Don't Let It VAPpen:

Exploring Antimicrobial Prophylaxis for Ventilator-Associated Pneumonia

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Disclosures

The planners and speakers have indicated that there are no relevant financial relationships with any in eligible companies to disclose.

Learning Objectives

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

Recognize

- Recognize the pathophysiology of ventilator-associated pneumonia

Identify

- Identify various prophylactic strategies for ventilator-associated pneumonia

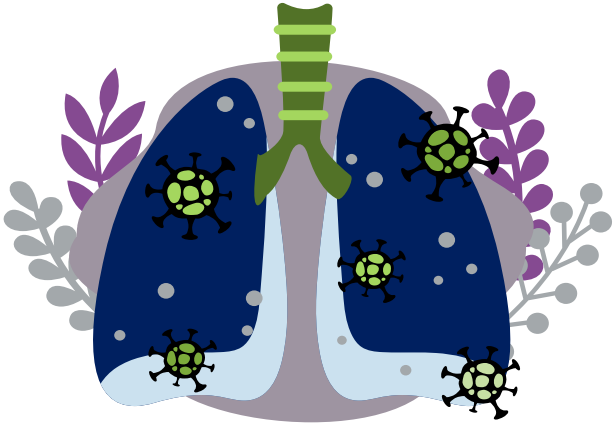
Recall

- Recall findings from recent literature surrounding antimicrobial prophylaxis for ventilator-associated pneumonia

Select

- Select an evidence-based approach to using antimicrobial prophylaxis for ventilator-associated pneumonia in select patients

BACKGROUND



Definitions

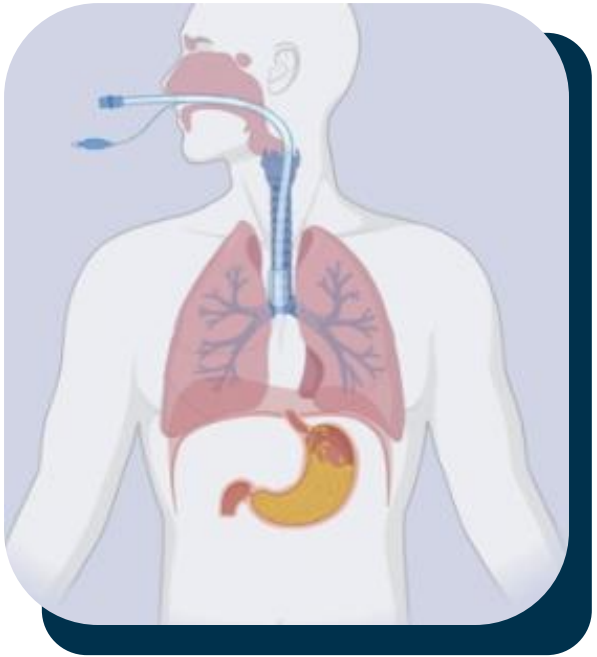
Community-Acquired Pneumonia	Hospital-Acquired Pneumonia	Ventilator-Associated Pneumonia
Acquired outside of hospital or LTCF in the community or <48 hours after hospital admission	Acquired ≥48 hours after hospital admission, non-mechanical ventilation related	Acquired ≥48 hours after endotracheal intubation

LTCF: Long-term care facility

Howroyd F, et al. *Respir Med.* 2025;247:108275.
Kalil AC, et al. *Clin Infect Dis.* 2016;63(5):e61–e111.

Pathophysiology

- Colonization of the aerodigestive tract by pathogenic bacteria
- Subsequent aspiration of contaminated secretions into the lower respiratory tract
- Biofilm formation acts as reservoir for persistent infection
- Inflammatory response



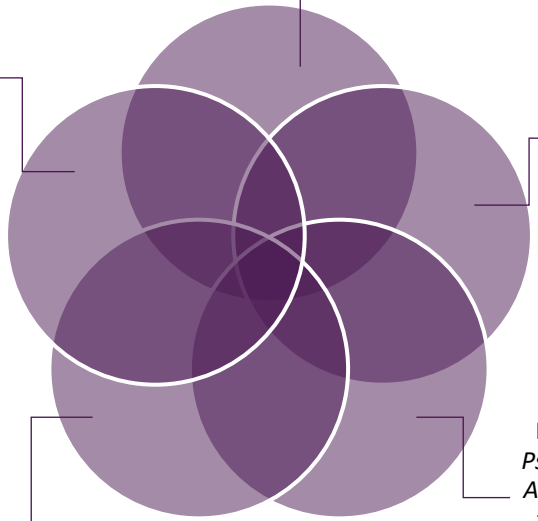
ETT: Endotracheal tube
VAP: Ventilator-associated pneumonia

Howroyd F, et al. *Respir Med.* 2025;247:108275.
Kalil AC, et al. *Clin Infect Dis.* 2016;63(5):e61–e111.

Colonization

Respiratory tract colonization often precedes VAP in mechanically ventilated patients

Pre-VAP endotracheal aspirate cultures may help guide empiric therapy, though not all colonization progresses to VAP



Colonizers may originate from endogenous or exogenous sources

Aspiration of colonized secretions into the lower respiratory tract via the endotracheal tube contributes to infection

MDR organisms such as *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and MRSA are common colonizers and frequent VAP pathogens

MRSA: Methicillin-resistant *Staphylococcus aureus*
VAP: Ventilator-associated pneumonia
MDR: Multi-drug resistant

Joseph NM, et al. *Int J Infect Dis*. 2010;14(8):e723-e729.

Etiology & Epidemiology

VAP

- One of the most common ICU-acquired infections, affecting approximately 5–20% of patients who receive mechanical ventilation for ≥48 hours
- Leads to prolonged ICU and hospital stays and increased healthcare costs

Mortality

- Estimated at 10–45%, with higher rates in surgical intensive care units and patients with moderate severity of illness

MDR organisms

- Frequently implicated, with pathogens such as *Pseudomonas* spp., *Staphylococcus aureus, Klebsiella* spp., and *Acinetobacter baumannii*

ICU: Intensive care unit
Spp.: Species MDR: Multi-drug resistant
VAP: Ventilator-associated pneumonia

Dongol S, et al. *PloS One*. 2021;16(11):e0259634.
Wu D, et al. *Frontiers in Pharmacology*. 2019;10:482.
Xie J, et al. *Infectious Diseases Society of America*. 2018;67.
Papazian L, et al. *Intensive Care Medicine*. 2020;46(5):888-906.

Risk Factors

- Prolonged mechanical ventilation
- Prolonged ICU length of stay
- Male sex
- Older age (>70 years)
- High APACHE II scores
- Low serum albumin
- COPD, diabetes, obesity, alcoholism
- Trauma, burns, multi-organ injury
- Depressed consciousness, aspiration, elevated gastric pH, tracheostomy
- Use of sedatives, paralytics, and mandatory ventilation modes
- Prior antibiotic exposure and upper respiratory tract colonization by GNB

ICU: Intensive care unit
GNB: Gram Negative bacteria
COPD: Chronic obstructive pulmonary disease
APACHE II: Acute Physiology and Chronic Health Evaluation II

Dongol S, et al. *PloS One*. 2021;16(11):e0259634.
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Risk Factors For Multi-Drug Resistant Organisms

Intravenous antibiotics within the previous 90 days

- Broad-spectrum β-lactams
- Carbapenems
- Fluoroquinolones

Prolonged hospital or intensive care unit stay

- Hospitalization ≥5 days before ventilator associated pneumonia onset

Septic shock at the time of VAP

Acute respiratory distress syndrome before VAP

Acute renal replacement therapy prior to VAP

VAP: Ventilator-associated pneumonia

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Xie J, et al. *Infectious Diseases Society of America.* 2018;67.

Common Pathogens

Gram-Positive Bacteria

- *Staphylococcus aureus*:
  - Methicillin-susceptible
  - Methicillin-resistant
- *Streptococcus pneumoniae*

Gram-Negative Bacilli

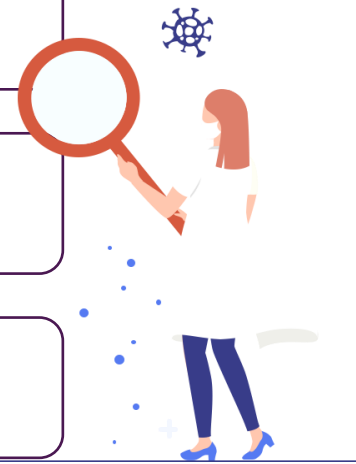
- Non-fermenting:
  - *Pseudomonas aeruginosa* → One of the top causes
  - *Acinetobacter baumannii* complex → Associated with high carbapenem resistance and mortality
  - *Stenotrophomonas maltophilia* → Inherently resistant to many antibiotics

Enterobacterales

- *Klebsiella* species (*K. pneumoniae, K. oxytoca*)
- *Enterobacter* species (*E. cloacae complex, E. aerogenes*)
- *Escherichia coli*
- *Proteus* species, *Citrobacter* species, *Morganella morganii*

Polymicrobial Infections

- Occur in 20–40% of ventilator-associated pneumonia cases
- Often involving combinations of:
  - S. *aureus* and Gram-negative rods (*Pseudomonas, Klebsiella, Enterobacter*)



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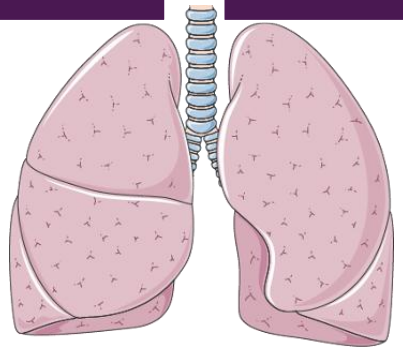
Diagnosis

New or progressive pulmonary infiltrate on chest radiograph after at least 48 hours of mechanical ventilation

Plus, at least two of the following:

- Fever (>38°C) or hypothermia (<36°C),
- Leukocytosis or leukopenia
- Purulent respiratory secretions



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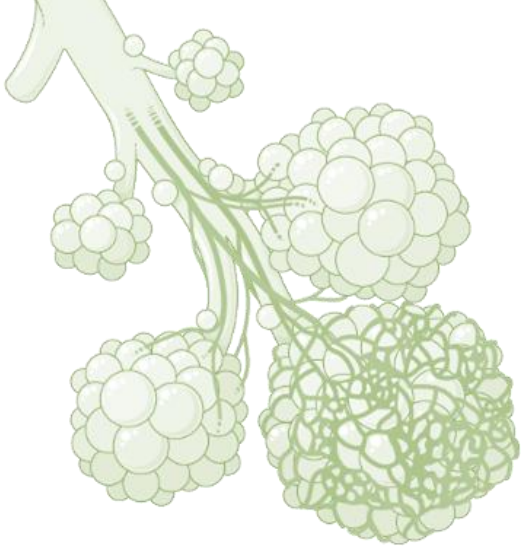
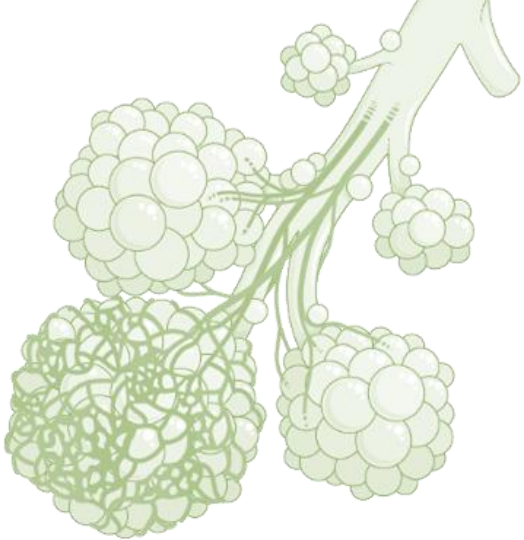
Assessment Question #1

Which pathophysiologic mechanism directly contributes to the development of ventilator-associated pneumonia?

A. Hematogenous spread from bloodstream infection
B. Microaspiration of colonized secretions around the endotracheal tube cuff
C. Reactivation of latent pulmonary infection
D. Viral-induced cytokine storm leading to alveolar injury





Ventilator-Associated Pneumonia Management

Ventilator-Associated Pneumonia Treatment

No Risk Factors for Antibiotic Resistance No Risk Factors for Gram-Negative Resistance MRSA < 10-20%	No Risk Factors for Gram-Negative Resistance MRSA ≥ 10-20%	Gram-Negative Resistance ≥ 10% MRSA > 10-20%
β-Lactam or Fluoroquinolone	β-Lactam or Fluoroquinolone and MRSA coverage	Two Agents: β-Lactam or Fluoroquinolone or Aminoglycoside and MRSA coverage
β-Lactam: • Piperacillin-tazobactam 4.5 g IV Q8H • Cefepime 2 g IV Q8H • Meropenem 1 g IV Q8H Fluoroquinolone: • Levofloxacin 750 mg IV Q24H	β-Lactam: • Piperacillin-tazobactam 4.5 g IV Q8H • Cefepime 2 g IV Q8H • Meropenem 1 g IV Q8H • Aztreonam 2 g IV Q12H Fluoroquinolone: • Levofloxacin 750 mg IV Q24H • Ciprofloxacin 400 mg IV Q8H MRSA coverage: • Vancomycin • Linezolid 600 mg IV Q12H	β-Lactam: • Piperacillin-tazobactam 4.5 g IV Q8H • Cefepime 2 g IV Q8H • Meropenem 1 g IV Q8H • Aztreonam 2 g IV Q12H Fluoroquinolone: • Levofloxacin 750 mg IV Q24H • Ciprofloxacin 400 mg IV Q8H Aminoglycosides: • Tobramycin 7 mg/kg IV MRSA coverage: • Vancomycin • Linezolid 600 mg IV Q12H

MRSA: Methicillin-resistant *Staphylococcus aureus*
IV: Intravenous
CrCl: Creatinine clearance
Q: Every
Kg: Kilogram
H: Hour

Kalil AC, et al. *Clin Infect Dis*. 2016;63(5):e61-e111.
Metlay JP, et al. *Am J Respir Crit Care Med*. 2019;200(7):e45-e67.

Pathogen-Specific Treatment

HAP/VAP due to *Pseudomonas*:

- Low concern for septic shock or mortality risk: monotherapy
- High concern for septic shock or mortality risk: consider combination with two antibiotics

HAP/VAP due to *Acinetobacter*:

- Ampicillin-sulbactam 9 g every 8 hours PLUS Minocycline 200 mg every 12 hours

HAP/VAP due to Carbapenem-Resistant Pathogens:

- Empiric therapy subject to local antibiogram
- Ceftazidime-avibactam
- Add aztreonam if empirically treating for IMP/VIM or NDM

Duration:

- HAP/VAP: 7 days
- Shorter/longer durations may be indicated based on improvement
- De-escalation preferred over fixed antibiotic therapy
- Clinical criteria should guide the discontinuation of antibiotic therapy

IMP/VIM: Imipenemase/Verona Integron-encoded Metallo-β-lactamase
HAP: Hospital-acquired pneumonia
VAP: Ventilator-associated pneumonia
NDM: New Delhi metallo-beta-lactamase

Kalil AC, et al. *Clin Infect Dis*. 2016;63(5):e61-e111.
Metlay JP, et al. *Am J Respir Crit Care Med.* 2019;200(7):e45-e67.

Importance Of Extended-Infusion β-Lactams

VAP Pathogens Often Have Higher MICs:
- *Pseudomonas aeruginosa*
- *Acinetobacter* species
- Enterobacterales

β-Lactams Are Time-Dependent Antibiotics:
- Efficacy depends on **%fT > MIC**
  - Carbapenems: 40%
  - Penicillins: 50%-60%
  - Cephalosporins: 60%-70%
  - Aztreonam: 50%

Critically Ill Patients May Have Altered Pharmacokinetics:
- Increased volume of distribution
- Augmented renal clearance
- Unpredictable drug exposure

Extended Infusions Improve Target Attainment:
- Maintain serum concentrations above MIC longer
- Increased probability of pharmacodynamic success
- Especially important in VAP with risk of MDR organisms

Recommended by Guidelines:
- IDSA/ATS VAP guidelines support optimized dosing
- SCCM endorses extended infusions

Examples:
- Piperacillin–tazobactam: **3–4 hour infusion**
- Cefepime: **3–4 hour infusion**
- Meropenem: **3 hour infusion**

In VAP, extended-infusion β-lactams improve time above MIC—helping overcome altered PK and higher MIC pathogens common in critically ill patients

%fT: Percent Free Time
VAP: Ventilator-associated pneumonia
MDR: Multi drug-resistant
IDSA/ATS: The Infectious Diseases Society of America/American Thoracic Society SCCM: Society of Critical Care Medicine
MIC: Minimum Inhibitory Concentration

Kalil AC, et al. *Clin Infect Dis*. 2016;63(5):e61-e111.
Metlay JP, et al. *Am J Respir Crit Care Med.* 2019;200(7):e45-e67.

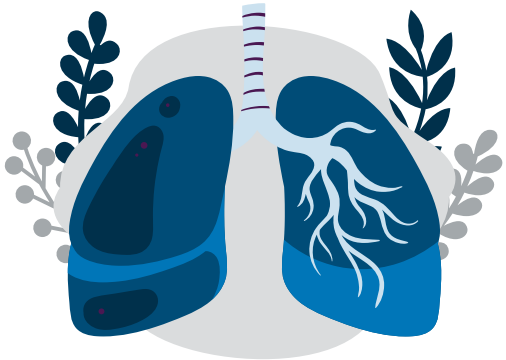
Inhaled Aminoglycosides at Advocate Health

Drug	Dose	Indications	Preparations on Formulary	Clinical Pearls
Tobramycin	≥6 years old: 300 mg every 12 hours OR 112 mg every 12 hours podhaler	**Common** adjunctive treatments to IV antibiotics in MDR Gram-negative pulmonary infections	300 mg/5 mL Inhalation solution	Expires 96 hours after preparation
Colistin	75 – 150 mg every 12 hours		150 mg/2 mL	Expires 4 hours after preparation Administer promptly after preparation to avoid polymyxin-induced toxicity
Amikacin	500 mg every 12 hours	**Less common** adjunctive treatments to IV antibiotics in MDR Gram-negative pulmonary infections	500 mg/2 mL Compounded dilution	Added to albuterol in nebulizer
Ceftazidime	1000 mg every 12 hours		1000 mg vial with 3 mL SWFI	Expires 8 hours after preparation

These are reserved for treatment of VAP, not prophylaxis

MDR: Multi-drug resistant
mg: Milligram ML: Milliliter
SWFI: Sterile water for injection

Le J, et al. *Pharmacother*. 2010;30(6):562-84.
Wood GC. *Expert Rev Anti Infect Ther*. 2011 Nov;9(11):993-1000.
Mogayzel PJ, et al. *Am J Respir Crit Care Med*. 2013 Apr 1;187(7):680-9.
ATS/IDSA Guidelines. Am J *Respir Crit Care Med*. 2005 Feb 15;171(4): 388-416.



Ventilator-Associated Pneumonia Prophylactic Strategies

Why Prevention Matters

High Morbidity and Mortality

VAP Increases:

- ICU mortality
- Length of stay
- Complications

Significant Resource Utilization

VAP Increases:

- Ventilation duration
- ICU days
- Healthcare costs

Antibiotic Exposure Has Consequences

- Resistance selection
- *Clostridioides difficile* infection
- Drug toxicity

Prevention Is Evidence-Based

- Bundled interventions decrease VAP rates

Examples of Preventive Strategies

- Head-of-bed elevation
- Daily sedation interruption and early mobility
- Oral care protocols
- Subglottic secretion drainage

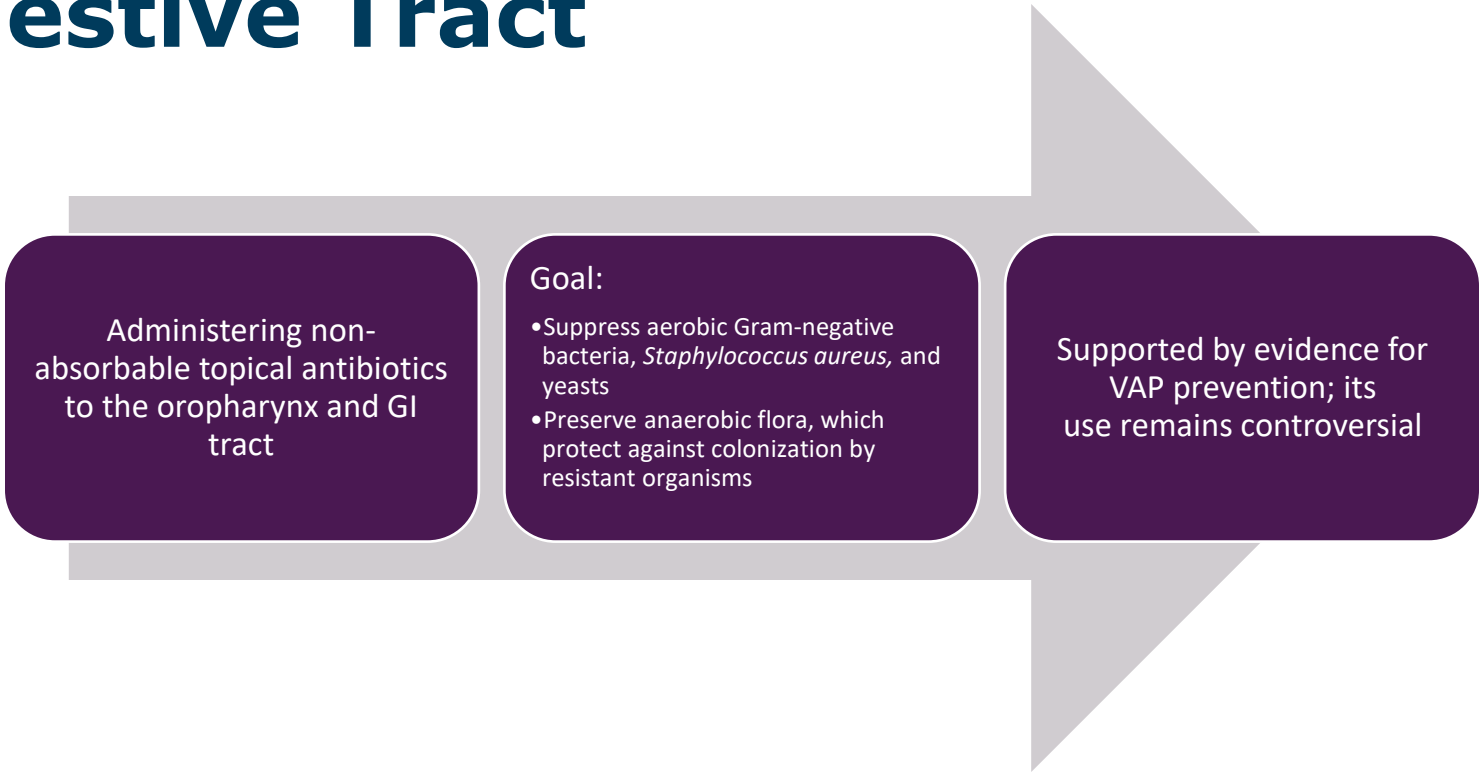
Limited Antibiotic Options

- Rising MDR pathogens
- Few new anti-Pseudomonal agents

VAP: Ventilator-associated pneumonia
ICU: Intensive care unit
MDR: Multi-drug resistance

Kalil AC, et al. *Clin Infect Dis*. 2016;63(5):e61-e111.
Metlay JP, et al. *Am J Respir Crit Care Med.* 2019;200(7):e45-e67.

Selective Decontamination Of The Digestive Tract

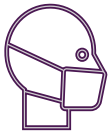


IV: Intravenous
GI: Gastrointestinal
VAP: Ventilator-associated pneumonia

Zhu D, et al. *J Hosp Infect.* 2024;145:174-186.

Non-Invasive Ventilation for Weaning

Using ventilatory support delivered via a mask to help a patient transition off invasive mechanical ventilation



After a patient is extubated, non-invasive ventilation (e.g., BiPAP or CPAP) is used to:

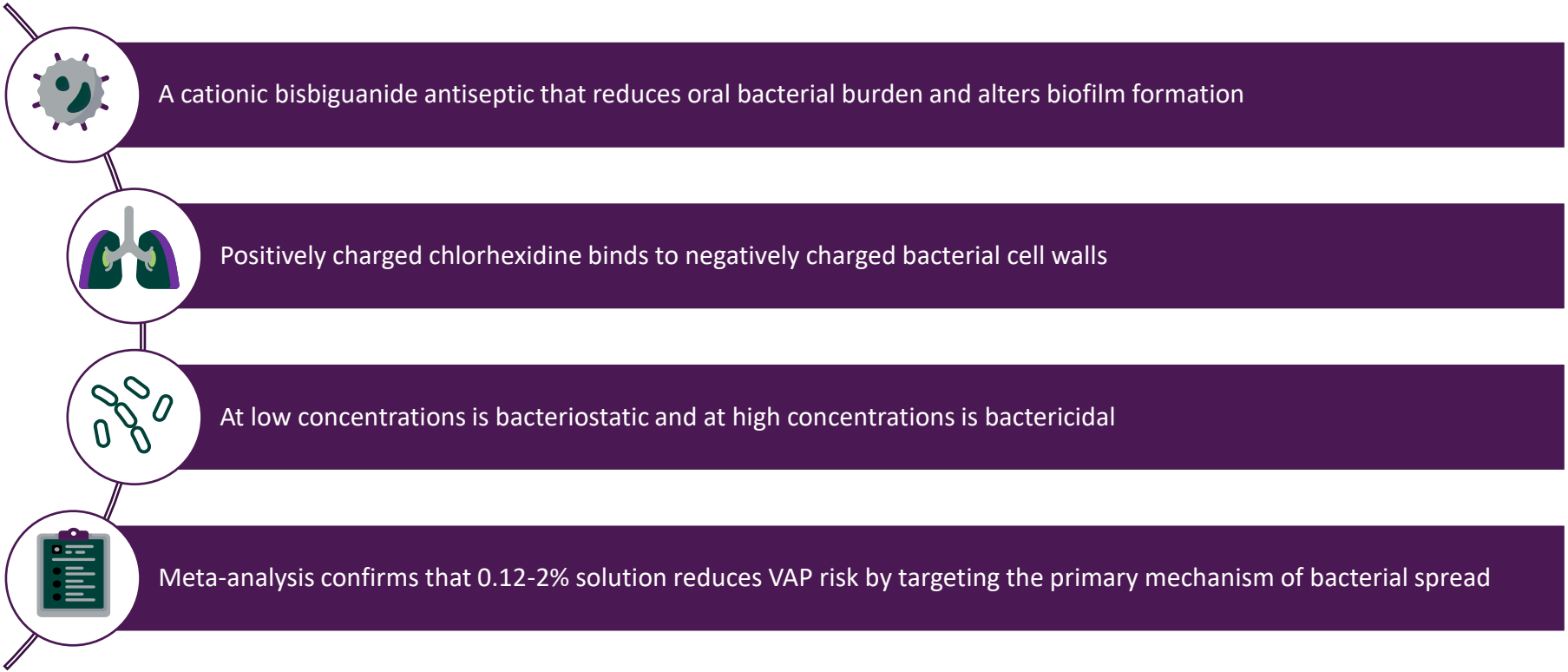
- Support breathing
- Reduce work of breathing
- Prevent respiratory failure while the lungs and respiratory muscles recover

Minimizes exposure to invasive mechanical ventilation, the single greatest risk factor for VAP development

BiPAP: Bilevel Positive Airway Pressure
CPAP: Continuous Positive Airway Pressure
VAP: Ventilator-associated pneumonia

Zhu D, et al. *J Hosp Infect.* 2024;145:174-186.

Chlorhexidine Oral Decontamination

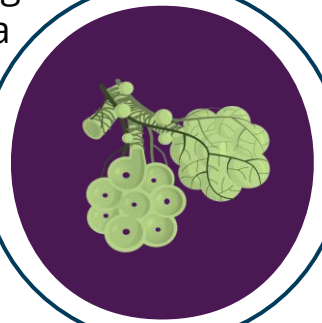


VAP: Ventilator-associated pneumonia

Koeman M, et al. *Am J Respir Crit Care Med*. 2006;173(12):1348-1355.

Early Mobilization

1. Improves secretion clearance, reducing pooling of bacteria in lower airways
2. Enhances lung expansion and V/Q matching which decreases atelectasis



3. Shortens duration of mechanical ventilation
4. Reduces sedation needs, decreasing aspiration risk and prevents ICU-acquired weakness

V/Q: Ventilation/perfusion
ICU: intensive care unit
VAP: Ventilator-associated pneumonia

Zhu D, et al. *J Hosp Infect.* 2024;145:174-186.

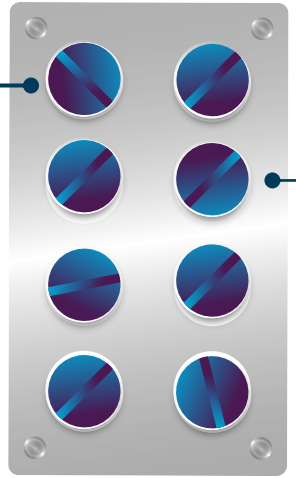
Prophylactic Probiotics and Antibiotics

Probiotics

Restores normal gut and oropharyngeal flora

Competitively inhibits pathogenic colonization, strengthens mucosal barriers, and modulates immune responses

Definitive evidence from large-scale trials remains pending



Antibiotics

Current guidelines do not recommend routine antibiotics for prevention

Resistance concerns

Appropriate antimicrobial stewardship

Suggested to prevent aerodigestive tract colonization

VAP: Ventilator-associated pneumonia

Zhu D, et al. *J Hosp Infect.* 2024;145:174-186.

Antimicrobial Prophylaxis Controversies

Resistance Concerns
Broad antibiotic exposure may promote development of MDR organisms
Long-term resistance effects remain uncertain

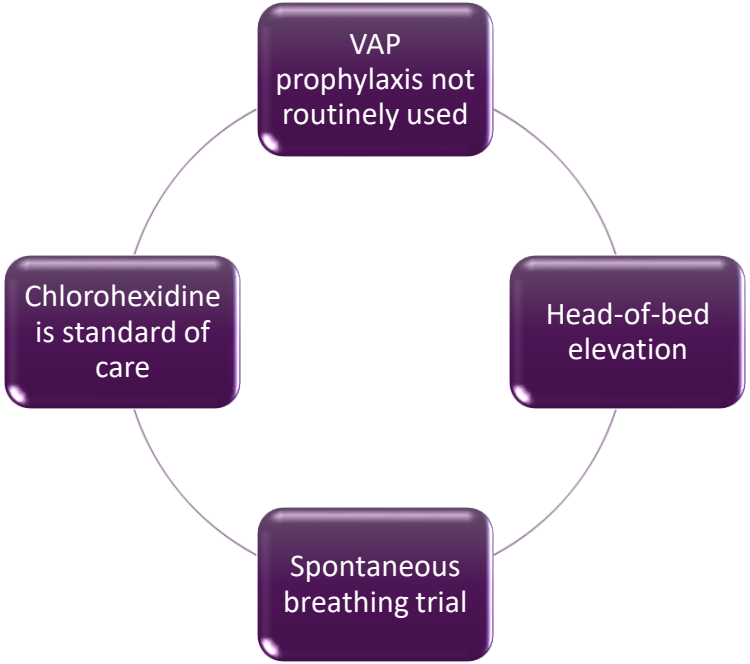
Generalizability of Data
Many studies conducted in low-resistance settings
Benefits may only be seen with certain patient populations

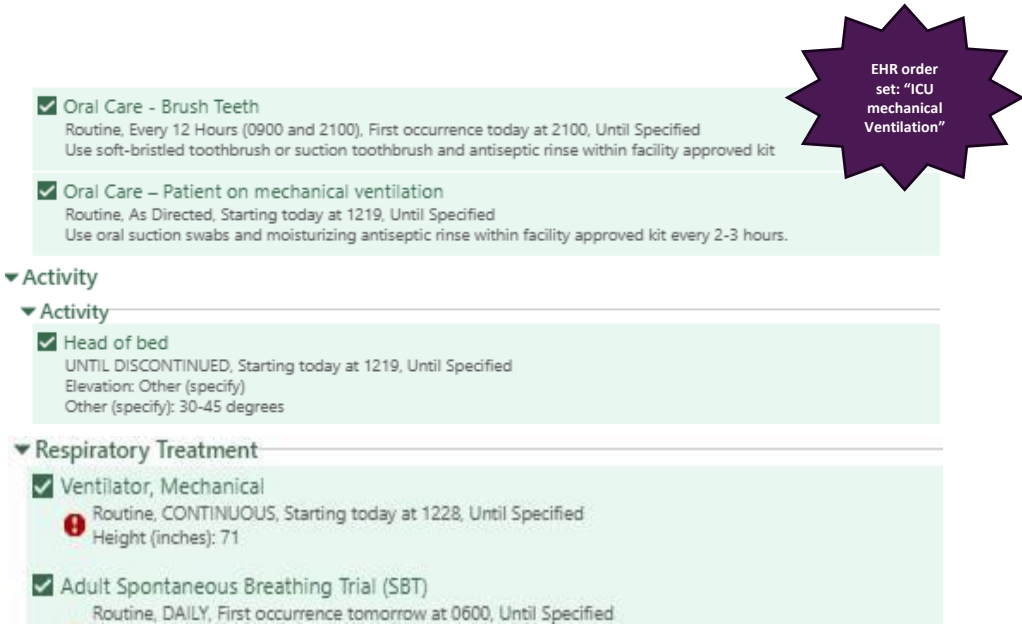
Mortality vs. Microbiologic Tradeoffs
Decrease in VAP incidence and colonization
Inconsistent impact on overall mortality
Microbiologic benefit does not confer clear survival benefit

MDR: Multi-drug resistant
VAP: Ventilator-associated pneumonia

Zhu D, et al. *J Hosp Infect.* 2024;145:174-186.

Advocate Health VAP Care Bundles





VAP: Ventilator-associated pneumonia
EHR: Electronic Health Record

AAH Pharmacy Practice Council. ICU Mechanical Ventilation (accessed 2026 April 14).

Shortcomings Of Current Prevention Strategies

Incomplete Risk Elimination	Diagnostic Uncertainty	Care Bundle Compliance Variability	Persistent Microaspiration	Does Not Address MDRO Colonization
• Care bundles do not eliminate VAP • Residual risk remains despite full compliance	• No gold standard for VAP diagnosis • Clinical criteria overlap with non-infectious causes	• Effectiveness depends on consistent execution • Human and system factors affect adherence	• Oral care and positioning reduce, but do not completely prevent aspiration • Endotracheal tubes remain a risk factor	• Non-antibiotic strategies do not directly modify airway flora • High-risk patients remain vulnerable

VAP: Ventilator-associated pneumonia
MDRO: Multi-drug-resistant organism

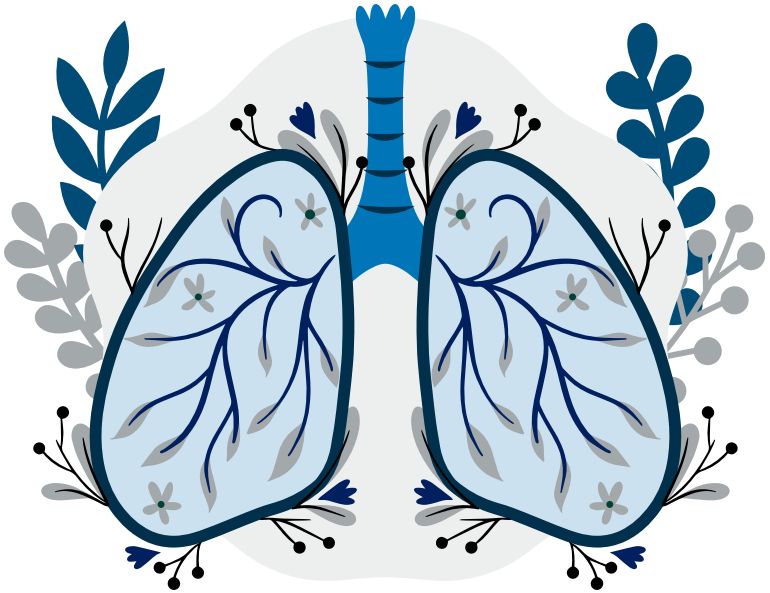
Assessment Question #2

Which of the following is considered a guideline-supported VAP prevention strategy commonly included in ventilator care bundles?

A. Use of ipratropium bromide/albuterol sulfate
B. Regular probiotic use
C. Daily sedation interruption and spontaneous breathing trials
D. Routine IV antibiotic prophylaxis

IV: Intravenous
VAP: Ventilator-associated pneumonia

Literature Review of Intravenous, Topical, and Inhaled Prophylactic Agents



Intravenous Prophylaxis

Ceftriaxone
and
Amoxicillin–Clavulanate

PROPHY-VAP Trial

Ceftriaxone to prevent early Ventilator-Associated pneumonia in patients with acute brain injury: a multicenter, randomized, double-blind, placebo-controlled, assessor-masked superiority trial		
Population	Adult patients with acute brain injury requiring mechanical ventilation for ≥48 hours and a GCS ≤12 • Enrolled: 345 patients • Demographics: 52% male, 48% female • Conducted in 9 ICUs across 8 French university hospitals	
Intervention	Single dose of IV ceftriaxone 2 grams administered within 12 hours of tracheal intubation	
Comparison	Placebo (saline) with standard VAP prevention bundle	
Primary Outcome	Early VAP incidence (days 2-7 of mechanical ventilation)	
Secondary Outcomes	• Overall antibiotic consumption despite prophylaxis • Hospital and ICU length of stay • 28-day survival • Ventilator-free and antibiotic-free days	
Results and Conclusion	Primary outcomes: • Ceftriaxone: 14% • Placebo: 32% • Hazard ratio 0.60 (95% CI 0.38-0.95), p=0.030 • Absolute risk reduction: 18%	Secondary outcomes: • Ventilator-free days: 9 vs. 5, p=0.023 • Antibiotic-free days: 21 vs. 15, p<0·0001 • Mortality: 15% vs. 25%; HR 0.62 (95% CI 0.39-0.97), p=0.036

IV: Intravenous
VAP: Ventilator-associated pneumonia
ICU: Intensive care unit
GCS: Glasgow Coma Scale

Nseir S, et al. *Lancet Respir Med*. 2023;11:475–486.

ANTHARTIC Trial

Prevention of Early Ventilator-Associated Pneumonia after Cardiac Arrest		
Population	• Multicenter double blind randomized placebo controlled trial • 194 adults after out-of-hospital cardiac arrest with initial shockable rhythm requiring mechanical ventilation • Treated with targeted temperature management at 32–34°C	
Intervention	• 99 participants received antibiotic vs. 95 received placebo • IV amoxicillin–clavulanate: 1000 mg/200 mg three times daily for 2 days initiated within 6 hour of return of spontaneous circulation vs. placebo	
Primary Outcome	• Incidence of early ventilator-associated pneumonia, occurring within the first 7 days of hospitalization	
Secondary Outcomes	• Incidence of late VAP >7 days • Ventilator-free days at day 28 • ICU length of stay • Mortality at day 28	• Other nosocomial infections • Emergence of antimicrobial resistance • Serious adverse events
Results and Conclusion	Early VAP incidence: • Amoxicillin–clavulanate: 19% • Placebo: 34% • p = 0.03	28-day mortality: • Amoxicillin–clavulanate: 41% • Placebo: 37% • HR 0.53 (95% CI, 0.31–0.92); p = 0.03

IV: Intravenous
VAP: Ventilator-associated pneumonia
ICU: Intensive care unit

François B, et al. *N Engl J Med*. 2019;381:1831–1842.

PROTECT Trial

Ceftriaxone to Prevent Early-Onset Pneumonia in Comatose Patients Following Out-of-Hospital Cardiac Arrest		
Population	• 52 adults ≥18 years • Comatose survivors of out-of-hospital cardiac arrest undergoing targeted temperature management • No pneumonia at baseline	
Intervention	• Ceftriaxone 2 g IV every 12 hours for 3 days vs. a placebo (normal saline)	
Primary Outcome	• Early-onset pneumonia within ≤4 days of intubation • Confirmed by blinded adjudicators	
Secondary Outcomes	• Late-onset pneumonia • Microbiologically confirmed pneumonia • ICU and ventilator-free days	• Mortality • Antibiotic resistance gene acquisition • Open-label antibiotic use
Results	Primary Outcome: • Ceftriaxone: 38% • Placebo: 69% • RR 0.57 (95% CI 0.21–1.001); p = 0.05	Key Secondary Findings: • Decreased open-label antibiotic use: 54% vs. 85%, RR=0.64 (95% CI 0.43-0.94) • Decreased acquisition of resistance genes: IRR 0.30 (95% CI 0.13–0.70) • Increase in ICU & ventilator-free days: Higher in ceftriaxone group • Mortality: Lower unadjusted mortality (42% vs. 73%), RR=0.59 (95% CI 0.22-0.998)

Conclusion	• Trial was inconclusive for reducing early-onset pneumonia
	• Ceftriaxone associated with:
	  ○ Decreased antibiotic exposure
	  ○ Decreased resistance gene acquisition
	Trial suggests that IV ceftriaxone prophylaxis may reduce early VAP and antibiotic exposure without increasing resistance, but results were underpowered and inconclusive	

IV: Intravenous
VAP: Ventilator-associated pneumonia
ICU: Intensive care unit
IRR: incidence risk ratio

Gagnon DJ, et al. Chest. 2026;169(1):115–127.

IV Prophylaxis Literature Summary

Ceftriaxone

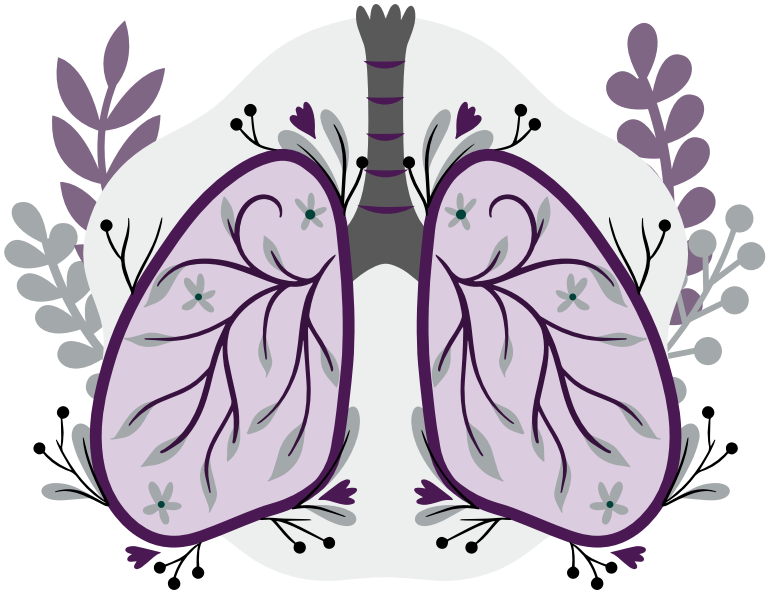
One 2 gram dose reduced early VAP incidence in acute brain injury patients

Amoxicillin–Clavulanate

A 2-day course reduced early VAP incidence after out-of-hospital cardiac arrest

IV: Intravenous
VAP: Ventilator-associated pneumonia

Nseir S, et al. *Lancet Respir Med*. 2023;11:475–486.
François B, et al. *N Engl J Med*. 2019;381:1831–1842.



Topical Prophylaxis

Chlorhexidine
and
Colistin, Tobramycin, Amphotericin B

DeRiso, et al. Trial

Chlorhexidine gluconate 0.12% oral rinse reduces the incidence of total nosocomial respiratory infection and nonprophylactic systemic antibiotic use in patients undergoing heart surgery		
Population	353 adults undergoing open-heart surgery in the cardiovascular ICU at a tertiary care hospital	
Intervention	• Chlorhexidine group: 173, placebo group: 180 • Chlorhexidine gluconate 0.12% oral rinse applied rigorously to buccal, gingival, pharyngeal, tongue, and tooth surfaces for 30 seconds preoperatively then twice daily post-operatively until ICU discharge or death • Comparator: placebo oral rinse	
Primary Outcome	Incidence of nosocomial respiratory infections, including VAP	
Secondary Outcomes	• Overall nosocomial infection rate • Gram-negative infection rates • Use of non-prophylactic systemic IV antibiotics • Duration of mechanical ventilation	• ICU and hospital length of stay • Re-intubation • In-hospital mortality • Antibiotic resistance patterns

Results and Conclusion	Key primary finding:
	• Total respiratory tract infections:
	  • Chlorhexidine: 2.9%
	  • Placebo: 9.4%
	  • 69% relative reduction ($p < 0.05$)
		Key Secondary Findings:
		• Overall nosocomial infections: 65% reduction with chlorhexidine ($p < 0.01$)
		• 67% reduction ($p < 0.05$) in GNB respiratory infections
		• Mortality: Chlorhexidine 1.16% vs. placebo 5.56% ($p < 0.05$)
		• Use of nonprophylactic IV antibiotics was lowered by 43% ($p<0.05$)
		• No increase in antibiotic resistance
		• No significant differences in ventilation duration, re-intubation rate, or hospital length of stay

VAP: Ventilator-associated pneumonia
ICU: Intensive care unit
GNB: Gram-negative bacilli

DeRiso AJ 2nd, et al. *N Engl J Med.* 1996;334(9):569–574.

DeRiso Conclusion

Twice-daily topical chlorhexidine 0.12% oral rinse significantly reduced incidence of nosocomial respiratory infections, particularly Gram-negative infections, in patients undergoing cardiac surgery

Use of chlorhexidine also reduced systemic antibiotic exposure and showed a statistically significant decrease in mortality

The intervention is low-cost, simple, and safe, with no observed increase in antimicrobial resistance

This trial provided high-quality evidence supporting targeted VAP prophylaxis, especially in cardiac surgery patients with short-term mechanical ventilation

VAP: Ventilator-associated pneumonia

DeRiso AJ 2nd, et al. *N Engl J Med.* 1996;334(9):569–574.

SuDDICU Trial

Selective Decontamination of the Digestive Tract during Ventilation in the ICU	
Population	• Combined international trial: 9,289 patients • Expected to require mechanical ventilation for ≥48 hours
Intervention	Selective decontamination of the digestive tract • Topical nonabsorbable antimicrobials: colistin, tobramycin, and amphotericin B applied to oropharynx and stomach via oral paste and gastric suspension vs. no topical antimicrobials
Primary Outcome	In-hospital mortality
Secondary Outcomes	• VAP incidence • ICU-acquired bacteremia • Duration of mechanical ventilation • ICU length of stay
Results and Conclusion	In-hospital mortality: 27.9% vs. 29.5% • OR 0.93 (95% CI 0.84–1.05), p=0.27 Secondary outcomes: • VAP incidence reduced: RR 0.44 (95% CI 0.36-0.54) • ICU-acquired bacteremia reduced: RR 0.68 (95% CI 0.57-0.81) • Duration of mechanical ventilation: Mean difference -0.73 days (95% CI -1.32 to -0.09) • ICU length of stay: Mean difference -0.86 days (95% CI -1.73 to 0) Demonstrated that SDD did not result in a statistically significant decrease in incidence of in-hospital death compared to standard care

SDD: Selective decontamination of the digestive tract
VAP: Ventilator-associated pneumonia
ICU: Intensive care unit
CI: Confidence interval

SuDDICU Investigators . *JAMA*. 2022;328(19):1911-1921.

Topical Prophylaxis Literature Summary

Chlorohexidine

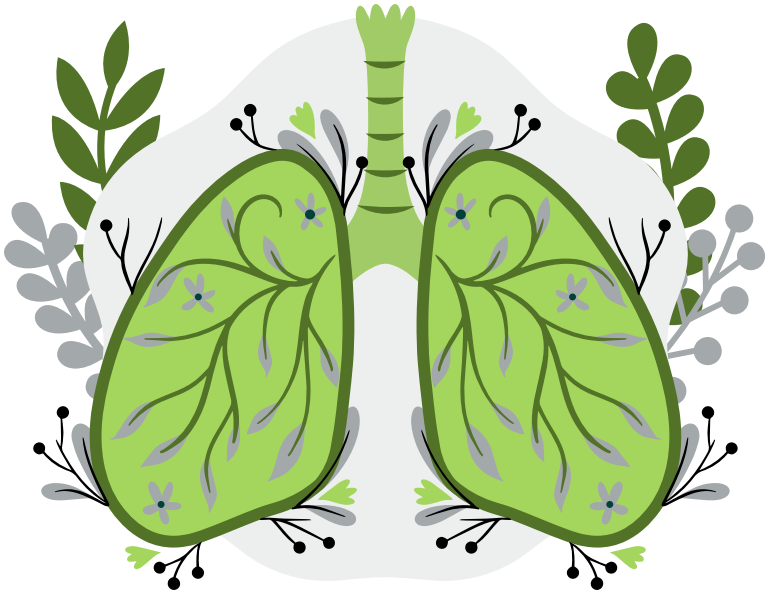
Chlorhexidine gluconate 0.12% showed a statistically significant reduction in nosocomial respiratory infections and the need for non-prophylactic systemic antibiotics in postoperative heart surgery patients

SDD

Selective decontamination of the digestive tract did not have a statistically significant reduction of in-hospital deaths compared to standard of care

SDD: Selective decontamination of the digestive tract

DeRiso AJ 2nd, et al. *N Engl J Med.* 1996;334(9):569–574.
SuDDICU Investigators . *JAMA.* 2022;328(19):1911-1921.



Inhaled Prophylaxis

Amikacin

AMIKINHAL Trial

Inhaled Amikacin to Prevent Ventilator-Associated Pneumonia		
Population	Critically ill adults receiving invasive mechanical ventilation for ≥72 hours enrolled between 72–96 hours of ventilation across 19 ICUs in France	
Intervention	Inhaled amikacin 20 mg/kg nebulized via vibrating mesh nebulizer once daily for three consecutive days	
Comparison	Comparator: nebulized 0.9% sodium chloride Both: received standard VAP prevention practices per international guidelines	
Primary Outcome	First episode of ventilator-associated pneumonia from randomization to day 28	
Secondary Outcomes	• Incidence density of VAP • VAP due to Gram-negative organisms susceptible to amikacin • VAE	• Systemic antibiotic exposure • Duration of mechanical ventilation, ICU and hospital length of stay • Mortality at day 28 and day 90
Results	Primary outcome – VAP at day 28: • Amikacin 15% vs. placebo 22% • Hazard Ratio +1.5 days (0.6 to 2.5) • P = 0.004	Secondary outcomes: • VAP due to amikacin-susceptible Gram-negative bacteria: Amikacin 7% vs. placebo 14%. (HR 1.9 (1.1 to 2.8)) • Ventilator-associated complications: Infection-related VAE reduced (HR 0.66) • Systemic antibiotic exposure: No statistically significant reduction in total antibiotic-days • ICU mortality: 24% vs. 26% (HR 0.89) • Hospital mortality: 29% vs. 32% (HR 0.91) • Antimicrobial resistance: No increase in resistant organism isolation • Safety: Serious adverse effects were rare (<2%) • Lower incidence of acute kidney injury in the amikacin group
Conclusion	A 3-day course of inhaled amikacin significantly reduced the incidence of VAP during 28 days of follow-up in patients ventilated for ≥3 days. Findings support selective prophylaxis in patients at sustained risk for VAP, but do not justify routine use for all mechanically ventilated patients.	

IBW: Ideal body weight VAP: Ventilator-associated pneumonia
ICU: intensive care unit VAE: Ventilator-associated event

Ehrmann S, et al. *N Engl J Med*. 2023;389:2052–2062.

Inhaled Antimicrobial Prophylaxis Summary

Amikacin

In patients who were mechanically ventilated for ≥72 hours, a short-course of inhaled amikacin statistically significantly reduced the burden of VAP at the 28 days follow-up mark

VAP: Ventilator-associated pneumonia

Ehrmann S, et al. *N Engl J Med*. 2023;389:2052–2062.
Vallés J, et al. *Intensive Care Med*. 2003;29(4):633–639.

Assessment Question #3

Which of the following statements accurately describes the literature surrounding the use of antimicrobial prophylaxis for VAP?

A. Routine antimicrobial prophylaxis is recommended for all mechanically ventilated patients because it consistently reduces mortality

B. Several antimicrobial prophylactic strategies have demonstrated reductions in VAP incidence in select populations, but inconsistent mortality benefit and resistance concerns limit routine use

C. Antimicrobial prophylaxis has not shown any benefit in reducing VAP incidence or bacterial colonization

D. Inhaled antibiotic prophylaxis is superior to all other strategies and is recommended as standard ICU practice

VAP: Ventilator-associated pneumonia
ICU: Intensive care unit

Summary

Intravenous Antimicrobials

Ceftriaxone:
- PROPHY-VAP Trial
- Acute brain injury
- Requiring mechanical ventilation for ≥48 hours
- One time dose of 2 g within 12 hours

Reduced early VAP incidence

Amoxicillin-Clavulanate:
- ANTHARTIC Trial
- After out-of-hospital cardiac arrest managed with TTM requiring mechanical ventilation
- Initiated within 6 hours of ROSC

Reduced early VAP incidence

Topical Antimicrobials

Chlorhexidine:
- DeRiso, et al. Trial
- Cardiac surgery
- Applied for 30 seconds preoperatively then twice daily postoperatively
- A part of Advocate Health care bundles

Reduced rate of respiratory infections

Colistin/tobramycin/ampB:
- SuDDICU Trial
- Mechanically ventilated ICU patients for ≥48 hours
- Applied to oropharynx and stomach
- Oral paste and gastric suspension

No mortality benefit

Inhaled Antimicrobials

Amikacin:
- AMIKINHAL Trial
- Critically ill patients
- Invasive mechanical ventilation ≥72 hours
- Amikacin 20 mg/kg nebulized
- 3-day course

Reduced VAP incidence with no mortality benefit

Key Takeaways

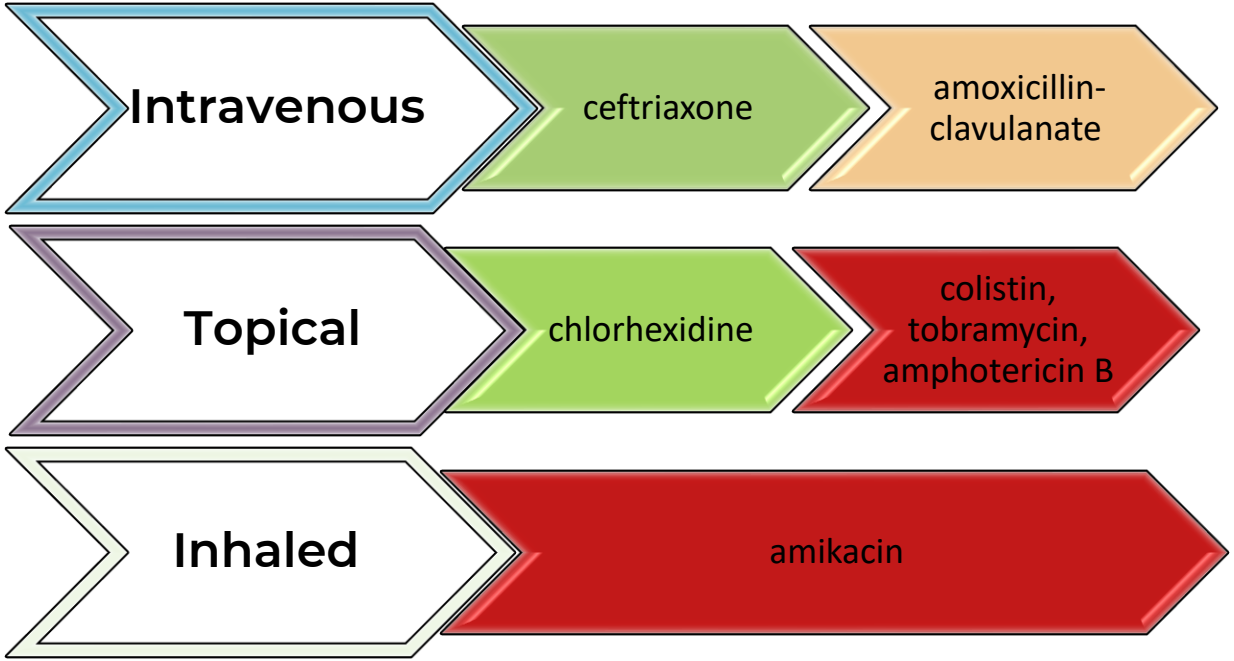
Numerous methods have been studied

Trials on IV ceftriaxone, IV amoxicillin-clavulanate, and topical chlorhexidine concluded positive outcomes in their designated patient populations

Inhaled antibiotics failed to demonstrate survival benefit when added to systemic antibiotics for VAP prophylaxis

VAP: Ventilator-associated pneumonia
ICU: Intensive care unit
IV: Intravenous
TTM: Targeted temperature management
ROSC: Return of spontaneous circulation

Summary (cont.)



Patient Populations To Consider

Severe acute brain injury

Out-of-hospital cardiac arrest with TTM

TTM: Targeted temperature management

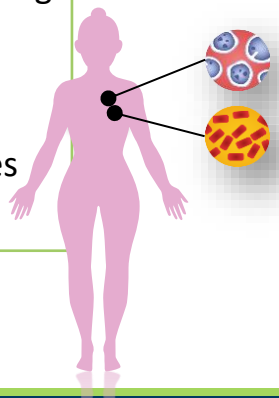
Assessment Question #4

A 58-year-old female is admitted to the ICU following elective abdominal surgery. She was intubated for airway protection preoperatively. Relevant information is listed below:

- Mechanical ventilation duration: 12 hours
- Expected extubation later today
- Temperature: 36.8°C
- WBC: 8.9 $\times 10^9$/L
- Chest X-ray: Proper tube placement, no ground glass opacities or infiltrates present
- No history of cardiac arrest or brain injury
- POD: 0

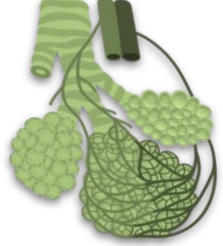
The ICU team asks if an antimicrobial agent should be initiated to prevent VAP. Which of the following is the most appropriate recommendation?

A. Initiate nebulized amikacin 20 mg/kg for three days to prevent VAP
B. Initiate IV ceftriaxone to prevent early VAP incidence
C. Do not initiate antimicrobial prophylaxis and continue standard ventilator care bundle measures
D. Initiate IV amoxicillin-clavulanate for 48 hours for VAP prevention



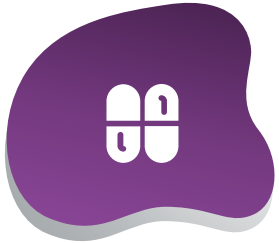
VAP: Ventilator-associated pneumonia
IV: Intravenous
WBC: White blood count
ICU: Intensive care unit
POD: Postoperative day

Key Takeaways



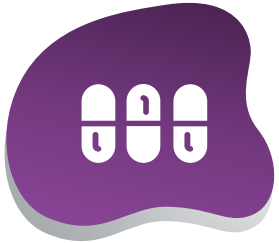
1

VAP remains common despite ventilator care bundles



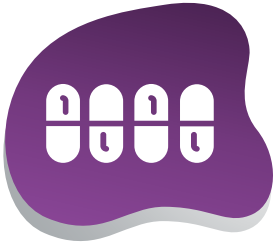
2

Select IV prophylaxis reduces early VAP incidence in specific populations



3

Inconsistent mortality benefit and increasing resistance concerns limit its use



4

Routine antimicrobial prophylaxis is not guideline-supported but may be considered case by case in certain patient populations

VAP: Ventilator-associated pneumonia
IV: Intravenous

Questions?

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