

# Surviving Sepsis Campaign: 2021 Guideline Update

---

Kaitly Abbott, PharmD

PGY1 Pharmacy Resident

[kaitlyn.abbott@ascension.org](mailto:kaitlyn.abbott@ascension.org)



# Speaker Disclosure

I have no financial relationships or affiliations to disclose.



# Objectives

1. Define sepsis and septic shock
2. Discuss the various screening tools used in sepsis
3. Describe the clinical presentation of a patient presenting with organ dysfunction
4. Explain the purpose of the Surviving Sepsis Campaign
5. Discuss the updates to the 2021 Surviving Sepsis Campaign guideline
6. Given a patient case, use the updated guidelines to make recommendations for a patient with septic shock



# Epidemiology

“Sepsis and septic shock are major healthcare problems, impacting millions of people around the world each year and killing between one in three and one in six of those it affects.”



# What is Sepsis?

Sepsis-3 Guidelines (2016):

- **Sepsis:** Life-threatening organ dysfunction caused by a dysregulated host response to infection
  - Acute change in total SOFA score  $\geq$  2 points
  
- **Septic shock:** Sepsis + persistent hypotension (MAP < 65 mmHg) requiring vasopressor use AND serum lactate > 2 mmol/L despite adequate fluid resuscitation (30 mL/kg of crystalloids)

# Formal Scoring Systems

## SIRS criteria

Temperature  $>38.3$  °C (101 °F) or  $<36.0$  °C (96.8 °F)  
 Tachycardia  $>90$  bpm  
 Tachypnea  $>20$  breaths/min or  $\text{PaCO}_2 <4.3$  kPa (32 mmHg)  
 Leukocytosis (WBC count  $>12 \times 10^9/\text{L}$  (12,000/ $\mu\text{L}$ )) or  
 Leukopenia (WBC count  $<4 \times 10^9/\text{L}$  (4000/ $\mu\text{L}$ )) or  
 Normal WBC count with  $>10\%$  immature neutrophils

<https://www.semanticscholar.org/paper/Criteria-for-Sepsis%3A-Systemic-Inflammatory-Response-Als-ulaiman-Kubiak/9aa7b65ea67c0cf1e3018109d81a9d95ee9a628>

**Table 2** Quick Sequential Organ Failure Assessment (SOFA) score

qSOFA (Quick SOFA) Criteria	Points
Respiratory rate $\geq 22/\text{min}$	1
Change in mental status	1
Systolic blood pressure $\leq 100$ mmHg	1

[https://cdn.amegroups.cn/static/magazine\\_modules/imgRender/dist/index.html?imgSource=https://cdn.amegroups.cn/journals/pbpc/files/journals/2/articles/12738/public/12738-PB4-R1.png](https://cdn.amegroups.cn/static/magazine_modules/imgRender/dist/index.html?imgSource=https://cdn.amegroups.cn/journals/pbpc/files/journals/2/articles/12738/public/12738-PB4-R1.png)

**Table 1** The Sequential Organ Failure Assessment (SOFA) score<sup>a</sup>

Organ system	SOFA score				
	0	1	2	3	4
Respiratory, $\text{PO}_2/\text{FiO}_2$ , 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, $\times 10^3/\text{mm}^3$	$\geq 150$	$<150$	$<100$	$<50$	$<20$
Liver, Bilirubin, mg/dL	$<1.2$	1.2–1.9	2.0–5.9	6.0–11.9	$>12.0$
Cardiovascular	MAP $\geq 70$ mmHg	MAP $<70$ mmHg	Dopamine $<5$ or dobutamine (any dose) <sup>b</sup>	Dopamine 5.1–15 or epinephrine $\leq 0.1$ or norepinephrine $\leq 0.1$ <sup>b</sup>	Dopamine $>15$ or epinephrine $>0.1$ or norepinephrine $>0.1$ <sup>b</sup>
Central nervous system, Glasgow Coma Scale	15	13–14	10–12	6–9	$<6$
Renal, Creatinine, mg/dL. Urine output, mL/d	$<1.2$	1.2–1.9	2.0–3.4	3.5–4.9 $<500$	$>5.0$ $<200$

<sup>a</sup>, adapted from Vincent *et al.* (7); <sup>b</sup>, Catecholamine doses are given as  $\mu\text{g}/\text{kg}/\text{min}$  for at least 1 hour.  $\text{FiO}_2$ , fraction of inspired oxygen; MAP, mean arterial pressure;  $\text{PO}_2$ , partial pressure of oxygen.

[https://cdn.amegroups.cn/static/magazine\\_modules/imgRender/dist/index.html?imgSource=https://cdn.amegroups.cn/journals/pbpc/files/journals/2/articles/12738/public/12738-PB4-R1.png](https://cdn.amegroups.cn/static/magazine_modules/imgRender/dist/index.html?imgSource=https://cdn.amegroups.cn/journals/pbpc/files/journals/2/articles/12738/public/12738-PB4-R1.png)

# Formal Scoring Systems

National Early Warning Score (NEWS)\*

PHYSIOLOGICAL PARAMETERS	3	2	1	0	1	2	3
Respiration Rate	≤8		9 - 11	12 - 20		21 - 24	≥25
Oxygen Saturations	≤91	92 - 93	94 - 95	≥96			
Any Supplemental Oxygen		Yes		No			
Temperature	≤35.0		35.1 - 36.0	36.1 - 38.0	38.1 - 39.0	≥39.1	
Systolic BP	≤90	91 - 100	101 - 110	111 - 219			≥220
Heart Rate	≤40		41 - 50	51 - 90	91 - 110	111 - 130	≥131
Level of Consciousness				A			V, P, or U

<https://openanesthesiajournal.com/VOLUME/12/PAGE/26/FULLTEXT/>

MEWS (Modified Early Warning System)

	3	2	1	0	1	2	3
Respiratory Rate per minute		Less than 8		9-14	15-20	21-29	More than 30
Heart Rate per minute		Less than 40	40-50	51-100	101-110	111-129	More than 129
Systolic Blood Pressure	Less than 70	71-80	81-100	101-199		More than 200	
Conscious level (AVPU)	<b>U</b> nresponsive	Responds to <b>P</b> ain	Responds to <b>V</b> oice	<b>A</b> lert	New agitation Confusion		
Temperature (°c)		Less than 35.0	35.1-36	36.1-38	38.1-38.5	More than 38.6	
Hourly Urine For 2 hours	Less than 10mls / hr	Less than 30mls / hr	Less than 45mls / hr				

<https://www.rn.com/nursing-news/patient-deterioration-early-warning-signs/>

---

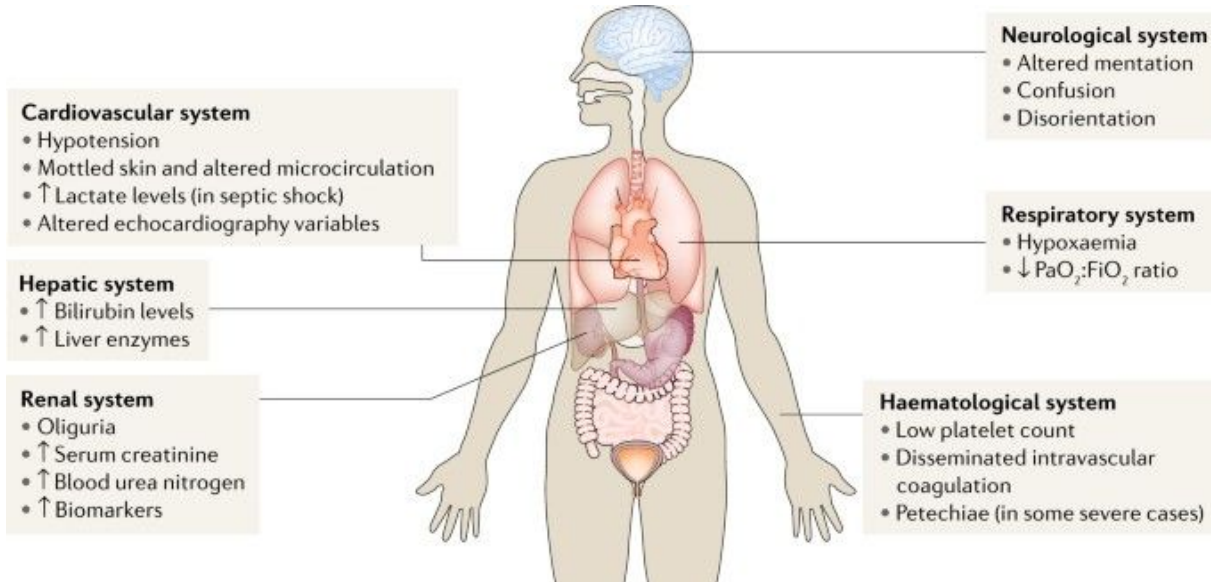
# Survey Question 1:

Which formal screening tool does you use? (Select all that apply)

- A. SOFA
- B. qSOFA
- C. SIRS
- D. NEWS
- E. MEWS
- F. Unsure



# Signs of Organ Dysfunction



<https://www.nature.com/articles/641581-018-0005-7>

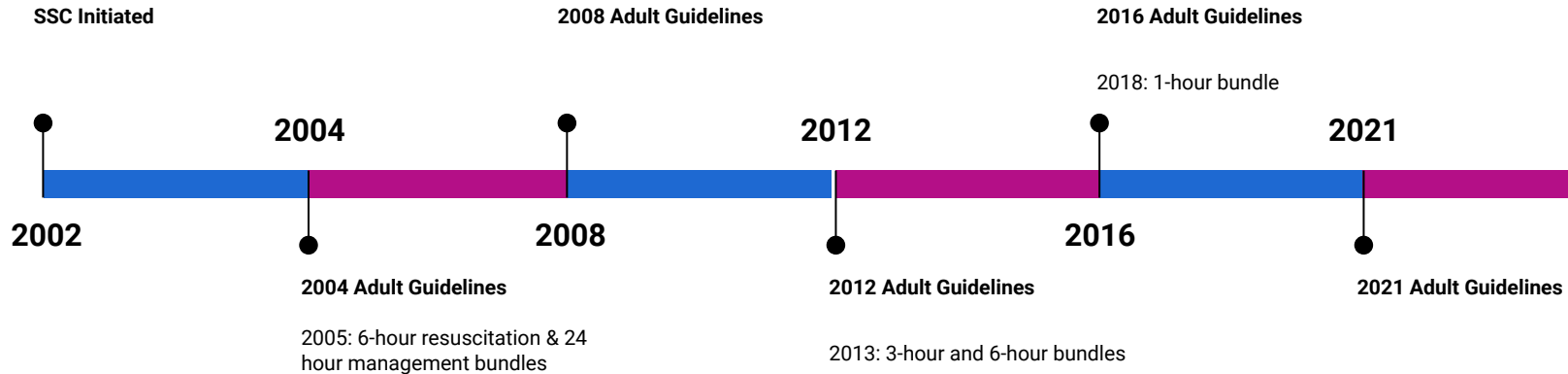
# Surviving Sepsis Campaign

**Goal:** Reduce mortality along with the following:

- Build awareness of sepsis
- Develop guidelines of care
- Educate healthcare professionals
- Implement performance improvement programs
- Improve diagnosis
- Increase the use of appropriate treatment
- Improve post-ICU care



# Surviving Sepsis Campaign



# The Surviving Sepsis Campaign: Hour-1 Sepsis Bundle



Initiate bundle upon recognition of sepsis/septic shock.

*May not complete all bundle elements within one hour of recognition.*

**1**

Measure lactate level.  
Remeasure lactate if initial lactate elevated ( $> 2$  mmol/L).

**2**

Obtain blood cultures before administering antibiotics.

**3**

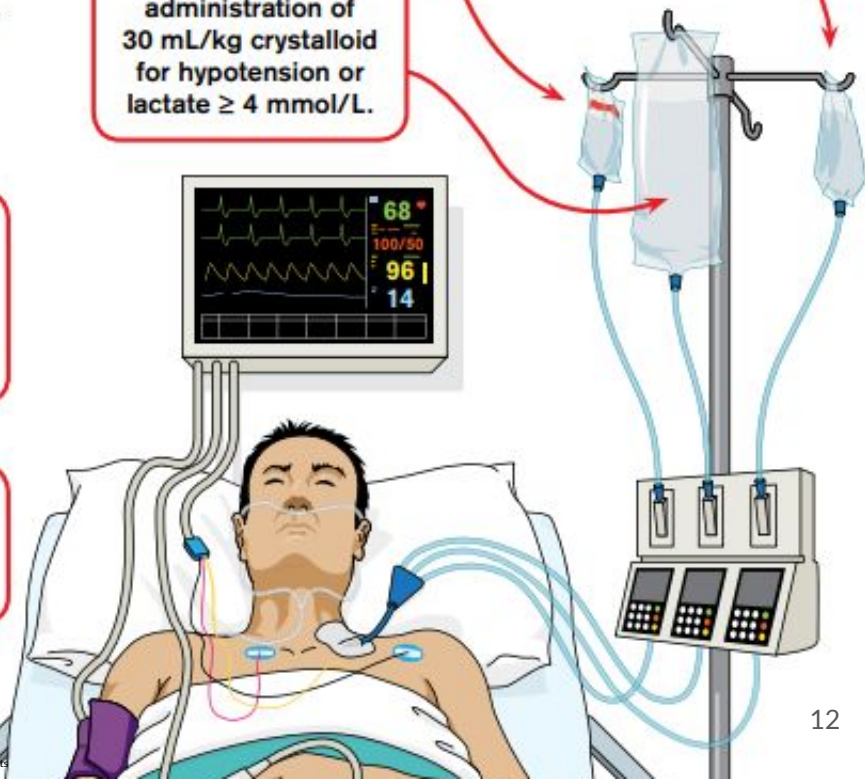
Administer broad-spectrum antibiotics.

**4**

Begin rapid administration of 30 mL/kg crystalloid for hypotension or lactate  $\geq 4$  mmol/L.

**5**

Apply vasopressors if hypotensive during or after fluid resuscitation to maintain a mean arterial pressure  $\geq 65$  mm Hg.



---

# 2021 Sepsis Guidelines



# 2021 Sepsis Guidelines

- GRADE system to assess the quality of evidence from high to very low, and to formulate recommendations as strong or weak, or best practice statement when applicable
- Highlights six sections:
  - Screening and Early Treatment
  - Infection
  - Hemodynamic Management
  - Ventilation
  - Additional Therapies
  - Long Term Outcomes and Goals of Care- *NEW*



# Screening

2016 Recommendation	2021 Recommendation
N/A	<p data-bbox="1000 574 1729 674"><b>We recommend against using qSOFA compared with SIRS, NEWS, or MEWS as a single screening tool for sepsis or septic shock</b></p> <p data-bbox="1074 718 1655 744"><i>Strong recommendation, moderate-quality evidence</i></p>



# Initial Resuscitation

2016 Recommendation	2021 Recommendation
<p>We recommend that in the initial resuscitation from sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloid fluid be given within the first 3 hours</p> <p><i>Strong , low quality of evidence</i></p>	<p><b>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 hours of resuscitation</b></p> <p><i>Weak, low quality of evidence</i></p>





# Initial Resuscitation

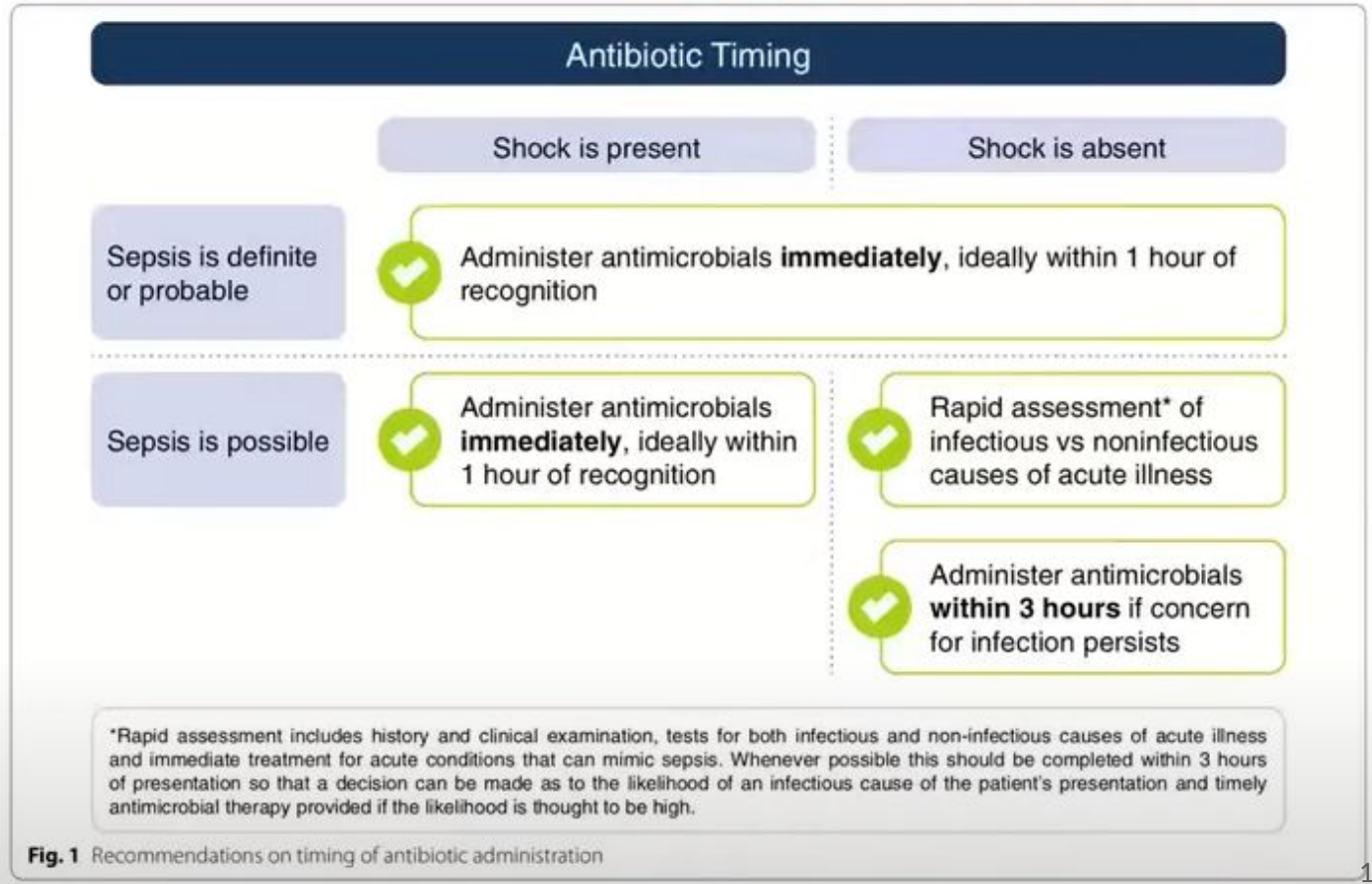
2016 Recommendation	2021 Recommendation
N/A	<p data-bbox="1000 573 1734 674"><b>For adults with septic shock, we suggest using capillary refill time to guide resuscitation as an adjunct to other measures of perfusion</b></p> <p data-bbox="1199 718 1534 743"><i>Weak, low quality of evidence</i></p>



# Infection

2016 Recommendation	2021 Recommendation
<p>We recommend that administration of intravenous antimicrobials should be initiated as soon as possible after recognition and within 1 hour for both a) septic shock and b) sepsis without shock</p> <p><i>Strong recommendation, moderate quality of evidence</i></p>	<p><b>For adults with possible septic shock or a high likelihood for sepsis, we recommend administering antimicrobials immediately, ideally within 1 hour of recognition</b></p> <p><i>Strong, low quality of evidence (Septic shock)</i></p> <p><i>Strong, very low quality of evidence (Sepsis without shock)</i></p>
	<p><b>For adults with a low likelihood of infection and without shock, we suggest deferring antimicrobials while continuing to closely monitor the patient</b></p> <p><i>Weak, very low quality of evidence</i></p>

# Infection





# Infection

2016 Recommendation	2021 Recommendation
<p>We recommend empiric broad-spectrum therapy with one or more antimicrobials for patients presenting with sepsis or septic shock to cover all likely pathogens (including bacterial and potentially fungal or viral coverage”</p> <p><i>Strong recommendation, moderate quality of evidence</i></p>	<p><b>For adults with sepsis or septic shock at high risk of MRSA, we recommend using empiric antimicrobials with MRSA coverage over using antimicrobials without MRSA coverage</b></p> <p><i>Best practice statement</i></p>
	<p><b>For adults with sepsis or septic shock at low risk of MRSA, we suggest against using empiric antimicrobials with MRSA coverage, as compared with using antimicrobials without MRSA coverage</b></p> <p><i>Weak recommendation, low quality of evidence</i></p>



# Infection

2016 Recommendation	2021 Recommendation
<p>We recommend empiric broad-spectrum therapy with one or more antimicrobials for patients presenting with sepsis or septic shock to cover all likely pathogens (including bacterial and potentially fungal or viral coverage”</p> <p><i>Strong recommendation, moderate quality of evidence</i></p>	<p><b>For adults with sepsis or septic shock and high risk for multidrug resistant (MDR) organisms, we suggest using two antimicrobials with gram-negative coverage for empiric treatment over one gram-negative agent</b></p> <p><i>Weak, very low quality of evidence</i></p>
	<p><b>For adults with sepsis or septic shock and low for multidrug resistant (MDR) organisms, we suggest against using two gram-negative agents for empiric treatment, as compared to one gram-negative agent</b></p> <p><i>Weak, very low quality of evidence</i></p>



# Infection

2016 Recommendation	2021 Recommendation
<p>We recommend empiric broad-spectrum therapy with one or more antimicrobials for patients presenting with sepsis or septic shock to cover all likely pathogens (including bacterial and potentially fungal or viral coverage”</p> <p><i>Strong recommendation, moderate quality of evidence</i></p>	<p><b>For adults with sepsis or septic shock at high risk of fungal infection, we suggest using empiric antifungal therapy over no antifungal therapy</b></p> <p><i>Weak, low quality of evidence</i></p>
	<p><b>For adults with sepsis or septic shock at low risk of fungal infection, we suggest against empiric use of antifungal therapy</b></p> <p><i>Weak, low quality of evidence</i></p>



# Hemodynamic Management

2016 Recommendation	2021 Recommendation
<p data-bbox="222 573 956 638">We suggest using either balanced crystalloids or saline for fluid resuscitation of patients with sepsis or septic shock</p> <p data-bbox="425 682 753 715"><i>Weak, low quality of evidence</i></p>	<p data-bbox="1014 573 1709 671"><b>For adults with sepsis or septic shock, we recommend using balanced crystalloids instead of normal saline for resuscitation</b></p> <p data-bbox="1197 715 1526 748"><i>Weak, low quality of evidence</i></p>







# Hemodynamic Management



	Human plasma	0.9% saline	Balanced crystalloids	
			Lactated Ringer's	Plasma-Lyte A©
Sodium (mEq/L)	135–145	154	130	140
Potassium (mEq/L)	4.5–5.0	0	4	5
Chloride (mEq/L)	94–111	154	109	98
Calcium (mEq/L)	2.2–2.6	0	2.7	0
Magnesium (mEq/L)	0.8–1.0	0	0	3
Bicarbonate (mEq/L)	23–27	0	0	0
Lactate (mEq/L)	1–2	0	28	0
Acetate (mEq/L)	0	0	0	27
Gluconate (mEq/L)	0	0	0	23

<http://www.emdocs.net/lactated-ringers-versus-normal-saline-myths-and-pearls-in-the-ed/>



# Hemodynamic Management

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

-  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.



# Ventilation

2016 Recommendation	2021 Recommendation
N/A	<p data-bbox="996 573 1731 671"><b>For adults with sepsis induced hypoxemic respiratory failure, we suggest the use of high flow nasal oxygen over noninvasive ventilation</b></p> <p data-bbox="1199 715 1528 742"><i>Weak, low quality of evidence</i></p>



# Ventilation

2016 Recommendation	2021 Recommendation
<p>We suggest using neuromuscular blocking agents for <math>\leq 48</math> hours in adult patients with sepsis-induced ARDS and a <math>\text{PaO}_2/\text{FiO}_2</math> ratio <math>&lt; 150</math> mmHg</p> <p><i>Weak recommendation, moderate quality of evidence</i></p>	<p><b>For adults with sepsis induced moderate-severe ARDS, we suggest using intermittent NMBA boluses, over NMBA continuous infusion</b></p> <p><i>Weak, moderate-quality evidence</i></p>



# Ventilation

2016 Recommendation	2021 Recommendation
N/A	<p data-bbox="996 574 1733 710"><b>For adults with sepsis-induced severe ARDS, we suggest using venovenous (VV) ECMO when conventional mechanical ventilation fails in experienced centers with the infrastructure in place to support its use</b></p> <p data-bbox="1199 754 1530 781"><i>Weak, low quality of evidence</i></p>



## Additional Therapies

2016 Recommendation	2021 Recommendation
<p>We suggest against using IV hydrocortisone to treat septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability. If this is not achievable, we suggest IV hydrocortisone at a dose of 200 mg/day</p> <p><i>Weak, low quality of evidence</i></p>	<p><b>For adults with septic shock and an ongoing requirement for vasopressor therapy, we suggest using IV corticosteroids</b></p> <p><b><i>Weak, moderate-quality evidence</i></b></p>



## Additional Therapies

2016 Recommendation	2021 Recommendation
N/A	<b>For adults with sepsis or septic shock we suggest against using IV vitamin C</b>  <i>Weak, low quality of evidence</i>



## Additional Therapies

2016 Recommendation	2021 Recommendation
<p>We suggest against the use of sodium bicarbonate therapy to improve hemodynamics or to reduce vasopressor requirements in patients with hypoperfusion-induced lactic acidemia with pH <math>\geq 7.15</math></p> <p><i>Weak recommendation, moderate quality of evidence</i></p>	<p><b>For adults with septic shock and severe metabolic acidemia (pH <math>\leq 7.2</math>) and acute kidney injury (AKIN score 2 to 3), we suggest using sodium bicarbonate therapy</b></p> <p><i>Weak, low quality of evidence</i></p>



## Long-Term Outcomes and Goals of Care

2016 Recommendation	2021 Recommendation
N/A	<p data-bbox="1002 573 1723 671"><b>For adults with septic shock, we recommend discussing goals of care and prognosis with patients and families over no such discussion</b></p> <p data-bbox="1232 718 1493 743"><i>Best practice statement</i></p>





## Long-Term Outcomes and Goals of Care

2016 Recommendation	2021 Recommendation
N/A	<p data-bbox="996 572 1731 749">For adults with sepsis or septic shock, we recommend that the principles of palliative care (which may include palliative care consultation based on clinician judgement) be integrated into the treatment plan, when appropriate, to address patient and family symptoms and suffering</p> <p data-bbox="1232 790 1495 816"><i>Best practice statement</i></p>



## Long-Term Outcomes and Goals of Care

2016 Recommendation	2021 Recommendation
N/A	<p data-bbox="996 574 1734 710"><b>For adults with septic shock and their families, we recommend screening for economic and social support (including housing, nutritional, financial, and spiritual support), and make referrals where available to meet these needs</b></p> <p data-bbox="1232 754 1499 779"><i>Best practice statement</i></p>



## Long-Term Outcomes and Goals of Care

2016 Recommendation	2021 Recommendation
N/A	<p data-bbox="996 574 1731 637"><b>For adult survivors of sepsis or septic shock, we suggest referral to a post-critical illness follow-up program if available</b></p> <p data-bbox="1232 681 1495 705"><i>Best practice statement</i></p>



## Lets Practice!

AP is a 65-year-old male who presents to the ED. On arrival he is confused and bradycardic.

PMH: Type 2 diabetes, hypertension, and COPD

Temperature: 101 °F      HR: 53      RR: 24      BP: 88/46 with MAP of 60      SpO<sub>2</sub>: 95% on 4L NC

Physical assessment: Oriented to person only

Chest XR: focal consolidations consistent with pneumonia



## Question 1:

AP is given adequate fluid resuscitation. His MAP is now 62. The healthcare team collected a lactate level and sent blood cultures. The lactate is 3.

Does this patient have sepsis, septic shock, or neither?

- A. Sepsis
- B. Septic shock
- C. Neither

# What is Sepsis?

Sepsis-3 Guidelines (2016):

- **Sepsis:** Life-threatening organ dysfunction caused by a dysregulated host response to infection
    - Acute change in total SOFA score  $\geq 2$  points
  
  - **Septic shock:** Sepsis + persistent hypotension (MAP < 65 mmHg) requiring vasopressor use AND serum lactate > 2 mmol/L despite adequate fluid resuscitation (30 mL/kg of crystalloids)
-



## Question 2:

The health care team has measured a lactate and sent blood cultures to the lab. AP's MAP is still 62. What fluids should be started?

- A. 0.9% sodium chloride
- B. Dextrose 5%
- C. Lactated Ringer's
- D. 3% sodium chloride

# Hemodynamic Management

2016 Recommendation	2021 Recommendation
<p data-bbox="222 573 956 638">We suggest using either balanced crystalloids or saline for fluid resuscitation of patients with sepsis or septic shock.</p> <p data-bbox="425 682 753 715"><i>Weak, low quality of evidence</i></p>	<p data-bbox="1014 573 1709 671"><b>For adults with sepsis or septic shock, we recommend using balanced crystalloids instead of normal saline for resuscitation.</b></p> <p data-bbox="1197 715 1526 748"><i>Weak, low quality of evidence</i></p>













## Question 3: Hemodynamics

AP has been given appropriate fluid resuscitation. The patient is also on norepinephrine 0.4 mcg/kg/minute to increase MAP. Current MAP is 62. What is the most appropriate adjunct agent?

- A. Dopamine
- B. Epinephrine
- C. Vasopressin
- D. Phenylephrine

# Hemodynamic Management

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

 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.*



## Question 4: Infection

The patient has been admitted to the ED for 30 minutes, and it has been determined that he is in septic shock. AP's wife reports the patient was previously admitted 1 month ago and was treated with IV antibiotics.

Allergies: NKDA

Does the patient need MRSA coverage?

- A. Yes
- B. No
- C. Unsure

# Infection

2016 Recommendation	2021 Recommendation
<p>We recommend empiric broad-spectrum therapy with one or more antimicrobials for patients presenting with sepsis or septic shock to cover all likely pathogens (including bacterial and potentially fungal or viral coverage.”</p> <p><i>Strong recommendation, moderate quality of evidence</i></p>	<p><b>For adults with sepsis or septic shock at high risk of MRSA, we recommend using empiric antimicrobials with MRSA coverage over using antimicrobials without MRSA coverage</b></p> <p><i>Best practice statement</i></p>
	<p><b>For adults with sepsis or septic shock at low risk of MRSA, we suggest against using empiric antimicrobials with MRSA coverage, as compared with using antimicrobials without MRSA coverage.</b></p> <p><i>Weak recommendation, low quality of evidence</i></p>

---

# Questions?



## References

1. Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8):801-810.
2. Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. *Crit Care Med*. 2021;49(11):e1063-e1143
3. Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock; 2016. *Crit Care Med*. 2017;46(3):486-552.
4. SCCM: Adult patients. Society of Critical Care Medicine (SCCM). (n.d.).<https://www.sccm.org/SurvivingSepsisCampaign/Guidelines/Adult-Patients>
5. SCCM/LearnICU: Surviving sepsis campaign hour-1 bundle teaching slides. Society of Critical Care Medicine (SCCM) - LearnICU. (n.d.).<https://www.sccm.org/LearnICU/Resources/Surviving-Sepsis-Campaign-Hour-1-Bundle-Teaching-S>
6. Gordon AC, Mason AJ, Thirunavukkarasu N, et al. VANISH Randomized Clinical Trial: Effect of early vasopressin vs norepinephrine on kidney failure in patients with septic shock. *JAMA*. 2016; 316(5): 509-518.