

# Sepsis

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# Objectives

1. Define sepsis and septic shock according to the Third International Definition published in 2016. Define the SIRS criteria and describe its limitations.
2. Describe the SOFA score and qSOFA score.
3. Describe the management of sepsis including the volume of resuscitation, the type of fluid recommended, goal MAP, timing of antibiotic therapy and the importance of source control.
4. Understand the prognosis and utility of lactate levels and the appropriate vasopressor to use in sepsis refractory to fluids.

# By the numbers

According to the CDC:

- > 1.7 million people are diagnosed with sepsis each year in the US
- 270,000 people die every year from sepsis, leading cause of death in hospitals
- 1 in 3 patients who dies in the hospital have sepsis
- Sepsis begins outside the hospital in 87% of patients
- Most common sources: lungs (25%), urine (25%), skin (11%), gut (11%)

# Surviving Sepsis Campaign

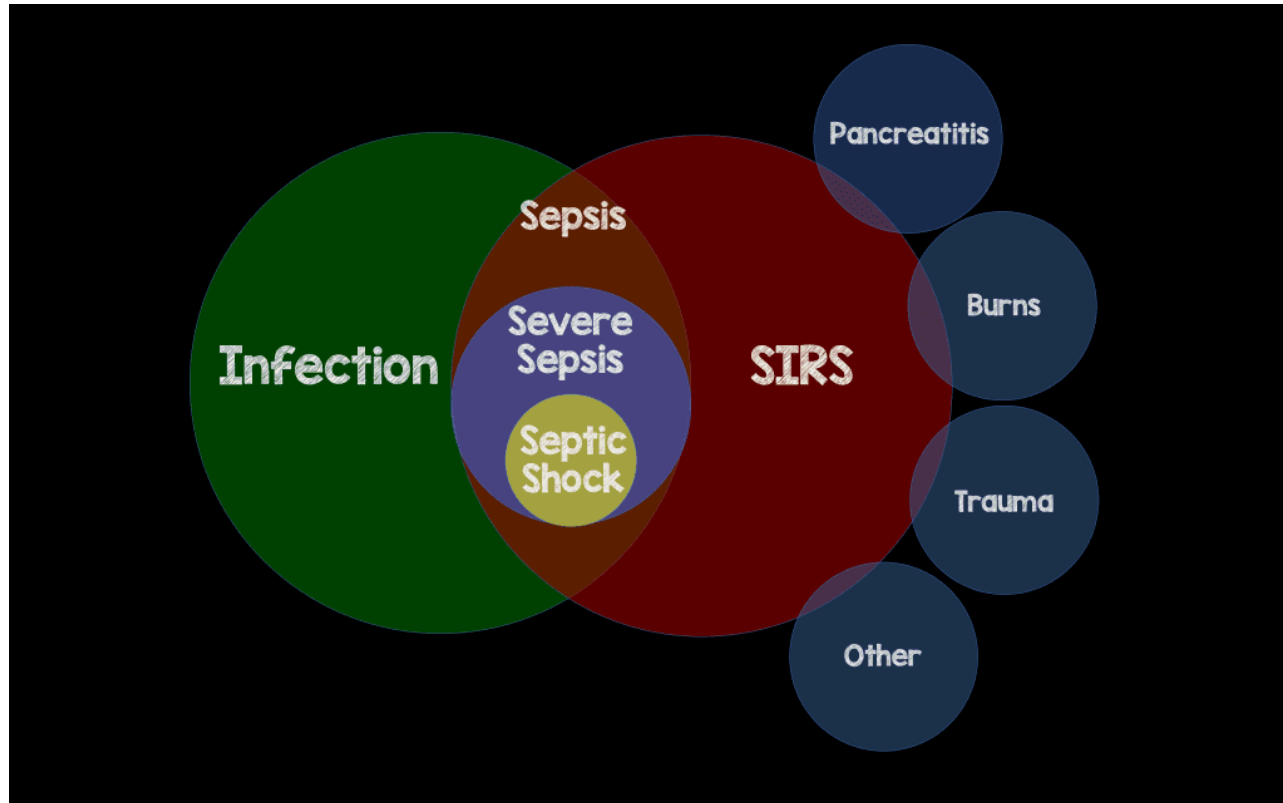
- The European Society of Intensive Care Medicine and The Society of Critical Care Medicine convenes a task force of critical care, infectious disease, surgical, and pulmonary specialists periodically, most recently in 2021
- When compiled, the task force recommendations with supporting evidence, including original research, are circulated to major international societies and other relevant bodies for peer review and endorsement (24 endorsing societies)

# The “Old” Sepsis

## Sepsis 2.0 Definitions

- SIRS
  - Temp > 100.4 or < 95.0
  - RR > 20 or PaCO<sub>2</sub> < 32mmHg
  - HR > 90/min
  - WBC >12k or <4k or Band > 10%
- Sepsis = 2 SIRS criteria + infection
- Severe Sepsis = sepsis + organ dysfunction
- Septic Shock = severe sepsis + persistent hypotension after 30cc/kg IVF resuscitation
- The biggest issue with these definitions is infection isn't the only thing that can cause SIRS (poor specificity, but, maybe, poor sensitivity as well).

# The “Old” Sepsis



## Sepsis 3.0

Sepsis - 3 consensus definition: ***life-threatening organ dysfunction secondary to a dysregulated host response to infection.***

There is no gold standard diagnostic test that exists to diagnose sepsis. Instead it is a constellation of clinical signs and symptoms in a patient with suspected infection.

Organ dysfunction can be identified as an acute change in total SOFA score  $\geq 2$  points due to the infection

## Sequential [Sepsis-Related] Organ Failure Assessment (SOFA) Score

System	0	1	2	3	4
Respiration PaO <sub>2</sub> /FiO <sub>2</sub> , mmHg (kPa)	$\geq 400$ (53.3)	$< 400$ (53.3)	$< 300$ (40)	$< 200$ (26.7) with respiratory support	$< 100$ (13.3) with respiratory support
Coagulation Platelets, $\times 10^3/\mu\text{L}$	$\geq 150$	$< 150$	$< 100$	$< 50$	$< 20$
Liver Bilirubin, mg/dL ( $\mu\text{mol/L}$ )	$< 1.2$ (20)	1.2 - 1.9 (20 - 32)	2.0 - 5.9 (33 - 101)	6.0 - 11.9 (102 - 204)	$> 12.0$ (204)
Cardiovascular	MAP $\geq 70\text{mmHg}$	MAP $< 70\text{mmHg}$	Dopamine $< 5$ or Dobutamine (any dose)	Dopamine 5.1 - 15 or Epinephrine $\leq 0.1$ or Norepinephrine $\leq 0.1$	Dopamine $> 15$ or Epinephrine $> 0.1$ or Norepinephrine $> 0.1$
CNS GCS Score	15	13 - 14	10 - 12	6 - 9	$< 6$
Renal Creatinine, mg/dL ( $\mu\text{mol/L}$ ) Urine Output, mL/d	$< 1.2$ (110)	1.2 - 1.9 (110 - 170)	2.0 - 3.4 (171 - 299)	3.5 - 4.9 (300 - 440)  $< 500$	$> 5.0$ (440)  $< 200$
*Catecholamine Doses = $\mu\text{g/kg/min}$ for at least 1hr					

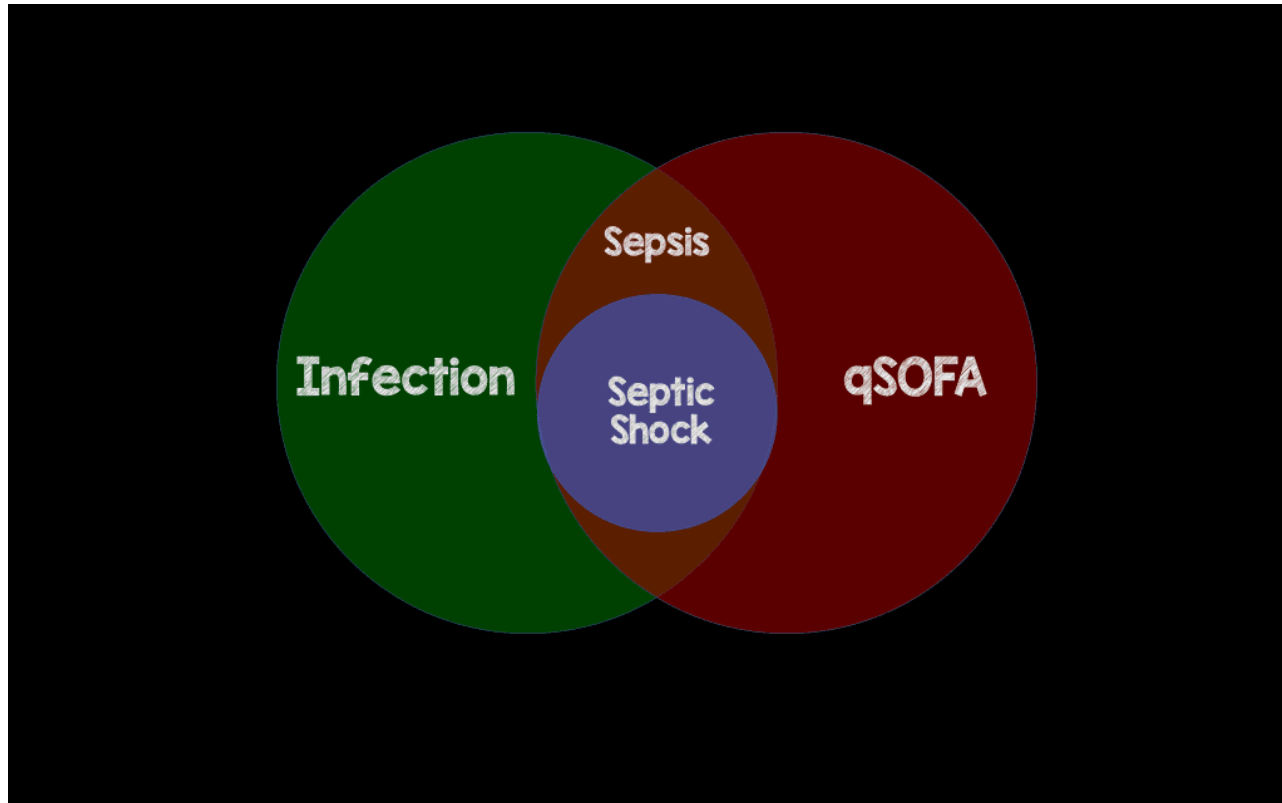


# qSOFA



Easier to calculate at the bedside, no labs needed

# Sepsis 3.0

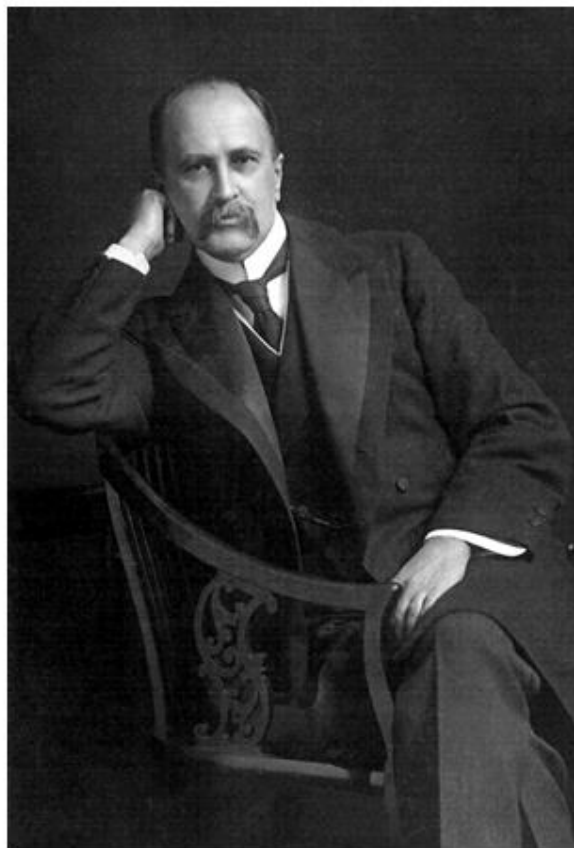


## Sepsis 3.0.1

*2021 update:* Neither qSOFA nor SOFA are intended to be a stand-alone definition of sepsis and that failure to meet 2 or more qSOFA or SOFA criteria should not defer investigation or treatment of infection or delay any other aspect of clinical care

Regardless of semantics/definitions, sepsis is a **MEDICAL EMERGENCY**.

Early recognition and aggressive treatment are key to improved outcomes.



- “Patients don’t die of their disease, they die of the physiologic abnormalities of their disease.”

- Sir William Osler

# Sepsis Management

*Sepsis standard operating procedures, initially specified as Early Goal Directed Therapy have evolved to “usual care” which includes a standard approach with components of the sepsis bundle, **early identification, lactate, cultures, antibiotics, and fluids.***

-SSC 2021 Guidelines

# Identification of Sepsis



## Screening for sepsis

PICO Question	2021 Recommendation	Recommendation Strength and Quality	Change from 2016
In acutely ill patients should we use qSOFA criteria to screen for the presence of sepsis?	<b>We recommend against using qSOFA compared with SIRS, NEWS, or MEWS as a single-screening tool for sepsis or septic shock.</b>	Strong, moderate-quality evidence	New recommendation

# Guiding resuscitation

## INITIAL RESUSCITATION

4. Sepsis and septic shock are medical emergencies, and we recommend that treatment and resuscitation begin immediately.	<b>Best practice statement</b>	
5. For patients with sepsis induced hypoperfusion or septic shock we suggest that at least 30 mL/kg of IV crystalloid fluid should be given within the first 3 hr of resuscitation.	<b>Weak</b> , low quality of evidence	<b>DOWNGRADE</b> from <b>Strong</b> , low quality of evidence “We <b>recommend</b> that in the initial resuscitation from sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloid fluid be given within the first 3 hr”
6. For adults with sepsis or septic shock, we suggest using dynamic measures to guide fluid resuscitation, over physical examination, or static parameters alone.	<b>Weak</b> , very low quality of evidence	
7. For adults with sepsis or septic shock, we suggest guiding resuscitation to decrease serum lactate in patients with elevated lactate level, over not using serum lactate.	<b>Weak</b> , low quality of evidence	
8. For adults with septic shock, we suggest using capillary refill time to guide resuscitation as an adjunct to other measures of perfusion.	<b>Weak</b> , low quality of evidence	<b>NEW</b>

# Hemodynamics

$$V = I \times R$$

$$P = F \times R$$

## MEAN ARTERIAL PRESSURE

9. For adults with septic shock on vasopressors, we recommend an initial target mean arterial pressure (MAP) of 65mm Hg over higher MAP targets. **Strong, moderate-quality evidence**





# Guiding resuscitation

## Surviving Sepsis Campaign



LOW

7

For adults with sepsis or septic shock, we **suggest** guiding resuscitation to decrease serum lactate in patients with elevated lactate level, over not using serum lactate.



LOW

8

For adults with septic shock, we **suggest** using capillary refill time to guide resuscitation as an adjunct to other measures of perfusion.

### Early Goal-Directed and Lactate-Guided Therapy in Adult Patients With Severe Sepsis and Septic Shock: A Meta-Analysis of Randomized Controlled Trials

Mortality benefit associated with lactate-guided resuscitation

### Effect of a Resuscitation Strategy Targeting Peripheral Perfusion Status vs Serum Lactate Levels on 28-Day Mortality Among Patients With Septic Shock: The ANDROMEDA-SHOCK Randomized Clinical Trial

34.9% vs. 43.4% mortality,  $P = 0.06$

Gu WJ, Zhang Z, Bakker J. Early lactate clearance-guided therapy in patients with sepsis: a meta-analysis with trial sequential analysis of randomized controlled trials. *Intensive Care Med*. 2015 Oct;41(10):1862-1863.

Ding XF, Yang ZY, Xu Z, et al. Early goal-directed and lactate-guided therapy in adult patients with severe sepsis and septic shock: a meta-analysis of randomized controlled trials. *J Transl Med*. 2018 Nov 29;16(1):331.

Hernandez G, Ospina-Tascon GA, Damiani LP, et al. Effect of a resuscitation strategy targeting peripheral perfusion status vs serum lactate levels on 28-day mortality among patients with septic shock: the ANDROMEDA-SHOCK randomized clinical trial. *JAMA*. 2019 Feb 19;321(7):654-664.

# Fluid choice

## HEMODYNAMIC MANAGEMENT

32. For adults with sepsis or septic shock, we recommend using crystalloids as first-line fluid for resuscitation.

**Strong**, moderate-quality evidence

33. For adults with sepsis or septic shock, we suggest using balanced crystalloids instead of normal saline for resuscitation.

**Weak**, low quality of evidence

**CHANGED from weak recommendation**, low quality of evidence.

“We suggest using either balanced crystalloids or saline for fluid resuscitation of patients with sepsis or septic shock”







34. For adults with sepsis or septic shock, we suggest using albumin in patients who received large volumes of crystalloids.



**Weak**, moderate-quality evidence

35. For adults with sepsis or septic shock, we recommend against using starches for resuscitation.

**Strong**, high-quality evidence




# Pressors, inotropes?

	 Use norepinephrine as first-line vasopressor.
<i>For patients with septic shock on vasopressors</i>	<div> Target a MAP of 65 mm Hg.</div> <div> <b>Consider</b> invasive monitoring of arterial blood pressure.</div>
<i>If central access is not yet available</i>	<div> <b>Consider</b> initiating vasopressors peripherally.*</div>
<i>If MAP is inadequate despite low-to-moderate norepinephrine</i>	<div> <b>Consider</b> adding vasopressin.</div>
<i>If cardiac dysfunction with persistent hypoperfusion is present despite adequate volume status and blood pressure</i>	<div> <b>Consider</b> adding dobutamine or switching to epinephrine.</div>

 Strong recommendations are displayed in green  
 Weak recommendations are displayed in yellow.

*\*When vasopressors are used peripherally, they should be administered only for a short period of time and in a vein proximal to the antecubital fossa.*

# Antimicrobials

	 <b>Shock is present</b>	 <b>Shock is absent</b>
<b>Sepsis is definite or probable</b>	<input checked="" type="checkbox"/> Administer antimicrobials <b>immediately</b> , ideally within 1 hour of recognition.	<input checked="" type="checkbox"/> Administer antimicrobials <b>immediately</b> , ideally within 1 hour of recognition.
<b>Sepsis is possible</b>	<input checked="" type="checkbox"/> Administer antimicrobials <b>immediately</b> , ideally within 1 hour of recognition.	<input checked="" type="checkbox"/> Rapid assessment* of infectious vs. noninfectious causes of acute illness.
<p><i>*Rapid assessment includes history and clinical examination, tests for both infectious and noninfectious causes of acute illness, and immediate treatment of acute conditions that can mimic sepsis. Whenever possible, this should be completed within 3 hours of presentation so that a decision can be made as to the likelihood of an infectious cause of the patient's presentation and timely antimicrobial therapy provided if the likelihood is thought to be high.</i></p>		<input checked="" type="checkbox"/> Administer antimicrobials <b>within 3 hours</b> if concern for infection persists.

A 58-year-old man is evaluated in the hospital for fever, hypotension, and altered mental status. He was hospitalized 2 days ago for an infected arm wound and was treated with intravenous piperacillin/tazobactam and vancomycin. This morning he developed new pain in the middle of his back and difficulty urinating. His medical history is significant for type 2 diabetes mellitus treated with metformin.

On physical examination, temperature is 39.1 °C (102.4 °F), blood pressure is 83/48 mm Hg, pulse rate is 109/min, and respiration rate is 21/min. Oxygen saturation is 98% breathing 2 L/min of oxygen through nasal cannula. He is somnolent but arousable and oriented when awake. There is erythema surrounding the wound on his right upper arm with no drainage or tenderness. There is tenderness to percussion in the middle of his back and a palpable bladder.

Laboratory studies reveal a blood serum leukocyte count of 22,000/ $\mu$ L ( $22 \times 10^9$ /L), and plasma glucose of 160 mg/dL (8.88 mmol/L).

Chest radiograph is unremarkable.

- A. IV insulin
- B. IV fluid bolus
- C. MRI of the spine
- D. Surgical exploration of the arm wound

A 51-year-old man is evaluated for fever, hypotension, and confusion. He was admitted to the ICU 8 days ago for observation after complications resulting from an outpatient surgical procedure. He had experienced unexpected bleeding in the recovery room and had a central venous catheter inserted emergently for blood transfusion. On the first postoperative day he was weaned from mechanical ventilation, vomited once but recovered, and has been receiving supplemental oxygen through nasal cannula. Today he developed a fever, hypotension, and confusion. His hemoglobin has remained stable.

On physical examination, temperature is 38.6 °C (101.5 °F), blood pressure is 89/50 mm Hg, pulse rate is 101/min, and respiration rate is 23/min. Oxygen saturation is 100% on 2L/min of oxygen through nasal cannula. Lung examination reveals clear breath sounds.

Laboratory studies reveal a leukocyte count of 15,000/ $\mu$ L ( $15 \times 10^9$ /L) and a serum creatinine of 1.2 mg/dL (106.1  $\mu$ mol/L).

An intravenous fluid bolus of 30 mL/kg of body weight is now infusing. Blood and respiratory cultures have been obtained and broad spectrum antibiotics are administered.

- A. Administer glucocorticoids
- B. Administer norepinephrine
- C. Obtain procalcitonin
- D. Remove the central venous catheter