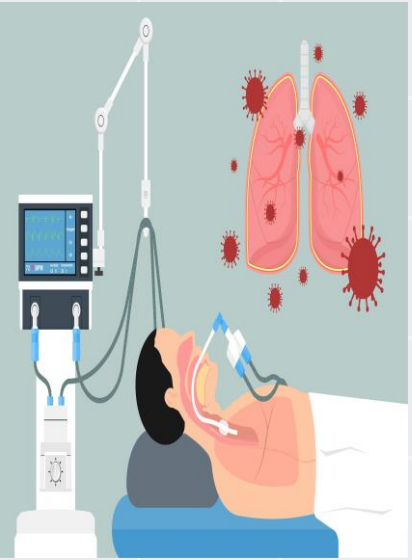

بسم الله الرحمن الرحيم

Treatment of Ventilator-Associated Pneumonia



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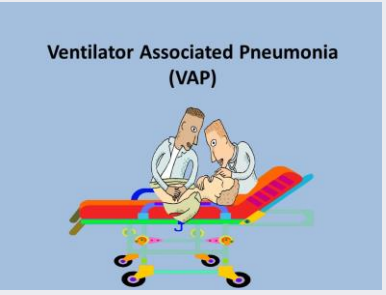
Assistant professor of Shahid Beheshti Medical University

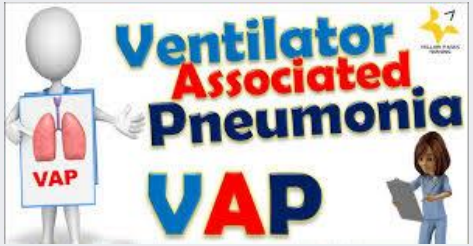
EMPIRIC THERAPY of VAP

- When VAP is suspected clinically
  - Obtain microbiological
  - Start antimicrobial therapy in:
    - Signs of septic shock or
    - Rapidly progressive organ dysfunction



Empiric regimens for VAP are determined by multiple factors

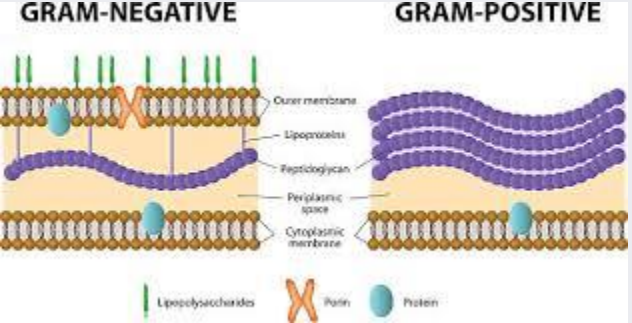
- Local known distribution of pathogens causing VAP
- Patient's individual risk factors for MDR
- Results of a good-quality Gram stain
- Results of PCR multiplex
- Potential adverse effects of antimicrobial agents
- Potential drug interactions
- Drug cost and availability
- Patient's severity of illness
- Clinician's familiarity with different antibiotics



Risk factors for MDR pathogens

(*Pseudomonas aeruginosa*, other gram-negative bacilli, and MRSA):

- Intravenous (IV) antibiotic use within the previous 90 days
- Septic shock at the time of VAP
- Acute respiratory distress syndrome (ARDS) preceding VAP
- ≥5 days of hospitalization prior to the occurrence of VAP
- Acute renal replacement therapy prior to VAP onset



Risk factors specifically for MDR *Pseudomonas aeruginosa* and other gram-negative bacilli:

- Treatment in an ICU in which >10 percent of gram-negative bacilli associated with VAP are **resistant** to piperacillin-tazobactam and/or cefepime
- Treatment in an ICU in which local antimicrobial susceptibility rates among gram-negative bacilli are not known
- **Colonization** with **and/or** prior isolation of MDR *Pseudomonas* or other gram-negative bacilli on culture from any body site (but especially from the respiratory tract)

Risk factors specifically for MRSA

- Treatment in a unit in which >10 to 20 percent of S. aureus isolates associated with VAP are methicillin resistant
- Treatment in a unit in which the prevalence of MRSA is not known
- Colonization with and/or prior isolation of MRSA on culture from any body site (but especially the respiratory tract)

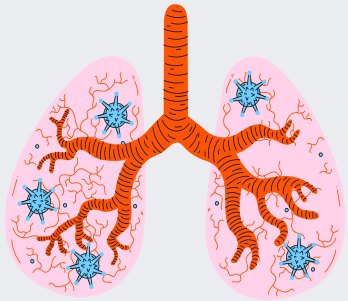
Legionella spp (rare)

- Increased susceptibility in
  - Compromised immune systems
  - Diabetes mellitus
  - Renal disease
  - Structural lung disease
  - Recently treated with glucocorticoids

- Add empiric anti-Legionella therapy (azithromycin or a fluoroquinolone)
  - Clinical syndrome is consistent with Legionella pneumonia (eg, severe illness, bilateral patchy infiltrates) +
    - Legionella spp outbreak or
    - Patient is not improving on initial empiric therapy

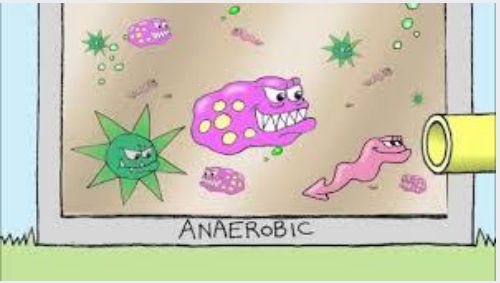
Viruses and fungi

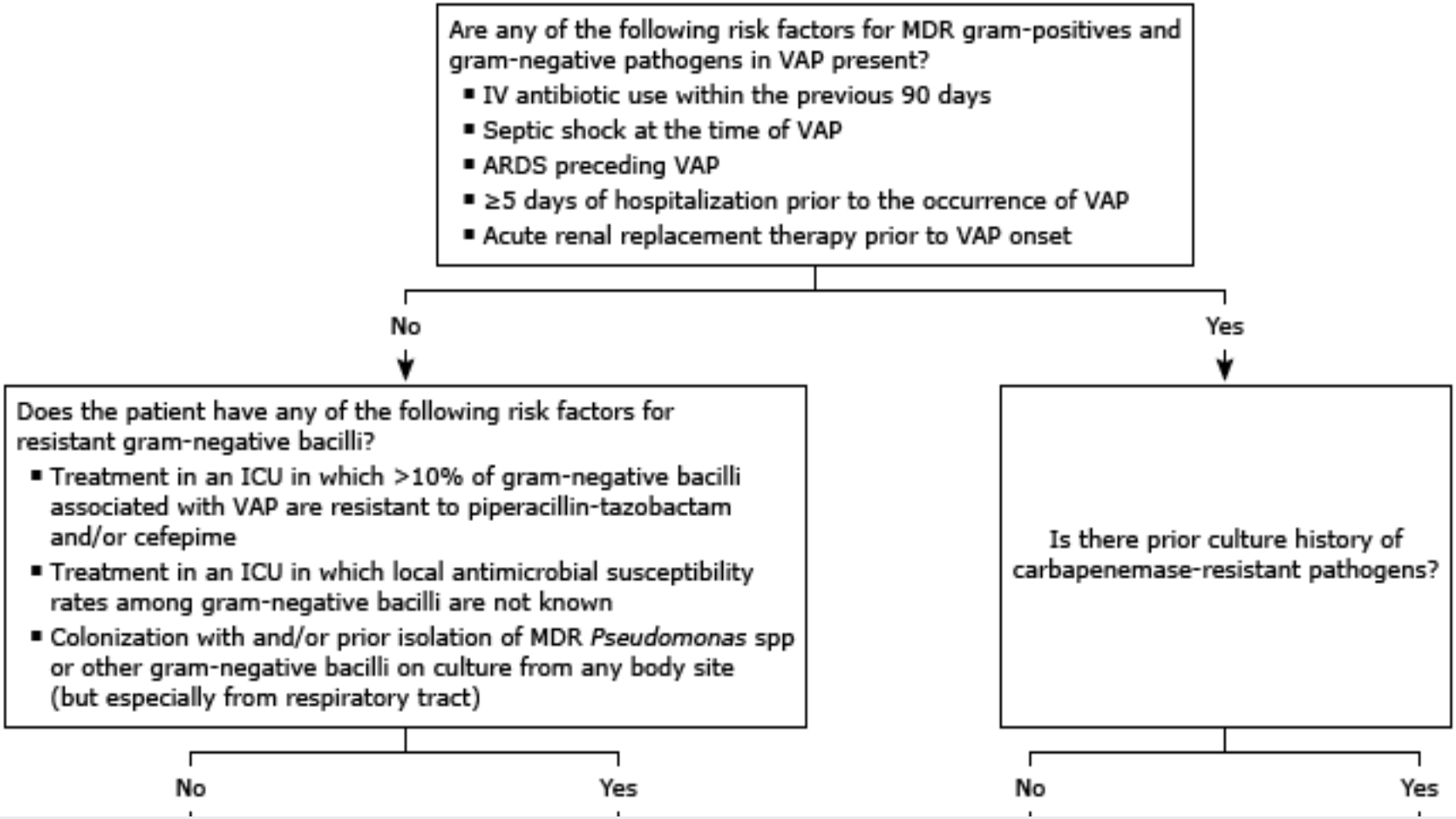
- All HAP/VAP is NOT caused by bacteria.
- Viruses (COVID-19, influenza) and fungi can cause similar clinical presentations, especially in patients with severe immunocompromise

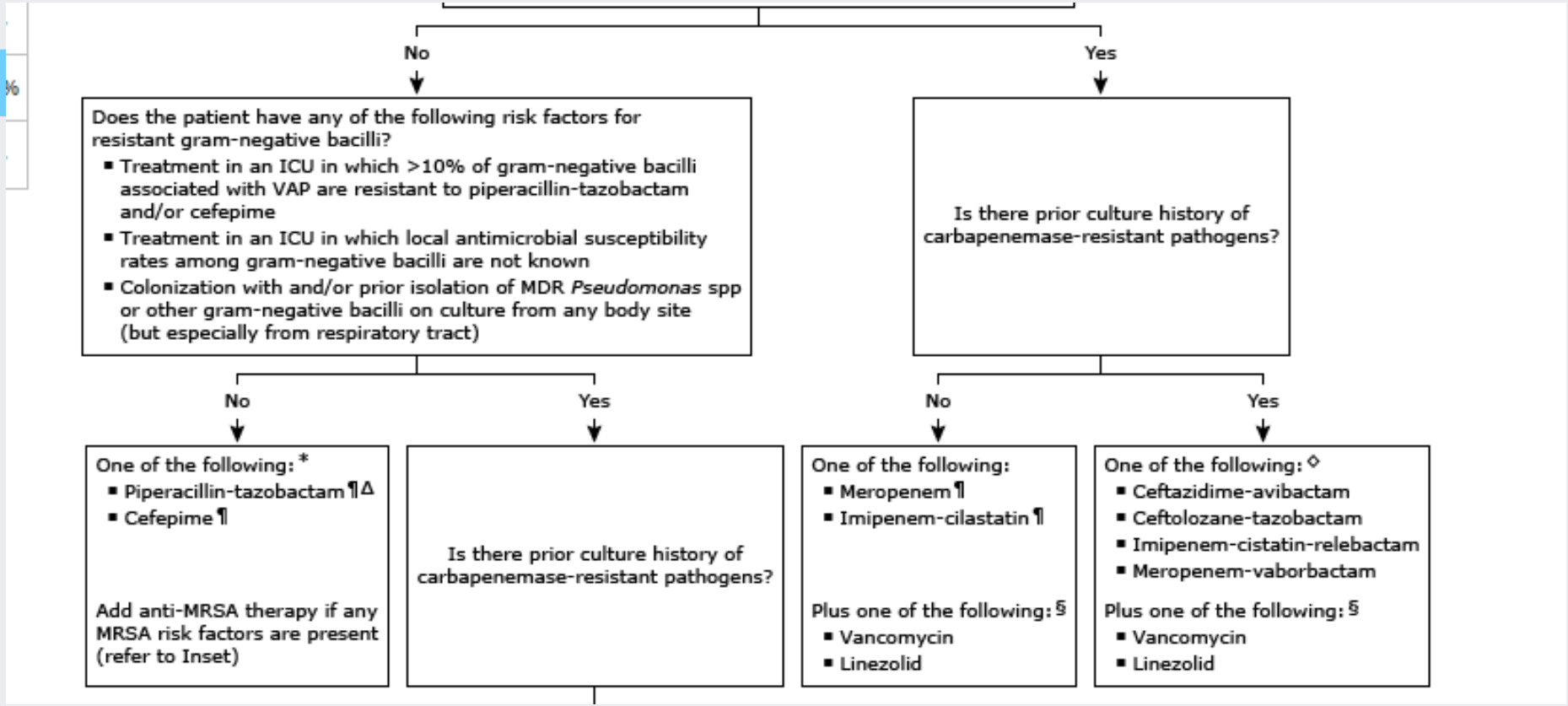


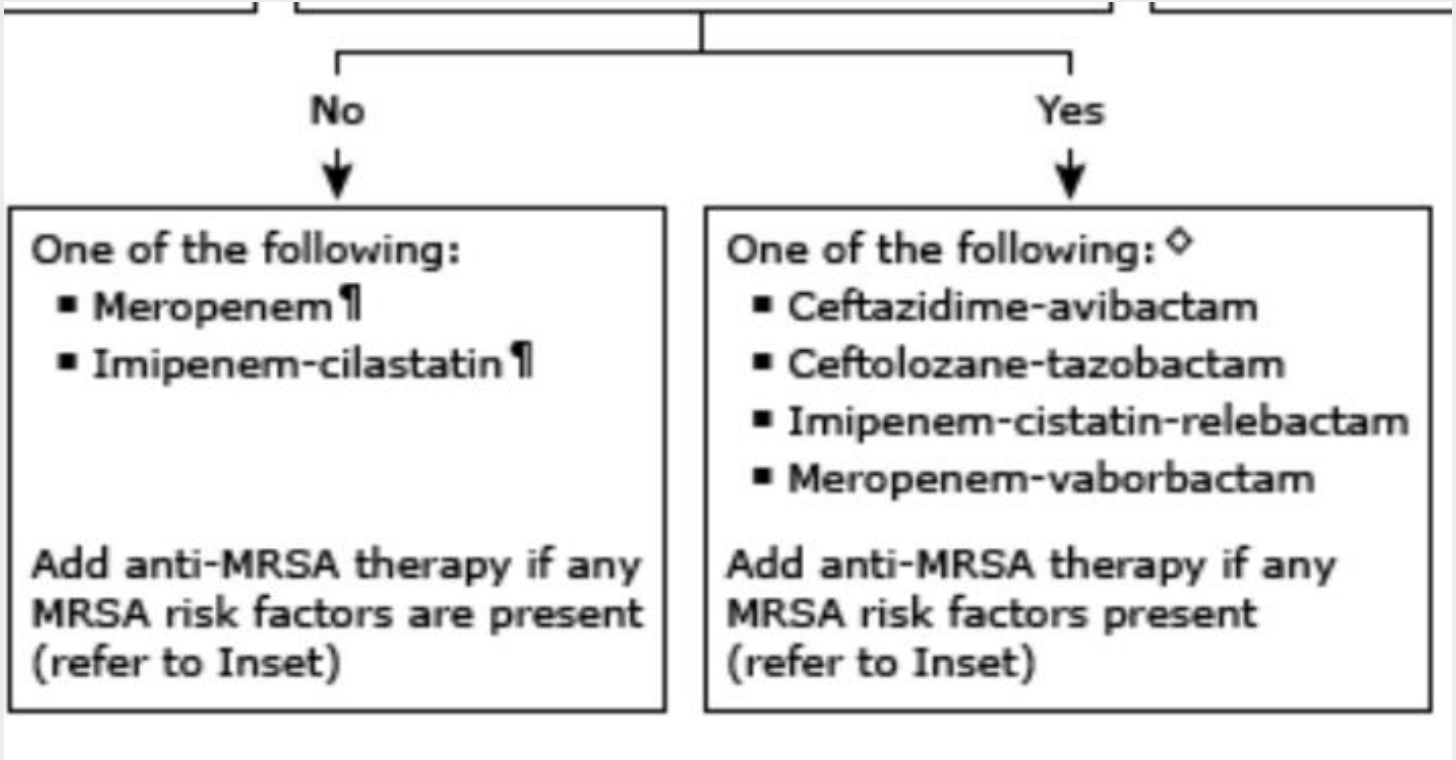
Anaerobes (rare)

- Empiric treatment (beta-lactam-betalactamase inhibitor, a carbapenem, metronidazole, moxifloxacin, or clindamycin) in
    - frank and/or gross aspiration (inhalation of vomitus),
    - Poor dentition
    - Recent abdominal surgery
    - Presence of possible lung abscess
    - Not improving on initial empiric therapy
    - A good-quality (eg, from BAL) Gram stain demonstrates polymicrobial organisms or polymicrobial oral flora

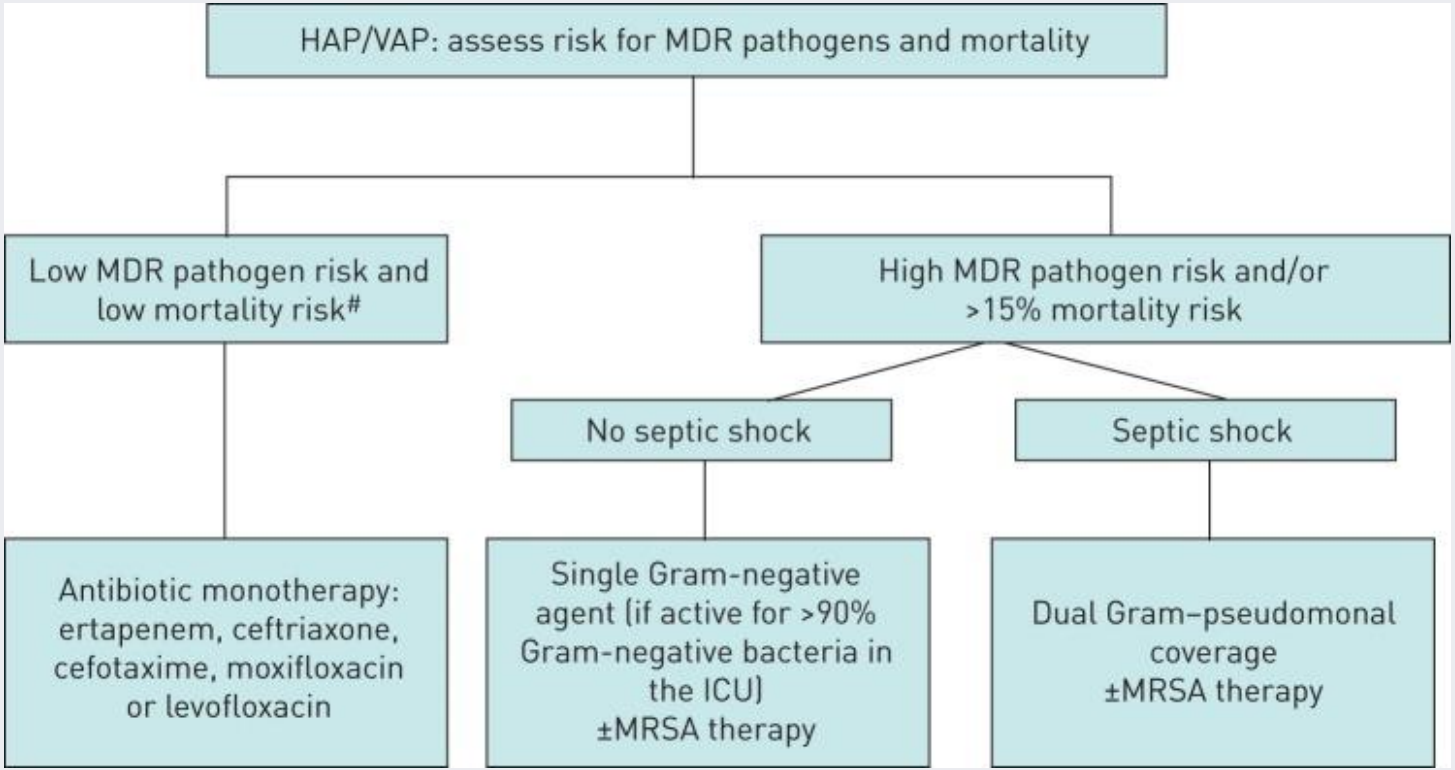



Are any of the following risk factors for MDR gram-positives and gram-negative pathogens in VAP present?
IV antibiotic use within the previous 90 days
Septic shock at the time of VAP
ARDS preceding VAP
≥5 days of hospitalization prior to the occurrence of VAP
Acute renal replacement therapy prior to VAP onset
No
Yes
Does the patient have any of the following risk factors for resistant gram-negative bacilli?
Treatment in an ICU in which >10% of gram-negative bacilli associated with VAP are resistant to piperacillin-tazobactam and/or cefepime
Treatment in an ICU in which local antimicrobial susceptibility rates among gram-negative bacilli are not known
Colonization with and/or prior isolation of MDR Pseudomonas spp or other gram-negative bacilli on culture from any body site (but especially from respiratory tract)
Is there prior culture history of carbapenemase-resistant pathogens?
No
Yes
No
Yes


No
Yes
Does the patient have any of the following risk factors for resistant gram-negative bacilli?
▪ Treatment in an ICU in which >10% of gram-negative bacilli associated with VAP are resistant to piperacillin-tazobactam and/or cefepime
▪ Treatment in an ICU in which local antimicrobial susceptibility rates among gram-negative bacilli are not known
▪ Colonization with and/or prior isolation of MDR *Pseudomonas* spp or other gram-negative bacilli on culture from any body site (but especially from respiratory tract)
Is there prior culture history of carbapenemase-resistant pathogens?
No
Yes
No
Yes
One of the following: *
▪ Piperacillin-tazobactam ¶ Δ
▪ Cefepime ¶
Add anti-MRSA therapy if any MRSA risk factors are present (refer to Inset)
Is there prior culture history of carbapenemase-resistant pathogens?
One of the following:
▪ Meropenem ¶
▪ Imipenem-cilastatin ¶
Plus one of the following: §
▪ Vancomycin
▪ Linezolid
One of the following: ◇
▪ Ceftazidime-avibactam
▪ Ceftolozane-tazobactam
▪ Imipenem-cistatin-relebactam
▪ Meropenem-vaborbactam
Plus one of the following: §
▪ Vancomycin
▪ Linezolid


No
Yes
One of the following:
Meropenem ¶
Imipenem-cilastatin ¶
Add anti-MRSA therapy if any MRSA risk factors are present (refer to Inset)
One of the following: ◇
Ceftazidime-avibactam
Ceftolozane-tazobactam
Imipenem-cistatin-relebactam
Meropenem-vaborbactam
Add anti-MRSA therapy if any MRSA risk factors present (refer to Inset)

International ERS/ESICM/ESCMID/ALAT guidelines



- If the beta-lactam beta-lactamase agents are not available

+

- High suspicion for carbapenem-resistant gram-negative bacilli

→ Addition of one of the following agents **along with** a carbapenem :

  - Tobramycin
  - Colistin
  - Aztreonam
  - Levofloxacin
  - Ciprofloxacin

Aminoglycosides

- Are not recommended as monotherapy for gram-negative infections
  - Poor lung penetration
  - Increased risk of nephrotoxicity and ototoxicity
  - Poorer clinical response rates
- As part of the initial empiric regimen in patients with (prefer tobramycin)
  - Septic shock or
  - Rapidly progressive disease when there are little or no alternative options
- Aminoglycoside should be discontinued
  - Isolated microorganism is susceptible to a beta-lactam
  - After two or three days in patients who have improved clinically
  - Cultures are negative

- **Polymyxins** (intravenous colistin or polymyxin B) in :
  - Highly resistant Pseudomonas spp, Acinetobacter spp, Enterobacterales (including Klebsiella pneumoniae) and
  - Newer beta-lactam beta-lactamase agents are not available

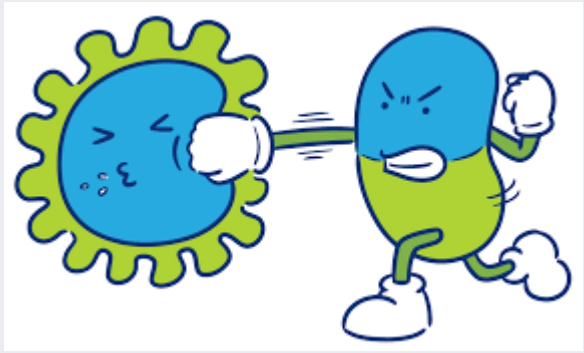
- **Aztreonam**
  - As a second agent for gram-negative bacteria with another beta-lactam

- **Anti-pseudomonal fluoroquinolones**
  - Second agent for gram negative bacilli

No clinical improvement after 48 to 72 hours

- Evaluation of:
  - Complications (eg, empyema, lung abscess)
  - Other sites of infection
  - Alternate diagnoses (eg, thromboembolic disease, pulmonary edema, malignancy, hypersensitivity reaction, etc).
- Obtain additional diagnostic pulmonary cultures
- Expand empiric regimen
- Consider viral infections or Legionella
- In immunocompromised patients: Consider fungal, viral, parasitic, and less common bacterial pathogens

DURATION



- Suggestion: seven days
- longer than seven days in:
  - Metastatic infection
  - Gram-positive bacteremia
  - Slow response to therapy
  - Immunocompromise
  - Pyogenic complications such as empyema or lung abscess

- Monitoring serial procalcitonin levels can help guide the decision to discontinue antibiotics

Aerosolized antibiotics

- Aerosolized colistin, polymyxin, or aminoglycosides can be used as adjunctive therapy (in combination with IV antibiotics) in patients with VAP MDR gram-negative bacilli, such as *A. baumannii or P. aeruginosa*

antibiotics

MDPI

Review

Aerosolized Antibiotics to Manage Ventilator-Associated Infections: A Comprehensive Review

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Abstract: Background: Ventilator-associated lower respiratory tract infectious complications in critically ill patients cover a wide spectrum of one disease process (respiratory infection), initiating from tracheal tube and/or tracheobronchial colonization, to ventilator associated tracheobronchitis (VAT) and ventilator-associated pneumonia (VAP). VAP occurence has been associated with increased intensive care unit (ICU) morbidity (ventilator days, as well as length of ICU and hospital stay) and ICU mortality. Therefore, treatments that aim at VAP/VAT incidence reduction are a high priority. Aim: The aim of the present review is to discuss the current literature concerning two major aspects: (a) can aerosolized antibiotics (AA) administered in a pre-emptive way prevent the occurrence of ventilator-associated infections? and (b) can VAT treatment with aerosolized avert the potential evolution to VAP? Results: There were identified eight studies that provided data on the use of aerosolized antibiotics for the prevention of VAT/VAP. Most of them report favorable data on reducing the colonisation rate and the progression to VAP/VAT. Another four studies dealt with the treatment of VAT/VAP. The results support the decrease in the incidence to VAP transition and/or the improvement in signs and symptoms of VAP. Moreover, there are concise reports on higher cure rates and microbiological eradication in patients treated with aerosolized antibiotics. Yet, differences in the delivery modality adopted and resistance emergence issues preclude the generalisability of the results. Conclusion: Aerosolized antibiotic therapy can be used to manage ventilator-associated infections, especially those with difficult to treat resistance. The limited clinical data raise the need for large randomized controlled trials to confirm the benefits of AA and to evaluate the impact on antibiotic selection pressure.

Keywords: aerosolized antibiotics; intensive care unit; lower respiratory tract infections; nebulized antibiotics; tracheal tube colonization; treatment; ventilator-associated pneumonia; ventilator-

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ORIGINAL RESEARCH

Ceftazidime-Avibactam in the Treatment of Patients with Bacteremia or Nosocomial Pneumonia: A Systematic Review and Meta-analysis

Ryan K. Shields · Juan P. Horcajada · Shweta Kamat · Paurus M. Irani · Margaret Tawadrous · Tobias Welte

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ABSTRACT

Introduction: Ceftazidime-avibactam (CAZ-AVI) is a combination of the third-generation cephalosporin ceftazidime and the novel, non-β-lactam β-lactamase inhibitor avibactam that is approved for the treatment of pediatric (≥ 3 months) and adult patients with complicated infections including hospital-acquired and ventilator-associated pneumonia (HAP/VAP), and bacteremia. This systematic literature review and meta-analysis (PROSPERO registration: CRD42022362856) aimed to provide a quantitative and qualitative synthesis to evaluate the effectiveness of CAZ-AVI in treating adult patients with bacteremia or nosocomial pneumonia caused by carbapenem-resistant *Enterobacterales* (non metallo-β-lactamase-producing strains) and multi-drug resistant (MDR) *Pseudomonas aeruginosa* infections.

Methods: The databases included in the search, until November 7, 2022, were Embase and PubMed. A total of 24 studies (retrospective: 22, prospective: 2) with separate outcomes for patients with bacteremia or pneumonia were included.

Results: The outcomes assessed were all-cause mortality, clinical cure, and microbiological cure. Qualitative (24 studies) and quantitative (8/24 studies) syntheses were performed. The quality of the studies was assessed using the MINORS checklist and the overall risk of bias was moderate to high.

Tobias Welte: Deceased 10 March 2024.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40121-024-00999-y.

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Combined Rifampin and Sulbactam Therapy for Multidrug-Resistant Acinetobacter Baumannii Ventilator-Associated Pneumonia in Pediatric Patients

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[2]Department of Anesthesiology and Pain Medicine, University of California Davis Health, Sacramento, CA, USA.

Abstract

Background: With essentially no drug available to control the infection caused by the extensively drug-resistant Acinetobacter baumannii (XDR-Ab) in infants and young children, this study explored the clinical outcomes of pediatric patients with drug-resistant XDR-Ab who were treated with rifampicin in combination with sulbactam sodium.

Methods: The data for clinical outcomes, microbiological responses, and side effects were collected and evaluated for 12 critically ill infants and young children diagnosed with ventilator-associated pneumonia caused by XDR-Ab following surgical treatment for congenital heart disease in a pediatric cardiac intensive care unit. This study was approved by local institutional review board (IRB).

Results: Two patients died from the complex underlining diseases. The other 10 patients were weaned off the mechanical ventilation successfully within 4–15 days after the start of treatment with rifampicin combined with sulbactam sodium and discharged home. Three cases experienced adverse side effects, including severe rash and elevated aminotransferase level.

Conclusion: The combination of rifampicin and sulbactam sodium appeared to be an effective and safe therapy for severe ventilator-associated pneumonia caused by XDR-Ab in infants and young children. Side effects such as skin rashes and elevated aminotransferase levels can be reversed once rifampicin is discontinued in time. (Funded by the Department of Cardiovascular Surgery, The Second Xiangya Hospital, Central South University, Changsha, China; the Departments of Anesthesiology and Pain Medicine of University of California Davis Health; and the National Institutes of Health.)

Acinetobacter baumannii (Ab) is one of the most common gram-negative bacteria in nosocomial infection. Extensively drug-resistant Ab (XDR-Ab) has become a global

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SAGE

Preliminary experience of tigecycline treatment in critically ill children with ventilator-associated pneumonia

Shupeng Lin[1], Lingfang Liang[2], Chenmei Zhang[2] and Sheng Ye[2]

Abstract

Objective: Ventilator-associated pneumonia (VAP) is a life-threatening complication for children who are treated in a paediatric intensive care unit. Tigecycline treatment of children with VAP has not been well studied. This study aimed to describe tigecycline use in children with VAP in a tertiary care hospital.

Methods: We conducted a retrospective chart review in a tertiary hospital from May 1, 2012 to May 1, 2017.

Results: Twenty-four children (20 girls) with median age of 8 months (range, 27 days to 6 years and 9 months) were treated with tigecycline. In-hospital mortality was 41.7% (10/24). The primary diagnosis was congenital heart disease (15/24). A total of 70.8% (17/24) of patients received a loading dose (1.5 mg/kg), followed by 1 mg/kg every 12 hours. The median duration of tigecycline therapy was 10.75 days (range, 3–21.5 days). Sulperazone was the most frequently used concomitant antibiotic. Eighteen pathogens were isolated in 16 cases. Tigecycline therapy failed in 41.6% (10/24) of patients and 20.8% (5/24) died. The pathogen was eradicated in 37.5% (6/16) of patients. No serious adverse effects were detected.

Conclusion: Tigecycline combined with other agents as salvage therapy in children with VAP is well tolerated. Our preliminary results show a positive clinical response.


وَالصُّبحِ إِذَا تَنَفَّسَ
و قسم به صبح روشن وقتی که دم زند
(و عالم را به روی خود بیفروزد).
سوره تکویر – آیه ۱۸