

# Epidemiology and Microbiology of Hospital-Acquired Pneumonia

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## ABSTRACT

Hospital-acquired pneumonia (HAP) is the second most common nosocomial infection in the critically ill patient and is associated with the greatest mortality and increased morbidity and cost of care. The major risk factor for the development of HAP in intensive care is the occurrence of intubation and mechanical ventilation, giving rise to the term *ventilator-associated pneumonia* (VAP). Incidence of VAP varies in different populations of critically ill patients and generally ranges from 9 to 20%, with an overall rate of 10 to 15 cases per 1,000 ventilator days. The cumulative risk of developing VAP is ~1% per day of mechanical ventilation (MV). The crude mortality rate of VAP is 60% and the estimates of attributable risk range from 27 to 43%. Mortality from VAP is influenced by host factors, the virulence of the pathogens, and the adequacy of initial antimicrobial therapy. The etiologic agents for VAP differ according to the population studied, duration of hospital stay, time after intubation, and prior antimicrobial therapy. Risk factors include nonmodifiable factors like age, chronic obstructive pulmonary disease, severe head trauma, and multiple trauma, and modifiable factors like large volume gastric aspiration, duration of MV, elevated gastric pH, histamine type 2 blocker therapy, ventilator circuit change frequency, self-extubation, and reintubation. The impact that diagnosis using invasive diagnostic techniques may have on the epidemiological characteristics of VAP are unknown, but may potentially reduce problems resulting from misclassification of this entity.

**KEYWORDS:** Ventilator-associated pneumonia, antimicrobial therapy, intensive care unit, mechanical ventilation

**Objectives:** Upon completion of this article, the reader should appreciate the magnitude of hospital-acquired pneumonia, specifically in intubated and mechanically ventilated patients, with a focus on incidence, mortality, morbidity and costs, responsible microorganisms, and risk factors.

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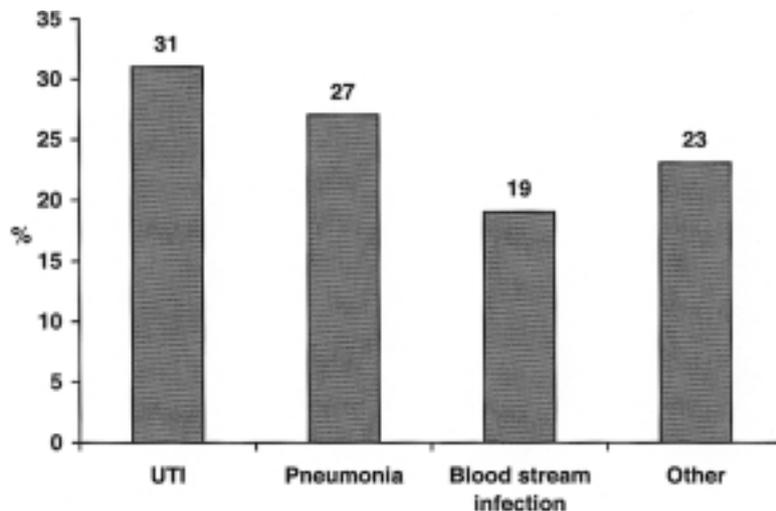
Hospital-Acquired Pneumonia; Editor in Chief, Joseph P. Lynch, III, M.D.; Guest Editor, Mark J. Rumbak, M.D. *Seminars in Respiratory and Critical Care Medicine*, volume 23, number 5, 2002. Address for correspondence and reprint requests: John E. McGowan Jr., M.D., Department of Epidemiology (Rm 442), Rollins School of Public Health of Emory University, 1518 Clifton Road, Atlanta, GA 30322. E-mail: jmcgowa@sph.emory.edu. <sup>1</sup>Division of Pulmonary and Critical Care Medicine, Emory University, Atlanta, Georgia; <sup>2</sup>Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, Georgia. Copyright © 2002 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662. 1069-3424,p;2002,23,05,415,426,ftx,en;srm00170x.

Hospital-acquired pneumonia (HAP) is defined as parenchymal lung infection occurring more than 48 hours after admission to the hospital. Most cases of HAP are associated with use of mechanical ventilation, although some cases occur in absence of this risk.<sup>1</sup> Associated factors in nonventilated patients include outbreaks associated with bronchoscopy,<sup>2</sup> noninvasive ventilation,<sup>3</sup> and superinfection with bacteria after initial viral infection (for example, when pneumonia due to *Staphylococcus aureus* follows hospitalization for pneumonia due to influenza virus A).<sup>4</sup> Aspiration of oropharyngeal contents represents a hazard for hospitalized patients whether they are intubated or not.<sup>5</sup> Patients who have undergone surgery may develop pneumonia regardless of whether their intubation during surgery required further ventilator assistance.<sup>6</sup>

According to surveillance data from the National Nosocomial Infections Surveillance (NNIS) System, pneumonia is the second most common nosocomial (hospital-associated) infection in the intensive care unit (ICU), accounting for 27% of all nosocomial infections in ICUs, and 86% of all HAP was associated with mechanical ventilation<sup>7</sup> (Fig. 1). In the ICU, therefore, the epidemiology and microbiology associated with HAP closely resemble that for ventilator-associated pneumonia (VAP). Thus, the remainder of this article focuses mainly on epidemiology and microbiology of VAP.

VAP is defined as development of clinical signs and symptoms of pneumonia occurring more than 48 hours after intubation and mechanical ventilation.<sup>8</sup> VAP is associated with significant morbidity, hospital cost, and mortality.<sup>7,9</sup> VAP has been further categorized as early-onset (occurring within the first 4 days of mechanical ventilation) and late-onset (which develops 5 or more days after initiation of mechanical ventilation).<sup>10</sup> The causative organisms and prognosis differ in these two categories; however, this difference is also affected by the hospital stay prior to ICU admission.<sup>10,11</sup>

The pathogenesis of VAP requires bacterial colonization of the aerodigestive tract and the aspiration of contaminated secretions into the lower airways. Insertion of the endotracheal tube not only compromises the natural barrier between oropharynx and trachea, but may also facilitate the pooling and leakage of the contaminated secretions around the endotracheal tube cuff, and finally entry of bacteria into the lung.<sup>12</sup> Several other factors such as supine position, frequency of ventilator circuit change, tracheal suctioning, and contaminated respiratory care equipment are additional risk factors for aspiration of these contaminated secretions. The role of the gastrointestinal tract as a source of oropharyngeal and tracheal colonization remains controversial.<sup>13-15</sup> Several studies have shown a sequence of events leading to colonization from the stomach to the trachea, with increasing frequency in direct correlation to the gastric pH—27 to 45% of patients have primary colonization of the gastric juice and subsequent colonization of the tracheobronchial tree ~2 days later.<sup>16-19</sup> In addition, other studies have shown, by means of various diagnostic techniques, that the gastric juice of intubated patients is aspirated into the tracheobronchial tree within a few hours.<sup>20-23</sup> In contrast, some studies failed to show that the gastropulmonary route of infection is important for development of VAP.<sup>13,24,25</sup> For example, in a study by de Latorre et al, 19 of 72 patients developed tracheal colonization after pharyngeal or gastric colonization by the same organisms. In 10 of 12 patients who developed VAP, the microorganisms responsible had already colonized the trachea, but only 10 of the 21 responsible microorganisms isolated from VAP had previously colonized the pharynx or stomach.<sup>24</sup> Furthermore, the use of antimicrobial therapy to eliminate gastric organism reservoirs has generally failed to prevent VAP.<sup>26,27</sup> Thus, the relationship between VAP and tracheal, pharyngeal, and gastric colonization remains to be defined for intubated patients on mechanical ventilation.



**Figure 1** Nosocomial infection rates in the medical intensive care units (MICUs) in the United States. National Nosocomial Infections Surveillance Study data from 1992 to 1997 in 181,993 patients in 112 MICUs. (Adapted from Richards MJ, Edwards JR, Culver DM, Gaynes RP. Nosocomial infections in medical intensive care units in the United States. National Nosocomial Infection System. Crit Care Med 1999;27:887-892.)

Our understanding of VAP remains limited despite several studies describing different aspects of its epidemiology. The greatest limitation of available reports is the almost uniform reliance on nonspecific clinical and radiographic criteria to define cases of nosocomial pneumonia.<sup>28</sup> Unfortunately, these conventional criteria have been unable to reliably diagnose cases of nosocomial pneumonia that have been confirmed by autopsy, histopathology, or other more stringent diagnostic approaches. Moreover, even criteria for histological diagnosis of pneumonia may not be universally accepted.<sup>29–32</sup> Estimates of occurrence and of microbiology are hindered by these problems with diagnosis.

Currently, there is no well-accepted “gold standard” for diagnosis, but rather, there are a variety of diagnostic procedures with variable sensitivity and specificity.<sup>33,34</sup> The variability in diagnostic accuracy has fueled controversies for the last 2 decades on the role of invasive diagnostic techniques for establishing VAP. Bronchoscopy with the use of bronchoalveolar lavage (BAL) or protected specimen brush (PSB) has greater specificity than a clinical diagnosis.<sup>33,34</sup> Nonbronchoscopic methods, such as blinded BAL or quantitative endotracheal aspiration, with and without use of a clinical pulmonary infection score, are more specific than clinical diagnosis.<sup>33–35</sup> Invasive diagnostic techniques for bacteriological confirmation of suspected VAP are thought to have potential promise.<sup>36</sup> Regardless of the diagnostic method used, the American Thoracic Society, in a consensus statement, suggested empiric initial therapy based on the severity of the patient’s disease and the stage of onset, using antibiotics to cover certain pathogens in patients with specific risk factors.<sup>12</sup> This extensive use of empiric treatment hinders true classification of a patient as having pneumonia, interferes with assessment of the true microbiological picture, promotes selection of multiple drug-resistant pathogens, and increases hospital costs.

With these limitations in mind, this discussion will provide an update on epidemiological considerations on nosocomial pneumonia in intubated and mechanically ventilated patients. The issues discussed in this review include the incidence, mortality, morbidity, economic impact, microbiology, and risk factors.

## INCIDENCE

The incidence of VAP varies by type of ICU and among different critically ill patient populations. The data from NNIS and a similar study from Europe suggested that the majority of ICU infections are associated with mechanical ventilation.<sup>7,9</sup> Over a decade ago, the European Prevalence of Infection in Intensive Care (EPIC) study revealed that almost 50% of prevalent ICU infections were VAP.<sup>9</sup> Other studies have shown that VAP accounted for more than 50% of nosocomial infections in

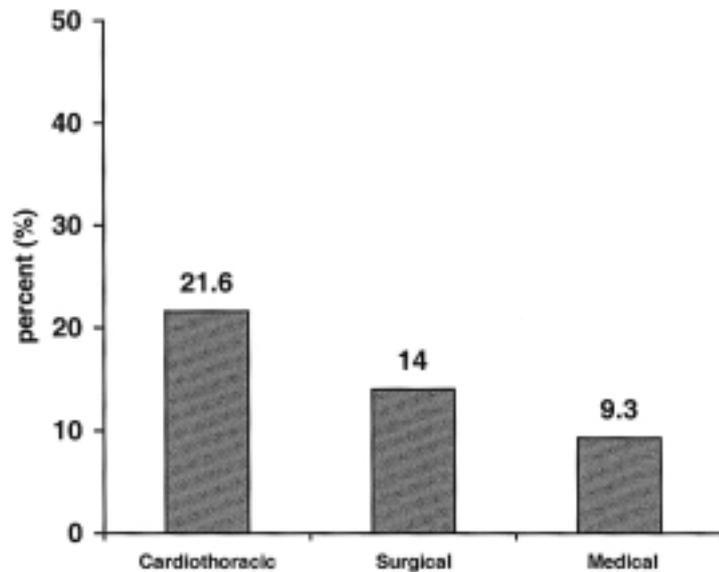
mechanically ventilated patients.<sup>37,38</sup> Rates of pneumonia are increased six- to 21-fold for intubated patients and show a further rise with the duration of mechanical ventilation.<sup>39–42</sup> The incidence of VAP ranges from six to 52 cases per 100 patients, depending upon the population studied.<sup>37,40,43–46</sup>

Crude rates of VAP are usually 1 to 3% per day of intubation and mechanical ventilation.<sup>47</sup> In a study by the Canadian Critical Care Trials Group, 177/1014 (17.5%) of patients developed VAP 9.0 ± 5.9 days after ICU admission (median 7 days, interquartile range 5, 10 days). The risk of developing VAP increased cumulatively, with an overall rate of 14.8 cases per 1000 ventilator days. These investigators found that the VAP rates were 3% per day for the first week of ventilation and decreased to 2% per day in the second week of ventilation and 1% per day in the third week and thereafter. This decreasing hazard suggested a high risk of early VAP and low risk of developing VAP in long-term residents of the ICU. In contrast, however, other studies have shown that the incremental risk of developing pneumonia is virtually constant throughout hospital stay and is around 1% per day of mechanical ventilation. For example, in a study by Fagon and coworkers, the actuarial risk of VAP was 6.5% at 10 days, 19% at 20 days, and 28% at 30 days of ventilation.<sup>48</sup>

In the NNIS study, rates of VAP varied from five cases per 1000 ventilator days in pediatric patients to 16 cases per 1000 ventilator days in patients with thermal injury and trauma.<sup>7</sup> Rates of VAP are generally higher in surgical ICU patients than in medical ICU patients.<sup>35,45</sup> In a study by Kollef,<sup>35</sup> VAP occurred more often in cardiothoracic patients (21.6%) compared with surgical patients (14%) and medical patients (9.3%) (Fig. 2).

The NNIS data analysis, which allows hospitals to compare the rates of nosocomial infections in their institution to national experience, is an important infection control tool. For example, infection control surveillance data for VAP from our institution, Crawford W. Long Hospital, a community hospital with academic affiliation in Atlanta, Georgia, has shown the rate of VAP to be 11 cases per 1000 ventilator days in cardiothoracic patients, seven cases per 1000 ventilator days in the surgical patients, and eight cases per 1000 ventilator days in the medical ICU patients over the last 1-year period. Comparing these rates with the NNIS standard (Fig. 3) assists in focusing the implementation of infection control measures in the two ICUs where local rates equal or exceed those reported by NNIS.

How does employing invasive diagnostic techniques change the epidemiological landscape of VAP? The impacts that BAL or PSB may have on these estimates of occurrence are unclear. In general, the incidence of VAP in studies in which invasive diagnostic methods are used is lower when compared with rates in those studies in which the diagnosis is made by clinical criteria alone (Fig. 4) (Table 1).<sup>35,44,47–57</sup>



**Figure 2** Incidence rates of different critically ill patient populations. Adapted from Kollef.<sup>35</sup>

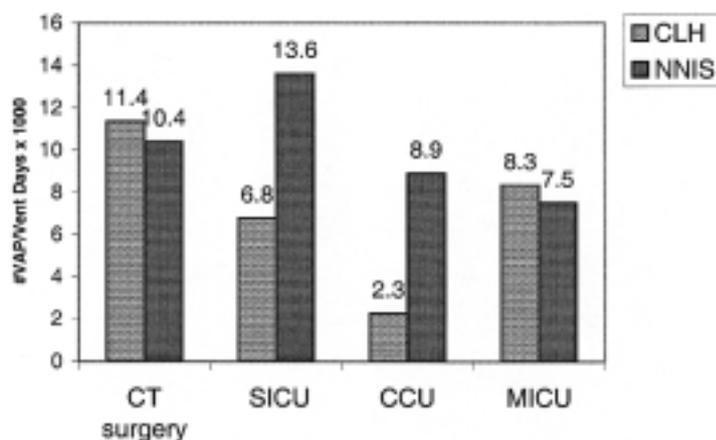
Based on the data presented, it appears that the incidence of VAP varies in different critically ill patient populations, and generally ranges from 9 to 20%, even with the use of stringent diagnostic criteria. Depending on the population studied, overall rates can also be expressed as about 10 to 15 cases per 1000 ventilator days for ICU patients. The cumulative risk of developing VAP is around 1% per day of mechanical ventilation.

### MORTALITY

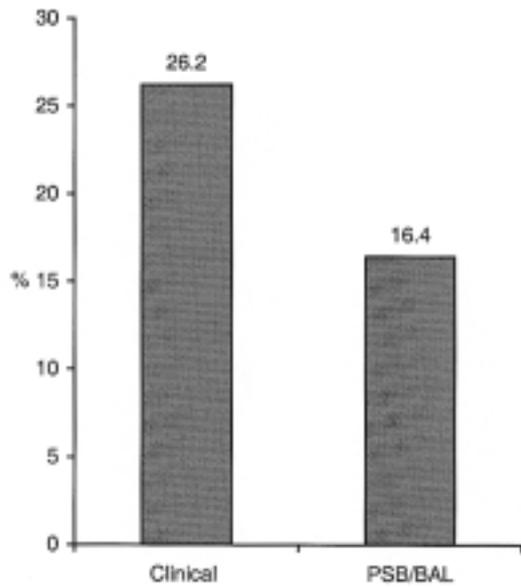
Nosocomial pneumonia in intubated and mechanically ventilated ICU patients is not only common, but is also associated with significant morbidity and mortality.<sup>8</sup> Crude mortality rates are generally higher in patients with VAP than in those without VAP.<sup>58,59</sup> Although urinary tract infections are the most common nosocomial infections, their attributable mortality rate is usually less than 4%. In comparison, the attributable mortality im-

pact of nosocomial pneumonia is much higher—up to 27%.<sup>58</sup> The mortality rate appears to be two- to 10-fold higher in patients with VAP than in those without VAP.<sup>40,44,53,60</sup> In a case-control study of 200 patients who died in the hospital, nosocomial pneumonia was a contributing factor in 60% of patients with infection-related mortality. In addition, a review of 1000 autopsy reports showed that pneumonia was associated with 7.5% of the deaths and was the most common nosocomial infection contributing to death.<sup>61,62</sup>

There are data to suggest that mortality rates associated with VAP are linked to the bacterial organism recovered. Mortality rates in patients with VAP associated with isolation of aerobic gram-negative bacilli (GNB), especially nonfermenters, are considerably higher than those for infections associated with recovery of other gram negative and gram-positive pathogens.<sup>48,63,64</sup> In one study, death rate attributed to *Pseudomonas aeruginosa* or *Acinetobacter* pneumonia was 87%,



**Figure 3** Ventilator-associated pneumonia (VAP) incidence rate at Crawford Long Hospital as compared with National Nosocomial Infections Surveillance (NNIS) System data over 1-year period. (Unpublished data from M Maher and J Steinberg.) CLH, Crawford Long Hospital; NNIS, National Nosocomial Infections Surveillance System; CT surgery, cardiothoracic surgery; SICU, surgical intensive care unit; CCU, coronary care unit; MICU, medical intensive care unit.



**Figure 4** Incidence rate (mean) of ventilator-associated pneumonia (VAP) based upon diagnostic criteria utilized: clinical alone (26.2%)<sup>35,44,49,50,52</sup> versus protected specimen brush/ bronchoalveolar lavage (PSB/BAL) (16.4%).<sup>48,54-57</sup>

compared with a death rate of 55% in pneumonias attributed to other organisms.<sup>48</sup> Similarly, in a study by Kollef and coworkers, patients with VAP associated with high-risk pathogens (*P. aeruginosa*, *Acinetobacter* spp., and *Stenotrophomonas maltophilia*) had a mortality rate (65%) that was significantly higher than that of patients with late onset VAP due to other organisms (31%) or patients without late onset VAP (37%).<sup>63</sup> In a study by Rello and coworkers, mortality due to VAP caused by

methicillin-resistant *Staphylococcus aureus* (MRSA) was found to be 86% as compared with 12% mortality in VAP associated with methicillin-sensitive strains of *Staphylococcus aureus* (MSSA).<sup>65</sup>

In contrast to crude mortality rates, Fagon et al demonstrated that the mortality rate attributable to VAP (“attributable mortality”), using a case-control methodology, was 27%, and the risk ratio for death was 2.0.<sup>58</sup> Again, the mortality rate increased to 43% when the causative agent was *P. aeruginosa* or *Acinetobacter* spp. (the risk ratio was 2.5).<sup>58</sup> Attributable mortality also depends on the type of patient population studied.<sup>35,66</sup> For example, in a study by the Canadian Critical Care Trials group, the attributable mortality was higher for medical patients than for surgical patients.<sup>66</sup>

There are data to suggest that mortality can be altered by the type of diagnostic technique utilized. A study by Fagon et al evaluated the efficacy of an invasive strategy utilizing both PSB and BAL compared with the traditional, noninvasive strategy.<sup>36</sup> The invasive management strategy was based on direct examination of bronchoscopic PSB samples or BAL samples and their quantitative cultures. The noninvasive (clinical) management strategy was based on clinical criteria, isolation of microorganisms by nonquantitative analysis of endotracheal aspirates, and clinical practice guidelines. These investigators found that those patients who received invasive management had reduced mortality at day 14 (16.2%) compared with patients who received clinical management (25.8%). Patients in the invasive strategy group also had decreased organ dysfunction, more antibiotic-free days, and less colonization or infection with candida species. It appeared that a reduction in

**Table 1** Incidence of Ventilator-Associated Pneumonia

Investigator	Year of Publication	Reference	Incidence (%) by Diagnostic Criteria		
			Clinical	Clinical-PSB/BAL	PSB/BAL
Craven	1986	44	21	—	—
Kerver	1987	49	67	—	—
Driks	1987	50	18	—	—
Salata	1987	51	—	41*	—
Langer	1989	52	9	—	—
Fagon	1989	48	—	—	12
Torres	1990	53	—	24	—
Kollef	1993	35	16	—	—
Baker	1996	54	—	—	5
Fagon	1996	55	—	—	28
Timsit	1996	56	—	—	15
Cook	1998	47	—	24	—
Tejada Artigas	2001	57	—	—	22

\*Clinical-autopsy diagnosis  
PSB, protected specimen brush; BAL, bronchoalveolar lavage.

mortality was conferred because of appropriate initial antibiotic selection based upon a more accurate diagnostic technique. Furthermore, using an invasive strategy resulted in the reduction of misclassification of "true" pneumonia.

Other studies suggest that mortality from VAP is positively influenced by correct diagnosis and appropriate initial antimicrobial treatment.<sup>67</sup> In contrast, several studies have shown increased fatality in VAP associated with inappropriate initial therapy.<sup>43,67-69</sup> For example, in a study by Alvarez-Lerma, the attributable mortality and number of patients who developed shock after the onset of VAP were significantly higher for patients with inappropriate initial antimicrobial therapy than for other patients<sup>67</sup> (Fig. 5).

### MORBIDITY AND ECONOMIC IMPACT

Several investigators have reported that nosocomial pneumonia increased the duration of hospitalization two- to threefold compared with patients without pneumonia.<sup>58,59</sup> In a study by Ibrahim et al, patients who developed VAP had significantly longer stays in the ICU (23.9 days vs 5.9 days) and in the hospital (38.6 days vs 15.2 days) compared with patients without VAP.<sup>59</sup> Also, in the study by Fagon and coworkers, the mean length of stay was 34 days with VAP and 21 days for matched ventilator-assisted patients without VAP.<sup>58</sup>

In a study by the Canadian Critical Care Trials group, patients with VAP stayed in the ICU 4.3 days longer and had a trend toward an increase in risk of death.<sup>66</sup> The attributable ICU length of stay was longer for medical than surgical patients (6.5 versus 0.7 days,  $p < 0.004$ ), and for patients thought to be infected with "high risk" organisms (*Pseudomonas* species, *Acinetobacter*, *Stenotrophomonas*, and MRSA) as compared with "low risk" organisms (all others) (9.1 versus 2.9 days).

Although more specific data are needed, hospital costs appear to be dramatically increased in survivors of nosocomial pneumonia. A precise evaluation of such

costs associated with VAP is difficult, as it depends on a wide variety of factors that differ from one hospital to another, one country to another, and so forth. The average excess hospital charges for nosocomial pneumonia was estimated to be US\$1255 per patient in 1982 in a study by Pinner and coworkers,<sup>70</sup> and US\$2863 per patient in 1985 in another study by Beyt and coworkers.<sup>71</sup> A study by Croce and coworkers in a trauma ICU suggested that discontinuing antibiotics after negative bronchoscopic cultures could lead to savings of more than US\$1700 per patient with suspected VAP.<sup>72</sup>

### MICROBIOLOGY

The bacteria recovered from patients with VAP may vary by the method of diagnosis and population studied. About half of VAP cases are polymicrobial,<sup>8</sup> so it is difficult to define the role of individual microorganisms in the genesis of this infection. Nosocomial pathogens may be part of the host's endogenous flora or may be acquired from other patients, staff, devices, or the hospital environment. Early-onset VAP, occurring during the first 4 days of mechanical ventilation, is often associated with recovery of bacteria such as *Streptococcus pneumoniae*, *Hemophilus influenzae*, *Moraxella catarrhalis*, or (uncommonly) anaerobes, especially if the patient has not previously received antibiotics. By comparison, bacteria associated with late-onset VAP, occurring  $> 4$  days after admission, more commonly are *Pseudomonas aeruginosa*, *Acinetobacter* or *Enterobacter* spp., or MRSA (Fig. 6). Many of the recovered strains of GNB such as *P. aeruginosa* and *Acinetobacter* spp., and of gram-positive cocci such as *S. aureus*, are resistant to many antibiotics.

*S. aureus* is isolated in approximately 20 to 40% of cases and is particularly common in persons with intravenous drug abuse, neurological disease, thermal injury, or wound infection, and in patients who have received prior antibiotic therapy or have had a prolonged stay in the ICU. Compared to patients with VAP asso-

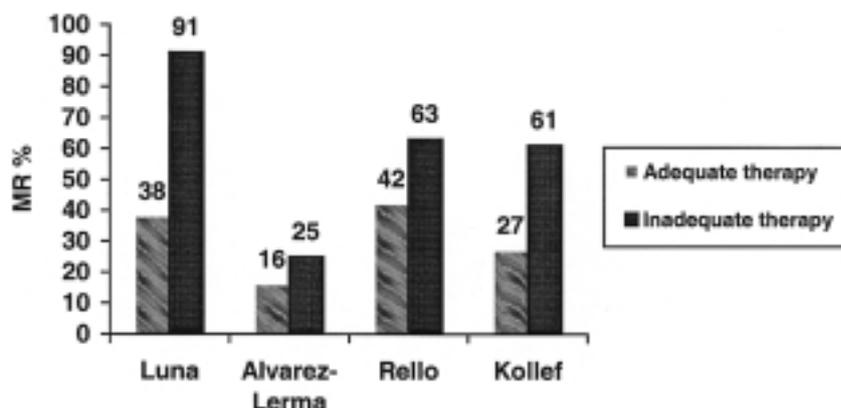
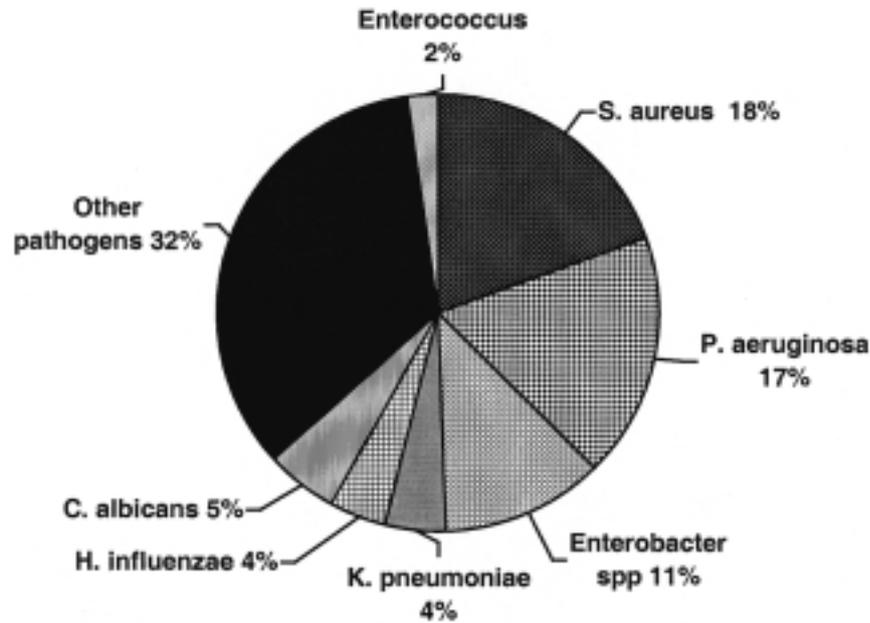


Figure 5 Effect of adequacy of initial antimicrobial therapy on mortality rates for ventilator-associated pneumonia (VAP).<sup>43,67-69</sup>



**Figure 6** Pathogens most frequently associated with nosocomial pneumonia in the intensive care unit. [National Nosocomial Infections Surveillance (NNIS) System report. Data summary from January 1990–May 1999, issued June 1999. Am J Infect Control 1999;27:520–532.]

ciated with MSSA, those whose cases are associated with MRSA are often older and significantly more likely to have had previous chronic lung disease, antibiotic therapy, steroid therapy, and > 6 days of mechanical ventilation. Bacteremia, shock, and mortality are usually higher in the MRSA group.<sup>65</sup>

As already noted, increased rates of polymicrobial infection in VAP have been shown in several studies.<sup>48,73–75</sup> In a study by Fagon et al of 52 consecutive cases of VAP diagnosed by PSB, 40% of the cases were polymicrobial.<sup>48</sup> Aerobic GNB, including *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* spp., *Serratia* spp., *P. aeruginosa*, and *Acinetobacter* spp., are most frequently isolated, particularly in patients with late-onset disease or a serious underlying disease.<sup>48,73–75</sup>

High rates of *H. influenzae*, *S. pneumoniae*, MSSA, or susceptible *Enterobacteriaceae* were constantly found in early-onset VAP, whereas recovery of *P. aeruginosa*, *Acinetobacter* spp., MRSA, and multiresistant GNB was significantly more frequent in late-onset VAP.<sup>12,76,77</sup> This different distribution between early- and late-onset VAP is linked to frequent administration of prior antimicrobial therapy before recognition of late-onset VAP.<sup>78</sup> The paradigm of early-onset and late-onset VAP loses its significance in patients who have been on broad spectrum antibiotics prior to intubation and mechanical ventilation.

Potential pathogens like anaerobes, fungi, *Legionella*, viruses, and even opportunistic pathogens like *Pneumocystis carinii* are not commonly reported in VAP.<sup>79–82</sup> However, it is likely that some of these

agents are underreported due to difficulties involved in the diagnostic techniques used to identify their presence. The probability of recovering anaerobes is particularly high in patients with aspiration and orotracheal intubation.<sup>79</sup>

Interpreting the clinical relevance of a positive culture for fungi poses a problem in mechanically ventilated patients. More frequently, yeasts are isolated from the respiratory tract in the apparent absence of disease. *Candida* species are very commonly isolated. For example, one study looked at the relevance of isolating *Candida* spp. from 25 nonneutropenic patients who had been on mechanical ventilation for at least 72 hours.<sup>82</sup> Multiple cultures and biopsy specimens were collected by bronchoscopic techniques soon after the patient's death. Only two patients had evidence of invasive pneumonia, as demonstrated by histologic examination of 10 patients who had at least one biopsy specimen positive for *Candida* spp. Many of the bronchoscopic procedures yielded positive cultures for *Candida* spp. but did not contribute to diagnosis of invasive disease. Based on this study, use of bronchoscopic and nonbronchoscopic techniques currently appears to be insufficient for the diagnosis of *Candida* pneumonia.

## RISK FACTORS

Risk factors that are likely to increase the frequency of aspiration, increase the quantity of the microorganism inoculated, impair local respiratory tract defenses, or impair systemic immunity have been demonstrated in

**Table 2 Risk Factors for Ventilator-Associated Pneumonia**

	Modifiable	Nonmodifiable
<i>Host</i>		Increased age Cardiorespiratory disease Chronic obstructive pulmonary disease Adult respiratory distress syndrome Coma Neurosurgery Head trauma, multiple trauma Burns Organ system failure
<i>Ventilator and Airway Management</i>	Duration of mechanical ventilation Intracuff pressure < 20 cm H <sub>2</sub> O Reintubation and Tracheostomy 24-hour circuit changes, PEEP	
<i>General ICU Management or Intervention</i>	Enteral nutrition Supine positioning Large-volume gastric aspiration Histamine-2-receptor antagonists or antacids Paralytic agents Antibiotics Transport out of the ICU	

ICU, intensive care unit; PEEP, positive end-expiratory pressure.

several studies of VAP.<sup>11,35,37,39,44,47,53,83-85</sup> Factors that might be expected to increase the risk of nosocomial VAP can be divided into two categories: modifiable and nonmodifiable (Table 2). Modifiable risk factors include duration of mechanical ventilation, large-volume gastric aspiration, alterations in gastric pH, histamine-type 2 receptor blocker or antacid therapy, ventilator circuit changes at 24-hour intervals, positive end-expiratory pressure, reintubation or self-extubation, and tracheostomy, whereas nonmodifiable risk factors include age, chronic obstructive pulmonary disease, severe head trauma, multiple trauma, and fall-winter season.

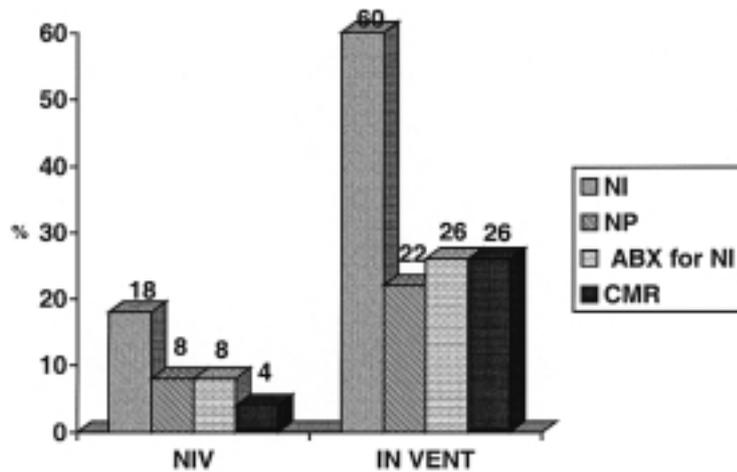
Alteration in gastric pH has been directly associated with gastric colonization by bacteria and subsequent development of VAP. Several studies have shown lower rates for VAP in patients who received sucralfate, a gastroprotective agent, rather than for agents that neutralize gastric secretions (antacids) or block gastric acid secretion (H<sub>2</sub> blockers).<sup>50,85-88</sup> In a randomized study of 244 mechanically ventilated patients that compared stress ulcer prophylaxis with antacids, ranitidine, or sucralfate, late-onset VAP was observed in only 5% of the patients in the sucralfate group as compared with 16% and 21% in patients who received antacids or ranitidine, respectively.<sup>86</sup> Patients in the sucralfate group also had a lower median gastric pH and less frequent gastric colonization compared with the other groups. Molecular typing showed that 84% of the patients with late-onset, gram-negative bacterial pneumonia had gastric colonization with the same strain before develop-

ment of VAP. Other investigations have suggested that sucralfate may not be associated with a lower incidence of VAP.<sup>89,90</sup> In fact, Markowicz et al demonstrated that the use and duration of sucralfate exposure were associated with an increased risk of VAP in a selected acute respiratory distress syndrome (ARDS) population.<sup>90</sup>

Prolonged intubation has been associated with persistent tracheal colonization and subsequent pneumonia. The role of early tracheostomy has been controversial in prevention of VAP, with some studies showing benefit<sup>91-93</sup> and other studies failing to show any benefit.<sup>94-96</sup> Furthermore, the implementation of noninvasive ventilation has been associated with decreased rates of VAP<sup>3</sup> (Fig. 7).

## SUMMARY

HAP is the second most common nosocomial infection in the critically ill patient and is associated with the greatest mortality and increased morbidity and cost of care. The major risk factor for the development of HAP is the occurrence of intubation and mechanical ventilation. VAP is the most common cause of nosocomial infection-related mortality. The incidence of VAP varies among different critically ill patient populations. The pathogens causing VAP are most likely to be multiresistant organisms, making empiric antibiotic choices potentially more problematic. Mortality associated with VAP is influenced by the virulence of the causative pathogens, inappropriate initial antimicrobial therapy,



**Figure 7** Association of noninvasive ventilation with nosocomial pneumonia survival in critically ill patients. Adapted from Girou et al.<sup>3</sup> NIV, noninvasive ventilation; inv vent, invasive ventilation; NI, nosocomial infection; NP, nosocomial pneumonia; ABX, antibiotics; CMR, crude mortality rate.

and host defense mechanisms. VAP is associated with increased ICU stay, hospital stay, and increased cost of care. Risk factors for developing VAP are diverse and include some modifiable risk factors. Targeting the modifiable risk factors may decrease the incidence and mortality related to this common ICU problem. In addition, it may also have an economic impact on the healthcare of the patient. Additional research is needed to further evaluate new preventive strategies and health care-related issues for VAP as well as for other sources of HAP.

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