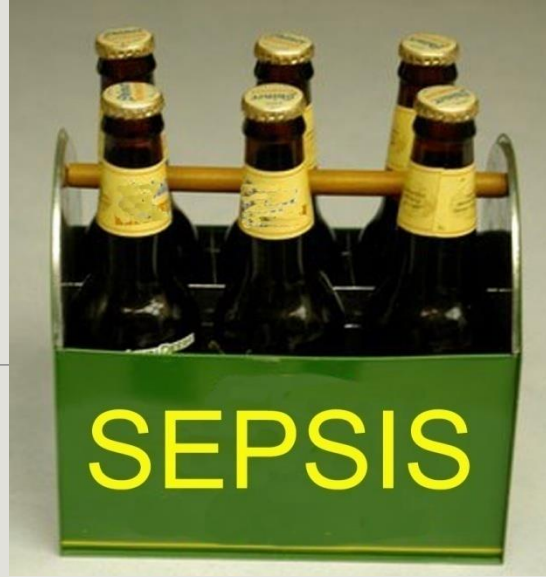
Mortality from sepsis increases 8% every hour that treatment is delayed[4]

EARLY DETECTION IS CRITICAL

As many as 80% of sepsis deaths could be prevented with rapid diagnosis and treatment[4]

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%

The New England Journal of Medicine

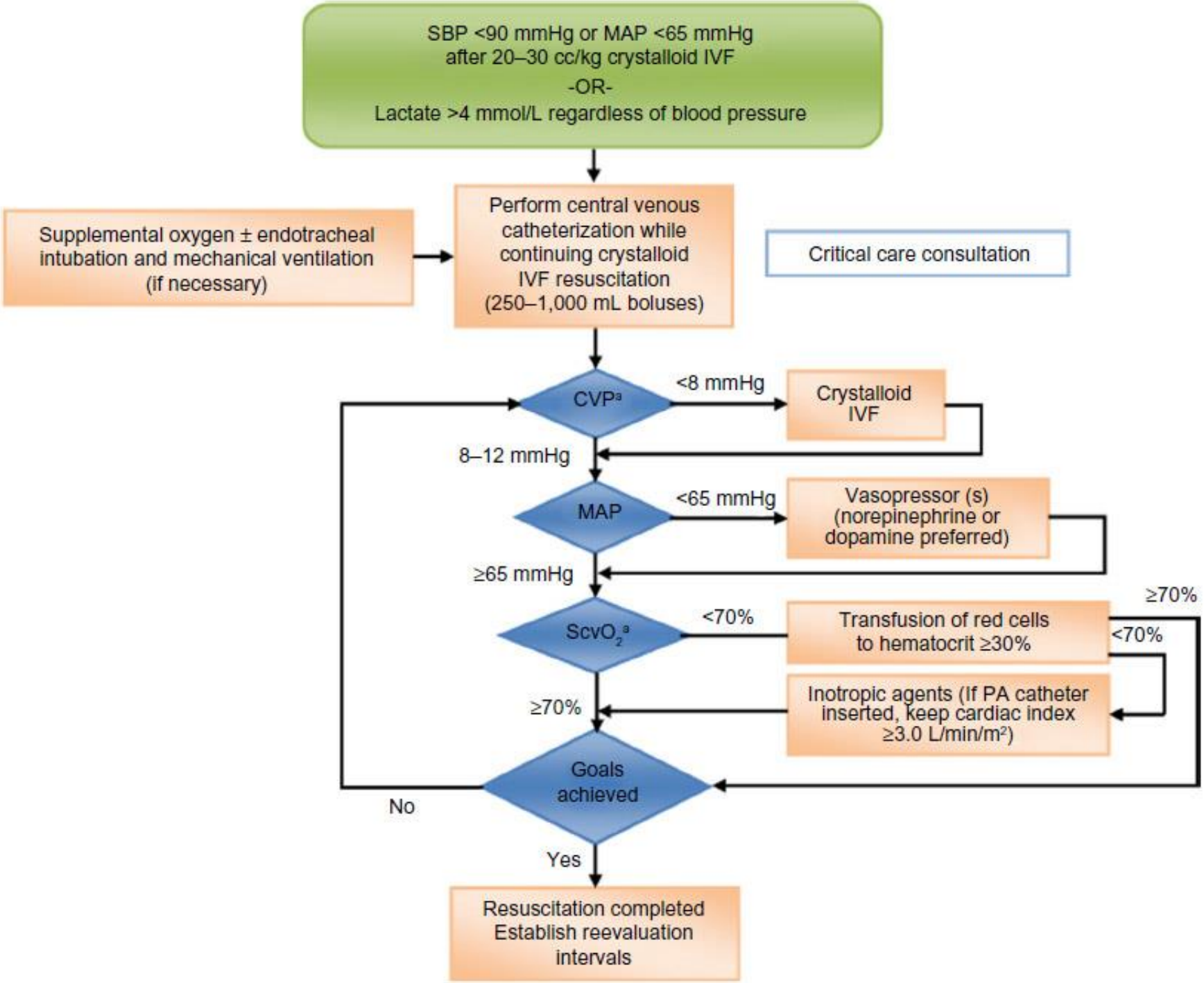
EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

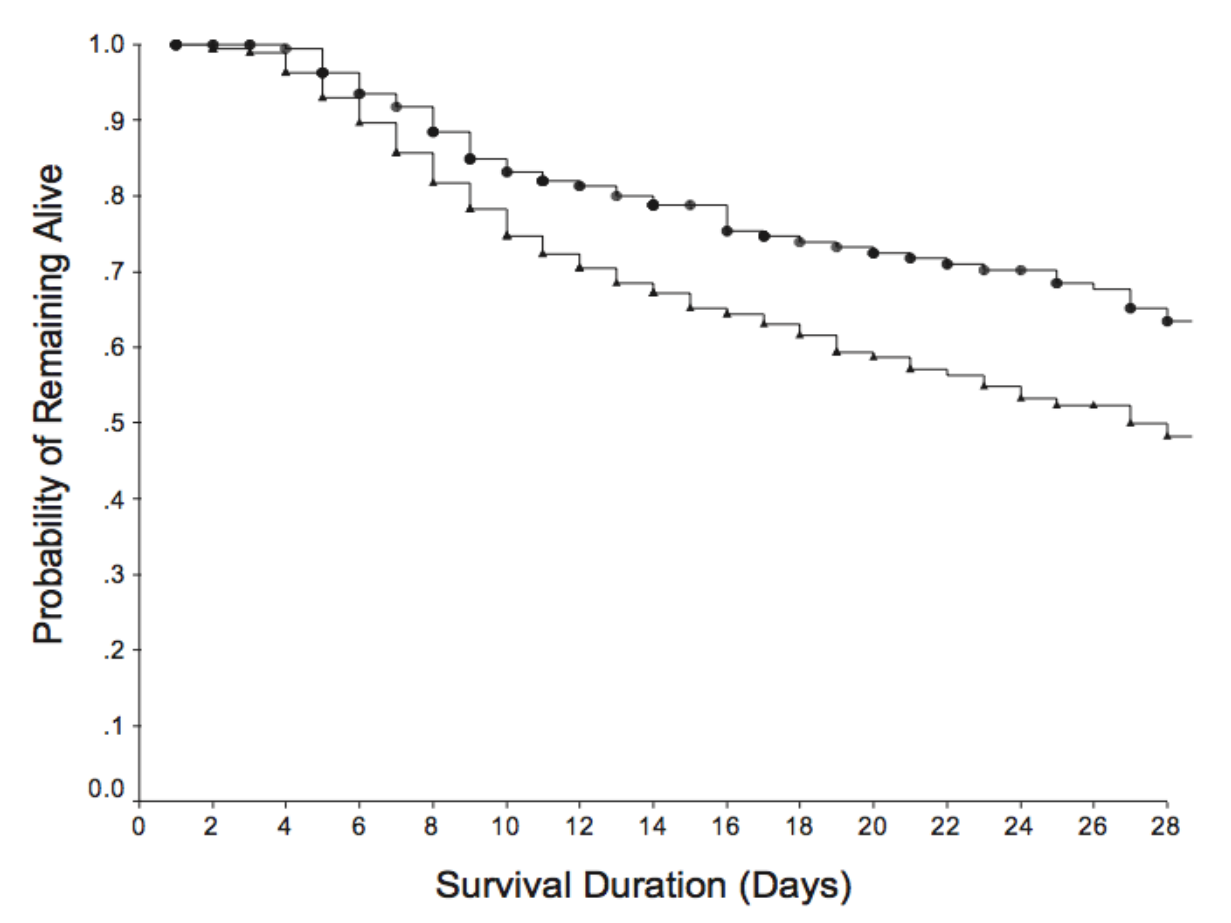
INCLUSION = Sepsis AND [BP < 90 after fluid OR Lactate > 4]

Control	Intervention	EGDT
CVP 8-12	Fluids	CVP 8-12
MAP > 65	Vasopressors	MAP > 65
	Transfusions Dobutamine	ScvO2 > 70%
49% mortality		33% mortality LOS 4 less days $13-16,000 savings

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[a]
<8 mmHg
Crystalloid IVF
8–12 mmHg
MAP
<65 mmHg
Vasopressor (s) (norepinephrine or dopamine preferred)
≥65 mmHg
ScvO2[a]
<70%
Transfusion of red cells to hematocrit ≥30%
≥70%
<70%
Inotropic agents (If PA catheter inserted, keep cardiac index ≥3.0 L/min/m2)
≥70%
Goals achieved
No
Yes
Resuscitation completed
Establish reevaluation intervals

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



Thiel, S. W., Asghar, M. F., Micek, S. T., Reichley, R. M., Doherty, J. A., & Kollef, M. H. (2009). Hospital-wide impact of a standardized order set for the management of bacteremic severe sepsis*. *Critical Care Medicine*, *37*(3), 819–824. doi:10.1097/CCM.0b013e318196206b

Society of Critical Care Medicine

ESICM

SURVIVING SEPSIS GUIDELINES

Surviving Sepsis Campaign

COMPARISON OF RECOMMENDATIONS FROM 2012 TO 2016

New Surviving Sepsis Guidelines

Released in January 2017

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

Septic Shock

Severe Sepsis + Hypotension

Severe Sepsis

Sepsis + End Organ Damage

Sepsis

SIRS + Infection

SIRS

Temp. >38°C or <36°C, HR >90, RR >20 or $PaCO_2$ <32,
WBCs >12,000 or <4,000 or >10% bands

Let's Replace SIRS with qSOFA

The new diagnostic tool for Sepsis = qSOFA

<u>≥ 2 of the 3 indicators below:</u>

- Altered Mental Status
- SBP of < 100
- Respiration rate > 22

<u>Septic Shock Definitions</u>

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

JAMA. 2016;315(8):762-774. doi:10.1001/jama.2016.0288

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.**

JAMA. 2016;315(8):762-774. doi:10.1001/jama.2016.0288

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

JAMA. 2016;315(8):762-774. doi:10.1001/jama.2016.0288

Management of Sepsis 2017

Surviving Sepsis Campaign

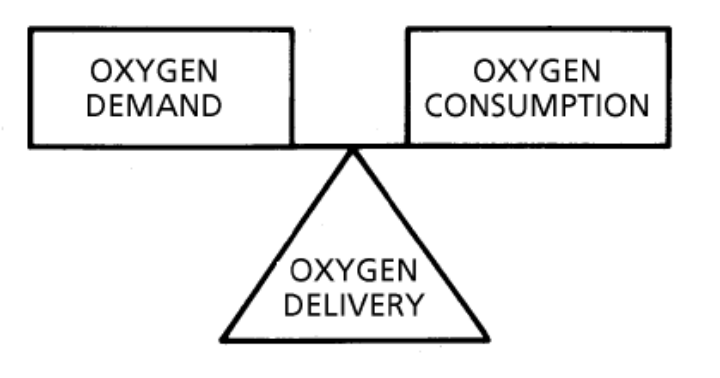
Sepsis Bundle

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 as a Predictor of Mortality

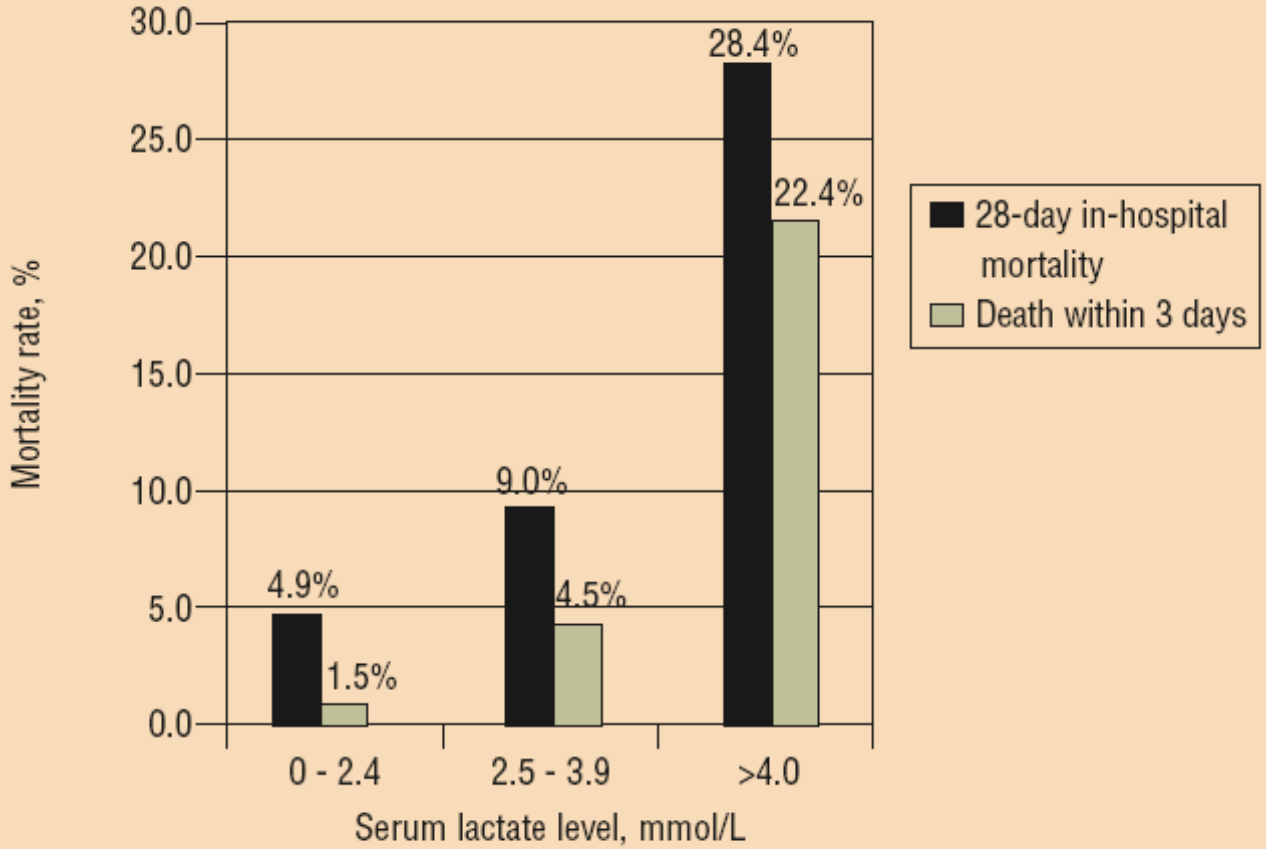


Figure 2 Serum lactate level as a predictor of mortality in patients with sepsis (n = 1278). The 28-day in-hospital mortality was 8.2% (105 patients); death occurred within 3 days in 4.3% (55 patients).

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

Kumar A, et al. Crit Care Med 2006;34:1589

Surviving Sepsis Campaign

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.

Technique	Examples
▪ Drainage	Intra-abdominal abscess, Thoracic empyema
▪ Debridement	Necrotizing fasciitis, Infected pancreatic necrosis
▪ Device removal	Infected vascular catheter, Urinary catheter
▪ Definitive control	Cholecystectomy, Sigmoid resection

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
    - (ie 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

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

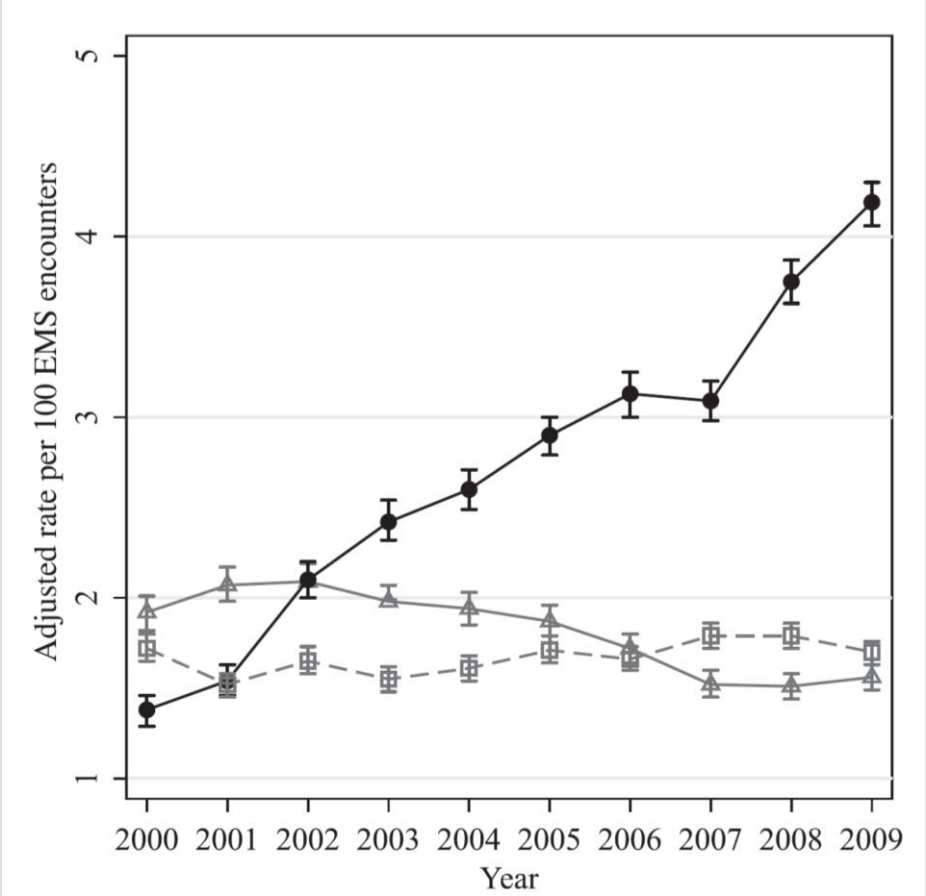
Analysis of Incidence, Care, and Outcome

Christopher W. Seymour[1,2], Thomas D. Rea[3,4], Jeremy M. Kahn[2,5], Allan J. Walkey[6], Donald M. Yealy[7], and Derek C. Angus[2,8]

Am J Respir Crit Care Med. 2012:186; 12: 1264–1271

EMS Sepsis Trend

Also increasing



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

ACI NSW Agency for Clinical Innovation

SEPSIS KILLS – RECOGNISE · RESUSCITATE · REFER

RECOGNISE

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?

- ❑ Respirations ≤ 10 or ≥ 25 per minute
- ❑ SpO_2 < 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

NO → Treat and re-assess simultaneously: **Sepsis may still be a concern** → **Re-assess**

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

EMS Sepsis Alert - *Hunter et al, 2016*

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)

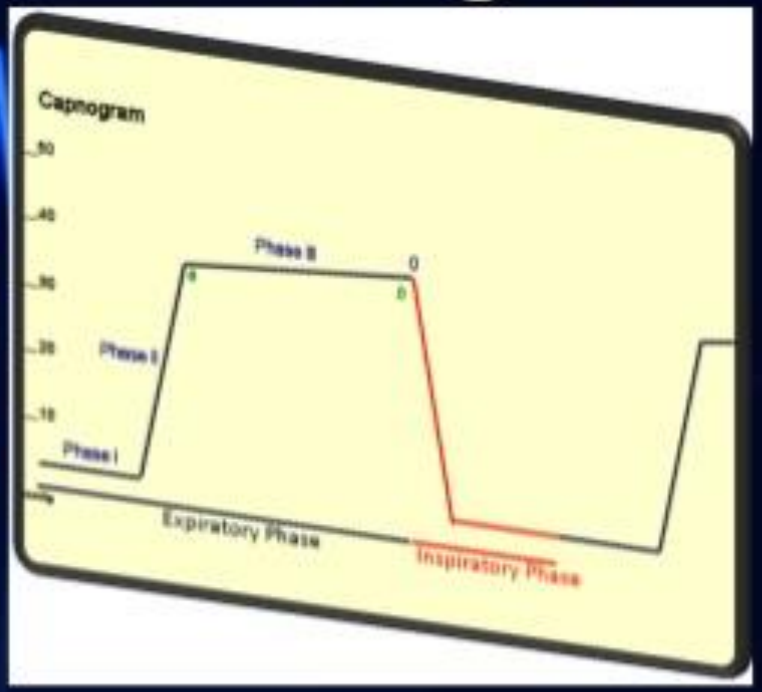
Decreased:

- 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

4th Edition



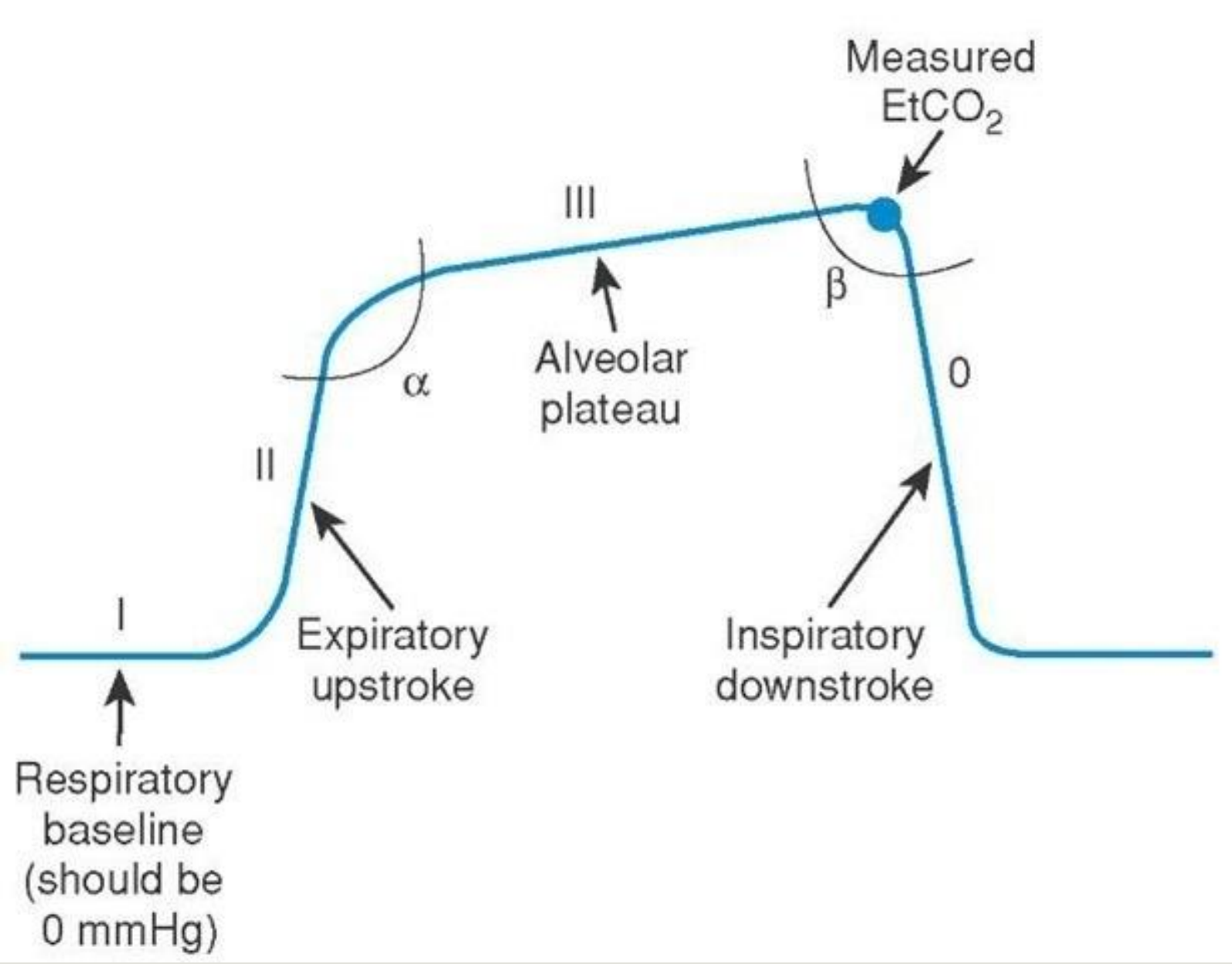
Capnography

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

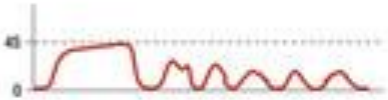

Measured
EtCO2
III
β
Alveolar
plateau
α
0
II
I
Expiratory
upstroke
Inspiratory
downstroke
Respiratory
baseline
(should be
0 mmHg)

Sudden loss of waveform

- ET tube disconnected, dislodged, kinked or obstructed
- Loss of circulatory function

Decreasing $EtCO_2$

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



CPR Assessment

- Attempt to maintain minimum of 10mmHg

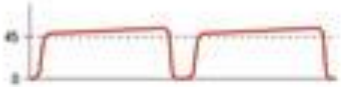
Sudden increase in $EtCO_2$

- Return of spontaneous circulation (ROSC)

Bronchospasm ("Shark-fin" appearance)

- Asthma
- COPD

Hypoventilation



Hyperventilation

Decreased $EtCO_2$

- Apnea
- Sedation

Abnormal $ETCO_2$

	Increased $ETCO_2$	Decreased $ETCO_2$
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

- ↓ cardiac output = ↓ $EtCO_2$

EtCO2 reflects pH

- CO_2 is transported in the blood as bicarbonate (HCO_3)
- ↓ HCO_3 = ↓ $EtCO_2$

EtCO2 reflects Lactate & Mortality

- Inverse, linear relationship
- ↓ $EtCO_2$ = ↑ lactate
- *Lactate requires blood testing - Capnography is instantaneous*

RECOGNIZE - RESUSCITATE - REFER

EMS - ER - ICU

Surviving Sepsis Campaign

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     - CVP, ScVO2, Bedside US,
     - Dynamic Assessment of fluid responsiveness to PLR or fluid bolus
7. Re-measure lactate (if initially elevated)

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?