

# Prevention of Postoperative Pneumonia

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**H**ospital-acquired pneumonia (HAP) is defined as pneumonia that develops 48 hours or more after hospital admission, which was not incubating at the time of admission (Table 1).

Ventilator-associated pneumonia (VAP) refers to pneumonia that develops more than 48 to 72 hours after endotracheal intubation. Postoperative pneumonia is HAP or VAP that occurs in a postoperative patient.

HAP is the second most common nosocomial infection in the United States after urinary tract infection but is the leading cause of mortality attributed to nosocomial infection.<sup>1</sup> Furthermore, HAP prolongs hospital stays for an average of 7 to 9 days and adds excess medical costs ranging from \$12,000 to \$40,000 per patient.<sup>2-4</sup> "Attributable mortality" from HAP is estimated to be between 33% and 50%.<sup>5-7</sup>

There is convincing evidence that specific interventions can be employed to prevent HAP/VAP and postoperative pneumonia. The higher morbidity, hospital mortality, and excess hospital costs attributable to these infections should make implementation of preventive strategies a priority among hospitals. Mandatory education programs for health care workers caring for postoperative patients, adherence to infection-control practices, and surveillance of local nosocomial infection rates are all important strategies for effective prevention of postoperative pneumonia. This article, which is the second in a series addressing recent evidence-based recommendations for improving the quality and safety of surgical care, reviews the etiology, pathogenesis, and prevention of postoperative pneumonia. In addition, an illustrative case is provided to demonstrate the approach to evaluating and treating a patient with postoperative pneumonia.

## ETIOLOGY AND PATHOGENESIS OF POSTOPERATIVE PNEUMONIA

### Etiology

Postoperative pneumonia is typically caused by bacteria and may be polymicrobial, especially in patients with acute respiratory distress syndrome (ARDS).<sup>8</sup> The majority of infections are caused by gram-negative aerobes; organisms commonly isolated include *Pseudomo-*

## TAKE HOME POINTS

- Postoperative pneumonia is defined as hospital-acquired or ventilator-associated pneumonia in a postsurgical patient.
- Postoperative pneumonia is usually caused by bacteria and may be polymicrobial. Most infections are caused by gram-negative aerobes.
- Three pathogenic mechanisms are responsible for the development of postoperative pneumonia: (1) colonization of the aerodigestive tract with pathogenic bacteria; (2) aspiration of contaminated secretions; and (3) impaired host defenses due to critical illness and its therapy or other nonmodifiable host factors.
- Prophylactic approaches may be nonpharmacologic and pharmacologic. In general, nonpharmacologic interventions are less expensive and easier to apply than pharmacologic interventions. Preventive measures should be tailored to the patient's specific risk factors for developing pneumonia.

*nas aeruginosa*, *Enterobacter* species, *Klebsiella pneumoniae*, *Acinetobacter* species, *Serratia* and *Citrobacter* species, and *Stenotrophomonas* species.<sup>9,10</sup> Methicillin-resistant *Staphylococcus aureus* (MRSA) is the predominant gram-positive pathogen accounting for nosocomial pneumonia in the United States<sup>11</sup> and is more common in patients with diabetes mellitus or head trauma.<sup>12</sup> Anaerobic bacteria rarely cause HAP/VAP despite being commonly associated with aspiration pneumonia in nonintubated patients.<sup>13</sup> Fungal and viral pathogens are very rare

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**Table I.** Clinical Definitions of Pneumonia

Category	Definition
Community-acquired pneumonia	Patient with a first positive bacterial culture obtained $\leq 48$ hr after hospital admission and lacking risk factors for health care–associated pneumonia
Health care–associated pneumonia	Patient with a first positive bacterial culture obtained $\leq 48$ hr after hospital admission and any of the following: <ul style="list-style-type: none"> <li>• Admission source indicates transfer from another health care facility</li> <li>• Receiving hemodialysis, wound, or infusion therapy as an outpatient</li> <li>• Prior hospitalization for <math>\geq 3</math> days within past 90 days</li> <li>• Immunocompromised state due to underlying disease or therapy</li> </ul>
Hospital-acquired pneumonia (HAP)	Patient with a first positive bacterial culture obtained $> 48$ hr after hospital admission
Ventilator-associated pneumonia (VAP)	Mechanically ventilated patient with a first positive bacterial culture obtained $> 48$ hr after hospital admission or tracheal intubation, whichever occurred first
Postoperative pneumonia	HAP or VAP occurring in a postoperative patient

NOTE: Clinical criteria for pneumonia include new or progressive lung infiltrate and at least 2 of the following: hyper- or hypothermia, elevated white blood cell count, purulent tracheal secretions or sputum, and worsening oxygenation.

causes of HAP/VAP in immunocompetent hosts.<sup>14</sup> Multidrug-resistant pathogens are an increasing problem, and prevalence varies by patient population and by hospital and type of intensive care unit (ICU), emphasizing the need for local surveillance programs.<sup>15</sup>

### Pathogenesis

Postoperative pneumonia risk is influenced by a number of risk factors that become relevant in hosts who are exposed to a nosocomial environment. Many of the risk factors are modifiable, and awareness of these factors as well as attempts to limit their occurrence is paramount to reducing HAP/VAP rates. All risk factors can be grouped into 1 of 3 pathogenetic mechanisms: colonization of the aerodigestive tract with pathogenic bacteria, aspiration of contaminated secretions, and impaired host defenses due to critical illness and its therapies or other nonmodifiable host factors.<sup>16</sup> Duration of exposure to the health care environment and prior antibiotic exposure also are important factors in the development of nosocomial pneumonia, including postoperative pneumonia.

Colonization of the aerodigestive tract by pathogens

is a prerequisite for postoperative pneumonia to develop.<sup>17</sup> The pathogens replace normal host flora for several reasons, including broad-spectrum antibiotic use, stress ulcer prophylaxis (which modifies the stomach pH and environment and predisposes to gastric colonization), and the presence of medical devices in the aerodigestive tract (eg, endotracheal and nasogastric tubes). The host airway becomes desiccated, and the mucociliary elevator system is bypassed or becomes ineffectual. The pathogens are able to adhere to epithelial cells in the upper and lower airway and flourish in this environment.<sup>18</sup> They release microbial products that contribute to biofilm formation and a continuous source of pathogenic bacteria, which can gain access to the tracheobronchial tree via aspiration of infected secretions with each cycle of the ventilator.<sup>19</sup>

Aspiration of secretions is ubiquitous in an environment where the glottis is bypassed. In addition, the supine position, gastric overdistention, and enteral feedings all contribute to aspiration risk.<sup>20</sup> Nebulization devices and ventilator circuits that become contaminated by purulent secretions enable pathogens to be aerosolized into the tracheobronchial tree with the help of positive pressure ventilation. Frequent patient transportation, inadequate subglottic suctioning, and low endotracheal tube cuff pressure may also contribute to VAP development.

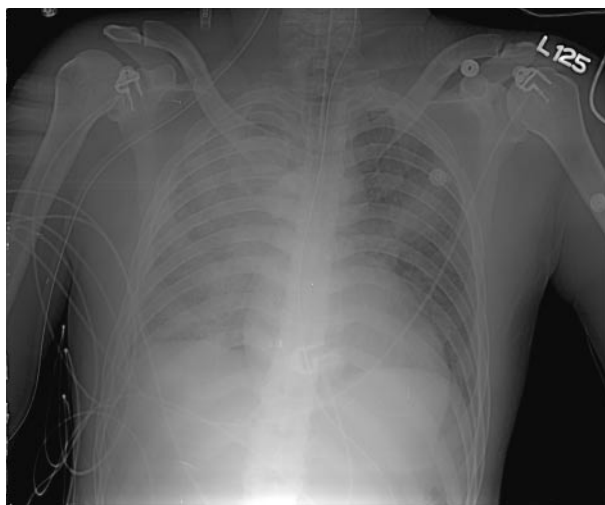
The patient may also exhibit a number of nonmodifiable risk factors that uniquely predispose to HAP/VAP by lowering host defense mechanisms. These include male sex, age greater than 60 years, ARDS, multisystem organ failure, coma, chronic obstructive pulmonary disease (COPD), tracheostomy placement, reintubation, neurosurgery, and head trauma with intracranial pressure monitoring.<sup>21</sup>

### APPROACH TO SUSPECTED POSTOPERATIVE PNEUMONIA

#### Case Presentation

A 68-year-old man with a history of adult-onset diabetes, congestive heart failure (ejection fraction, 32%), and hypertension is admitted to the hospital with abdominal pain. The patient has a 55 pack-year smoking history and admits to occasional alcohol ingestion. He was hospitalized 4 months earlier for pulmonary edema related to his underlying heart failure.

On hospital admission, the patient is found to have laboratory and radiographic evidence consistent with ischemic colitis and subsequently undergoes a complete colectomy. The preoperative chest radiograph showed cardiomegaly, with no acute pulmonary process. The surgical procedure was uneventful, and perioperative laboratory



**Figure 1.** Chest radiograph demonstrating a new pulmonary infiltrate involving the right lower and upper lobes.

evaluation showed no evidence of myocardial ischemia. Unfortunately, the patient does not liberate from mechanical ventilation due to poor respiratory efforts associated with spontaneous breathing trials. On the third hospital day, the patient's temperature is 38.5°C and white blood cell count is 16,000/ $\mu$ L, and a chest radiograph shows evidence of new pulmonary infiltrates (**Figure 1**).

• **What is the differential diagnosis for this patient's new pulmonary infiltrates?**

Postoperative pneumonia usually is suspected when a patient develops a new or progressive pulmonary infiltrate with fever, leukocytosis, and purulent tracheobronchial secretions.<sup>2,22</sup> However, these clinical criteria are nonspecific for the diagnosis of postoperative pneumonia, and therefore a number of noninfectious causes of fever and pulmonary infiltrates also must be considered (**Table 2**).

Several studies have demonstrated the limitations of using clinical and radiographic parameters alone for establishing the diagnosis of HAP/VAP.<sup>23,24</sup> Autopsy results in a series of patients with acute lung injury demonstrated that clinical criteria alone led to an incorrect diagnosis of VAP in 29% of clinically suspected cases.<sup>23</sup> In another study, the accuracy of clinical judgment in formulating treatment plans for patients with suspected VAP was compared with quantitative lower airway cultures obtained by bronchoscopy; clinical judgments about the presence of VAP were correct only 62% of the time when compared with culture specimens, and only 33% of the treatment plans based on clinical judgment alone were deemed to be effective.<sup>24</sup> Most clinical

**Table 2.** Noninfectious Causes of Fever and Pulmonary Infiltrates Mimicking Postoperative Pneumonia

Chemical aspiration without infection
Atelectasis
Pulmonary embolism
Acute respiratory distress syndrome
Pulmonary hemorrhage
Lung contusion
Infiltrative tumor
Radiation pneumonitis
Drug reaction
Bronchiolitis obliterans organizing pneumonia

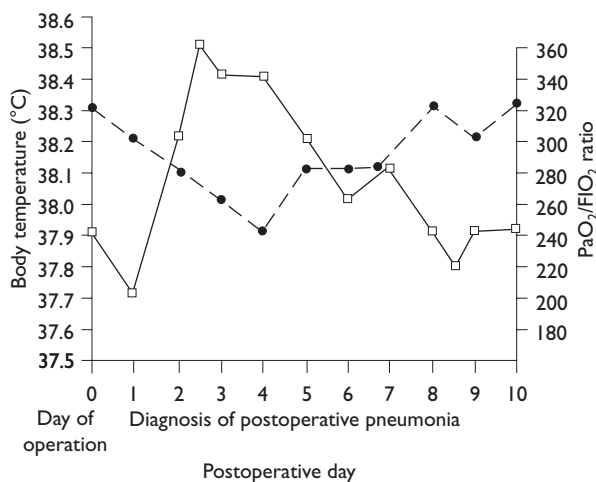
errors resulted in the unnecessary prescription of antibiotics, failure to diagnose VAP accurately, failure to treat all organisms causing polymicrobial VAP, and failure to treat VAP due to antibiotic-resistant pathogens.<sup>24</sup>

Not all studies, however, have concluded that clinical diagnosis of VAP is markedly inferior to other methods. For example, a study of 25 deceased mechanically ventilated patients found that the presence of radiographic infiltrates and 2 of 3 clinical criteria (fever, leukocytosis, purulent secretions) had a sensitivity of 69% and a specificity of 75%, with the combination of histologic evidence of pneumonia and positive postmortem cultures as the gold standard.<sup>25</sup>

• **How is the diagnosis of postoperative pneumonia in a ventilated patient confirmed?**

Lower respiratory sampling methods including bronchoalveolar lavage (BAL) and protected specimen brush can more accurately confirm the presence or absence of pneumonia and facilitate the modification of empirically prescribed antibiotic therapy. The airway of mechanically ventilated patients is commonly colonized with potentially pathogenic bacteria. Consequently, secretions obtained from an endotracheal or tracheostomy tube cannot consistently differentiate between upper airway colonization and lower respiratory tract infection.<sup>2</sup> Sampling methods that minimize contamination from the upper airway (eg, bronchoscopic or blind catheter BAL and brushing) offer the advantage of establishing a more precise microbiologic diagnosis of VAP to guide subsequent antimicrobial choices.<sup>26</sup>

The use of BAL for the microbiologic diagnosis of VAP appears to be associated with greater confidence among clinicians that the culture results actually reflect the presence or absence of VAP and the etiologic agents of infection.<sup>2</sup> The main apparent advantage



**Figure 2.** Graph of case patient's body temperature (solid line) and ratio of partial pressure of arterial oxygen to fraction of inspired oxygen (PaO<sub>2</sub>/FIO<sub>2</sub> ratio; dotted line) following surgery.

associated with obtaining properly collected and processed lower respiratory tract samples in patients with suspected VAP is to enable more specific modification of initial empiric antibiotic regimens. This has been demonstrated for both medical and surgical patients. A recent meta-analysis of 4 randomized trials comparing lower respiratory tract sampling with quantitative cultures to clinical criteria for the diagnosis of VAP found that initial antibiotic therapy was almost 3 times more likely to be modified among patients randomized to the former group.<sup>27</sup>

• **What is the next step in this patient's management?**

In patients with clinically suspected postoperative pneumonia, respiratory specimens for microbiologic processing should be obtained followed by timely administration of an empiric antibiotic regimen selected according to the presence or absence of risk factors for infection with antibiotic-resistant bacteria. Initial administration of an appropriate antibiotic (ie, to which the pathogens are sensitive based on in vitro susceptibility testing) is one of the primary determinants of hospital outcome over which the clinician has control. Use of an initial antibiotic regimen that is inappropriate for the microorganism(s) causing nosocomial pneumonia of all types has been associated with a significantly greater risk of death.<sup>28</sup> These findings strongly suggest that initial antimicrobial therapy for postoperative pneumonia should be selected according to the presence or absence of risk factors for health care-associated infection (eg, recent hospitalization, admission from a nursing home, current hemodialysis, immunocompromised state, late-onset in-

fection, or prior antibiotic exposure during the current hospitalization).<sup>29</sup> An initial combination antimicrobial regimen should be prescribed in patients with suspected postoperative pneumonia having these risk factors in order to appropriately treat potentially antibiotic-resistant pathogens including MRSA and *P. aeruginosa*.<sup>29</sup>

The subsequent availability of microorganism identification and antibiotic susceptibility testing allows for antimicrobial de-escalation to occur when appropriate. Antimicrobial de-escalation promotes narrowing of the initial antimicrobial regimen and use of the shortest duration of antibiotic therapy that is clinically effective. It is important that hospitals employ their own local microbiologic data in formulating appropriate initial antibiotic regimens for HAP/VAP.

**Case Conclusion**

The patient undergoes BAL followed by administration of broad-spectrum antimicrobial agents with coverage for MRSA and potentially resistant gram-negative bacteria. The Gram stain of the BAL specimen shows a predominance of neutrophils and gram-positive bacteria in clusters that subsequently are identified as MRSA. The patient is treated for MRSA pneumonia (linezolid 600 mg twice daily), and the antibiotic regimen is continued for 8 days. The patient's response to therapy is shown in **Figure 2**. Two sets of blood cultures drawn prior to beginning antibiotic therapy return negative for bacterial or fungal growth. The patient continues to do poorly with spontaneous breathing trials, and a percutaneous tracheostomy tube is placed on day 8 of mechanical ventilation. The patient is liberated from the ventilator on day 17 of mechanical ventilation and is discharged to a nursing facility 21 days following hospital admission. The patient's prolonged need for mechanical ventilation and hospitalization following surgery was attributed to postoperative pneumonia due to MRSA.

**PREVENTION OF POSTOPERATIVE PNEUMONIA**  
**Grading Risk and General Preventive Strategies**

Postoperative pulmonary complications are common following both thoracic and nonthoracic operations. To optimize the application of preventive strategies for postoperative pneumonia, clinicians must be able to identify patients at risk for this complication and its variants. Arozullah and coworkers<sup>30</sup> developed and validated a preoperative risk index for the prediction of postoperative pneumonia; the identified risk factors and their designated point values are shown in **Table 3**. The investigators then divided patients into 5 risk categories based on their cumulative risk scores

(ie, 1 = 0–15 points, 2 = 16–25 points, 3 = 26–40 points, 4 = 41–55 points, 5 = > 55 points); the incidence of postoperative pneumonia rose from 1% at a risk score of 1 to 15.3% at a risk score of 5 (Table 4). The implication of these data is that patients at higher risk should receive more aggressive and dedicated interventions aimed at the prevention of this complication.

In addition to the specific preventive interventions detailed below, a general plan for the prevention of postoperative pulmonary complications should be in place. This is important because patients with postoperative pulmonary complications spend more time in the hospital and more time on mechanical ventilation, 2 factors that increase their risk for postoperative pneumonia. A recent systematic review identified postoperative lung expansion maneuvers, selective nasogastric decompression, short-acting neuromuscular blockade, and laparoscopic (versus open) operation as interventions supported by the available medical literature to prevent postoperative pulmonary complications (Table 5).<sup>31</sup> The evidence for other interventions including smoking cessation, intraoperative neuraxial blockade, postoperative epidural analgesia, immunomodulating enteral nutrition, routine total parenteral or enteral nutrition, and right-heart catheterization was either conflicting or did not support the use of these specific interventions.<sup>31</sup>

### Specific Preventive Strategies

In 2005, the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) published guidelines for the management of adults with HAP, VAP, and health care–associated pneumonia.<sup>29</sup> The ATS/IDSA guidelines used an evidence-based grading system to rank recommendations, which was defined as follows: level I (high) evidence (evidence from well-conducted, randomized clinical trials); level II (moderate) evidence (evidence from well-designed, controlled trials without randomization, including cohort studies, patient series, and case-control studies; also, any large case series in which systematic analysis of disease patterns and/or microbial etiology was conducted, as well as reports of new therapies that were not collected in a randomized fashion); and level III (low) evidence (evidence from case studies and expert opinion). The following discussion summarizes ATS/IDSA recommendations regarding interventions that target modifiable risk factors for HAP.

**Nonpharmacologic interventions.** Nonpharmacologic approaches to the prevention of postoperative pneumonia (Table 6) are generally less expensive and easier to apply than pharmacologic interventions (Table 7). Most nonpharmacologic interventions tar-

**Table 3.** Postoperative Pneumonia Risk Index

Preoperative Risk Factor	Point Value
Type of surgery	
Abdominal aortic aneurysm repair	15
Thoracic	14
Upper abdominal	10
Neck	8
Neurosurgery	8
Vascular	3
Age	
≥ 80 yr	17
70–79 yr	13
60–69 yr	9
50–59 yr	4
Functional status	
Totally dependent	10
Partially dependent	6
Weight loss > 10% in past 6 mo	7
History of chronic obstructive pulmonary disease	5
General anesthesia	4
Impaired sensorium	4
History of cerebrovascular accident	4
Blood urea nitrogen level	
< 2.86 mmol/L (< 8 mg/dL)	4
7.85–10.7 mmol/L (22–30 mg/dL)	2
> 10.7 mmol/L (> 30 mg/dL)	3
Transfusion > 4 U	3
Emergency surgery	3
Steroid use for chronic condition	3
Current smoker within 1 yr	3
Alcohol intake > 2 drinks/day in past 2 wk	2

Adapted with permission from Arozullah AM, Khuri SF, Henderson WG. Development and validation of a multifactorial risk index for predicting postoperative pneumonia after major noncardiac surgery. *Ann Intern Med* 2001;135:853.

get the prevention of aspiration events. Basic infection control measures, which include hand disinfection and local microbiologic surveillance, are important to this approach. Pathogens causing postoperative pneumonia are ubiquitous in health care settings, and transmission of these bacteria to patients often occurs via health care workers, whose hands become contaminated or transiently colonized with the bacteria. Procedures such as tracheal suctioning and manipulation of ventilator circuits increase the opportunity for cross-contamination with these pathogens. This risk can be reduced by using aseptic technique and eliminating pathogens from the hands of personnel.<sup>32</sup> Alcohol-based foams and lotions can increase compliance with

**Table 4.** Distribution of Postoperative Pneumonia Risk Index Scores in Patients in the Development and Validation Cohorts

Variable	Risk Class				
	1 (0–15 points)	2 (16–25 points)	3 (26–40 points)	4 (41–55 points)	5 (> 55 points)
Development cohort patients, n (%)	69,333 (43)	55,757 (35)	32,103 (20)	3517 (2)	95 (0.1)
Average predicted probability of postoperative pneumonia in development cohort patients (95% CI), %	0.24 (0.24–0.25)	1.20 (1.19–1.20)	4.0 (3.98–4.01)	9.4 (9.34–9.42)	15.3 (15.1–15.5)
Rate of postoperative pneumonia in development cohort patients, %	0.24	1.19	4.0	9.4	15.8
Rate of postoperative pneumonia in validation cohort patients, %	0.24	1.18	4.6	10.8	15.9

Adapted with permission from Arozullah AM, Khuri SF, Henderson WG. Development and validation of a multifactorial risk index for predicting postoperative pneumonia after major noncardiac surgery. *Ann Intern Med* 2001;135:853.

CI = confidence interval.

hand disinfection between patient contacts and have been shown to allow hand disinfection to occur more efficiently.<sup>33,34</sup> Surveillance of ICU infections allows staff to take appropriate infection control measures for multidrug-resistant pathogens and aids in selecting empiric therapy in cases of suspected postoperative pneumonia.

*Avoid tracheal intubation/use noninvasive positive-pressure ventilation (level I evidence).* The critical roles that the endotracheal tube and ventilator circuit play in the pathogenesis of HAP/VAP emphasize the need for avoiding unnecessary intubations. Noninvasive positive-pressure ventilation (NIPPV) using a face mask can be an effective ventilatory mode in appropriately selected patients likely to benefit from this approach. The beneficial effects of NIPPV on the development of HAP/VAP and on survival have been established in randomized trials involving patients with acute exacerbations of COPD or acute lung injury with hypoxic respiratory failure and in immunosuppressed patients with pulmonary infiltrates, fever, and respiratory failure.<sup>35–40</sup> All attempts to avoid reintubation should be considered, as this is an important risk factor for developing VAP.<sup>41</sup>

*Shorten duration of mechanical ventilation (level II evidence).* The duration of mechanical ventilation is an important risk factor for the development of HAP/VAP. The risk of HAP/VAP is not constant over the time of ventilation and, in a large cohort study, was estimated to be 3% per day in the first week, 2% per day in the second week, and 1% per day in the third week and beyond.<sup>42</sup> Strategies that reduce the duration of mechanical ventilation have the potential to reduce HAP/VAP rates significantly. Sedation protocols that focus on minimizing sedative administration<sup>43,44</sup> and protocolized weaning of mechanical ventilation<sup>45,46</sup> are

good examples of such strategies, as they shorten the patient's exposure to the endotracheal tube and risk for aspiration of contaminated secretions.

*Maintain appropriate ICU staff levels (level II evidence).* Adequate nursing and respiratory therapy staffing may influence duration of stay of patients in ICUs and the development of HAP/VAP, presumably due to maintenance of infection control standards.<sup>47,48</sup> Lapses in basic infection control measures (eg, handwashing, patient isolation for multidrug-resistant pathogens) are more likely with increased workloads for registered nurses and increased reliance on less-trained health care personnel to deliver care.<sup>49–52</sup> The duration of mechanical ventilation can also be reduced by appropriate staffing levels.<sup>45,52</sup> Mandatory training of ICU staff aimed at HAP/VAP prevention is also important in preventing these nosocomial infections.<sup>53,54</sup>

*Use orotracheal/orogastric intubation (level II evidence).* Occlusion of one of the nares by a nasotracheal or nasogastric tube has been identified as a risk factor promoting sinusitis.<sup>55</sup> The presence of the foreign device prevents clearance of the secretions from the sinuses, which can become infected. Infected secretions are a risk factor for VAP from aspiration of the secretions into the lower respiratory tract.<sup>56,57</sup> The preferred route of tracheal and gastric intubation is via the oropharynx to prevent the development of nosocomial sinusitis and HAP/VAP.

*Control subglottic secretions (level I evidence).* Secretions tend to accumulate and pool above the endotracheal tube cuff in intubated patients.<sup>58</sup> These pooled secretions can become contaminated and leak around the cuff into the lower respiratory tract, precipitating HAP/VAP. A specially designed endotracheal tube with a separate dorsal lumen that allows for continuous aspiration of the subglottic secretions has been shown to significantly

**Table 5.** Strength of Evidence for Specific Interventions to Reduce the Risk for Postoperative Pulmonary Complications

Risk Reduction Strategy	Strength of Evidence	Type of Complication Studied
Postoperative lung expansion modalities	A	Atelectasis, pneumonia, bronchitis, severe hypoxemia
Selective postoperative nasogastric decompression	B	Atelectasis, pneumonia, aspiration
Short-acting neuromuscular blockade	B	Atelectasis, pneumonia
Laparoscopic (versus open) operation	C	Spirometry, atelectasis, pneumonia, overall respiratory complications
Smoking cessation	I	Postoperative ventilator support
Intraoperative neuraxial blockade	I	Pneumonia, postoperative hypoxia, respiratory failure
Postoperative epidural analgesia	I	Atelectasis, pneumonia, respiratory failure
Immunonutrition	I	Overall infectious complications, pneumonia, respiratory failure
Routine total parenteral or enteral nutrition	D	Atelectasis, pneumonia, empyema, respiratory failure
Right-heart catheterization	D	Pneumonia

Adapted with permission from Lawrence VA, Cornell JE, Smetana GW. Strategies to reduce postoperative pulmonary complications after noncardiothoracic surgery: systematic review for the American College of Physicians. *Ann Intern Med* 2006;144:605.

A = good evidence that the strategy reduces complications and benefit outweighs harm; B = at least fair evidence that the strategy reduces complications and benefit outweighs harm; C = at least fair evidence that the strategy may reduce complications, but the balance between benefit and harm is too close to justify a general recommendation; D = at least fair evidence that the strategy does not reduce complications or harm outweighs benefit; I = evidence of effectiveness of the strategy to reduce complications is conflicting, of poor quality, lacking, or insufficient, or the balance between benefit and harm cannot be determined.

reduce the incidence of early-onset VAP in randomized controlled trials, without a corresponding beneficial effect on mortality, ICU length of stay, or duration of mechanical ventilation.<sup>59–61</sup> These specialized endotracheal tubes cost approximately 20% to 25% more than standard endotracheal tubes. There is also level II evidence for maintaining endotracheal tube cuff pressure at greater than 20 cm H<sub>2</sub>O to prevent aspiration of subglottic secretions around the cuff and into the lungs.

*Avoid unnecessary ventilator circuit changes and manipulation/drain ventilator circuit condensate (level II evidence).* Studies have shown that the rate of bacterial contamination of inspiratory phase gas is not reduced by more frequent ventilator circuit changes.<sup>62</sup> Several prospective randomized trials have shown that VAP incidence is not affected by the frequency of ventilator circuit changes or by more frequent tubing changes.<sup>63–67</sup> However, vigilance is required by physicians, nurses, and respiratory therapists to prevent flushing of the ventilator circuit condensate into the lower respiratory tract with in-line medication administration and patient repositioning. The contaminated condensate within ventilator circuits predisposes the patient to VAP and also serves as a reservoir for the spread of nosocomial pathogens to other patients in the ICU.<sup>62</sup> Proper procedures must be followed when draining the condensate from the tubing and disposing of the condensate. Current recommendations are to change ventilator circuits based on visual contamination of the circuit with blood, emesis, or purulent secretions as

opposed to routine circuit changes based on duration. This recommendation may reduce the incidence of VAP, minimize risk to health care workers from exposure to infected aerosols, and result in cost savings.

*Heat-moisture exchanger (level I evidence).* Use of heat-moisture exchangers can reduce condensate accumulation significantly, which could translate into lower VAP rates.<sup>68,69</sup> One randomized trial found a lower incidence of late-onset VAP with humidification via a heat-moisture exchanger than with conventional heat-water humidification.<sup>70</sup> However, while heat-moisture exchangers do decrease ventilator circuit colonization, they have not consistently resulted in significantly reduced rates of VAP in clinical trials.<sup>69,71–74</sup>

*Keep patients in semirecumbent position (level I evidence).* The supine position is associated with aspiration of upper airway secretions, which is a particular problem during enteral feeding.<sup>75</sup> Studies using radiolabeled enteral feeds in patients undergoing mechanical ventilation have demonstrated higher endotracheal counts, consistent with higher aspiration rates, when patients were kept supine compared with a semirecumbent position (45°).<sup>75,76</sup> An important randomized trial demonstrated a three-fold reduction in the incidence of VAP and a trend toward a reduced hospital mortality rate in patients treated in the semirecumbent position (45°) compared with patients treated completely supine (0°).<sup>77</sup> However, more recent experiences have demonstrated that optimal patient positioning is difficult to maintain, and its influence on VAP prevention

**Table 6.** Nonpharmacologic Strategies to Prevent Nosocomial Pneumonia

Strategy	Evidence	
	Grade	References
Handwashing/disinfection	Level I	32–34
Noninvasive positive pressure ventilation	Level I	35–40
Avoid tracheal reintubation	Level I	41
Weaning/sedation protocols	Level II	43–46
Adequate nursing/therapist staffing	Level II	47–52
Education initiatives	Level II	53,54
Avoid nasotracheal intubation	Level II	55–57
Suctioning of subglottic secretions	Level I	59–61
Routine emptying of ventilator circuit condensate	Level II	62
Avoid ventilator circuit changes	Level II	63–67
Use of heat-moisture exchangers	Level I	69–74
Maintain semierect position	Level I	75–79
Use of enteral nutrition/small bowel feeds	Level I	82,83
Antibacterial coating of endotracheal tube	U/D	85–89
Kinetic therapy beds*	Level I	90,91
Chest physiotherapy†	U/D	92,93

U/D = undetermined at this point.

\*Benefit limited to specific patient types.

†Incentive spirometry/deep breathing maneuvers are more resource effective than chest physiotherapy.

is questionable.<sup>78,79</sup> Nevertheless, intubated patients should be kept in the semierect position at all times if possible, particularly during enteral feeding.

*Enteral nutrition is preferable to parental nutrition (level I evidence).* The optimal approach for providing nutrition to mechanically ventilated patients and the timing of initiation of nutritional support is complicated. Enteral nutrition is considered a risk factor for VAP, especially in the presence of large gastric volumes and the increased risk of aspiration of gastric contents.<sup>16,20,80</sup> The alternative of parenteral nutrition is associated with higher costs, complications from line insertion, intravascular device-associated infections, and loss of intestinal villous structure. Atrophy of intestinal villi may be a risk factor for intestinal microbial translocation. Use of enteral nutrition should precipitate measures to avoid gastric overdistention.<sup>81</sup> These measures include reducing narcotic and anticholinergic use, monitoring gastric residual volumes prior to intermittent gastric enteral feedings, using prokinetic agents, and using smaller bore feeding tubes.<sup>16,20</sup>

The available evidence supports small bowel or postpyloric feeding in critically ill patients. An analysis of 10 studies in critically ill patients found that, compared with gastric feeding, small bowel feeding was associated

**Table 7.** Pharmacologic Strategies to Prevent Nosocomial Pneumonia

Strategy	Evidence	
	Grade	References
Use of sucralfate for GI prophylaxis	Level I	96–99
Parenteral antibiotic prophylaxis*	Level I	102
Avoid unnecessary red blood cell transfusion	Level I	103–109
Blood glucose control with insulin	Level I	110,111
Antibiotic cycling/rotation	Level II	113–118
Shorter courses of antibiotics	Level I	120–122
Vaccines	U/D	124–127
Nebulized antimicrobials	U/D	128
Oral decontamination	Level I	129–131

GI = gastrointestinal; U/D = undetermined at this time.

\*Benefit for specific high-risk patients.

with a decrease in gastroesophageal regurgitation, an increase in protein and calorie delivery, and a shorter time to reaching feeding goals.<sup>82</sup> In addition, when the results of 7 randomized trials were aggregated statistically, patients who received small bowel feeds as opposed to gastric feeds had fewer episodes of pneumonia. However, there was no difference in mortality between the groups. The optimal time to initiate enteral nutrition is not clear. Although early nutritional support intuitively makes sense, a strategy of early goal-directed feeding (day 1 of intubation) compared with low-level early enteral feeding followed by goal-directed feeds (day 5 of intubation) showed higher VAP rates in the early goal-directed group.<sup>83</sup> Delaying the administration of goal-directed enteral feeds in selected patients with high aspiration risks may prevent HAP/VAP.

*Biofilm prevention technology (level of evidence undetermined).* Biofilms form on surfaces (eg, endotracheal tube lumen) and consist of mucus, water channels, and slime-enclosed colonies of bacteria that settle in the biofilm and can intermittently become detached from it.<sup>19,84</sup> *Pseudomonas* species are particularly adept at forming biofilms, analogous to their propensity to infect patients with abnormal airways (eg, patients with cystic fibrosis). The recognition of the occurrence of biofilms on endotracheal tubes and their pathogenic potential has stimulated interest in approaches to limit biofilm formation. These include the use of surface coatings that impair bacterial adherence, oxygen-plasma processing of the polyvinyl chloride, and the administration of nebulized antibiotics.<sup>85–89</sup> Unfortunately, none of these approaches has yet undergone rigorous clinical investigation, and it is not clear whether such technolo-



gies will influence the adherence of airway secretions on the surface of the endotracheal tube.

*Kinetic therapy beds (level I evidence in neurosurgical/surgical patients only).* Critically ill patients tend to develop atelectasis and are unable to clear their secretions as a result of their immobility. Kinetic therapy beds, which continuously rotate patients, have reduced the risk of pneumonia in surgical and neurosurgical patient populations in randomized trials; however, these results could not be duplicated in medical patients.<sup>90,91</sup> Barriers to the use of kinetic therapy beds include cost, disconnection of intravenous catheters and other indwelling devices, and concerns about pressure ulcers. However, this modality can be considered in neurosurgical or surgical patients.<sup>90</sup>

*Chest physiotherapy (level of evidence undetermined).* The theoretical benefits of chest physiotherapy techniques (eg, postural drainage, manual lung hyperinflation) include more rapid resolution of atelectasis and enhanced airway clearance. A stratified, randomized trial in patients after abdominal surgery found incentive spirometry and deep breathing exercises to be more resource effective than chest physiotherapy.<sup>92</sup> A small, prospective nonrandomized trial showed a reduced incidence of VAP in patients receiving chest physiotherapy.<sup>93</sup> Barriers to the use of chest physiotherapy include limited universal access, optimal use of physical therapist time, and associated risks (eg, arterial hypoxemia). Larger randomized clinical trials are needed to evaluate this intervention.

**Pharmacologic interventions.** The following interventions should be tailored to the patient's specific risk factors.

*Avoid unnecessary use of stress ulcer prophylaxis (level I evidence).* Histamine<sub>2</sub>-receptor (H<sub>2</sub>-receptor) blockers and antacids are appropriate measures for stress ulcer prophylaxis but also are known risk factors for the development of VAP.<sup>94</sup> This risk presumably results from decreased intragastric acidity creating a favorable environment for colonization of the stomach by pathogens and via the increased intragastric volumes, which increases the risk for aspiration.<sup>95</sup> Sucralfate does not significantly increase gastric volume or decrease intragastric acidity. Numerous randomized trials in different patient populations and using different dosages have yielded conflicting results with respect to VAP risk.<sup>96-99</sup> In a large randomized trial, sucralfate use was associated with lower rates of late-onset VAP compared with H<sub>2</sub>-receptor blocker and antacid use.<sup>96</sup> The Canadian Critical Care Trials Group performed a large, double-blind, randomized trial comparing ranitidine with sucralfate and found a trend toward lower VAP rates with sucralfate use; however, clinically significant

gastrointestinal bleeding occurred 4% more frequently in the sucralfate group.<sup>97</sup> A reasonable strategy is to assess the risks and benefits of stress ulcer prophylaxis on an individual basis, taking into account each patient's specific risks for VAP and gastrointestinal bleeding.

*Avoid routine use of prophylactic antibiotics except in selected patients (level I evidence).* Prolonged use of prophylactic antibiotics in trauma patients was associated with the delayed onset of HAP/VAP but an increased incidence of pneumonia caused by antibiotic-resistant gram-negative bacteria and an increased overall incidence of nosocomial infections.<sup>100</sup> A multivariate analysis of VAP patients found prior administration of antibiotics to have an adjusted odds ratio of 3.1 (95% confidence interval, 1.4-6.9) for the development of late-onset VAP.<sup>101</sup> The greatest harm of prolonged prophylactic antibiotics is the potential for ensuing infection with antibiotic-resistant pathogens, which can be transmitted to other patients. However, prophylactic parenteral antibiotics may play a role in the prevention of HAP/VAP among specific high-risk populations, including patients with head trauma or coma. In a randomized trial, cefuroxime administration for 24 hours at the time of intubation in patients with closed head injury reduced the incidence of early-onset VAP.<sup>102</sup> Therefore, prophylactic antibiotics should be employed in appropriate high-risk patients (trauma, severe head injury, coma, high-risk surgical procedure), generally for less than 24 hours following intubation, surgery, or the initial trauma.

*Follow restricted (conservative) blood transfusion policy (level I evidence).* The transfusion of packed red blood cells has been associated with serious nosocomial infections, including VAP.<sup>30,103-106</sup> This is thought to result from the immunosuppressive effects of donor leukocyte-containing packed red blood cell units. In 1 study, transfusion of packed red blood cells was found to be an independent risk factor for the development of VAP.<sup>107</sup> A prospective, randomized trial using leukocyte-depleted red blood cell transfusions in a group of patients undergoing colorectal surgery resulted in a reduced incidence of pneumonia.<sup>108</sup> These data suggest that the unnecessary transfusion of packed red blood cells should be avoided to reduce the risk of nosocomial infections including HAP/VAP and that conservative "triggers" to transfusion in ICU patients in the absence of active bleeding or cardiac disease should be followed.<sup>109</sup>

*Optimize glycemic control (level I evidence).* Intensive insulin therapy to maintain blood glucose levels between 80 and 110 mg/dL in randomized surgical ICU patients resulted in reduced mortality, reduced bloodstream infections, less antibiotic use, shorter duration of mechanical ventilation, and shorter ICU stays.<sup>110</sup> A similar

study in critically ill medical patients failed to demonstrate a mortality benefit and found more episodes of hypoglycemia in the intensive insulin therapy group.<sup>111</sup> Intensive glycemic control has not been studied in patients with VAP, but avoidance of hyperglycemia and its adverse effects on neutrophil function is recommended.

*Antibiotic class rotation (level II evidence).* Predominant use of a single drug class to treat gram-negative bacterial infections has been associated with the emergence of antibiotic-resistant infections, including HAP/VAP.<sup>112</sup> The practice of a scheduled antibiotic class switch that simultaneously provides adequate empiric antimicrobial coverage and minimizes antimicrobial resistance is an appealing strategy based on the theory that cycling of antibiotic classes will reduce the selective pressure on bacteria to become resistant to a single class.<sup>113,114</sup> This strategy has been associated with reduced occurrence of VAP when increasing resistance to the baseline antibiotic class was recognized as the stimulus for the class switch.<sup>113</sup> However, this strategy has had inconsistent effects on antimicrobial resistance patterns and the development of nosocomial infections.<sup>115–118</sup> A policy of antibiotic rotation can be considered only in conjunction with the application of other strategies aimed at preventing the emergence of antibiotic-resistant infections (ie, short-course antibiotic therapy and adequate infection control measures).

*Use short-course antibiotic therapy (level I evidence).* Prolonged administration of antibiotics to ICU patients has been shown to be an important risk factor for the emergence of colonization and infection with antibiotic-resistant bacteria.<sup>15</sup> Attempts have been made to shorten the duration of antibiotic treatment in order to reduce subsequent hospital-associated infections caused by antibiotic-resistant bacteria.<sup>26,119</sup> Several clinical trials have found that 7 to 8 days of antibiotic treatment is acceptable for most nonbacteremic patients with VAP.<sup>26,120–122</sup> Several recently published guidelines for the antibiotic management of nosocomial pneumonia and severe sepsis recommend the discontinuation of empiric antibiotic therapy after 48 to 72 hours if cultures are negative or the signs of infection have resolved.<sup>29,123</sup>

*Vaccines (level of evidence undetermined).* Vaccination programs in adults and children have been successful in reducing the incidence of pneumonia caused by specific pathogens, including *Hemophilus influenzae*, *Streptococcus pneumoniae*, and influenza virus.<sup>124–127</sup> These pathogens are major causes of health care-associated pulmonary infections and can predispose to the development of HAP/VAP. At least 1 study showed that the use of a vaccine directed against a respiratory pathogen in a high-risk population reduced sub-

sequent hospitalization for pneumonia, supporting the benefit of this intervention.<sup>126</sup> Vaccines for the prevention of antibiotic-resistant bacterial infections are not currently available for use in the ICU setting.

*Nebulized antibiotics (level of evidence undetermined).* A study by Palmer et al<sup>128</sup> revealed that in ventilator-dependent patients who were colonized with gram-negative organisms and who had tracheostomy tubes in place, nebulized aminoglycosides resulted in a significant reduction in the volume of secretions and, in some patients, eradication of the gram-negative colonizers. This concept has not yet been studied in a randomized manner as a strategy to prevent VAP.

*Oropharyngeal decontamination (level I evidence).* The use of chlorhexidine solution for oropharyngeal decontamination has also been evaluated in patients undergoing heart surgery.<sup>129</sup> In these randomized clinical trials, patients receiving chlorhexidine oral rinses had significantly lower overall rates of HAP/VAP compared with patients receiving placebo. In 1 of these studies, the mortality rate and use of intravenous drugs were also decreased among patients receiving chlorhexidine rinses without changing bacterial resistance patterns.<sup>129</sup> The results of 2 large multicenter trials of chlorhexidine have been mixed.<sup>130,131</sup> However, given the low cost and lack of significant resistance, use of chlorhexidine for oropharyngeal decontamination should be employed in high-risk patients.

### Overcoming Barriers to Implementation of Preventive Strategies

The prevention of hospital-associated infections is an important management objective for all hospitals, but achieving effective implementation of preventive strategies is difficult. A comparison of French and Canadian ICUs regarding the use of 7 strategies to control secretions and to care for ventilator circuits revealed low overall compliance with specific VAP prevention guidelines (64% in French ICUs versus 30% in Canadian ICUs).<sup>132</sup> Two European surveys of physicians and nurses found that 37% of ICU physicians and 22% of nurses were not following published VAP prevention guidelines.<sup>133,134</sup> The reasons for nonadherence were disagreement with interpretation of trial data, lack of resources, fear of potential adverse events, and costs associated with the implementation of specific interventions. The use of standardized practices for HAP/VAP prevention along with focused educational modules for staff have been shown to overcome these barriers and to reduce infection rates.<sup>53,54</sup> **HP**

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