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Redefining Success for VAP: 360-Degree Approach

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FACULTY

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Target Audience

This activity has been developed for pharmacists who are responsible for the management of serious infections in hospitalized patients.

Learning Objectives

Upon reading this supplement, readers should be able to:

1. Identify therapeutic strategies that minimize the risk of resistance development during treatment of ventilator-associated pneumonia.
2. Recognize the importance of improving resource utilization in hospitals when treating serious infections.
3. Discuss the role of clinical pharmacists in the overall management of patients with ventilator-associated pneumonia.

Funding and Original Presentation of This Learning Activity

This CE supplement is jointly sponsored by Center for Independent Healthcare Education and Vemco MedEd and is published as an extension of the continuing education activity “Redefining Success for VAP: 360° Approach” that was held on December 9, 2008, in Orlando, Florida, during the 43rd ASHP Midyear Clinical Meeting and Exhibition. It is supported by an educational grant from Ortho-McNeil, Inc., administered by Ortho-McNeil Janssen Scientific Affairs, LLC.

Off-Label Use

In this educational activity, Dr. Burgess discusses the off-label (unapproved) use of doripenem for the treatment of ventilator-associated pneumonia.

Acknowledgement

Marco P. Cicero, PhD, of Vemco MedEd, LLC, contributed medical writing and editorial assistance.

Purpose Statement

The purpose of this activity is to educate pharmacists managing serious hospital infections on appropriate antimicrobial use to curb resistance development and improve resource utilization. With this knowledge, pharmacists will be able to fulfill an expanded role within the health care team.

Educational Overview

Among nosocomial infections, hospital-acquired pneumonia (including ventilator-associated pneumonia) is the leading cause of death associated with substantial health care costs in U.S. hospitals. Of serious concern are bacterial resistance and inappropriate antimicrobial management, which lead to compromised clinical outcomes. Early appropriate therapy is critical in (a) ensuring clinical success, (b) reducing the risk of resistance development, and (c) improving health care utilization—the 3 parameters of success of any management strategy. In this context, optimized dosing of antimicrobials, shortened duration of therapy, and de-escalation have proven to be successful strategies.

As equal partners in the health care team, pharmacists are responsible for appropriately and successfully managing these infections. Their increased responsibility in today's healthcare environment has made knowledge of the latest scientific evidence pertaining to successful management strategies an imperative.

Fee Information

There is no fee to participate in this educational activity.

Pharmacist Continuing Education

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Center requires faculty, planners, and others who are in a position to control the content of continuing education activities to disclose any real or apparent conflict of interest related to the activity. All identified conflicts of interest are reviewed to ensure fair balance, objectivity, and scientific rigor. The faculty is further required to disclose discussion of off-label uses.

Disclosure: Planning Committee

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What Is the 360-Degree Approach to Defining Success for VAP?

David P. Nicolau, PharmD, FCCP, FIDSA

VAP: Magnitude of the Problem

Nearly 1.6 million hospital-acquired infections (HAIs) occur annually in the United States (Table 1).¹ Predominant among these HAIs are urinary tract infections, bloodstream infections, surgical site infections, and hospital-acquired pneumonia (HAP). Of these, HAP is associated with the greatest infection-related morbidity and mortality.¹

In the intensive care unit (ICU) setting, HAP accounts for 25% of all HAIs.² Furthermore, nearly 90% of HAP cases occur during mechanical ventilation—this subcategory of HAP is referred to as ventilator-associated pneumonia (VAP).² Although VAP was originally thought to be restricted to the ICU setting, this disease process is increasingly prevalent in non-ICU populations, as severely ill patients are being managed in other care areas (i.e., transitional care, long-term rehabilitation units, etc). Therefore, prevention and management of VAP is a concern for all health care personnel.

The need for mechanical ventilation in these critically ill populations means that these patients will be at an increased risk for the development of pneumonia. This risk increases as the duration of mechanical ventilation increases—estimated at a 3% increase in incidence for each day during the first 5 days of mechanical ventilation.² Therefore, it is paramount to employ strategies to minimize the development of VAP.³ First and foremost among these is to identify patients who can be extubated as soon as possible to prevent VAP from occurring. Despite these efforts, a small proportion of the ventilated patient population will develop VAP. Given the high mortality associated with VAP, early appropriate therapy is critical for achieving successful outcomes for these patients.⁴ Selecting appropriate therapy can be challenging, as the nosocomial epidemiology of VAP can be diverse among differing patient populations or care settings. Moreover, the identified pathogens in this infected population commonly express resistance or multidrug resistance (MDR) to antimicrobials.⁵ Therefore, clinicians must recognize risk factors for infections caused by resistant organisms and be familiar with not only the epidemiology related to their patient population, but must also know the susceptibility profile of these pathogens if early appropriate therapy is to be initiated.

Prevention and Appropriate Management to Reduce Health Care Spending

HAIs have gained renewed attention as a targeted area to reduce health care spending, improve resource utilization, and achieve better patient outcomes. Insurance providers will continue to evaluate ways to conserve health care spending in hospitals and may follow the lead of recent government mandates regarding preventable hospital-acquired conditions.

The Center for Medicare and Medicaid Services (CMS) has

TABLE 1 The Burden of Hospital-Acquired Infections

Infection Type	Number in ICU	Number in Non-ICU	Number of Deaths
Urinary Tract	102,200	424,060	13,088
Bloodstream	81,942	133,368	30,665
Pneumonia	100,689	129,519	35,967
Surgical Site	28,725	244,385	8,205
Other	80,732	263,810	11,062
Total	394,288	1,195,142	98,987

Source: Klevens RM, et al. *Public Health Rep.* 2007;122(2):160-66.¹

ICU = intensive care unit.

listed a number of conditions (including catheter-associated urinary tract infection and vascular-catheter-associated infection) that it will no longer reimburse.⁶ This will put added pressure on institutions to minimize these infections and limit the resources used to manage patients with these infections. Although VAP is not included in the current CMS listing, this could change as funding shrinks and other preventable conditions are targeted for nonreimbursement.

VAP: Goals of Successful Management Strategy

It is estimated that approximately 38% to 70% of VAP episodes can be prevented.⁴ Thus, even in ideal situations, hospitals and ICUs will be confronted with a number of VAP episodes. Once a VAP case is identified, it will be important to achieve multiple goals for successful management (Figure 1).

The most important goal of a VAP management strategy is to achieve improved clinical outcomes and reduce morbidity and mortality. This can be achieved through early appropriate antimicrobial therapy. The second goal is to reduce the emergence of bacterial resistance. This is important, as infections caused by resistant pathogens are associated with increased morbidity, mortality, and cost, while the number of agents effective against MDR nosocomial pathogens is diminishing.^{7,8} The third goal of a VAP management strategy is to improve resource utilization.

Each of these goals is interrelated. If the first 2 goals are achieved through early appropriate antimicrobial therapy, this may reduce the hospital resources needed to successfully treat the patient, particularly by reducing hospital length of stay. The use of this clinical disease management approach coupled with other strategies, such as short-course or de-escalation of therapy, may provide additional opportunities to reduce overall hospital costs. These specific strategies, by reducing the unnecessary use or overuse of antimicrobials, may further reduce the risk of development of resistance.

FIGURE 1 360° Approach to Success in VAP

Success in VAP involves taking all aspects into consideration

VAP = ventilator-associated pneumonia.

What This Supplement Addresses

This supplement reviews tactics that can be used to achieve the 3 goals for success in VAP. Dr. David Burgess reviews the epidemiology of VAP, highlighting the importance of local epidemiology and antibiograms of the institution and specific hospital wards. Dr. Burgess continues his discussion on using pharmacokinetics and pharmacodynamics as the basis for optimizing antimicrobial dosing to reduce the risk of resistance emergence.

Dr. Keith Rodvold emphasizes the importance of efficiently using the available resources when managing patients with VAP. The clinical and economic burden of VAP is substantial, and clinicians must employ strategies that have been proven to be effective in reducing hospital costs and length of stay without compromising patient outcomes. The most effective means to reduce the cost of VAP is preventing it altogether, and a multidisciplinary team approach is imperative for implementing and continuing a successful VAP prevention program. As members of the ICU and infectious diseases team, clinical pharmacists can play an integral role in VAP prevention and should aim to be more proactive in helping achieve goals that minimize episodes of HAIs.

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Curbing Resistance Development: Maximizing the Utility of Available Agents

David S. Burgess, PharmD, FCCP

ABSTRACT

BACKGROUND: Ventilator-associated pneumonia (VAP) in hospital intensive care units (ICUs) is associated with high morbidity and mortality. Effective treatment of VAP can be challenging due to a high prevalence of *Pseudomonas aeruginosa* and multidrug-resistant (MDR) pathogens as causative organisms.

OBJECTIVE: To present the etiology of VAP in the United States (including national resistance trends of common nosocomial pathogens) and review dosing strategies aimed to optimize pharmacokinetic-pharmacodynamic parameters of antimicrobial agents.

SUMMARY: The majority of nosocomial pneumonia cases are caused by gram-negative pathogens, most commonly *P. aeruginosa*, *Enterobacter* spp., *A. baumannii*, and *K. pneumoniae*. *S. aureus* is the most common gram-positive pathogen, with 55% of VAP isolates exhibiting methicillin resistance. Combination therapy is recommended when MDR pathogens and *P. aeruginosa* are suspected, although short-course therapy and de-escalation should be considered when appropriate to reduce the risk of resistance. Optimized dosing strategies are important in increasing the probability of achieving successful outcomes. For example, when administering intravenous β -lactam therapy, prolonged infusion can be effective in increasing the T > MIC.

CONCLUSION: Clinicians need to be familiar with local antibiograms as well as regional resistance trends in order to choose appropriate therapy for VAP. Optimized dosing strategies can be effective in increasing the probability of attaining pharmacokinetic-pharmacodynamic targets predictive of successful clinical outcomes.

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Marco P. Cicero, PhD, of Vemco MedEd, LLC, contributed medical writing and editorial assistance.

Off-Label Disclosure Statement

In this article, the following off-label use of an antimicrobial agent is discussed: doripenem for the treatment of ventilator-associated pneumonia.

Introduction

Ventilator-associated pneumonia (VAP) is among the most common nosocomial infections originating in the intensive care unit (ICU), affecting 9% to 27% of all intubated patients.^{1,2} The attributable mortality can be as high as 33% to 50%.^{1,2} The risk of VAP is correlated to the length of stay (LOS) in the hospital or ICU as well as to the duration of mechanical ventilation.² *Pseudomonas aeruginosa* and multidrug-resistant (MDR) organisms account for over 20% of VAP infections, with higher rates observed in those with prolonged hospitalization.³ Infection by these problematic pathogens is associated with increased mortality, duration of mechanical ventilation, and hospital LOS.³ Therefore, when managing patients at high risk for VAP, it is important to recognize the local epidemiology and resistance trends in order to select the most appropriate initial antimicrobial therapy.

Etiology of Hospital-Acquired Pneumonia

Surveillance data from the National Healthcare Safety Network (NHSN, formerly the National Nosocomial Infections Surveillance System) have shown that gram-negative pathogens are the predominant cause of nosocomial pneumonia, accounting for approximately 70% of infections.⁴ Among the infections caused by gram-negative pathogens, *P. aeruginosa* is the leading cause (accounting for approximately 20%) followed by *Enterobacter* spp., *Klebsiella pneumoniae*, and *Acinetobacter baumannii*.⁴ The proportion of infections due to *Acinetobacter* has nearly doubled over the past 2 decades (from 4% in 1986 to 7% in 2003). However, there has been a gradual trend of increasing infections due to gram-positive pathogens, mainly *Staphylococcus aureus*.

The etiology of VAP can vary based on (a) local epidemiological trends as well as (b) the timing of onset of infection. According to the 2006–2007 NHSN data, the most common pathogen associated with VAP is *S. aureus* (24.4%) followed by *P. aeruginosa* (16.3%), *Enterobacter* spp. (8.4%), *A. baumannii* (8.4%), and *K. pneumoniae* (7.5%) (Table 1).⁵ The time of onset is also an important predictor of causative pathogens. Early-onset VAP, defined as VAP occurring within the first 5 days of hospitalization, is caused by enteric gram-negative bacteria (including *Escherichia coli*, *K. pneumoniae*, and *Enterobacter* spp.), *Haemophilus influenzae*, *Streptococcus pneumoniae*, and methicillin-susceptible *S. aureus* (MSSA).^{2,6} Late-onset VAP, defined as VAP occurring after 5 days of hospitalization, is more likely to be caused by MDR pathogens,^{2,6} including those associated with early-onset VAP as well as *P. aeruginosa* and *A. baumannii*. The variety and complexity of pathogens associated with VAP make choosing an appropriate initial therapy challenging.

Appropriate Antimicrobial Therapy for VAP

The American Thoracic Society (ATS) and the Infectious Diseases

TABLE 1 Pathogens Associated With VAP, NHSN Data 2006-2007

Species	Isolates (%) (n = 5,960)
<i>S. aureus</i>	24.4
<i>P. aeruginosa</i>	16.3
<i>Enterobacter</i> spp.	8.4
<i>A. baumannii</i>	8.4
<i>K. pneumoniae</i>	7.5
<i>E. coli</i>	4.6

Source: Hidron AI, et al. *Infect Control Hosp Epidemiol.* 2008;29(11):996-1011.⁵

Society of America (IDSA) guidelines on the management of VAP released in 2005 recommend combination therapy for late-onset infections or when *P. aeruginosa*, *A. baumannii*, or an MDR pathogen is suspected.² Gram-negative coverage should include an antipseudomonal cephalosporin or an antipseudomonal carbapenem or an antipseudomonal β -lactam/ β -lactamase inhibitor. In addition, an antipseudomonal fluoroquinolone or an aminoglycoside is recommended to ensure adequate coverage. If methicillin-resistant *Staphylococcus aureus* (MRSA) is also suspected, the regimen should include either vancomycin or linezolid.

The appropriate selection of specific agents depends on local susceptibility trends. Therefore, it is critical to be familiar with the antibiogram of the institution as well as specific hospital wards. As discussed earlier, national surveillance data indicate a predominance of *S. aureus* as causative pathogen for VAP.⁵ Moreover, MRSA now accounts for nearly 55% of all *S. aureus* VAP isolates. This is important, as MRSA infections are associated with increased mortality, LOS, and hospital costs as compared with MSSA infections.⁷⁻⁹

Among the gram-negative pathogens, the most concerning are MDR *P. aeruginosa*, carbapenem-resistant *Acinetobacter* spp., and third-generation cephalosporin-resistant *E. coli* and *Klebsiella* spp.¹⁰ *P. aeruginosa* exhibits elevated rates of resistance to fluoroquinolones and carbapenems and has been trending toward greater resistance to other antimicrobial classes (Figure 1).¹¹ Over one-third of *Acinetobacter* isolates from VAP patients exhibit resistance to carbapenems—moreover, carbapenem-resistant isolates typically exhibit resistance to multiple antimicrobial classes.⁵ MDR *Acinetobacter* isolates commonly have low susceptibility rates to fluoroquinolones, aminoglycosides, and β -lactams, including carbapenems.¹² Therefore, for infections due to *Pseudomonas* or *Acinetobacter*, it is particularly important to know the local antibiogram in order to select the most appropriate combination of agents.

Recommendations for treating infections due to *Acinetobacter* range from the use of combination therapy with an antipseudomonal β -lactam plus an aminoglycoside to combination therapy with colistin plus 1 or more other agents.¹³ The resurgence in the use of colistin in hospitals is likely the result of the

FIGURE 1 *P. aeruginosa* Resistance in U.S. ICUs

Source: Obritsch MD, et al. *Antimicrob Agents Chemother.* 2004;48(12):4606-10.¹¹

increased prevalence of *Acinetobacter* infections and a lack of other effective agents. It is important to note that colistin should not be used as monotherapy, since resistance to this agent can occur frequently when used alone.^{14,15}

The prevalence of extended-spectrum β -lactamase (ESBL)-producing gram-negative *E. coli* and *K. pneumoniae* has increased in the past several years (Figure 2).⁴ These bacteria are resistant not only to third-generation cephalosporins but to other classes of antibiotics as well.¹⁶ ESBL production can be conferred chromosomally or via a plasmid—plasmid-mediated resistance often carries resistance to aminoglycosides and other drug classes as well.² Therefore, when treating infections due to ESBL-producing *E. coli* and *K. pneumoniae*, cephalosporins, including fourth-generation cephalosporins, should not be given as monotherapy. There is also a high likelihood of resistance to fluoroquinolones and aminoglycosides.¹⁷ These strains are usually susceptible to carbapenems, which are, therefore, the preferred class for treating these infections. Extensive clinical experience also supports the use of carbapenems for these infections.^{2,17} However, it is important to note that multiple mechanisms for resistance to carbapenems have been identified and the prevalence of resistant strains should be carefully monitored.¹⁸

Treatment Strategies to Minimize Resistance Development

Hospital infections will be more challenging given the rising resistance rates observed in nosocomial pathogens coupled with the lack of antimicrobial agents in development targeting these pathogens.¹⁰ Therefore, the available agents must be used judiciously and effectively to reduce the risk of further development of resistance. Treatment strategies that may reduce the further development of resistance, while achieving similar clinical outcomes, include short-course therapy and de-escalation or streamlining therapy.

A prospective, multicenter, randomized study by Chastre et al. compared 8 days ($n=197$) with 15 days ($n=204$) of appropriate initial therapy for VAP.¹⁹ After 28 days, there were no significant differences in mortality (18.8% for 8-day vs. 17.2% for 15-day treatment groups; treatment difference=1.6%; 90% CI=-3.7% to 6.9%) or recurrence rates (28.9% for 8-day vs. 26.0% for 15-day treatment; treatment difference=2.9%; 90% CI=-3.2% to 9.1%) between the 2 treatment groups. Patients receiving the short-course regimen had significantly more antibiotic-free days ($P<0.001$). However, for patients with infections caused by nonfermenting gram-negative bacteria, including *P. aeruginosa*, short-course therapy resulted in higher rates of pulmonary infection recurrence (40.6% vs. 25.4%, treatment difference=15.2%; 90% CI=3.9% to 26.6%). Short-course therapy, therefore, may be appropriate for VAP, except in cases involving nonfermenting gram-negative bacteria.

As mentioned earlier, when *P. aeruginosa* or MDR pathogens are suspected, initial combination therapy increases the probability of providing adequate coverage. However, once the culture and susceptibility results are available and the patient shows signs of improvement, de-escalation of therapy to narrow coverage to only what is necessary should be considered. This is appropriate if an anticipated organism (such as MRSA, *P. aeruginosa*, or *Acinetobacter* spp.) was not recovered or if the organism was susceptible to a more narrow-spectrum agent than initially used.² By decreasing total antimicrobial usage, de-escalation of therapy can potentially reduce the risk of emergence of resistance to agents that are no longer deemed necessary for clinical success.

Optimizing Pharmacokinetic-Pharmacodynamic Parameters

The main goals of antimicrobial therapy are to maximize efficacy while minimizing the development of resistance. Strategies that can help achieve these goals include antimicrobial stewardship, infection control, and optimizing pharmacokinetic/pharmacodynamic (PK/PD) parameters.

This review will not discuss antimicrobial stewardship or infection control tactics. A number of publications provide a thorough understanding of the benefits of antimicrobial stewardship.²⁰⁻²² The recent guidelines released by the IDSA and the Society for Healthcare Epidemiology of America (SHEA) state the importance of the clinical pharmacist in implementing an antimicrobial stewardship program at institutions.²⁰ Infection control is traditionally not the focus of clinical pharmacists, but given the new mandates affecting reimbursement for hospital-acquired infections (HAIs) and heightened efforts to reduce HAIs, all health care personnel should be aware of infection control tactics. The SHEA and IDSA recently released a compendium of strategies to prevent various health care-associated infections in acute care hospitals that can be a valuable resource for hospital-based clinicians.²³

This review will focus on optimizing PK/PD parameters.

FIGURE 2 Resistance of Nosocomial Isolates to 3rd-Generation Cephalosporins: Nosocomial Infections Surveillance System, 1986–2003

Source: Gaynes R, et al. Clin Infect Dis. 2005;41(6):848-54.⁴

^aProportions of *K. pneumoniae* and *E. coli* that were resistant were significantly higher in 2003 compared with 1986 ($P<0.001$ for both, by the Cochran-Armitage χ^2 test for trend).

Antimicrobial agents can be divided into those that exhibit concentration-dependent bacterial killing or time-dependent bacterial killing.

For concentration-dependent agents, the PK/PD parameters predictive of successful clinical outcomes include the peak to minimum inhibitory concentration (MIC) ratio ($C_{max}:MIC$ for aminoglycosides) or the area under the concentration-time curve (AUC:MIC for fluoroquinolones). This was illustrated in a pivotal study by Forrest et al. who evaluated the clinical and microbiologic success rates in nosocomial pneumonia patients based on drug exposure following fluoroquinolone therapy.²⁴ For patients with an AUC:MIC ratio below 125, microbiologic success rates were consistently below 40% (Figure 3). For those with an AUC:MIC ratio above 125, microbiologic success rates were greater than 80%. It is important to recognize that meeting the PK/PD target does not necessarily guarantee a successful outcome but only predicts a greater chance of clinical success. Patient and pathogen factors can also impact the probability of a successful outcome.

For time-dependent agents such as the β -lactams, the PK/PD parameter predictive of clinical success is the time above the MIC ($T>MIC$). The $T>MIC$ required for clinical success can vary depending on the particular antimicrobial class.²⁵ The carbapenems require a $T>MIC$ of 40% for maximal effect while the cephalosporins require $T>MIC$ of 60% to 70%.²⁵ This variation among the classes can reflect differences in their bactericidal activity as well as the post-antibiotic effect of the agents.

When using intravenous β -lactam therapy, extending the

FIGURE 3 Fluoroquinolone Therapy for Nosocomial Pneumonia: Correlation Between Drug Exposure and Clinical Outcome

Source: Forrest A, et al. *Antimicrob Agents Chemother.* 1993;37(5):1073-81.²⁴

infusion period can be used to increase the $T > MIC$ and lower the peak concentration.^{26,27} The infusion period can be extended through either (a) continuous infusion (i.e., administering a loading dose and then a pump to administer the total daily intravenous dose over a 24-hour period), or (b) prolonged infusion (i.e., administering the same dose and dosing interval but increasing the duration of infusion, such as from 30 minutes to 3 hours).

The use of prolonged infusion has been studied extensively with doripenem. In 1 study, the concentration-time profiles of a 500 mg dose were compared with various infusion times ranging from 1 hour to 6 hours (Figure 4).²⁸ The impact of longer infusion times were then evaluated by determining the probability of meeting the $T > MIC$ target of 40%. For pathogens with an MIC of 1 $\mu\text{g/mL}$, 1-hour and 3-hour infusions were effective in meeting the PK/PD target. However, for pathogens with an MIC of 2 $\mu\text{g/mL}$, a 1-hour infusion had a 77% probability of meeting the PK/PD target compared a 100% probability with a 3-hour infusion. For pathogens with an MIC of 4 $\mu\text{g/mL}$, a 5-hour infusion was required to achieve a 99% probability of meeting the PK/PD target.

The PK/PD study with doripenem was instrumental in designing a clinical trial comparing doripenem with imipenem for the treatment of VAP.²⁹ Doripenem (500 mg every 8 hours; $n=264$) was administered via a 4-hour infusion and compared with an imipenem treatment (500 mg every 6 hours via a 30-minute infusion or 1,000 mg every 8 hours via a 60-minute infusion; $n=267$). In the clinically evaluable population, there was no significant difference in overall clinical success between the 2 treatment groups (68.3% for doripenem vs. 64.8% for

FIGURE 4 PK/PD Profile of Doripenem 500 mg

Republished with permission from Bhavnani SM, Hammel JP, Cirincione BB, Wilker MA, Ambrose PG. Use of pharmacokinetic-pharmacodynamic target attainment analyses to support phase 2 and 3 dosing strategies for doripenem. *Antimicrob Agents Chemother.* 2005;49(9):3944-47;²⁸ published by American Society for Microbiology; Copyright © 2005 American Society for Microbiology. LLQ = lower limit of quantification; PK/PD = pharmacokinetic-pharmacodynamic.

imipenem; treatment difference = 3.5%; 95% CI = -9.1% to 16.1%). However, patients treated with doripenem had higher success rates for infections caused by *P. aeruginosa* (80.0% vs. 42.9%) and *K. pneumoniae* (66.7% vs. 50.0%), although neither difference was statistically significant. Such studies illustrate the significance of applying pharmacokinetics-pharmacodynamics when choosing optimal dosing strategies to achieve clinical success.

Pharmacokinetics-pharmacodynamics can also be important in selecting dosing strategies to suppress the development of resistance. A study by Tam et al. used an in vitro model to determine the dosing regimen of meropenem that suppresses development of resistance by *P. aeruginosa*.^{30,31} In experiments with a wild-type strain, a large reduction in bacterial burden was observed within the first 24 hours of each regimen tested, although substantial regrowth occurred after 3 days for regimens that maintained $T > MIC$ of 100% and had a $C_{\min}:MIC$ of 1.7. Suppression of resistant subpopulations required $T > MIC$ of 100% and a $C_{\min}:MIC$ ratio of 6.2 or greater. Achieving these levels would be impractical in a clinical setting, which illustrates the difficulty in suppressing the development of resistance for this problematic pathogen. Lower concentrations of meropenem and the addition of tobramycin was effective in suppressing the development of resistance, confirming the importance of combination therapy for patients suspected with infections by *P. aeruginosa*.

Summary

VAP caused by *P. aeruginosa* and MDR pathogens presents a challenge to clinicians when selecting appropriate initial antimicrobial therapy. Current recommendations point to combination therapy to ensure adequate coverage of potential pathogens followed by de-escalation of therapy once culture and susceptibility results become available. Given the dearth of new antimicrobial agents in the pipeline, de-escalation of therapy can be critical in reducing the potential for development of resistance against available agents and prolonging their effectiveness. Optimized dosing strategies that take into account PK/PD parameters can also be important in increasing the probability of successful outcomes as well as in reducing the risk of development of resistance. Certain tactics, such as prolonged infusion of β -lactam agents, can improve the probability of PK/PD target attainment, although this does not necessarily guarantee a successful outcome.

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Collaborative Strategies for Improving Clinical Resource Utilization: How Pharmacists Can Make a Difference

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ABSTRACT

BACKGROUND: Ventilator-associated pneumonia (VAP) is associated with substantial health care costs that place a significant burden on scarce hospital resources. Preventative measures and appropriate management strategies can be effective in reducing the incidence of VAP and in improving VAP-related resource utilization.

OBJECTIVE: To provide an overview of the economic costs associated with VAP and of strategies that can be used to meet the goals of improving the efficiency of resource utilization without negatively impacting clinical outcomes.

SUMMARY: The substantial costs attributed to VAP are mainly due to the prolonged hospital length of stay (LOS) associated with these patients. Initial appropriate antimicrobial therapy is critical in achieving successful outcomes—including reducing LOS, mechanical ventilation days, and mortality. Initial treatment includes combination therapy when a multidrug-resistant pathogen or *Pseudomonas aeruginosa* is suspected. Once microbiologic results are available, de-escalation of therapy should be considered to reduce the unnecessary use of antimicrobials without impacting clinical outcomes. VAP prevention programs can also be an effective means to improve resource utilization in hospitals, although it is important to adopt a multidisciplinary team approach for acceptance of such programs and adherence to them.

CONCLUSION: In the current health care environment of increased transparency and accountability, renewed efforts must be made to not only prevent VAP but also to appropriately manage patients with VAP. All health care personnel involved in the management of patients with VAP must take a proactive role in reducing its incidence.

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DISCLOSURES

Keith A. Rodvold has served as a consultant to Johnson & Johnson, Astellas, GlaxoSmithKline, Theravance, Targanta, and Intranasal Therapeutics; participated in advisory committees for Johnson & Johnson, Targanta, Baxter, and Pfizer; and served on speakers bureaus for Johnson & Johnson, Wyeth, Pfizer, and Schering-Plough.

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Introduction

Although largely considered preventable, ventilator-associated pneumonia (VAP) is among the most common nosocomial infections acquired by adults and children in the intensive care unit (ICU), affecting approximately 9% to 27% of patients undergoing mechanical ventilation.¹ With an incidence that can be as high as 10 episodes per 1,000 ventilator-days,² VAP is associated with an attributable mortality of 33% to 50%.¹ In addition, the economic burden is substantial due to extended periods of mechanical ventilation, prolonged length of stay (LOS) in the ICU and hospital, overconsumption of antimicrobial agents, and increased health care costs.³

Given the economic impact of VAP and that it is generally preventable in most cases, renewed efforts must be made by all health care personnel to implement and adhere to strategies that prevent VAP or minimize the risk of VAP. It is critical for health care professionals and administrators to be aware of strategies that have been proven effective in improving resource utilization and to adopt strategies that can be appropriately implemented at their institutions.

The Clinical and Economic Costs of VAP

A number of studies have evaluated the clinical and economic impact of VAP. The Society for Healthcare Epidemiology of America (SHEA) released guidelines in 2007 on how to make a business case for infection control programs at hospitals.⁴ The report included costs attributable to different types of hospital-acquired infections (HAIs), including VAP, catheter-related bloodstream infection, coronary artery graft bypass surgery-associated surgical site infection, and catheter-related urinary tract infection. VAP was found to be associated with the highest attributable costs (an additional \$23,000 per episode on average), compared with bloodstream infection (\$18,432), surgical site infection (\$17,944), and urinary tract infection (\$1,257). An episode of VAP was also associated with a mean increase in the LOS by nearly 10 days.

A prospective, cohort study conducted by Warren et al. at a community hospital evaluated the impact of VAP on clinical outcomes and costs.⁵ The study included patients from the medical and surgical ICU from 1998 to 1999 and compared outcomes in patients who developed VAP with those who did not develop VAP. A total of 819 patients were included in the analysis, of which 127 had developed VAP. Patients with VAP were found to have a higher APACHE II (Acute Physiology and Chronic Health Evaluation) score, higher rate of congestive heart failure on admission, higher rate of hemodialysis, and longer duration of central venous catheter use and mechanical ventilation (Table 1). When considering patient outcomes, the LOS was significantly longer for patients with VAP—over 20 days longer on average for both ICU LOS and hospital LOS. Total hospital costs for patients with VAP were \$48,948 higher. When these costs were adjusted for disease severity, the attributable cost was \$11,897 for each case of VAP. Mortality rates were also significantly higher in patients with VAP (50% vs. 34%, $P < 0.001$).

TABLE 1 Outcomes and Attributable Costs of Ventilator-Associated Pneumonia

Variable	No VAP (n = 692)	VAP (n = 127)	P Value
APACHE II score, mean (IQR)	23 (9)	26 (8)	<0.001
CHF (%)	44	54	0.04
Hemodialysis (%)	10	23	<0.001
CVC days/patient, mean	9	27	<0.001
Ventilator days, median	2	15	<0.001
Outcomes			
ICU LOS, mean (days)	4	26	<0.001
Hospital LOS, mean (days)	13	38	<0.001
Total hospital costs, mean (\$)	21,620	70,568	<0.001
Death (%)	34	50	<0.001

Source: Warren DK, et al. *Crit Care Med.* 2003;31(5):1312-17.⁵

APACHE = Acute Physiology and Chronic Health Evaluation; CHF = congestive heart failure; CVC = central venous catheter; ICU = intensive care unit; IQR = interquartile range; LOS = length of stay; VAP = ventilator-associated pneumonia.

Muscedere et al. reviewed the published literature and institutional data to assess the impact of VAP on the Canadian health care system.² In this study, the incidence of VAP in Canada was estimated at 10.6 cases per 1,000 ventilator-days, which equated to approximately 4,000 VAP cases each year. VAP increased the mean ICU LOS by 4.3 days per episode and resulted in a total excess cost of CAN \$46 million (about \$11,500 per VAP case). The attributable mortality was estimated to be 5.8%, or 232 deaths each year. The authors emphasized that eradication of this preventable infection will significantly impact VAP-associated mortality rates and health care resources. The excess ICU LOS reported by Muscedere et al. was much less than what was reported in the Warren study (22 additional days by VAP patients);⁵ this difference may be due to differences in the methodology and patient selection of the 2 studies. The Warren study compared all ICU patients (with and without VAP) requiring >24 hours of mechanical ventilation during a set time period, while the Muscedere analysis was based on 1 matched cohort study (cases included patients requiring >48 hours mechanical ventilation and developed VAP).

Cost Distribution of VAP

The excess costs associated with VAP can be directly linked to the prolonged LOS. Warren et al. analyzed the cost distribution associated with VAP and determined that room and nursing costs accounted for nearly 50% of the total hospital costs.⁵ Pharmacy costs, including antimicrobial therapy, accounted for approximately 20% of the total costs with the remainder of costs attributed to operating room, laboratory, respiration therapy, radiology, and other expenses.

The cost distribution among ICU infected patients with and without VAP was also evaluated in a matched cohort study in Switzerland.⁶ The matching procedure identified 97 pairs of mechanically ventilated patients and revealed that the largest proportion of costs (approximately 75%) for patients with and

TABLE 2 Cost Burden of Methicillin-Resistant *Staphylococcus aureus* (MRSA) vs. Methicillin-Susceptible *Staphylococcus aureus* (MSSA) Ventilator-Associated Pneumonia

Dependent Variable	MRSA Estimate (95% CI) ^a	P Value
Total MV (days)	4.4 (0.6–8.2)	0.03
VAP MV (days)	4.5 (1.0–8.1)	0.01
Total LOS (days)	3.8 (-0.5–8.0)	0.08
VAP LOS (days)	3.7 (-0.5–8.0)	0.08
Total ICU (days)	5.3 (1.0–9.7)	0.02
VAP ICU (days)	4.4 (0.4–8.4)	0.03
Total Cost (US \$)	7,731 (-8,392–23,856)	0.35

Adapted from Shorr AF, et al. *Crit Care.* 2006;10(3):R97.¹⁰

^aMRSA estimate represents excess resources required for patients with MRSA compared with patients with MSSA.

ICU = intensive care unit; LOS = length of stay; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-susceptible *Staphylococcus aureus*; MV = mechanical ventilation; US = United States; VAP = ventilator-associated pneumonia.

without VAP was related to the costs of the ward (or fixed costs) (Figure 1). These costs also included the expenses related to physicians and nurses. For patients who remained free of any ICU-acquired infection, the total cost was less than one-third of the cost for ICU patients with VAP.

Cost Burden: Impact of Resistance

The increasing prevalence of resistant and multidrug-resistant pathogens can impact the cost of managing patients with VAP. Antimicrobial resistance can increase the risk of inappropriate therapy, which potentially increases mortality rates as well as LOS and duration of mechanical ventilation.⁷⁻⁹

A retrospective, cohort study was conducted to compare the clinical and economic outcomes for patients with early-onset VAP infected with methicillin-resistant *S. aureus* (MRSA) versus methicillin-susceptible *S. aureus* (MSSA).¹⁰ A total of 154 patients with *S. aureus* infections were included (59 patients with MRSA) in the multivariate analysis. MRSA infections were associated with a significant increase in mechanical ventilation days and ICU LOS (Table 2) and an insignificant increase in total LOS (3.8 days more) and total costs (\$7,731 higher). These results imply that there is a greater use of resources for managing patients with MRSA-related VAP compared with patients with MSSA-related VAP. Strategies should, therefore, be employed to quickly diagnose patients with VAP caused by MRSA to reduce morbidity and hospital costs.

Clinical Burden: Initial Inappropriate Therapy

Initial inappropriate therapy for VAP is associated with significantly higher mortality rates than initial appropriate therapy.⁷⁻⁹ In a retrospective, observational cohort study, the 30-day mortality rates were determined in 76 patients with VAP caused by potentially resistant gram-negative bacteria (*P. aeruginosa*, *Acinetobacter* spp., and *Stenotrophomonas maltophilia*).¹¹ Those who received

FIGURE 1 Comparison of Mean Costs for ICU Patients With VAP (Cases), Matched ICU Patients Requiring Mechanical Ventilation Without Pneumonia (Controls), and Patients Not Infected and Did Not Require Time in the ICU (Noninfected Patients)

Reprinted with permission from Hugonnet S, Eggimann P, Borst F, Maricot P, Chevrolet JC, Pittet D. Impact of ventilator-associated pneumonia on resource utilization and patient outcome. *Infect Control Hosp Epidemiol.* 2004;25(12):1090-96.⁶ Published by University of Chicago Press; © 2003 The University of Chicago Press. All rights reserved.

appropriate antimicrobial therapy (n=59) within 24 hours of bronchoalveolar lavage sampling had a significantly lower 30-day mortality rate compared with those who received inappropriate therapy (n=17; 17.2% vs. 50.0%, $P=0.005$). Due to an increased mortality and shorter hospital LOS of patients with inappropriate antimicrobial therapy, there was no significant difference in total hospital costs between the 2 patient populations.

A meta-analysis conducted by Kuti et al. evaluated the impact of initial inappropriate antibiotic therapy on mortality of VAP patients.¹² All studies published from 1966 to December 2006 were included if they met all of the following criteria: (a) observational studies, (b) compared patients receiving appropriate and inappropriate antibiotic therapy, and (c) reported data on incidence of mortality. Appropriate therapy was defined as treatment with at least 1 antibiotic having in vitro activity against the cultured pathogen. A total of 9 studies (813 total patients) met the inclusion criteria. Unadjusted mortality data revealed that inappropriate therapy significantly increased the risk of death in patients with VAP (odds ratio [OR]=2.34, 95% CI=1.51-3.63). An adjusted analysis was performed that included only those studies that used an appropriate analytic method to estimate an adjusted effect, adjusted ORs, and CIs. Three studies (323 patients) were included in the adjusted mortality analysis and showed similar results (OR=3.03, 95% CI=1.12-8.19). The authors suggest that the data show a clear association between inappropriate therapy and mortality in VAP patients. Clinicians should attempt to adopt protocols that help ensure initial appropriate therapy for these patients.

Improving Resource Utilization Through Appropriate Antimicrobial Therapy

Ideal therapy for VAP involves appropriate initial therapy while avoiding unnecessary antimicrobial use. These goals have been emphasized in the American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) guidelines pertaining to management of hospital-acquired pneumonia.¹ The ATS/IDSA guidelines recommend early, appropriate antimicrobials in adequate doses while avoiding excessive antimicrobial use through de-escalation of initial therapy and shortening the duration of therapy to the minimum effective period. The guidelines further state that antimicrobial selection and therapeutic adjustment should be based on microbiologic cultures and clinical response of the patient.

Selecting the appropriate initial therapy can be challenging, given the variety of causative pathogens and the difficulty in predicting their susceptibility profile. Because of the importance of appropriate initial antimicrobial therapy for VAP, the ATS/IDSA guidelines recommend initial combination therapy when a multidrug-resistant pathogen or *P. aeruginosa* is suspected.¹ However, to limit the excessive use of antimicrobials, the guidelines recommend de-escalation of therapy once microbiologic results are available.

De-escalation of Therapy

De-escalation of therapy reduces the unnecessary use of antimicrobials and has the potential to decrease the risk of development of resistance without affecting clinical outcomes. How to de-escalate is still controversial; while more research is needed to arrive at the optimal approach, several steps have been outlined on adopting this strategy.^{1,13,14} The following steps can serve as a useful guide in adopting a strategy of de-escalation. However, adjustments to this model should be made based on the individual patient characteristics and specific conditions at each institution.

Step 1. Obtain microbiologic samples. Microbiologic samples should be obtained as soon as VAP is suspected due to the significant time needed to obtain culture and susceptibility results.

Step 2. Begin empiric antimicrobial therapy. Therapeutic selection should be based on patient risk factors for MDR pathogens as well as local susceptibility patterns. Patients should be carefully monitored for clinical improvement based on their temperature, white blood cell count, chest X-ray, $\text{PaO}_2/\text{FiO}_2$, organ function, and hemodynamic parameters.

Step 3. Evaluate and de-escalate. Response to appropriate therapy can take 48 to 72 hours, so the selected antimicrobial regimen should not be changed during this time unless progressive deterioration of the patient occurs or initial microbiologic results suggest otherwise. Once culture results and susceptibility profiles are obtained, de-escalation of therapy can be considered.

If the patient shows clinical improvement, it may be possible to narrow (de-escalate) the antimicrobial spectrum based on the microbiologic results. After 7 to 8 days of therapy, the patient should be re-assessed for the need of continued therapy. An exception to short duration of therapy for VAP includes

infections caused by nonfermenting gram-negative pathogens, such as *P. aeruginosa* or *Acinetobacter* spp., which may require longer antimicrobial courses (e.g., 15 days or longer).¹⁵

If the patient shows no or little sign of clinical improvement, the patient should be re-assessed based on pathogen resistance to therapy, the presence of a complication (such as an abscess), a noninfectious diagnosis, or inadequate tissue penetration of the drug to the site of infection.

Use of Institutional Guidelines in VAP Management and Prevention

The use of VAP management guidelines can be effective in improving appropriate antimicrobial therapy and decreasing resource utilization. Recent evidence-based clinical guidelines by Muscedere et al. incorporate many of the aspects discussed in this review and can serve as an important reference when managing patients with VAP.¹⁶

A recent report from Canada assessed the value of de-escalation of therapy once culture results became available.¹⁷ All 740 patients included in the study received empiric broad-spectrum therapy and were then stratified depending on if they received targeted therapy based on culture results. Targeted therapy in this study was defined as a narrower spectrum of antimicrobial therapy based on culture and susceptibility results or discontinuation of antibiotics when cultures were negative. For those with positive cultures (n=412), the clinical progression of infection, multiple organ dysfunction scores, and mortality were not significantly different between the 2 patient populations. However, those who receive targeted therapy (n=320) had more days alive and off broad-spectrum antimicrobials (14.5 vs. 13.2 days, $P=0.04$). Those with negative cultures (n=327) and treated with targeted therapy (n=230) had more days alive and off broad-spectrum therapy (15.9 vs. 13.1 days, $P<0.001$) and fewer days on mechanical ventilation (9.8 vs. 14.7 days, $P=0.03$). The authors concluded that targeted therapy resulted in less antimicrobial use without any clinical compromise.

A report from a university-affiliated teaching hospital in Seattle, Washington, compared outcomes before and after the implementation of VAP management guidelines based on local microbiologic data.¹⁸ The guidelines promoted the use of quantitative bronchoscopy for diagnosis and initiated empiric therapy based on local microbiologic findings and resistance patterns. Therapy was then tailored based on culture results, and the duration of therapy was carefully considered based on clinical response. Following implementation of the guidelines, there were significant increases in the rate of tailoring therapy based on culture results and the use of definitive therapy, as well as a decrease in the mean duration of therapy (Table 3). The implementation of the guidelines led to a significant improvement in antimicrobial use practices, although no improvement was observed in the all-cause mortality rate of these patients.

Finally, a university teaching hospital in Kansas reported the effects of implementing evidence-based VAP prevention strategies on the incidence of infection in ventilated trauma patients.¹⁹ The VAP prevention protocol was modified to include elevation of the head of the bed, twice-daily chlorhexidine oral cleansing,

TABLE 3 Outcomes Before and After Implementation of VAP Management Guidelines

Outcomes	Before Period (n = 168)	After Period (n = 216)	P Value
Therapy tailored based on culture	61.3%	69.4%	0.034
Use of appropriate definitive therapy	80.4%	89.4%	0.001
Mean duration of therapy, days	12.0	10.7	0.001
All-cause mortality	22.6%	21.3%	0.756

Source: Dellit TH, et al. *Infect Control Hosp Epidemiol*. 2008;29(6):525-33.¹⁸

VAP = ventilator-associated pneumonia.

a once-daily respiratory therapy-driven weaning attempt, and conversion from a nasogastric to an orogastric tube whenever possible. In 2003 (prior to guidelines), there were 1,600 days of ventilator support compared with 703 days of ventilation in 2004 (following guideline implementation). Following implementation of these guidelines, the incidence of VAP decreased from 6.9 per 1,000 ventilator-days to 2.8 per 1,000 ventilator-days. This had a significant impact on resource utilization given that VAP patients had, on average, greater hospital LOS (an additional 25.4 days per episode), greater ventilator days (an additional 11.3 days per episode), and greater hospital charges (an additional \$233,000 per episode). This study illustrates the importance of considering improved preventative strategies as an effective means to reduce resource utilization among patients with VAP.

Multidisciplinary Team Model for VAP Prevention

Improving resource utilization when managing patients with VAP will require greater efforts in education of health care personnel, improved early and accurate diagnosis, appropriate empiric therapy, and the use of prevention measures.

The goals of VAP prevention programs are to decrease morbidity and mortality associated with these infections and to reduce hospital costs. Achieving these goals will require implementing tactics that reduce the risk of infection, which can include improved infection control, reduced inappropriate antimicrobial use, and limiting device days. Initially, it may be practical for an institution to focus on implementing a few proven cost-effective strategies.

The Institute for Healthcare Improvement (IHI) 100,000 Lives Campaign recommends a VAP "bundle" that includes 4 components: (a) elevation of head of the bed to between 30 degrees and 45 degrees, (b) daily "sedation vacations" and assessment for readiness to extubate, (c) prophylaxis for peptic ulcer disease, and (d) prophylaxis for deep vein thrombosis.²⁰ Initial reports have shown a dramatic decrease in VAP rates once these tactics were implemented at institutions.^{21,22}

VAP prevention programs require widespread support within the institution for implementation and adherence. Prevention programs should be multidisciplinary and evidence-based and should translate prevention strategies into hospital practice focused on patient safety and quality improvement.²³ Dr. Donald

Craven, in his guidelines for VAP prevention, suggests that a prevention program be led by a “champion leader” while other core members include administration, nursing, infectious disease and critical care physicians, respiratory therapists, and microbiologists, among others.²³ Although clinical pharmacists are not specifically listed, several reports have described and documented the impact of critical care pharmacists within a multidisciplinary ICU team.²⁴⁻²⁷ Evaluations of clinical pharmacists in the ICU setting have demonstrated the potential for improved patient outcomes and cost savings in critically ill patients, including those with VAP.²⁵⁻²⁷

One of the greatest barriers to implementing a prevention program is gaining administrative support and funding. However, as previously described, there is a wealth of information available demonstrating the high costs of these infections. This aspect should be emphasized when presenting to the administrators the need for improved prevention programs that will lead to improved clinical outcomes and decreased resource utilization. Today’s environment of increased transparency and accountability at hospitals should also provide incentive to implement strategies that lead to fewer cases of VAP.

Summary

When managing patients with VAP, clinicians must find a balance between (a) initiating appropriate therapy that provides adequate coverage, and (b) avoiding the overuse of antimicrobial agents. This approach will be important in achieving successful clinical outcomes while efficiently using scarce hospital resources. Strategies aimed at reducing hospital LOS will be most effective in improving resource utilization for patients with VAP. However, the greatest reduction in hospital costs will be through the implementation of preventative strategies that effectively reduce the actual number of VAP episodes. A multidisciplinary team approach will be critical in the success of these programs, and clinical pharmacists can play an integral role as part of the critical care team.

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Redefining Success for VAP: 360-Degree Approach

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DO YOU HAVE (1) ANY SUGGESTIONS FOR IMPROVING THIS SUPPLEMENT or (2) ANY ADDITIONAL COMMENTS?

Posttest Worksheet: Redefining Success for VAP: 360-Degree Approach

1. The approximate number of annual deaths caused by hospital-acquired infections in the United States is:
 - a. 50,000
 - b. 75,000
 - c. 100,000
 - d. 150,000
2. During the first 5 days of mechanical ventilation, the risk of developing VAP has been estimated to increase by:
 - a. 1% per day
 - b. 3% per day
 - c. 5% per day
 - d. 8% per day
3. The leading cause of VAP in the United States is:
 - a. *P. aeruginosa*
 - b. *S. pneumoniae*
 - c. *S. aureus*
 - d. *K. pneumoniae*
4. What percentage of *S. aureus* isolates from VAP patients exhibit methicillin resistance?
 - a. 30%
 - b. 40%
 - c. 55%
 - d. 75%
5. Which is the preferred class of agents to treat infections caused by ESBL-producing *E. coli* and *K. pneumoniae*?
 - a. Aminoglycosides
 - b. Fluoroquinolones
 - c. Third-generation cephalosporins
 - d. Carbapenems
6. In a study comparing 8 days versus 15 days of appropriate therapy for VAP, the short-course regimen resulted in:
 - a. Higher overall mortality rate
 - b. Higher overall recurrence rate
 - c. More antibiotic-free days
 - d. Lower failure rate for *P. aeruginosa* infections
7. Which of the following classes of agents does not exhibit time-dependent bactericidal activity?
 - a. Aminoglycosides
 - b. β -lactams
 - c. Cephalosporins
 - d. Carbapenems
8. A study by Forrest et al. showed that successful treatment of nosocomial pneumonia with a fluoroquinolone will require an AUC:MIC ratio of:
 - a. 30
 - b. 50
 - c. 125
 - d. 250
9. For VAP patients, the greatest portion of hospital costs are associated with:
 - a. Room charges
 - b. Pharmacy
 - c. Respiration therapy
 - d. Radiology
10. In a study comparing VAP patients with MRSA versus MSSA, the presence of MRSA significantly increased all of the following EXCEPT:
 - a. Total mechanical ventilation days
 - b. Total ICU days
 - c. Mechanical ventilation days during VAP
 - d. Total costs
11. When considering de-escalation of therapy for VAP, infections caused by which organism should NOT be considered for short duration of therapy?
 - a. *A. baumannii*
 - b. *E. coli*
 - c. *K. pneumoniae*
 - d. *E. cloacae*
12. Which of the following is NOT included in the Institute for Healthcare Improvement's VAP bundle?
 - a. Elevation of the head of the bed to between 30 degrees and 45 degrees
 - b. Antimicrobial prophylaxis
 - c. A daily "sedation vacation"
 - d. Daily assessment for readiness to extubate

To complete this activity online, go to
www.amcp.org (CE/CME Center) to access the posttest and evaluation form.

Posttest Answers and Evaluation: Redefining Success for VAP: 360-Degree Approach

Your evaluation and suggestions will help improve the quality of future continuing education activities. Please answer the following general questions, provide written comments, and evaluate the individual authors. Additional space for your comments and suggestions is available in this evaluation. Thank you for your cooperation.

ANSWERS TO POST TEST

1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____ 7. _____ 8. _____ 9. _____ 10. _____ 11. _____ 12. _____

LEARNING OBJECTIVES After reading this supplement, are you able to	Yes	Somewhat	No
1. Identify therapeutic strategies that minimize the risk of resistance development during treatment of ventilator-associated pneumonia			
2. Recognize the importance of improving resource utilization in hospitals when treating serious infections			
3. Discuss the role of clinical pharmacists in the overall management of patients with ventilator-associated pneumonia			

AUTHORS Evaluate the knowledge and expertise of the authors in the subject.	Excellent	Good	Fair	Poor
David P. Nicolau, PharmD				
David S. Burgess, PharmD				
Keith A. Rodvold, PharmD				

OVERALL EVALUATION	Yes	Somewhat	No
1. This supplement met my expectations.			
2. The content was relevant to my practice.			
3. This supplement was fair and balanced.			
4. This supplement was without commercial bias.			
If you answered "No" to 3 or 4, please explain.			

PRACTICE APPLICATION
1. What aspects of this supplement were most relevant to your practice?
2. Please list at least one strategy to minimize the risk of resistance development during the treatment of VAP that you learned from this supplement?
3. Do you intend to make changes to your practice based on this supplement? If yes, please specify.
4. What aspects of managing VAP do you need to learn more about to improve your practice performance?

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