# Sepsis & Septic Shock

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# Objectives

- Define Sepsis and Septic Shock
- Demonstrate effective interventions to reduce mortality and morbidity
- Discuss the use of lactic acid and procalcitonin levels in sepsis

# Sepsis

- Single most expensive condition in US
- 1.7 million cases/ year
- 270,000 deaths
- 30 day readmission – most common
- 30-50% hospital deaths
- < 1/3 Medicare patient's d/c home

# US Death rates

# Sepsis Definitions 1992

- Systemic Inflammatory Response Syndrome (SIRS)
- Sepsis
- Severe Sepsis
- Septic shock

Bone RC, Balk RA, Cerra FB, et al. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med. 1992;20(6):864–874

# Sepsis-3 2016

## The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP[1]; Clifford S. Deutschman, MD, MS[2]; Christopher Warren Seymour, MD, MSc[3]; Manu Shankar-Hari, MSc, MD, FFICM[4]; Djillali Annane, MD, PhD[5]; Michael Bauer, MD[6]; Rinaldo Bellomo, MD[7]; Gordon R. Bernard, MD[8]; Jean-Daniel Chiche, MD, PhD[9]; Craig M. Coopersmith, MD[10]; Richard S. Hotchkiss, MD[11]; Mitchell M. Levy, MD[12]; John C. Marshall, MD[13]; Greg S. Martin, MD, MSc[14]; Steven M. Opal, MD[12]; Gordon D. Rubenfeld, MD, MS[15,16]; Tom van der Poll, MD, PhD[17]; Jean-Louis Vincent, MD, PhD[18]; Derek C. Angus, MD, MPH[19,20]

*JAMA.* 2016;315(8):801-810. doi:10.1001/jama.2016.0287.

# Sepsis

…is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.

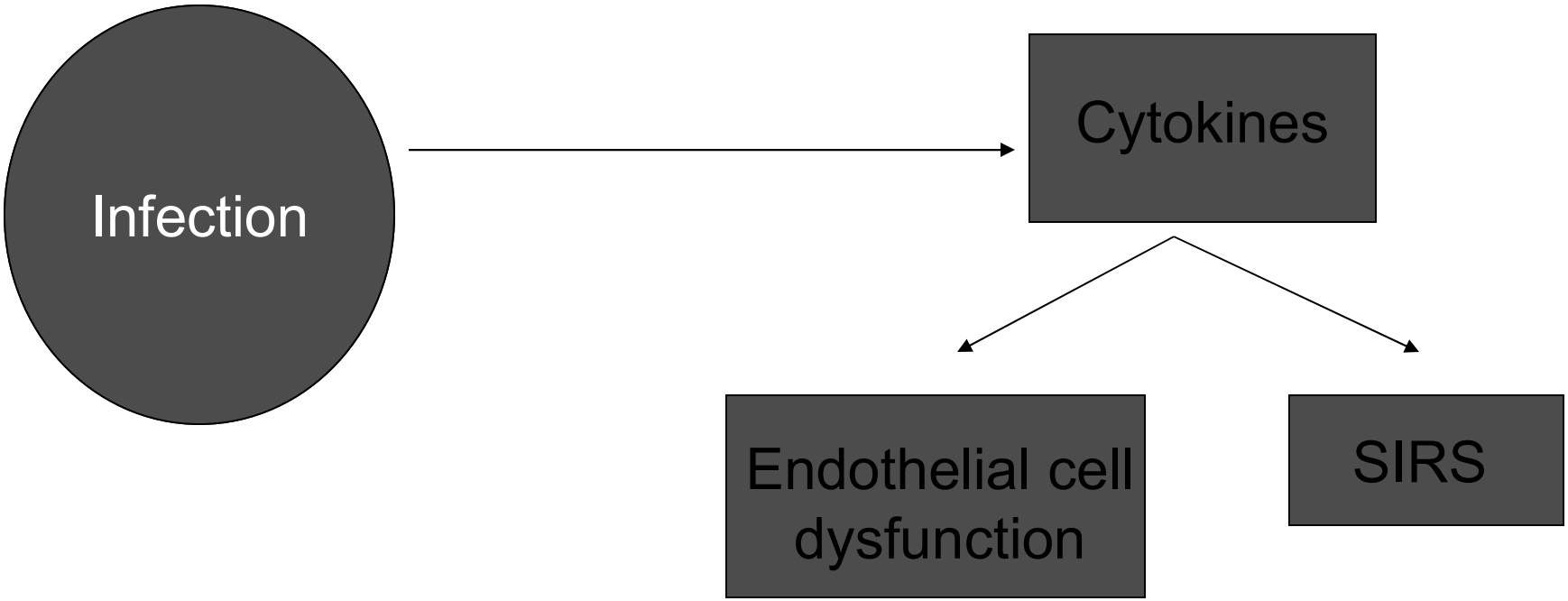
*JAMA*. 2016;315(8):801-810

# In lay terms…

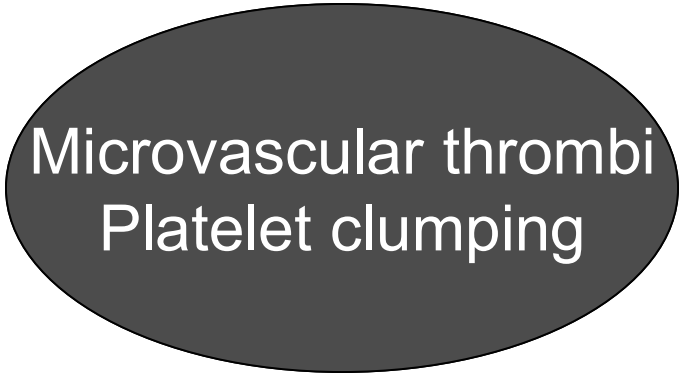
Sepsis is a life-threatening condition that arises when the body's response to infection injures its own tissues and organs.

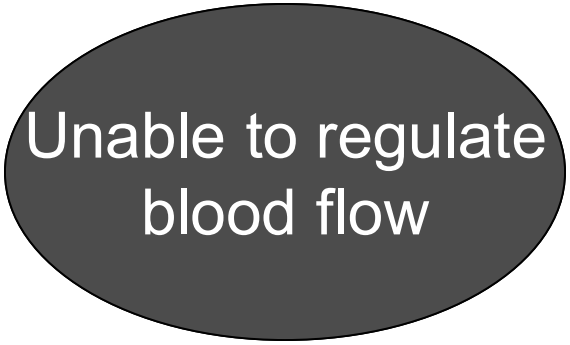
*JAMA*. 2016;315(8):801-810

# Proinflammatory Mediators

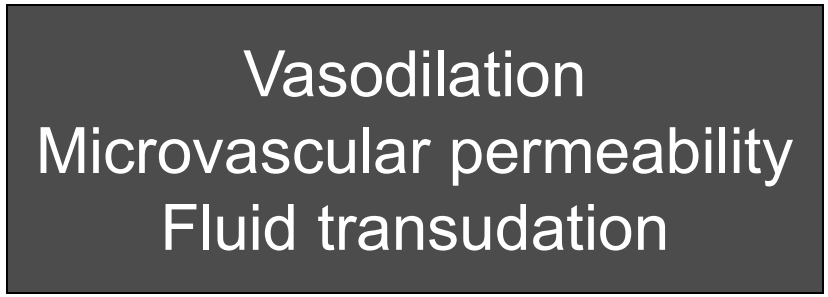


# Endothelial Cell Dysfunction








# Sequential Organ Failure Assessment

## SOFA Score

- $PaO_2/FiO_2$ ratio
- Platelet count
- Bilirubin
- MAP
- Glascow Coma Scale
- Creatinine & urine output

# qSOFA (quick)

- Respiratory rate ≥ 22
- Altered mentation
- Systolic BP ≤ 100 mmHg

- Early recognition
- Aggressive and immediate intervention

# Edgar vs Earl

- 80 yo man fever, productive cough
- T39 BP110/70 HR112 RR20
- CXR RLL infiltrate

- 77 yo change in mental status
- T38.5 BP90/60 HR96 RR26
- CXR RLL infiltrate

# What should you do next?

1) Administer antibiotics
2) Start IV fluids
3) Begin “vasopressors”
4) Obtain sputum Gram stain

# Fill the Tank!

Initial bolus…

Lactated Ringers*

30 mL/kg (1.5-3 liters)

Wide Open!

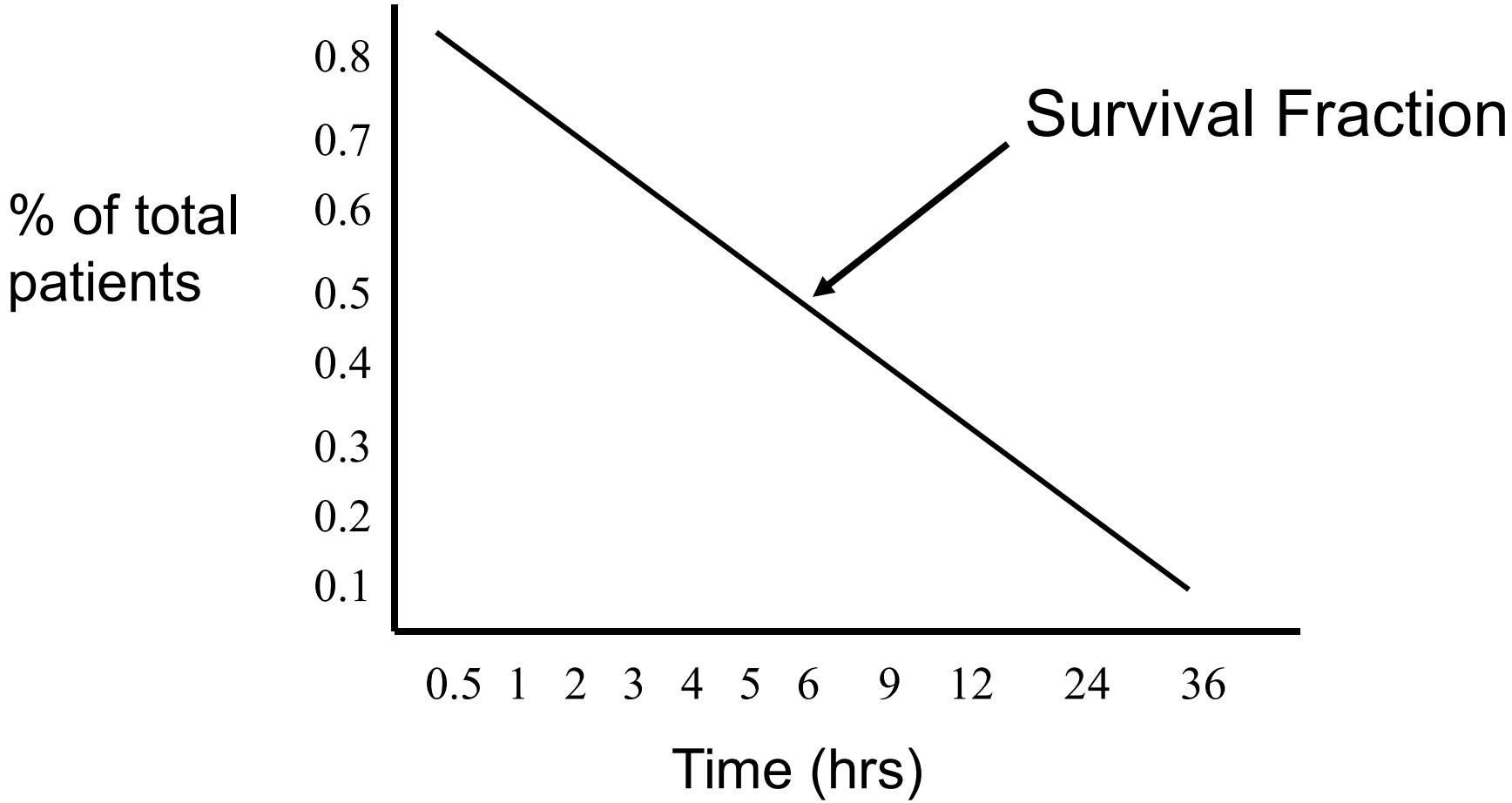

Brown RM, Semier MW, Fluid management in sepsis. *J Intensive Care Med*, 2019 May; 34(5): 364-373

# Fluid Resuscitation

- Blood pressure/ HR response
- Urine output
- Cardiothoracic US
- CVP/$ScvO_2$  Pulse pressure variation
- Lactate clearance/ normalization
- Dynamic measurements

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

# Antibiotic Timing




Kumar A, *Crit Care Med.* 2006; 34(6): 1589-96

# Antibiotic Timing

… every hour delay was associated with an approximately 12% decreased probability of survival…

Kumar A, *Crit Care Med* 2006; 34(6): 1589-96

# Antibiotic Timing

- Goal < 1 hour
- Delays
  - morbidity & mortality
  - acute kidney injury, acute lung injury

Kumar A. Systematic bias in meta-analyses of time to antimicrobial in sepsis studies. *Crit Care Med.* 2016; 44:e234–e235

Liu VX, Fielding-Singh V, Greene JD. The Timing of Early Antibiotics and Hospital Mortality in Sepsis. *Am J Respir Crit Care Med*. 2017 Mar 27.

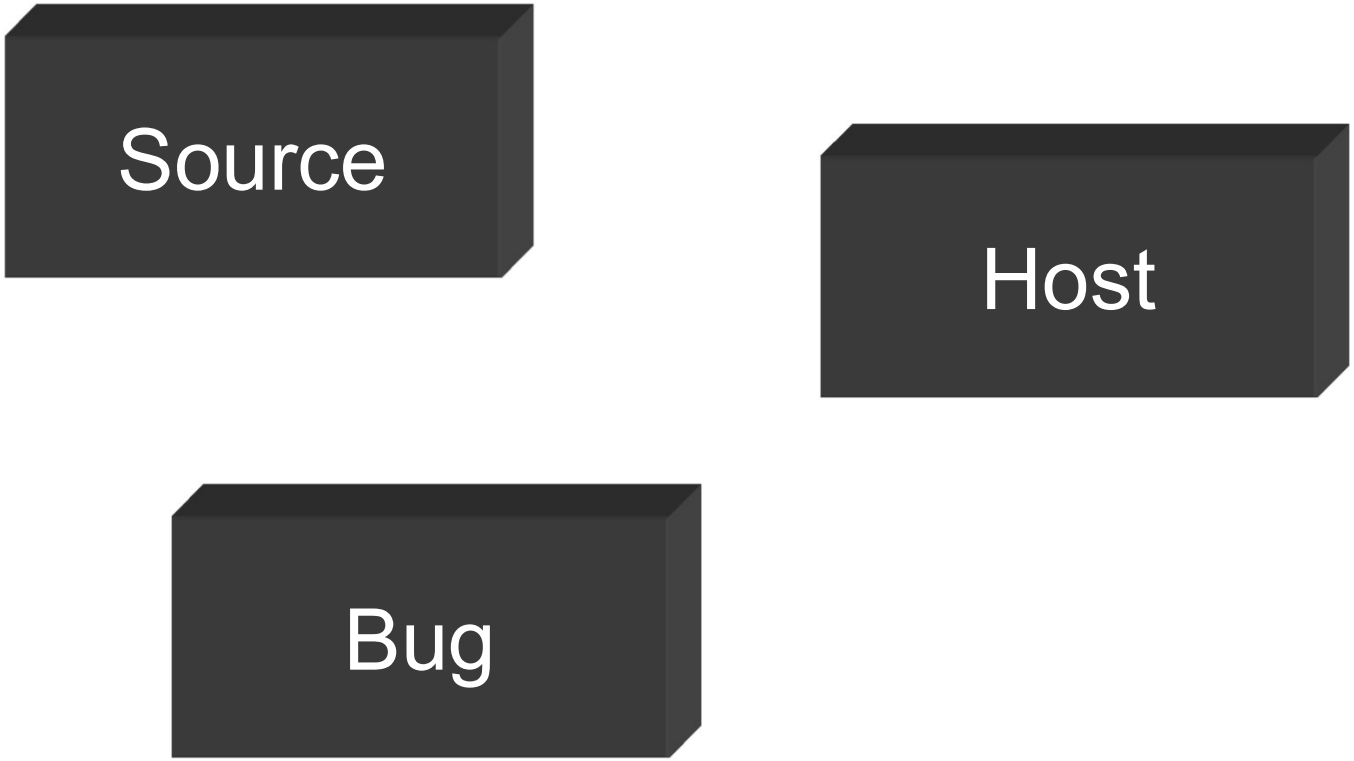
# Empiric Antibiotics

- Blood Stream Infections (BSI)

| | Mortality |
|---|---|
| – appropriate | 20% |
| – inappropriate | 34% |

Leibovici L, J Intern Med 1998; 244:379-386

# Antibiotic Choices



# Antibiotic Stewardship

Empiric broad-spectrum therapy

Narrow: pathogen ID/ sensitivities
&/or clinical improvement

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

# 1 Hour Bundle

- Measure lactate
- Obtain blood cultures
- Administer broad-spectrum antibiotics
- Begin 30mL/kg crystalloids for ↓BP or lactate > 4
- Vasopressors for persistent hypotension

The Surviving Sepsis Campaign Bundle: 2018 Update
DOI: 10.1097/CCM.0000000000003119

# Lactate

- Global tissue hypoxia
- Anaerobic respiration
- Trending lactate levels

# Jennifer

- 28 yo woman with 3 day h/o abdominal pain following laparoscopy
- confusion, BP 80/40  HR 140  R 32  T 38°  diffuse abdominal tenderness, rigidity
- WBC 24k  Hgb 15  Hct 45%  Bands 46%  Platelets 104,000  Lactate 8.7

# Control the Source

# Glucose control

- Maintain serum glucose ≤180 mg/dL
- IV vs. SQ insulin
- Start enteral nutrition ASAP

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

# Septic Shock

…is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.

*JAMA*. 2016;315(8):801-810

# Septic Shock

Sepsis with…

- persistent hypotension* requiring vasopressors and
- Lactate > 2 mmol/L

*despite adequate fluid resuscitation

*JAMA*. 2016;315(8):801-810

# Vasopressors

- Norepinephrine
- Vasopressin
- Epinephrine
- Phenylephrine

- Angiotensin II (ATHOS-3)

# Steroids?

- Unresponsive to vasopressors
- “Stress” dosing
- Hydrocortisone 50mg IV q6h

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

# Procalcitonin

- Bacterial infection w/ severe inflammatory reaction (>2.0)
- Early and highly specific
- Not elevated (<0.5) in viral, chronic inflammatory or  most autoimmune disorders
- Elevated in trauma, post op, rare cancer

# Procalcitonin MOnitoring SEpsis (MOSES) Study

- Daily Procalcitonin levels
- Decrease 80% by day 4
- Increased mortality two fold

Schuetz,P, et al *Crit Care Med*. 2017 May;45(5):781-789

# What about Vitamin C?

- Paul Marik, MD
  Vitamin C, thiamine, hydrocortisone
  Single center, 47 patients, before & after
- VITAMINS Clinical Trial
  - No benefit
- VICTAS Study
  RCT, 2000 patients

# Keys to Success

- Recognize (qSOFA)
- Aggressive IV fluid (30mL/kg)
- Early empiric antibiotics
- Vasopressors (steroids?)
- Source control
- Glucose control

# Citations


1. Bone RC, Balk RA, Cerra FB, et al. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med. 1992;20(6):864–874.

2. Levy MM, Fink MP, Marshall JC, et al. International Sepsis Definitions Conference. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Intensive Care Med. 2003;29(4):530–538.

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4. Brown RM, Semier MW, Fluid management in sepsis. *J Intensive Care Med*, 2019 May; 34(5): 364-373

5. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

# Citations


6. Kumar A, et al, Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med* 2006; 34(6): 1589-96
7. Kumar A. Systematic bias in meta-analyses of time to antimicrobial in sepsis studies. *Crit Care Med.* 2016; 44:e234–e235
8. Liu VX, Fielding-Singh V, Greene JD. The Timing of Early Antibiotics and Hospital Mortality in Sepsis. *Am J Respir Crit Care Med*. 2017 Mar 27.
9. The Surviving Sepsis Campaign Bundle: 2018 Update DOI: 10.1097/CCM.0000000000003119
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12. Marik PE, et al. Hydrocortisone, Vitamin C, and Thiamine for the Treatment of Severe Sepsis and Septic Shock. *Chest*. 2017; 151:1229-1238.

13. Fuji T, et al. Effect of Vitamin C, Hydrocortisone, and Thiamine vs Hydrocortisone Alone on Time Alive and Free of Vasopressor Support Among Patients with Septic Shock. *JAMA*. 2020;323(5):423-431.

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