

Don't Let It VAPpen:

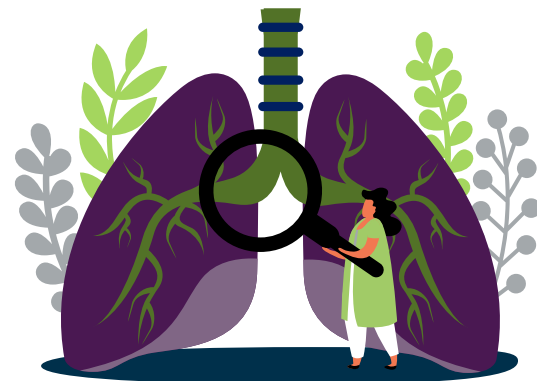
Exploring Antimicrobial Prophylaxis for Ventilator-Associated Pneumonia

04/21/2026

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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

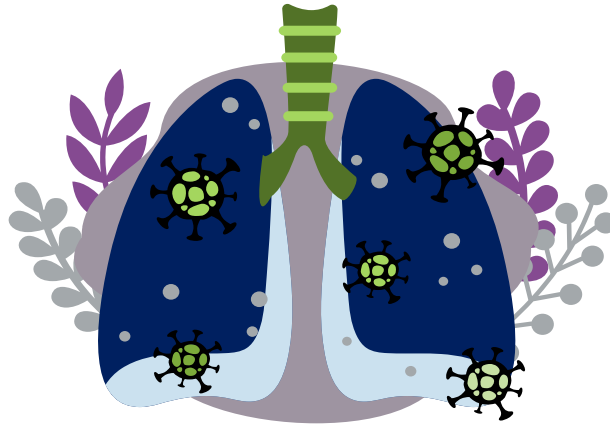
Recall

- 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

Acquired outside of hospital or LTCF in the community or <48 hours after hospital admission

Hospital-Acquired Pneumonia

Acquired ≥ 48 hours after hospital admission, non-mechanical ventilation related

Ventilator-Associated Pneumonia

Acquired ≥ 48 hours after endotracheal intubation

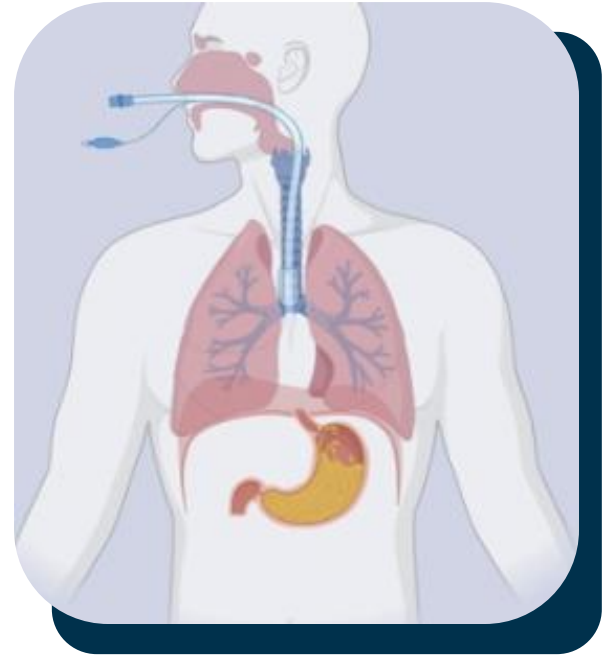
Pathophysiology

Colonization of the aerodigestive tract by pathogenic bacteria

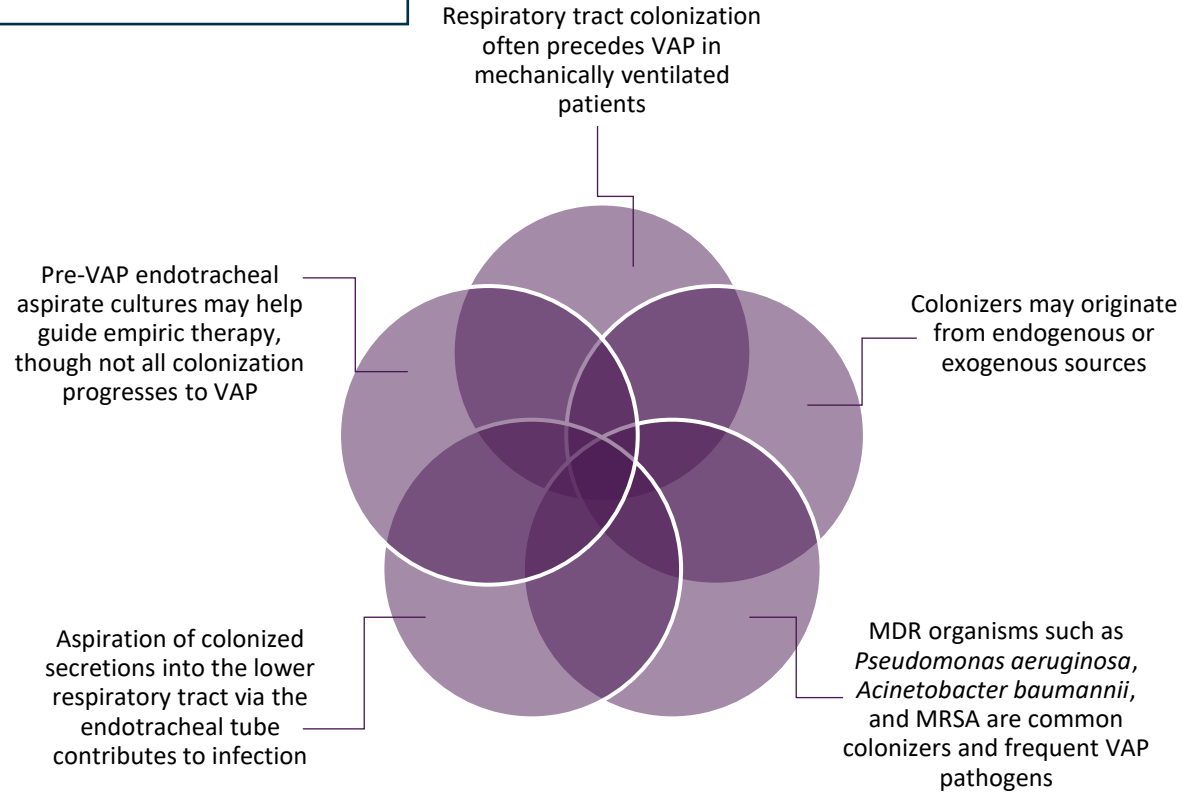
Subsequent aspiration of contaminated secretions into the lower respiratory tract

Biofilm formation acts as reservoir for persistent infection

Inflammatory response



Colonization



MRSA: Methicillin-resistant *Staphylococcus aureus*

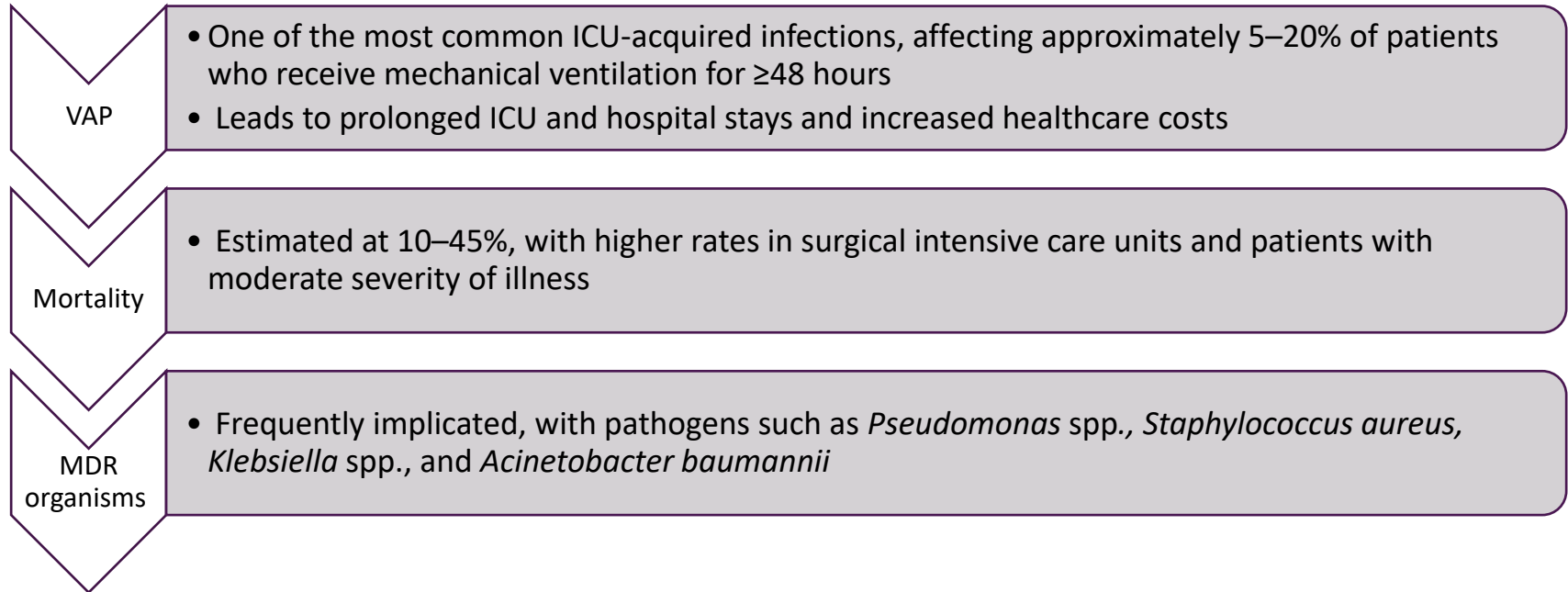
VAP: Ventilator-associated pneumonia

MDR: Multi-drug resistant

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

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Etiology & Epidemiology



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

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

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*)

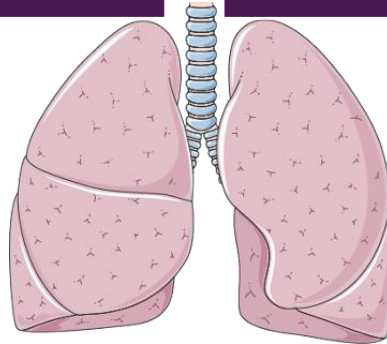


Diagnosis

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

Plus, at least two of the following:

- Fever ($>38^{\circ}\text{C}$) or hypothermia ($<36^{\circ}\text{C}$),
- Leukocytosis or leukopenia
- Purulent respiratory secretions



Assessment Question #1

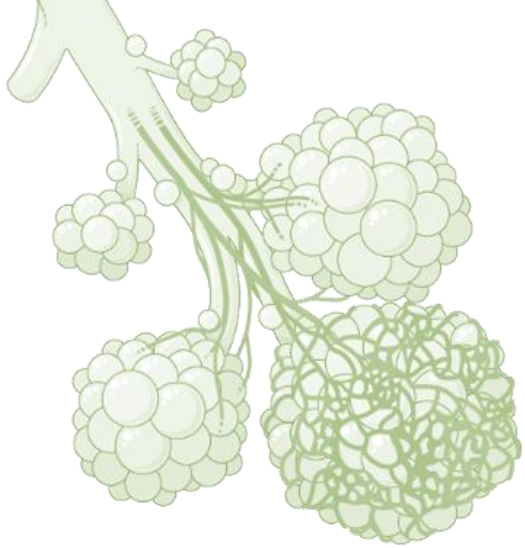
Which pathophysiologic mechanism directly contributes to the development of ventilator-associated pneumonia?

- 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

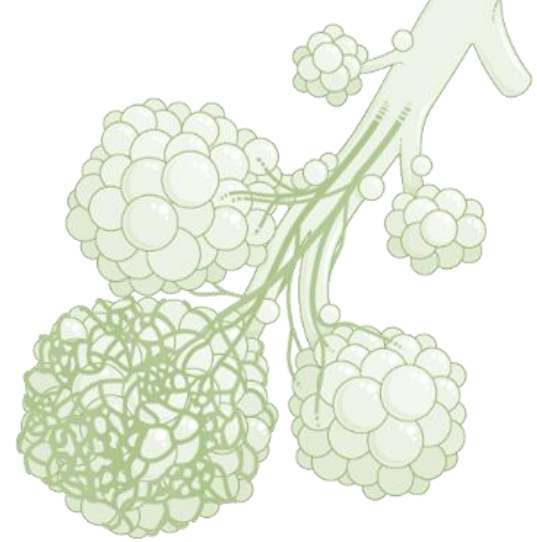
Assessment Question #1 Answer

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

- A. Hematogenous spread from bloodstream infection
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- C. Reactivation of latent pulmonary infection
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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%
<p style="text-align: center;">β-Lactam or Fluoroquinolone</p>	<p style="text-align: center;">β-Lactam or Fluoroquinolone and MRSA coverage</p>	<p style="text-align: center;">Two Agents: β-Lactam or Fluoroquinolone or Aminoglycoside and MRSA coverage</p>
<p>β-Lactam:</p> <ul style="list-style-type: none"> • Piperacillin-tazobactam 4.5 g IV Q8H • Cefepime 2 g IV Q8H • Meropenem 1 g IV Q8H <p>Fluoroquinolone:</p> <ul style="list-style-type: none"> • Levofloxacin 750 mg IV Q24H 	<p>β-Lactam:</p> <ul style="list-style-type: none"> • Piperacillin-tazobactam 4.5 g IV Q8H • Cefepime 2 g IV Q8H • Meropenem 1 g IV Q8H • Aztreonam 2 g IV Q12H <p>Fluoroquinolone:</p> <ul style="list-style-type: none"> • Levofloxacin 750 mg IV Q24H • Ciprofloxacin 400 mg IV Q8H <p>MRSA coverage:</p> <ul style="list-style-type: none"> • Vancomycin • Linezolid 600 mg IV Q12H 	<p>β-Lactam:</p> <ul style="list-style-type: none"> • Piperacillin-tazobactam 4.5 g IV Q8H • Cefepime 2 g IV Q8H • Meropenem 1 g IV Q8H • Aztreonam 2 g IV Q12H <p>Fluoroquinolone:</p> <ul style="list-style-type: none"> • Levofloxacin 750 mg IV Q24H • Ciprofloxacin 400 mg IV Q8H <p>Aminoglycosides:</p> <ul style="list-style-type: none"> • Tobramycin 7 mg/kg IV <p>MRSA coverage:</p> <ul style="list-style-type: none"> • Vancomycin • Linezolid 600 mg IV Q12H

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

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:

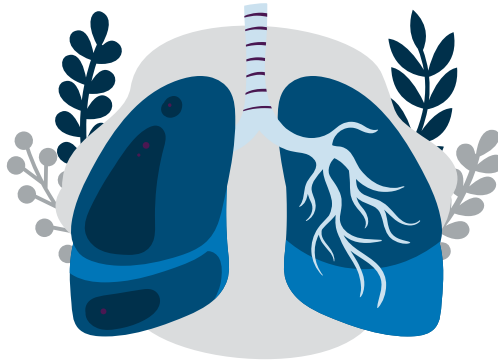
- Piperacillin–tazobactam: **3–4 hour infusion**
- Cefepime: **3–4 hour infusion**
- Meropenem: **3 hour infusion**

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

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



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

Selective Decontamination Of The Digestive Tract

Administering non-absorbable topical antibiotics to the oropharynx and GI tract

Goal:

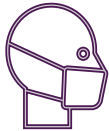
- Suppress aerobic Gram-negative bacteria, *Staphylococcus aureus*, and yeasts
- Preserve anaerobic flora, which protect against colonization by resistant organisms

Supported by evidence for VAP prevention; its use remains controversial

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

Chlorhexidine Oral Decontamination



A cationic bisbiguanide antiseptic that reduces oral bacterial burden and alters biofilm formation



Positively charged chlorhexidine binds to negatively charged bacterial cell walls

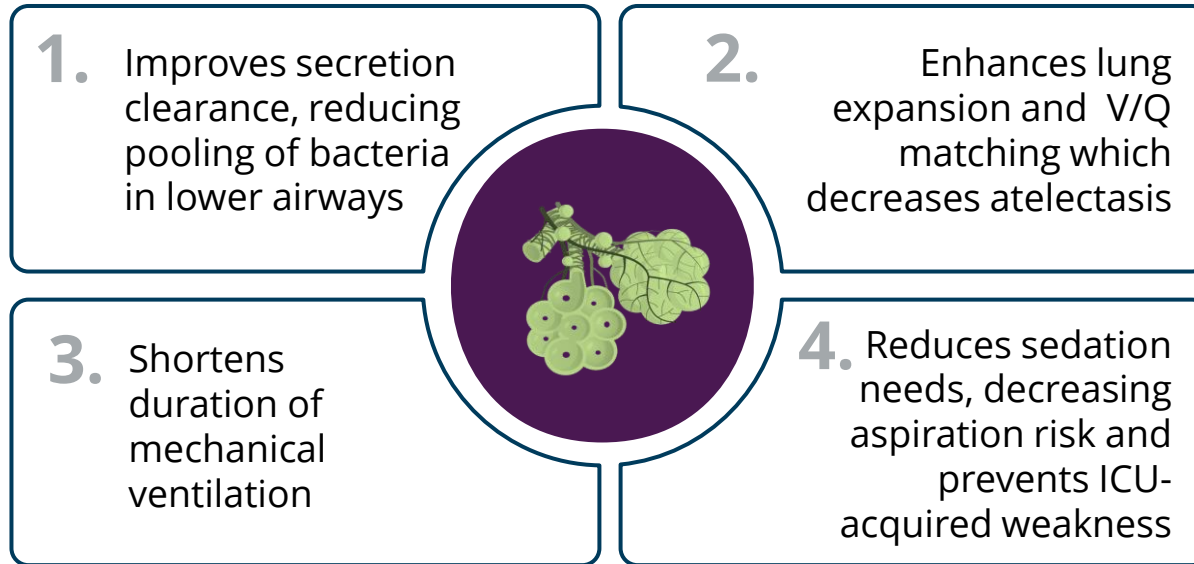


At low concentrations is bacteriostatic and at high concentrations is bactericidal



Literature confirms that the 0.12-2% solution reduces VAP risk by targeting the primary mechanism of bacterial spread

Early Mobilization



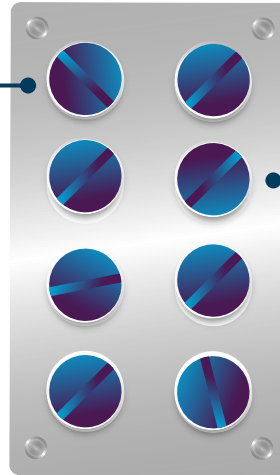
Prophylactic Probiotics and Antibiotics

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

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



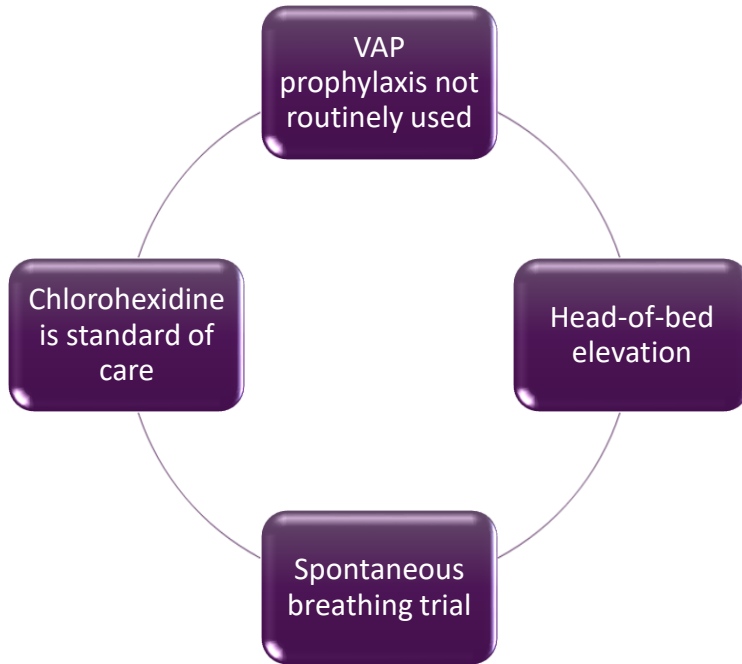
Mortality vs. Microbiologic Tradeoffs

Decrease in VAP incidence and colonization

Inconsistent impact on overall mortality

Microbiologic benefit does not confer clear survival benefit

Advocate Health VAP Care Bundles




- Oral Care - Brush Teeth
Routine, Every 12 Hours (0900 and 2100), First occurrence today at 2100, Until Specified
Use soft-bristled toothbrush or suction toothbrush and antiseptic rinse within facility approved kit
- Oral Care – Patient on mechanical ventilation
Routine, As Directed, Starting today at 1219, Until Specified
Use oral suction swabs and moisturizing antiseptic rinse within facility approved kit every 2-3 hours.

▼ Activity

▼ Activity

- Head of bed
UNTIL DISCONTINUED, Starting today at 1219, Until Specified
Elevation: Other (specify)
Other (specify): 30-45 degrees

▼ Respiratory Treatment

- Ventilator, Mechanical
Routine, CONTINUOUS, Starting today at 1228, Until Specified
 Height (inches): 71
- Adult Spontaneous Breathing Trial (SBT)
Routine, DAILY, First occurrence tomorrow at 0600, Until Specified

Shortcomings Of Current Prevention Strategies

Incomplete Risk Elimination

- Care bundles do not eliminate VAP
- Residual risk remains despite full compliance

Diagnostic Uncertainty

- No gold standard for VAP diagnosis
- Clinical criteria overlap with non-infectious causes

Care Bundle Compliance Variability

- Effectiveness depends on consistent execution
- Human and system factors affect adherence

Persistent Microaspiration

- Oral care and positioning reduce, but do not completely prevent aspiration
- Endotracheal tubes remain a risk factor

Does Not Address MDRO Colonization

- Non-antibiotic strategies do not directly modify airway flora
- High-risk patients remain vulnerable

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

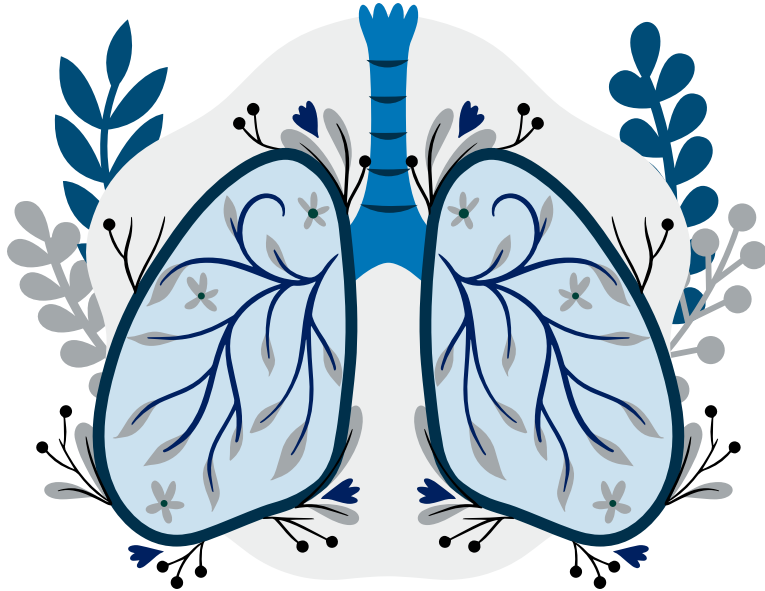
Assessment Question #2 Answer

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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	<p>Adult patients with acute brain injury requiring mechanical ventilation for ≥ 48 hours and a GCS ≤ 12</p> <ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Overall antibiotic consumption despite prophylaxis • Hospital and ICU length of stay • 28-day survival • Ventilator-free and antibiotic-free days 	
Results and Conclusion	<p>Primary outcomes:</p> <ul style="list-style-type: none"> • Ceftriaxone: 14% • Placebo: 32% • Hazard ratio 0.60 (95% CI 0.38-0.95), $p=0.030$ • Absolute risk reduction: 18% 	<p>Secondary outcomes:</p> <ul style="list-style-type: none"> • 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), $p=0.036$

ANTHARTIC Trial

Prevention of Early Ventilator-Associated Pneumonia after Cardiac Arrest	
Population	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Incidence of early ventilator-associated pneumonia, occurring within the first 7 days of hospitalization
Secondary Outcomes	<ul style="list-style-type: none"> • 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	<p>Early VAP incidence:</p> <ul style="list-style-type: none"> • Amoxicillin–clavulanate: 19% • Placebo: 34% • $p = 0.03$ <p>Mortality at 28-days:</p> <ul style="list-style-type: none"> • Amoxicillin–clavulanate: 41% • Placebo: 37% • HR 0.53 (95% CI, 0.31–0.92); $p = 0.03$

PROTECT Trial

Ceftriaxone to Prevent Early-Onset Pneumonia in Comatose Patients Following Out-of-Hospital Cardiac Arrest

Population	<ul style="list-style-type: none"> • 52 adults ≥18 years • Comatose survivors of out-of-hospital cardiac arrest undergoing targeted temperature management • No pneumonia at baseline 	
Intervention	<ul style="list-style-type: none"> • Ceftriaxone 2 g IV every 12 hours for 3 days vs. a placebo (normal saline) 	
Primary Outcome	<ul style="list-style-type: none"> • Early-onset pneumonia within ≤4 days of intubation • Confirmed by blinded adjudicators 	
Secondary Outcomes	<ul style="list-style-type: none"> • Late-onset pneumonia • Microbiologically confirmed pneumonia • ICU and ventilator-free days 	<ul style="list-style-type: none"> • Mortality • Antibiotic resistance gene acquisition • Open-label antibiotic use
Results	<p>Primary Outcome:</p> <ul style="list-style-type: none"> • Ceftriaxone: 38% • Placebo: 69% • RR 0.57 (95% CI 0.21–1.001); p = 0.05 	<p>Key Secondary Findings:</p> <ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Trial was inconclusive for reducing early-onset pneumonia • Ceftriaxone associated with: <ul style="list-style-type: none"> ○ Decreased antibiotic exposure ○ Decreased resistance gene acquisition <p>Trial suggests that IV ceftriaxone prophylaxis may reduce early VAP and antibiotic exposure without increasing resistance, but results were underpowered and inconclusive</p>	

IV Prophylaxis Literature Summary



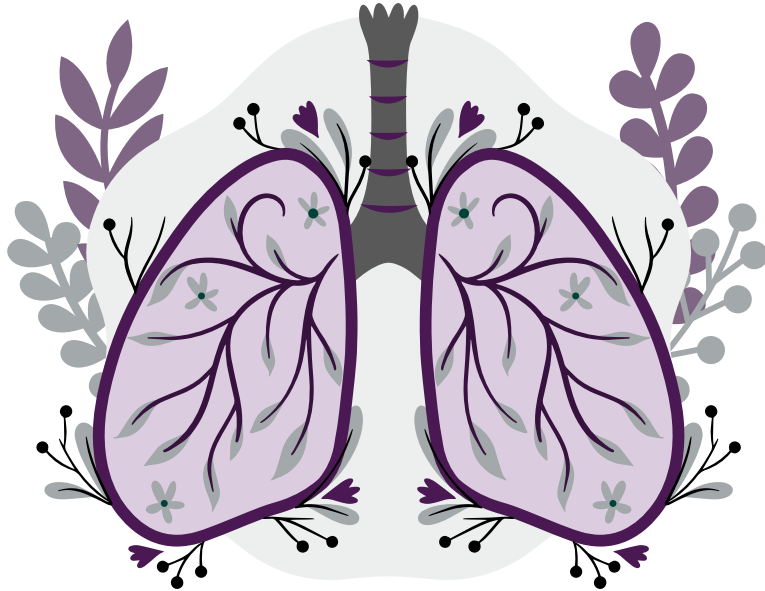
Ceftriaxone

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



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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Overall nosocomial infection rate Gram-negative infection rates Use of non-prophylactic systemic IV antibiotics Duration of mechanical ventilation 	<ul style="list-style-type: none"> ICU and hospital length of stay Re-intubation In-hospital mortality Antibiotic resistance patterns
Results and Conclusion	<p>Key Primary Finding:</p> <ul style="list-style-type: none"> Total respiratory tract infections: <ul style="list-style-type: none"> Chlorhexidine: 2.9% Placebo: 9.4% 69% relative reduction ($p < 0.05$) 	<p>Key Secondary Findings:</p> <ul style="list-style-type: none"> 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

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

SuDDICU Trial

Selective Decontamination of the Digestive Tract during Ventilation in the ICU	
Population	<ul style="list-style-type: none"> • Combined international trial: 9,289 patients • Expected to require mechanical ventilation for ≥ 48 hours
Intervention	<p>Selective decontamination of the digestive tract</p> <ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • VAP incidence • ICU-acquired bacteremia • Duration of mechanical ventilation • ICU length of stay
Results and Conclusion	<p>In-hospital mortality: 27.9% vs. 29.5%</p> <ul style="list-style-type: none"> • OR 0.93 (95% CI 0.84–1.05), $p=0.27$ <p>Secondary outcomes:</p> <ul style="list-style-type: none"> • 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) <p>Demonstrated that SDD did not result in a statistically significant decrease in incidence of in-hospital death compared to standard care</p>

Topical Prophylaxis Literature Summary



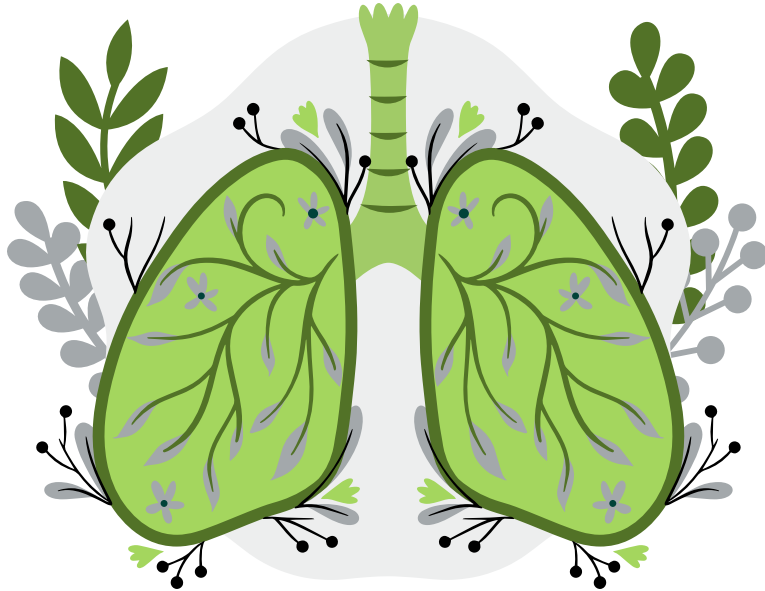
Chlorhexidine

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



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	<ul style="list-style-type: none"> 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	<p>Primary outcome – VAP at day 28:</p> <ul style="list-style-type: none"> Amikacin 15% vs. placebo 22% Hazard Ratio +1.5 days (0.6 to 2.5) P = 0.004 <p>Secondary outcomes:</p> <ul style="list-style-type: none"> 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.

Inhaled Antimicrobial Prophylaxis Summary



Amikacin

In patients who were mechanically ventilated for ≥ 72 hours, inhaled amikacin statistically significantly reduced the burden of VAP at the 28 days follow-up mark. With no mortality benefit.

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

Assessment Question #3 Answer

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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

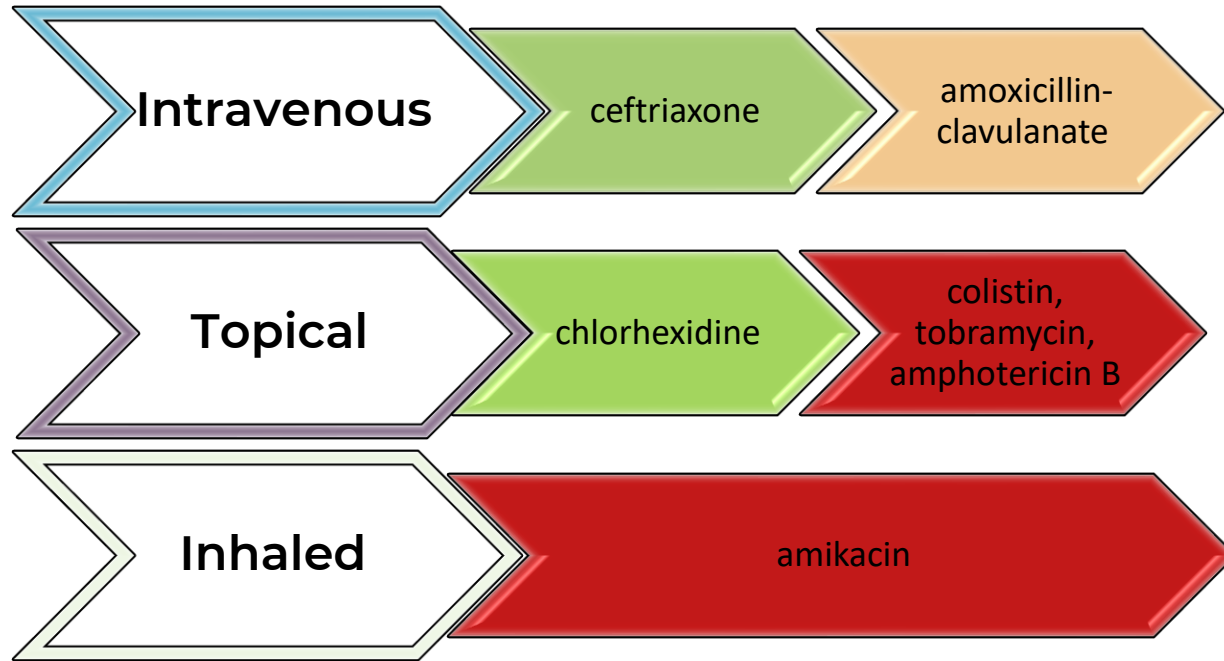
Key Takeaways

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

Summary (cont.)



Patient Populations To Consider

Severe acute
brain injury

Out-of-hospital
cardiac arrest
with TTM



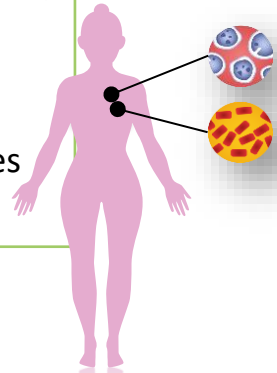
Assessment Question #4

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



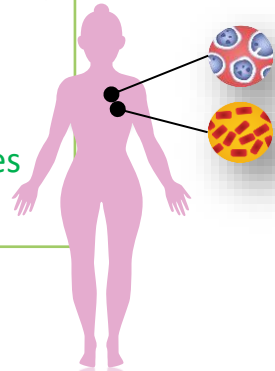
Assessment Question #4 Answer

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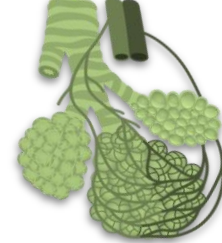
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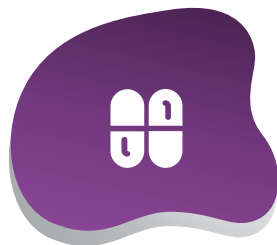


Key Takeaways



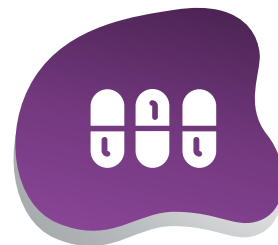
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VAP remains common despite ventilator care bundles



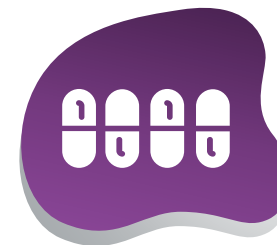
2

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

Questions?

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