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Sepsis Smackdown: New Evidence, Smarter Strategies & Winning the Fight Against Infection Chaos

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CE Deadline: 09/30/25



Today's Presenters



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Howdy!

Disclosures



The presenters have no real or perceived conflicts of interest related to this presentation

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Learning Objectives



At the end of this session, participants should be able to:

- Recognize key concepts and updated evidence in sepsis management as outlined in guidelines.
- Identify evidence-based empiric antibiotic strategies for treating sepsis and implications for clinical practice.
- Recall strategies to address challenges in applying sepsis management protocols, including interdisciplinary coordination and decision-making under time pressure.

Abbreviations



- ARDS – Acute respiratory distress syndrome
- C. Auris – *Candida auris*
- E.Coli – *Escherichia coli*
- ED – Emergency department
- ICU – Intensive care unit
- IV – Intravenous
- MAP – Mean arterial pressure
- MEWS – Modified early warning score
- MRSA – Methicillin-resistant *Staphylococcus aureus*
- NEWS – National early warning score
- SIRS – Systemic inflammatory response syndrome
- Staph – *Staphylococcus aureus*
- Strep – *Streptococcus spp.*
- SOFA – Sequential organ failure assessment
- qSOFA- Quick sequential organ failure assessment

The Sepsis Challenge



- Sepsis causes **life-threatening organ dysfunction** due to a **dysregulated host response** to infection
 - Septic shock
 - Underlying circulatory, cellular and metabolic abnormalities with greater risk of mortality
- Major healthcare problem, 20% of all-cause deaths globally

In the United States

- 1.7 million adults affected
- 270,000 sepsis-related deaths
- \$ 62B annual economic burden

Source: Guarino M, et al. *J Clin Med*. 2023.12(9):3188

The Sepsis Challenge



- Increase in incidence of sepsis attributed to
 - Advanced average age
 - Increased invasive procedures
 - Wide use of immunosuppressive drugs and chemotherapy
 - Antibiotic resistance
- **Early identification and prompt management is crucial**



Sources:

1. Getty Images. Used with permission of HealthTrust.
2. Guarino M, et al. *J Clin Med*. 2023.12(9):3188

Evolution of the Definition of Sepsis



Sepsis-1 (1991)



- Systemic inflammatory response syndrome (SIRS)
- Sepsis: systemic response to infection and meets ≥ 2 SIRS criteria
- Severe sepsis
- Septic shock

Sepsis-2 (2001)



- Role of early diagnosis
- Documented or suspected categories: inflammatory, hemodynamic, organ dysfunction, and tissue perfusion variations, and biochemical indicators

Sepsis-3 (2016)



- Life-threatening organ dysfunction caused by dysregulated host response to infection
- Septic shock
- Sequential Organ Failure Assessment (SOFA) score

Source: Gul F, et al. *Turk J Anaesthesiol Reanim*. 2017. 45:123-138.

Early Recognition Tools



Sequential Organ Failure Assessment (SOFA)

- Comprehensive organ dysfunction assessment requiring lab values
- ≥ 2 points indicate organ dysfunction

Quick SOFA (qSOFA)

- Rapid bedside assessment with 3 criteria met

National Early Warning Score (NEWS)

- Aggregate scoring system using vital signs
- Superior sensitivity for predicting clinical deterioration vs. qSOFA

Modified Early Warning Score (MEWS)

- Aggregates vital signs and physiological parameters to determine risk of catastrophic deterioration

Sources:

1. Guarino M, et al. *J Clin Med*. 2023;12(9):3188
2. Evans L, et al. *Intensive Care Med*. 2021;47(11):1181-1247.

Ready, Set, Sepsis: Hour–1 Sepsis Bundle



Laboratory Collection	Antibiotic Administration	Fluid Resuscitation	Vasopressors
<ul style="list-style-type: none">• Measure & remeasure lactate levels• Obtain blood cultures	<ul style="list-style-type: none">• Antimicrobial selection and administration	<ul style="list-style-type: none">• Administer 30 mL/kg crystalloid fluid for hypotension or lactate \geq 4 mmol/L• Initiate within first hour	<ul style="list-style-type: none">• For persistent hypotension during or after fluid resuscitation• Used to maintain MAP \geq 65 mmHg

Sources:

1. Guarino M, et al. *J Clin Med*. 2023.12(9):3188
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2. Evans L, et al. *Intensive Care Med*. 2021;47(11):1181-1247.

Fluid Resuscitation



- Fluid volume
 - Administer 30 mL/kg within first 3 hours
 - May consider reduced volume for patients at high risk for fluid overload
- Fluid choice
 - Balance crystalloids preferred over 0.9% normal saline
 - Reduced risk of hyperchloremia and acute kidney injury
 - Lactated Ringer's, PlasmaLyte
- Fluid monitoring
 - Use of dynamic measures to assess fluid responsiveness



Sources:

1. Guarino M, et al. *J Clin Med*. 2023;12(9):3188
2. Getty Images. Used with permission of HealthTrust.

Fluid Resuscitation, *continued*



- Fluid resuscitation – one size does not fit all
- Risk of fluid overload
 - Cardiac (heart failure) history
 - Kidney disease (hemodialysis)
 - Liver cirrhosis
- May consider giving lower volume fluid bolus & re-assess continued need



Sources:

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2. Evans L, et al. *Intensive Care Med*. 2021;47(11):1181-1247.

Vasopressor Selection



Maintain mean arterial pressure
(MAP) \geq 65 mmHg

Norepinephrine

First-line vasopressor

Vasopressin

Added to reduce norepinephrine rate in refractory hypotension

Epinephrine

Considered when additional agent is needed for adequate perfusion

Dobutamine

Consider for patients with myocardial dysfunction and persistent hypoperfusion



Sources:

1. Evans L, et al. Intensive Care Med. 2021;47(11):1181-1247.
2. Getty Images. Used with permission of HealthTrust.

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Tailoring Antibiotic Therapy



Identify the Source

Time-Sensitive Intervention

Risk/Benefit Assessment

Multidisciplinary Approach

Empiric Antibiotic Selection



- Select empiric coverage based on most likely source of infection

Likely Gram-positive Sources

Respiratory
Skin and soft tissue
Bone

Staph and Strep

Likely Gram-negative Sources

Genitourinary
Abdominal
Bloodstream

E. Coli and Klebsiella

- Pseudomonas Considerations

Sources:

1. Savage RD, *CMAJ Open*. 2016;4(4):E569.
2. Getty Images. Used with permission of HealthTrust.

Empiric Antibiotic Selection, *continued*



- Consider broader coverage
 - History of multidrug resistant organism infection or colonization – MRSA or C. Auris
 - Recent hospitalization – Pseudomonal Coverage
 - Recent parenteral antimicrobials in the past 90 days – Consider Resistance
 - Immunocompromised – Antiviral and Antifungal
- **Appropriate selection is key to mortality impact**
 - 34% vs. 18% when correct choice is made
 - Overuse also reduced effectiveness

Sources:

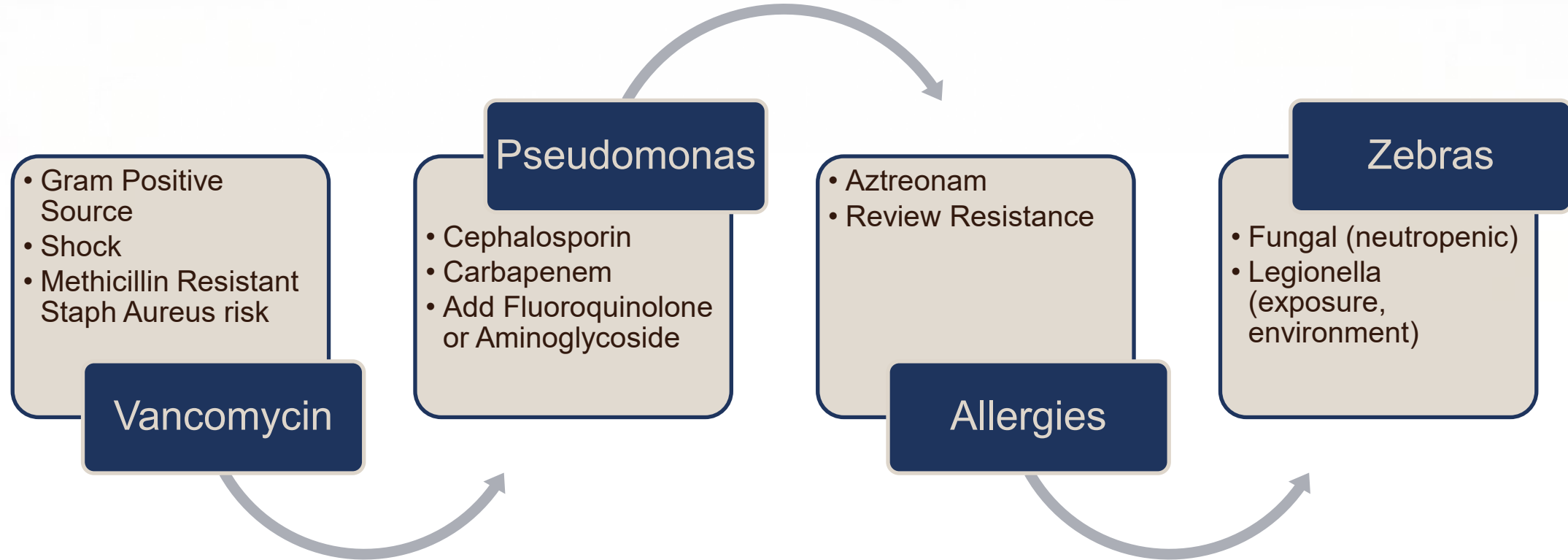
1. Leibovici L et al. *Antimicrob Agents Chemother.* 1997; 41(5):1127
2. Getty Images. Used with permission of HealthTrust

Tailoring Antibiotic Therapy



Patient Factor	Consideration
Recent Antibiotic Use	Increased risk for resistant organisms
Healthcare Exposure	Cover for MRSA and resistant gram-negatives
Renal / Hepatic Dysfunction	Dose adjustments and close monitoring
Immunosuppression	Broad coverage including fungal pathogens
Local Antibigram	Guide empiric therapy based on local patterns

Antibiotic Choices



Sources:

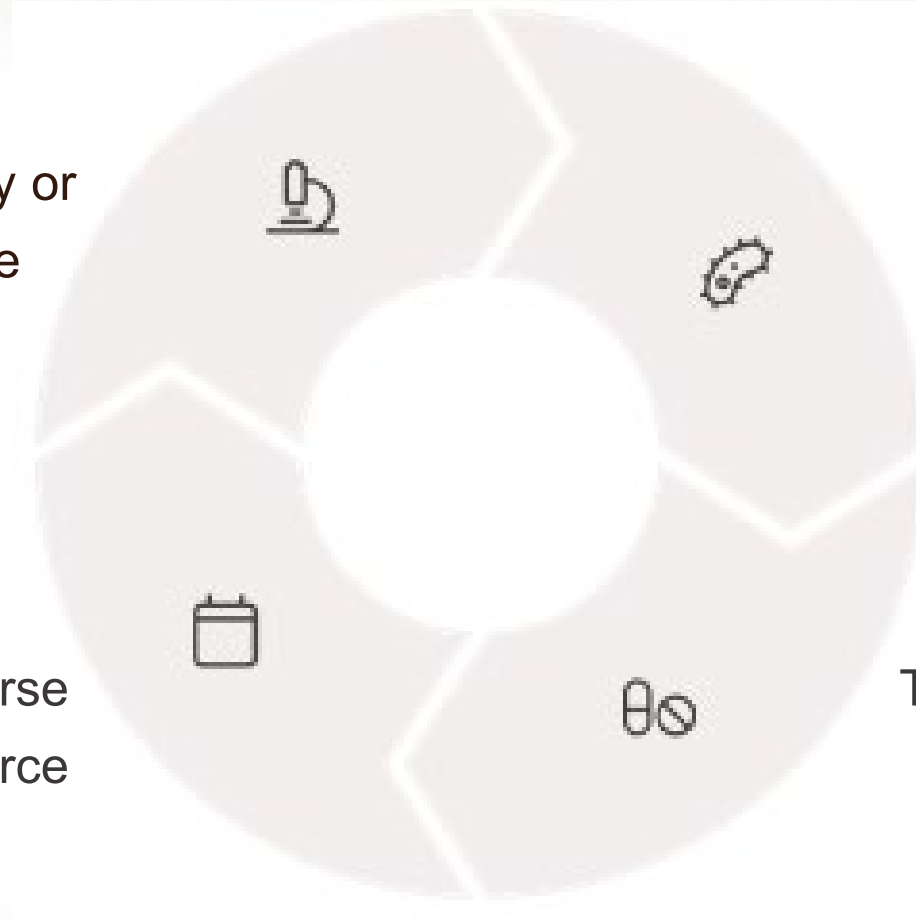
1. Savage RD, *CMAJ Open*. 2016;4(4):E569.
2. Qian ET, et al, *JAMA*. 2023; 330(16):1557.

De-escalation Strategies



Obtain Cultures

Collect blood, urine, respiratory or wound culture when possible



Identify Pathogen

Use both conventional and rapid diagnostic methods

Optimize Duration

Limit to shortest effective course based on response and source

Narrow Therapy




Target identified organisms with most appropriate antibiotic

Source:

1. Matuszak SS, et al. *Antibiotics*. 2025.14(5); 467

Adjunctive Therapies



Corticosteroids 	Lung-protective Ventilation 	Renal Replacement 
Consider IV hydrocortisone ONLY if fluid and vasopressors do not restore hemodynamic stability Hydrocortisone 200mg/day	Sepsis-related ARDS Low tidal volumes	For acute kidney injury with life-threatening complications May be done intermittently or continuously

Sources:

1. Guarino M, et al. *J Clin Med*. 2023;12(9):3188
2. Evans L, et al. *Intensive Care Med*. 2021;47(11):1181-1247.



- Faster resolution of shock
- No reduction in overall mortality
- Helps selected few

Corticosteroids Round-up

- Refractory Septic Shock
- ARDS
- COVID-19
 - Not Influenza
- Community Acquired Pneumonia
 - Significant Hypoxia
 - Mechanical Ventilation
- Steroid Responsive Underlying Condition
 - Acute Eosinophilic Pneumonia
 - Organizing Pneumonia, Cryptogenic Pneumonia
- Best Benefits from Hydrocortisone and Fludrocortisone (50mg intravenous every 6 hours and 50mcg daily by mouth)

Back to the Basics

Supportive Therapies

- Blood product infusion
- Nutrition
- Stress ulcer prophylaxis
- Venous thromboembolism prophylaxis
- External cooling and antipyretics
- Intensive insulin therapies



Interdisciplinary Coordination



Pharmacists

Antibiotic stewardship,
dosing optimization and
drug interactions

Laboratory

Rapid diagnostic
testing and results
communications

Nurses

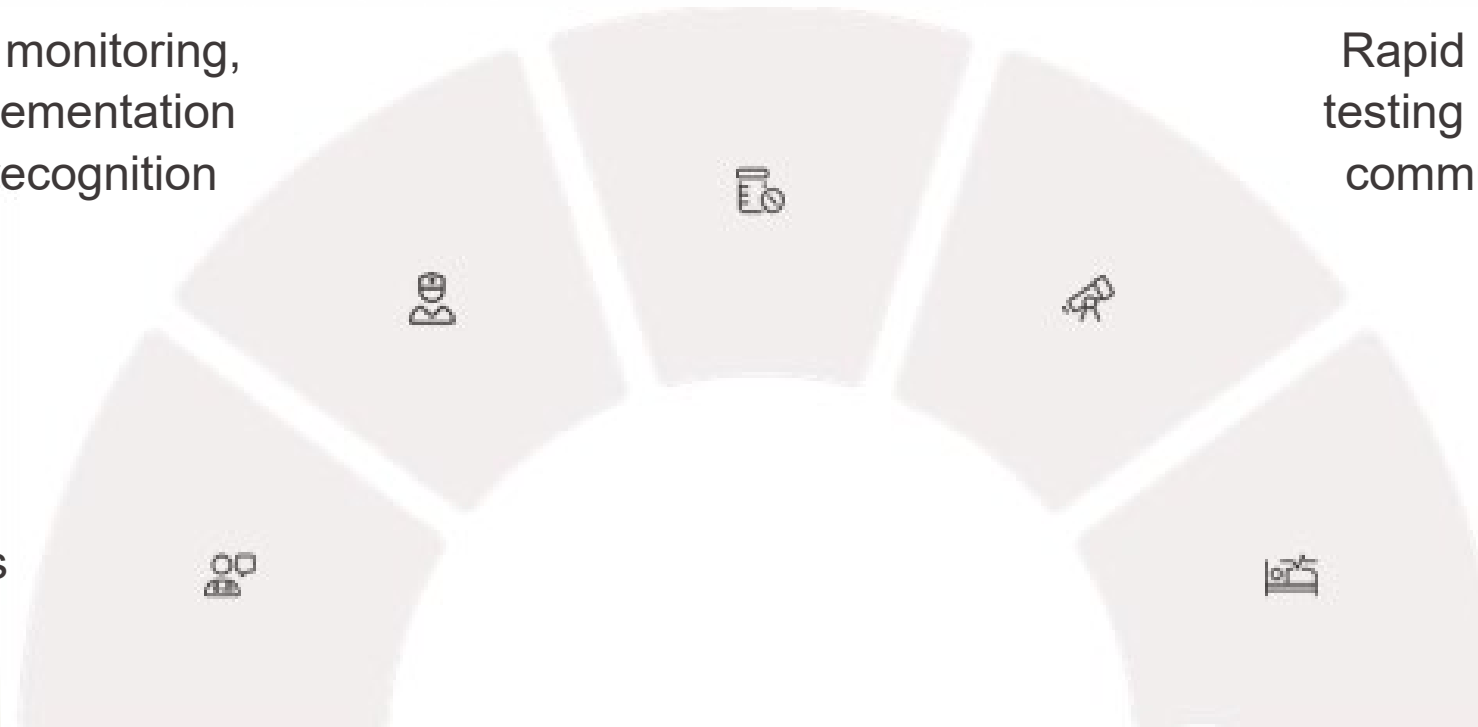
Continuous monitoring,
bundle implementation
and early recognition

Physicians

Diagnosis,
treatment decisions
and overall
management

Specialists

Source control
procedures and
specialized
interventions



Implementation Barriers



Resource Limitations

Inadequate staffing, equipment and laboratory capabilities can delay bundle implementation



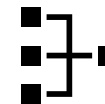
Time Constraints

High and competing clinical demands inhibit protocol adherence



Knowledge Gaps

Varying awareness and compliance with current guidelines across disciplines and experience levels



Systematic Issues

Electronic health record limitations and workflow disruptions can impede protocol adoption

Sources:

1. Sasmito P, et al. *Acute Crit Care*. 2024. 39(4):545-553.
2. Roberts N, et al. *Scand J Trauma Resusc Emerg Med*. 2017.19; 25:96.

Overcoming Implementation Challenges



Protocol Adaptation

- Develop guidelines based on local resources and constraints
- Create abbreviated versions for different settings (ED, ICU, floor)

Automated Systems

- Implement electronic alerts (best practice advisories)
- Develop one-click order sets for sepsis bundles

Education Initiatives

- Provide ongoing multidisciplinary training
- Regular sepsis simulations with debriefing

Performance Feedback

- Monitor and share compliance data and outcomes (i.e., Monthly sepsis dashboard with metrics)
- Celebrate improvements and identify barriers

Sources:

1. Sasmito P, et al. *Acute Crit Care*. 2024. 39(4):545-553.
2. Roberts N, et al. *Scand J Trauma Resusc Emerg Med*. 2017.19; 25:96.

Key Takeaways



Time is Tissue

Implement hour-1 bundle promptly. Every hour of delay increases mortality risk.



Target Appropriately

Tailor antibiotic selection to likely source, patient factors and local resistance patterns.



Team Approach

Leverage interdisciplinary expertise. Clear communication enhances coordination under pressure.



Continuous Improvement

Adapt protocols to local needs. Monitor outcomes and adjust approaches based on evidence.

A New Lack of Clarity in 2025



The Effect of Severe Sepsis and Septic Shock Management Bundle (SEP-1) Compliance and Implementation on Mortality Among Patients with Sepsis: A Systematic Review

- 4,403 unique references, and 17 studies were included
 - All 17 studies were observational, and none had low risk of bias
 - 12 studies assessed the relationship between SEP-1 compliance and mortality
 - 5 showed statistically significant benefit, whereas 7 did not
 - 4 had a flawed methodology
 - 1 had significant benefit
- Sepsis management bundle (SEP-1) demonstrated benefit in the septic shock population; however, the benefit appeared to be from use of vasopressors

Source: Ford JS et al. *Ann Intern Med.* 2025; 178(4):543

SEPSIS SMACKDOWN: NEW EVIDENCE, SMARTER STRATEGIES &



WINNING THE FIGHT AGAINST INFECTION CHAOS





Assessment Question 1

The Sepsis Hour-1 Bundle includes the following:

- A. Measure lactate level
- B. Begin fluid resuscitation
- C. Draw blood cultures
- D. Administer antimicrobials
- E. All of the above



Answer: Assessment Question 1

The Sepsis Hour-1 Bundle includes the following:

- A. Measure lactate level
- B. Begin fluid resuscitation
- C. Draw blood cultures
- D. Administer antimicrobials
- E. **All of the above**



Assessment Question 2

40-year-old female without any past medical history or hospitalizations presents with fever of 102 F, hypotension and altered mentation. MAP<65. HCG neg and urine is cloudy. Lungs are clear. Her partner says she was experiencing some urinary problems prior to this. No history of drug use. The best initial antibiotics would be:

- A. Piperacillin-Tazobactam
- B. Moxifloxacin and Piperacillin-Tazobactam and Vancomycin
- C. Ceftriaxone
- D. Vancomycin and Ceftazidime



Answer: Assessment Question 2

40-year-old female without any past medical history or hospitalizations presents with fever of 102 F, hypotension and altered mentation. MAP<65. HCG neg and urine is cloudy. Lungs are clear. Her partner says she was experiencing some urinary problems prior to this. No history of drug use. The best initial antibiotics would be:

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- B. Moxifloxacin and Piperacillin-Tazobactam and Vancomycin
- C. **Ceftriaxone**
- D. Vancomycin and Ceftazidime

Assessment Question 3



All of the following are tools to overcome implementation challenges in sepsis care, except:

- A. Monitor and share compliance and outcomes
- B. Provide ongoing multidisciplinary training
- C. Share published national and international guidelines
- D. Implement electronic alerts and best practice advisories to trigger timely interventions



Answer: Assessment Question 3

All of the following are tools to overcome implementation challenges in sepsis care, except:

- A. Monitor and share compliance and outcomes
- B. Provide ongoing multidisciplinary training
- C. Share published national and international guidelines**
- D. Implement electronic alerts and best practice advisories to trigger timely interventions

References



1. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Intensive Care Med.* 2021;47(11):1181-1247
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4. Gul F, Arslantas MK, et al. Changing Definitions of Sepsis. *Turk J Anaesthesiol Reanim.* 2017. 45: 129-138.
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8. Annane D, Renault A, et al. Hydrocortisone plus Fludrocortisone for Adults in Septic Shock. *N Engl J Med.* 2018. 378:809-818.
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Thanks y'all!



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