

2011

## Prevention of nosocomial pneumonia in the intensive care unit: Beyond the use of bundles

Marin H. Kollef  
*Washington University School of Medicine in St. Louis*

Follow this and additional works at: [https://digitalcommons.wustl.edu/open\\_access\\_pubs](https://digitalcommons.wustl.edu/open_access_pubs)

**Please let us know how this document benefits you.**

---

### Recommended Citation

Kollef, Marin H., "Prevention of nosocomial pneumonia in the intensive care unit: Beyond the use of bundles." *Surgical Infections*. 12, 3. 211-220. (2011).  
[https://digitalcommons.wustl.edu/open\\_access\\_pubs/2997](https://digitalcommons.wustl.edu/open_access_pubs/2997)

This Open Access Publication is brought to you for free and open access by Digital Commons@Becker. It has been accepted for inclusion in Open Access Publications by an authorized administrator of Digital Commons@Becker. For more information, please contact [vanam@wustl.edu](mailto:vanam@wustl.edu).

# Prevention of Nosocomial Pneumonia in the Intensive Care Unit: Beyond the Use of Bundles

Marin H. Kollef

## Abstract

**Background:** The occurrence of nosocomial pneumonia (NP) in the hospital setting is especially problematic, as it is associated with a greater risk of in-hospital death, longer stays on mechanical ventilation and in the intensive care unit (ICU), more need for tracheostomy, and significantly higher medical care costs.

**Methods:** Review of the pertinent English-language literature.

**Results:** The adverse effect of NP on healthcare outcomes has increased pressure on clinicians and hospital systems to prevent this infection. This brief review provides an overview of the current approaches to the prevention of NP, focusing primarily on ventilator-associated pneumonia (VAP).

**Conclusion:** Clinicians working in ICUs should consider the following recommendations: (1) Develop a VAP prevention bundle based on evidence-based guidelines; (2) monitor the rates of VAP prior to and during implementation of the program; (3) make adjustments according to VAP occurrence; and (4) integrate VAP prevention with other quality improvement programs.

**P**NEUMONIA ASSOCIATED with the need for mechanical ventilation in the intensive care unit (ICU) setting is one of the most common infections managed by intensivists. The current classification of pneumonia in the ICU includes community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), and nursing home-associated pneumonia (NHAP) (Table 1)[1–3]. Health care-associated pneumonia (HCAP) is the newest category of pneumonia and in many developed countries probably is the most common type necessitating ICU care. This is a distinct type of nosocomial pneumonia (NP), the others being HAP and VAP, that is present at the time of hospital or ICU admission where patients have specific underlying risk factors, including residence in a nursing home or long-term care facility; recent hospitalization or treatment with antibiotics; receipt of home or hospital-based intravenous therapy, wound care, or dialysis; and immunosuppression [2,3].

Patients with HCAP are more similar to patients with HAP and VAP and differ from patients with CAP because of the common presence of infection with multi-drug resistant (MDR) bacteria and the greater likelihood of co-morbidities, including cancer, chronic kidney disease, heart disease, chronic obstructive lung disease, immunosuppression, dementia, and impaired mobility [4–8]. From a prevention

standpoint, HAP and VAP are most amenable to useful strategies applied in the hospital setting. However, the prevention of pneumonias developing outside of the hospital (CAP, HCAP) also can be accomplished, to some extent, through the use of specific hospital-based strategies [9,10]. The medical literature and available clinical evidence currently is most robust for VAP and less developed for HAP and HCAP. Therefore, this review focuses on the prevention of VAP, and the reader should assume that the recommendations also apply to HAP and HCAP unless stated otherwise. However, it is important to recognize that not all VAP prevention studies are similar in the rigor with which infection was defined. That is, some studies used microbiologic criteria to confirm infection, whereas others employed less-specific clinical criteria. Readers should take this into account when considering including specific interventions in their prevention bundles, especially costly interventions or those carrying a risk to the patient or environment.

## Pathogenesis of Nosocomial Pneumonia

Under basal conditions, the lower respiratory tract is sterile. Thus, for pneumonia to develop, bacteria must be introduced into the lungs, typically by being aspirated from either the upper respiratory tract or the gastrointestinal tract.

TABLE 1. PNEUMONIA CLASSIFICATION FOR PATIENTS IN THE INTENSIVE CARE SETTING

|      |   |
|------|---|
| CAP  | Infection present at hospital admission in patients who do not meet the criteria for HCAP   |
| HCAP | Pneumonia present at hospital or ICU admission in patients with at least one of the following risk factors: <ul style="list-style-type: none"> <li>- Hospitalization for <math>\geq 2</math> days in an acute-care facility within 180 days of infection</li> <li>- Residence in a nursing home or long-term care facility</li> <li>- Antibiotic therapy, chemotherapy, or wound care within 30 days of current infection</li> <li>- Hemodialysis at a hospital or clinic</li> <li>- Home infusion therapy or home wound care</li> <li>- Family member with infection caused by MDR bacteria</li> <li>- Significant immunosuppression (corticosteroids, HIV, organ transplant)</li> </ul> |
| NHAP | Pneumonia occurring during residence in a nursing home or rehabilitation facility   |
| HAP  | Pneumonia occurring typically $\geq 48$ h after hospital admission in a non-intubated patient   |
| VAP  | Pneumonia occurring typically $\geq 48$ h after hospital admission and endotracheal intubation  |

CAP = community-acquired pneumonia; HCAP = healthcare-associated pneumonia; HIV = human immunodeficiency virus; MDR = multi-drug resistant; NHAP = nursing home-associated pneumonia; HAP = hospital-acquired pneumonia; VAP = ventilator-associated pneumonia; ICU = intensive care unit.

Introduction generally is associated with impairment of host defenses, both locally and systemically. The pathogenesis of VAP thus is a dual process requiring colonization of the aerodigestive tract with potentially causative pathogens followed by aspiration of secretions contaminated with these pathogens that overcome lower respiratory tract defense mechanisms, resulting in infection.

A leading hypothesis regarding the pathogenesis of VAP, and NP in general, is that the oropharynx is overgrown by microorganisms, which subsequently are aspirated into the lungs and colonize the airway. This hypothesis is supported by the observation that whereas enteric gram-negative bacteria are absent from the oropharynx under basal conditions, they can be detected in that site in nearly 75% of critically ill patients [11]. A comparison of bacterial DNA samples on the tongues of critically ill patients with organisms recovered from bronchoalveolar lavage (BAL) samples supports this theory [12]. Upper airway colonization by enteric bacteria occurs in 45% to 100% of intubated patients. Besides being colonized by aspirated endogenous flora, the airways may be colonized by exogenous flora as a result of cross-contamination from other ICU patients through inadvertent transmission by healthcare workers.

A complementary hypothesis is that the upper gastrointestinal tract plays a critical role in the pathogenesis of VAP. According to this view, the stomach is a primary site of colonization that may subsequently infect the lung through bacterial overgrowth and retrograde movement, followed by aspiration of organisms from the oropharynx. The small decrease in the mortality rate seen in certain ICU patient populations after selective decontamination of the digestive tract (SDD) supports the idea that gut flora play a role in the pathogenesis of VAP and possibly HAP and HCAP. Chronic infection of biofilms on an endotracheal tube also may play a role [13].

### Prevention of Nosocomial Pneumonia

#### Pharmacologic approaches (Table 2)

**Topical iseganan.** Iseganan is an antimicrobial peptide with activity against gram-positive and gram-negative bacteria and yeast. In a multicenter randomized trial, topical oropharyngeal administration of iseganan was not associated with a reduction in VAP [14].

**Orodigestive decontamination.** Orodigestive decontamination (ODD) is the use of a prophylactic antimicrobial

TABLE 2. PHARMACOLOGIC-BASED STRATEGIES FOR PREVENTION OF VENTILATOR-ASSOCIATED PNEUMONIA

| Strategy   | Recommendation                 | Evidence level <sup>a</sup> | References |
|--|--------------------------------|-----------------------------|------------|
| Topical iseganan   | No                             | 1                           | 14         |
| Orodigestive decontamination<br>(topical/topical plus intravenous antibiotics) | No#                            | 1                           | 15,16      |
| Oral chlorhexidine   | Yes                            | 1                           | 19–22      |
| Aerosolized antibiotics  | No recommendation <sup>b</sup> | 1                           | 23,24      |
| Intravenous antibiotics  | No recommendation <sup>b</sup> | 1                           | 25         |
| Specific stress ulcer prophylaxis regimen                                      | No                             | 1                           | 27         |
| Short-course antibiotic therapy<br>(when clinically applicable)                | Yes                            | 1                           | 30–32      |
| Routine antibiotic cycling/rotation/heterogeneity <sup>c</sup>                 | No                             | 2                           | 33–35      |
| Restricted (conservative) blood transfusion                                    | Yes                            | 2                           | 36–38      |
| Vaccines (influenza, pneumococcal) <sup>d</sup>                                | Yes                            | 1                           | 40,41      |

<sup>a</sup>1 = Supported by randomized trials; 2 = supported by prospective or retrospective cohort studies; 3 = supported by case series.

<sup>b</sup>Routine use of intravenous, topical, or aerosolized antibiotics for prophylaxis cannot be recommended because of the emergence of antibiotic resistance [see references 17 and 18] and insufficient data on aerosolized and intravenous antibiotics used alone.

<sup>c</sup>May be useful in specific clinical circumstances (as an adjunct to controlling an outbreak of a multi-drug resistant bacterial infection).

<sup>d</sup>General recommendation without specific evidence for ventilator-associated pneumonia.

regimen that includes nonabsorbable antibiotics applied to the oropharynx and gastrointestinal tract along with a short course of intravenous antibiotics. The technique has been studied for more than 25 years, and more than 10 meta-analyses have been written [15]. Despite a fairly consistent demonstration of modest decreases in the mortality rate and in blood stream infections, ODD is not in widespread use, primarily because of concerns about promoting antimicrobial resistance and uncertain cost-effectiveness. A randomized trial in more than 6,000 patients was published recently comparing ODD, oral decontamination with topical agents alone, and standard care [16]. Compared with standard care, ODD led to a 28-day mortality rate decrease from 27.5% to 26.9%. The 28-day mortality rate in the oral decontamination group was similar to that in the ODD group at 26.6%. Because antimicrobial resistance may take time to develop, however, its emergence may not be noticed during clinical trials, and this remains a major concern with the widespread implementation of ODD. Indeed, a followup of this study showed that increasing bacterial resistance emerged in the ICUs employing ODD [17,18]. Therefore, the routine use of ODD for the prevention of VAP cannot be recommended.

**Oral chlorhexidine.** Like the use of ODD, oral chlorhexidine administration has been associated with reductions in nosocomial infections, including VAP, primarily in patients undergoing cardiac surgery [19,20]. The overall magnitude of the effect on the prevention of VAP seems to be modest and probably is dependent on both the frequency of its administration and the concentration of chlorhexidine, as demonstrated in non-cardiac surgery populations [21,22].

**Aerosolized antibiotics.** The most recent American Thoracic Society/American Infectious Diseases Association guidelines for the management of NP concluded that aerosolized antibiotics have not been proved to have value in VAP treatment but can be considered as an adjunct for VAP caused by MDR pathogens that are not responsive to standard therapy [3]. Several small studies have been published in support of the use of inhaled antibiotics for both VAP and tracheobronchitis [23,24]. Although these trials are promising, current data are lacking to support the use of inhaled antibiotics as more than an adjunctive therapy in non-improving patients. There is no current role for aerosolized antibiotics for the prevention of VAP.

**Intravenous antibiotics.** Long courses of intravenous antibiotics can be associated with the emergence of antibiotic resistance, and therefore, their use should be limited to treatment indications. One study of cefuroxime administration for 24 h at the time of intubation in patients with closed head injury produced a significant reduction in early-onset VAP [25].

**Specific stress ulcer prophylaxis.** Stress ulcer prophylaxis (antacids, histamine type-2 receptor antagonists, proton-pump inhibitors) neutralizes gastric acid or reduces gastric acid secretion, facilitating gastric colonization with potentially pathogenic bacteria and yeast, which can be aspirated into the lungs and cause lower respiratory tract infections. Significant debate has ensued regarding the role of stress ulcer prophylaxis as a promoter of VAP [26]. Nevertheless, no

convincing evidence exists to recommend one agent over another when stress ulcer prophylaxis is deemed necessary [27]. More recently, the use of proton-pump inhibitors has been associated also with the development of CAP, further linking alterations in upper gastrointestinal colonization to the development of pneumonia [28,29].

**Short-course antibiotic therapy.** Available evidence suggests that shorter courses of antibiotic therapy for VAP are clinically effective and associated with less emergence of antibiotic resistance [28–30]. When clinically acceptable, a seven- to eight-day course of antibiotic therapy should be considered adequate for patients demonstrating a clinical response to treatment (resolution of fever, reduced white blood cell count, improved oxygenation, and decreased respiratory secretions). Although this may not be a primary mode for the prevention of VAP, it can result in less emergence of antibiotic-resistant VAP [28].

**Routine antibiotic cycling/rotation.** In view of the available evidence, the routine use of antibiotic cycling or rotation cannot be recommended for the prevention of VAP [31–33].

**Restricted use of blood transfusion.** Transfusion of red blood cells has been associated with the development of nosocomial infections, including VAP [36–38]. Restricted use of transfusion therefore seems appropriate to minimize this risk [39].

**Vaccines.** Appropriate use of influenza and pneumococcal vaccines is recommended to reduce the incidence of respiratory failure related to these infections, which could secondarily increase the occurrence of VAP [40,41]. Clinicians should follow national recommendations regarding vaccination policies and chemoprophylaxis in order to minimize the impact of respiratory illness outbreaks in the community [42].

### **Non-Pharmacologic Approaches to Preventing Nosocomial Pneumonia (Table 3)**

#### *Use of non-invasive mask ventilation*

The endotracheal tube plays an important role in the pathogenesis of VAP, which has led some authors to rename this nosocomial infection “endotracheal-tube associated pneumonia” [43]. Avoidance of endotracheal intubation by using mask ventilation reduces the occurrence of VAP and nosocomial sinusitis [44–46].

#### *Avoid re-intubation*

Re-intubation is associated with a higher risk of VAP by facilitating aspiration [47]. Appropriate interventions and surveillance should be in place to minimize unplanned extubations resulting in the need for re-intubation. Clinicians must balance the occurrence of re-intubations as part of the planned ventilator weaning process with the aim of minimizing the duration of mechanical ventilation, which also can help to prevent VAP.

#### *Avoid patient transport*

Unnecessary patient transport out of the ICU should be avoided, as such travel has been associated with VAP [48].

TABLE 3. NON-PHARMACOLOGIC-BASED STRATEGIES FOR PREVENTION OF VENTILATOR-ASSOCIATED PNEUMONIA

| Strategy  | Recommendation | Evidence level <sup>a</sup> | References |
|---|----------------|-----------------------------|------------|
| Use of non-invasive mask ventilation              | Yes            | 1                           | 43–46      |
| Avoid re-intubation                               | Yes            | 2                           | 47         |
| Avoid patient transports                          | Yes            | 2                           | 48         |
| Orotracheal intubation preferred                  | Yes            | 1                           | 49         |
| Orogastric intubation preferred                   | Yes            | 2                           | 50         |
| Early tracheostomy                                | No             | 1                           | 51,52      |
| Routine ventilator circuit changes                | No             | 1                           | 53,54      |
| Use of heat-moisture exchanger                    | Yes            | 1                           | 56–58      |
| Closed endotracheal suctioning                    | Yes            | 1                           | 61–63      |
| Subglottic secretion drainage                     | Yes            | 1                           | 64–67      |
| Shortening the duration of mechanical-ventilation | Yes            | 1                           | 71,72      |
| Adequate intensive care unit staffing             | Yes            | 2                           | 73,74      |
| Silver-coated endotracheal tube                   | Yes            | 1                           | 76,77      |
| Polyurethane endotracheal tube cuff               | Yes            | 1                           | 79,80      |
| Semi-erect positioning                            | Yes            | 1                           | 81,82      |
| Rotational beds                                   | Yes            | 1                           | 83–85      |
| Chest physiotherapy                               | No             | 1                           | 86–88      |
| Use of protocols/bundles                          | Yes            | 2                           | 89–91      |

<sup>a</sup>1 = Supported by randomized trials; 2 = supported by prospective or retrospective cohort studies; 3 = supported by case series.

#### *Orotracheal and orogastric intubation*

Orotracheal and orogastric intubation have been associated with reduced incidences of VAP and nosocomial sinusitis [49,50]. Therefore, the oral route is preferred when intubation of the trachea and esophagus is necessary in a critically ill patient.

#### *Early tracheostomy*

One trial suggested that early tracheostomy could prevent VAP [51]. However, a more recent rigorously conducted study found no benefit [52].

#### *Routine ventilator circuit changes*

Manipulation and changing of ventilator circuits may promote aspiration and increase the occurrence of VAP [53,54]. Therefore, ventilator circuit changes should be made only when the circuit is damaged or visibly soiled. When significant condensate accumulates in a circuit, it should be removed to avoid aspiration and VAP [55].

#### *Routine use of heat-moisture exchangers*

Use of heat-moisture exchangers (HMEs) for humidification does not reduce the occurrence of VAP consistently compared with water humidification methods [56–58]. Therefore, deciding on their use is left to the treating physicians. Prolonged use of HMEs has not been associated with a higher risk of VAP [59,60].

#### *Closed versus open endotracheal suctioning*

According to clinical studies, closed and open endotracheal suctioning systems are linked to similar rates of VAP [61,62]. However, closed systems create less aerosolization of potentially infected airway secretions. Available evidence suggests that closed suctioning systems need to be changed only when malfunctioning or visibly soiled [63].

#### *Subglottic suction drainage*

Aspiration of subglottic secretions with a specially designed endotracheal tube has been associated with reductions in VAP [64–67]. However, subglottic suctioning can cause mucosal injury of the trachea and failure to aspirate secretions secondary to either increased viscosity or mucosal blockage of the suction port [68,69].

#### *Shortening the duration of mechanical ventilation*

The likelihood of VAP has been linked to the duration of mechanical ventilation [70]. Therefore, efforts to reduce the duration of mechanical ventilation by optimizing weaning attempts and utilizing sedation should be routine [71,72].

#### *Adequate intensive care unit staffing*

Inadequate staffing of ICUs has been associated with excess development of nosocomial infections and prolonged durations of mechanical ventilation [73,74]. Therefore, adequate staffing should be in place to ensure that protocols are followed to prevent VAP and other nosocomial infections, as well as to minimize patient exposure to mechanical ventilation.

#### *Silver-coated endotracheal tube*

Biofilm formation is an important pathogenic element in the development of VAP (75). Recent clinical investigations suggest that a silver-coated endotracheal tube is safe and can reduce the incidence of VAP by almost 50% during the first ten days of mechanical ventilation [76,77]. Additionally, a retrospective analysis of the NASCENT study suggests that use of a silver-coated endotracheal tube may be associated with better outcomes for patients developing VAP [78].

#### *Polyurethane cuffed endotracheal tubes*

Endotracheal tube cuffs made of ultrathin polyurethane rather than polyvinyl chloride theoretically reduce channel



formation and minimize the volume of secretions microaspirated around the cuff. Limited data from some populations have demonstrated their efficacy [79,80]. Various shapes of the ultrathin polyurethane cuffs have been employed in the commercially available endotracheal tubes (cylindrical, tapering funnel-like design). Unfortunately, head-to-head studies of the efficacy of various cuff designs for the prevention of aspiration and VAP are not available. The development of endotracheal tubes that combine multiple prevention features (ultrathin polyurethane cuff with subglottic suctioning) may allow even greater reductions in VAP occurrence, although this has yet to be confirmed in clinical trials.

#### *Semierect positioning*

Supine positioning facilitates aspiration in the intubated patient and should be avoided if possible [81]. However, achieving head elevation to 45° may be difficult in many clinical situations. Under those circumstances, the head of the bed should be raised to the highest level applicable [82].

#### *Rotational beds*

Several small trials have shown that rotating beds can reduce the occurrence of VAP [83–85]. However, because of the cost of these beds and the populations studied, their use should be based on perceived benefit and available resources in particular cases.

#### *Chest physiotherapy*

In view of the available evidence, the routine use of chest physiotherapy cannot be recommended for the prevention of VAP [86–88].

### **Protocols/bundles to Prevent Ventilator-Associated Pneumonia**

An increasing body of evidence suggests that the routine use of bundles or protocols aimed at preventing VAP can be successful [89–91]. The challenge is to ensure that compliance with the elements of the bundles and protocols is adhered to over time in order to sustain the early benefits. Additionally, clinicians must evaluate new technologies for inclusion in their established bundles. One example is the routine use of chlorhexidine baths for enhanced environmental control in order to reduce the occurrence of nosocomial infections. The data on the use of these baths to prevent VAP are mixed [92,93]; however, the overall reduction in ICU-acquired infections resulting from their use can justify the inclusion of such baths in a VAP prevention bundle.

#### **Prevention Protocols**

An education-based program at Barnes-Jewish Hospital directed toward respiratory care practitioners and ICU nurses was developed by a multidisciplinary task force to highlight correct practices for the prevention of VAP [90]. Each participant was required to take a test before reviewing a study module and an identical test after completion of the module. Following implementation of the module, the rate of VAP decreased to 5.7/1,000 ventilator days from 12.6/1,000 ventilator days [90]. The estimated cost savings secondary to the lower rate of VAP for the 12 mos following the intervention

was estimated to exceed \$400,000. This educational protocol was then implemented across the four largest hospitals in the local healthcare system [89]. The VAP rates for all four hospitals combined dropped by 46%, from 8.75/1,000 ventilator days in the year prior to the intervention to 4.74/1,000 ventilator days in the 18 mos following the intervention ( $p < 0.001$ ). Statistically significant decreases in rates were observed at the pediatric hospital and at two of the three adult hospitals. No change in VAP rates was seen at the community hospital with the lowest rate of study module completion among respiratory therapists (56%). In addition to showing the effectiveness of a protocol for VAP prevention, these studies highlight the importance of compliance with the elements of the protocol to ensure its success. This same protocol also has been successful in the ICUs of a hospital in Thailand [91].

Lansford et al. developed a simple protocol for the prevention of VAP in trauma patients focusing on head-of-bed elevation, oral cleansing with chlorhexidine, a once-daily respiratory therapist-driven weaning attempt, and conversion of nasogastric to orogastric feeding tubes [50]. Implementation of the protocol was associated with a significant reduction in the rate of VAP (11 occurrences in 1,600 days of ventilator support [6.9/1,000 ventilator days] vs. two occurrences in 703 days of ventilation [2.8/1,000 ventilator days]). Elements of this protocol have proved effective in other surgical/trauma units as well [94]. However, compliance with infection control protocols often wanes over time and can be influenced significantly by staffing levels in the ICU [95,96]. Wahl et al. have shown that a computerized flow sheet employed in the ICU could improve compliance with care measures involved in the prevention of VAP, as well as other protocols [97].

Most recently, Bouadma et al. illustrated the benefits of a bundled approach to the prevention of VAP [98]. Their program was implemented in a 20-bed medical ICU of a teaching hospital in France and involved all healthcare workers. The French intervention included a multidisciplinary task force, an educational session, direct observations with performance feedback, technical improvements, and scheduled reminders. It focused on eight targeted measures based on well-recognized published guidelines, easily and precisely defined acts, and the bedside behavior of directly concerned healthcare workers. Compliance assessment consisted of five four-week periods (before the intervention and one, six, 12, and 24 mos thereafter). Hand hygiene and glove-and-gown use compliances were high (68% and 80%) initially and remained stable over time. Compliance with all other preventive measures was low initially but increased steadily over the two-year period of the study: backrest elevation (5–58%) and tracheal cuff pressure maintenance (40–89%), which improved after simple technical equipment implementation; orogastric tube use (52–96%); gastric overdistention avoidance (20–68%); good oral hygiene (47–90%); and elimination of nonessential tracheal suctioning (41–92%). The VAP prevalence rate decreased by 51% after implementation of the intervention ( $p < 0.001$ ). This long-lasting program for preventing VAP increased compliance with preventive measures that are directly dependent on healthcare workers' bedside performance. The use of a multidimensional framework appeared to be critical for the success of this program, as has been demonstrated for similar bundled approaches to VAP prevention [89,90].

TABLE 4. SMART APPROACHES FOR THE PREVENTION OF VENTILATOR-ASSOCIATED PNEUMONIA USING BUNDLES

**Specific interventions**

- Identify bundle elements likely to be successful
- Review evidence in support of proposed bundle elements
- Consult with experts
- Do not become sold on any single bundle element without evidence that it actually works

**Measurable outcomes**

- Use clinically relevant criteria to define outcome (e.g.; ventilator-associated pneumonia)
- Demonstrated ability to accurately measure outcome of interest
- Be aware of reporting biases, especially when using before–after or time-series methods

**Achievable program**

- Develop prevention strategy according to availability of local resources
- Target one problem or outcome at a time
- Start with a smaller problem to refine the local approach then apply to larger problems

**Relevant**

- Target problems that have direct clinical significance and consequences to patient care
- Ensure that updated information is employed in the development of the prevention program
- Update prevention program over time as new technologies or prevention strategies become available

**Time-bound**

- Use discrete time periods for the implementation of the various phases of the prevention program
- Have a cutoff time at which to determine the success or failure of the prevention program
- Have specific time periods over which the prevention program will be re-evaluated to determine whether it needs updating or efforts to re-establish compliance with its components

VAP = ventilator-associated pneumonia.

Protocols, standardized order sets, checklists, and clinical practice teams all provide approaches for the prevention of VAP, as well as for the overall enhancement of critical care. Depending on local expertise and resources, an approach to quality care improvement in the ICU should be implemented and monitored over time (Table 4). The SMART approach for the prevention of nosocomial infections seems to be a concise framework for developing and implementing successful programs using available prevention strategies [99]. Evidence-based recommendations are available that reduce nosocomial ICU infection rates [100–102], especially when simple tactics are bundled. To increase the likelihood of success, the SMART approach, in which specific objectives or outcomes that are precisely defined and quantified (e.g., 25% reduction of VAP with protocol implementation), should be implemented. The outcome must be measurable, achievable, and, most important, clinically relevant. This will facilitate buy-in from stakeholders such as staff who have to carry out the protocols and bundles. Appointing a team to champion the intervention and collaboration with hospital administrators will help ensure the success of the interventions. Finally, the intervention must be time bound so that success or failure can be assessed objectively [98].

### Summary Recommendations and Conclusion

Optimal management and prevention of nosocomial infections in the ICU setting is an important element of care for the critically ill patient. Clinicians need to develop systems within ICUs aimed at optimizing the care of patients in order to improve their clinical outcomes. In the future, emerging advances in the design of endotracheal tubes [103], use of probiotics [104], and development of new antibiotics should further our ability to prevent and treat NP. In the meantime,

clinicians working in ICUs should consider the following recommendations:

1. Develop a VAP prevention bundle using evidence-based guidelines and the input of local experts in infection control and critical care;
2. Monitor the rates of VAP prior to and during the implementation of the prevention program to determine its success or failure;
3. Make adjustments to the prevention program according to VAP occurrence in terms of the bundle elements, strategies to enhance bundle compliance, and changes in patient mix, target pathogens, or changing definitions of VAP (e.g., U.S. Centers for Disease Control and Prevention Conference for Establishing a VAP Surveillance Definition, scheduled for Fall 2010);
4. Integrate VAP prevention with other quality improvement programs in the ICU to minimize redundancies and optimize the use of resources.

### Author Disclosure Statement

Development of this manuscript was supported by the Barnes-Jewish Hospital Foundation. Dr. Kollef has served on the speaker's bureau or as a consultant for Bard Medical, Covidien, Pfizer, Merck, Astellas, Astrazeneca, Johnson & Johnson, and Forest.

### References

1. Hiramatsu K, Niederman MS. Health-care-associated pneumonia: A new therapeutic paradigm. *Chest* 2005;128:3784–3787.
2. Kollef MH, Shorr A, Tabak YP, et al. Epidemiology and outcomes of health-care-associated pneumonia: Results

- from a large US database of culture-positive pneumonia. *Chest* 2005;28:3854–3862.
3. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med* 2005;71:388–416.
  4. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis* 2007;44(Suppl):S27–S72.
  5. Craven DE. What is healthcare-associated pneumonia, and how should it be treated? *Curr Opin Infect Dis* 2006;19:153–160.
  6. Anand N, Kollef MH. The alphabet soup of pneumonia: CAP, HAP, HCAP, NHAP, and VAP. *Semin Respir Crit Care Med* 2009;30:3–9.
  7. Friedman ND, Kaye KS, Stout JE, et al. Healthcare-associated bloodstream infections in adults: A reason to change the accepted definition of community-acquired infections. *Ann Intern Med* 2002;137:791–797.
  8. Muder RR, Aghababian RV, Loeb MB, et al. Nursing home-acquired pneumonia: An emergency department treatment algorithm. *Curr Med Res Opin* 2004;20:1309–1320.
  9. Talwar A, Lee H, Fein A. Community-acquired pneumonia: What is relevant and what is not? *Curr Opin Pulm Med* 2007;13:177–185.
  10. Morrow LE. Prevention strategies for healthcare-associated pneumonia. *Semin Respir Crit Care Med* 2009;30:86–91.
  11. Johanson WG, Pierce AK, Sanford JP. Changing pharyngeal bacterial flora of hospitalized patients: Emergence of gram-negative bacilli. *N Engl J Med* 1969;281:1137–1140.
  12. Bahrani-Mougeot FK, Paster BJ, Coleman S, et al. Molecular analysis of oral and respiratory bacterial species associated with ventilator-associated pneumonia. *J Clin Microbiol* 2007;45:1588–1593.
  13. Adair CG, Gorman SP, Feron BM et al. Implications of endotracheal tube biofilm for ventilator-associated pneumonia. *Intensive Care Med* 1999;25:1072–1076.
  14. Kollef M, Pittet D, Sánchez García M, et al. A randomized double-blind trial of iseganan in prevention of ventilator-associated pneumonia. *Am J Respir Crit Care Med* 2006;173:91–97.
  15. Liberati A, D'Amico R, Pifferi, et al. Antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving intensive care. *Cochrane Database Syst Rev* 2004;1:CD000022.
  16. de Smet AM, Kluytmans JA, Cooper BS, et al. Decontamination of the digestive tract and oropharynx in ICU patients. *N Engl J Med* 2009;360:20–31.
  17. Oostdijk EA, de Smet AM, Blok HE, et al. Ecological effects of selective decontamination on resistant gram-negative bacterial colonization. *Am J Respir Crit Care Med* 2010;181:452–457.
  18. Wunderink RG. Welkommen to our world: Emergence of antibiotic resistance with selective decontamination of the digestive tract. *Am J Respir Crit Care Med* 2010;181:426–427.
  19. Koeman M, van der Ven AJ, Hak E, et al. Oral decontamination with chlorhexidine reduces the incidence of ventilator-associated pneumonia. *Am J Respir Crit Care Med* 2006;173:1348–1355.
  20. Segers P, Speekenbrink RG, Ubbink DT, et al. Prevention of nosocomial infection in cardiac surgery by decontamination of the nasopharynx and oropharynx with chlorhexidine gluconate: A randomized controlled trial. *JAMA* 2006;296:2460–2466.
  21. Panchabhai TS, Dangayach NS, Krishnan A, et al. Oropharyngeal cleansing with 0.2% chlorhexidine for prevention of nosocomial pneumonia in critically ill patients: An open-label randomized trial with 0.01% potassium permanganate as control. *Chest* 2009;135:1150–1156.
  22. Scannapieco FA, Yu J, Raghavendran K, et al. A randomized trial of chlorhexidine gluconate on oral bacterial pathogens in mechanically ventilated patients. *Crit Care* 2009;13(4):R117.
  23. Palmer LB, Smaldone GC, Chen JJ, et al. Aerosolized antibiotics and ventilator-associated tracheobronchitis in the intensive care unit. *Crit Care Med* 2008;36:2008–2013.
  24. Wood GC, Boucher BA, Croce MA, et al. Aerosolized ceftazidime for prevention of ventilator-associated pneumonia and drug effects on the proinflammatory response in critically ill trauma patients. *Pharmacotherapy* 2002;22:972–982.
  25. Sirvent JM, Torres A, El-Ebiary M, et al. Protective effect of intravenously administered cefuroxime against nosocomial pneumonia in patients with structural coma. *Am J Respir Crit Care Med* 1997;155:1729–1734.
  26. Kahn JM, Doctor JN, Rubenfeld GD. Stress ulcer prophylaxis in mechanically ventilated patients: Integrating evidence and judgment using a decision analysis. *Intensive Care Med* 2006;32:1151–1158.
  27. Cook D, Guyatt G, Marshall J, et al. A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in patients requiring mechanical ventilation. *N Engl J Med* 1998;338:791–797.
  28. Gulmez SE, Holm A, Frederiksen H, et al. Use of proton pump inhibitors and the risk of community-acquired pneumonia: A population-based case-control study. *Arch Intern Med* 2007;167:950–955.
  29. Sarkar M, Hennessy S, Yang YX. Proton-pump inhibitor use and the risk for community-acquired pneumonia. *Ann Intern Med* 2008;149:391–398.
  30. Ibrahim EH, Ward S, Sherman G, et al. Experience with a clinical guideline for the treatment of ventilator-associated pneumonia. *Crit Care Med* 2001;29:1109–1115.
  31. Dennesen PJ, van der Ven AJ, Kessels AG, Ramsay G, Bonten MJ. Resolution of infectious parameters after antimicrobial therapy in patients with ventilator-associated pneumonia. *Am J Respir Crit Care Med* 2001;163:1371–1375.
  32. Chastre J, Wolff M, Fagon JY, et al. Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: A randomized trial. *JAMA* 2003;290:2588–2598.
  33. Kollef MH, Vlasnik J, Sharpless L, et al. Scheduled change of antibiotic classes: A strategy to decrease the incidence of ventilator-associated pneumonia. *Am J Respir Crit Care Med* 1997;156:1040–1048.
  34. Gruson D, Hilbert G, Vargas F, et al. Rotation and restricted use of antibiotics in a medical intensive care unit: Impact on the incidence of ventilator-associated pneumonia caused by antibiotic-resistant gram-negative bacteria. *Am J Respir Crit Care Med* 2000;162:837–843.
  35. Warren DK, Hill HA, Merz LR, et al. Cycling empirical antimicrobial agents to prevent emergence of antimicrobial-resistant gram-negative bacteria among intensive care unit patients. *Crit Care Med* 2004;32:2450–2456.



36. Shorr AF, Duh MS, Kelly KM, et al. Red blood cell transfusion and ventilator-associated pneumonia: A potential link? *Crit Care Med* 2004;32:666–674.
37. Taylor RW, Manganaro L, O'Brien J, et al. Impact of allogenic packed red blood cell transfusion on nosocomial infection rates in the critically ill patient. *Crit Care Med* 2002; 30:2249–2254.
38. Taylor RW, O'Brien J, Trottier SJ, et al. Red blood cell transfusions and nosocomial infections in critically ill patients. *Crit Care Med* 2006;34:2302–2308.
39. Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: A systematic review of the literature. *Crit Care Med* 2008;36:2667–2674.
40. Nichol KL, Nordin J, Mullooly J, et al. Influenza vaccination and reduction in hospitalizations for cardiac disease and stroke among the elderly. *N Engl J Med* 2003;348:1322–1332.
41. Klugman KP, Madhi SA, Huebner RE, et al. A trial of a 9-valent pneumococcal conjugate vaccine in children with and those without HIV infection. *N Engl J Med* 2003;349: 1341–1348.
42. U.S. Centers for Disease Control and Prevention. 2009 H1N1 flu. Available at [www.cdc.gov/swineflu](http://www.cdc.gov/swineflu) Accessed June 11, 2010.
43. Pneumatikos IA, Dragoumanis CK, Bouros DE. Ventilator-associated pneumonia or endotracheal tube-associated pneumonia? An approach to the pathogenesis and preventive strategies emphasizing the importance of endotracheal tube. *Anesthesiology* 2009;110:673–680.
44. Antonelli M, Conti G, Rocco M, et al. A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. *N Engl J Med* 1998;339:429–435.
45. Nava S, Ambrosino N, Clini E, et al. Noninvasive mechanical ventilation in the weaning of patients with respiratory failure due to chronic obstructive pulmonary disease: A randomized, controlled trial. *Ann Intern Med* 1998;128:721–728.
46. Brochard L, Mancebo J, Wysocki M, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 1995;333:817–822.
47. Torres A, Gatell JM, Aznar E, et al. Re-intubation increases the risk of nosocomial pneumonia in patients needing mechanical ventilation. *Am J Respir Crit Care Med* 1995;152:137–141.
48. Kollef MH, Von Harz B, Prentice D, et al. Patient transport from intensive care increases the risk of developing ventilator-associated pneumonia. *Chest* 1997;112:765–773.
49. Holzapfel L, Chastang C, Demingon G, et al. A randomized study assessing the systematic search for maxillary sinusitis in nasotracheally mechanically ventilated patients: Influence of nosocomial maxillary sinusitis on the occurrence of ventilator-associated pneumonia. *Am J Respir Crit Care Med* 1999;159:695–701.
50. Lansford T, Moncure M, Carlton E, et al. Efficacy of a pneumonia prevention protocol in the reduction of ventilator-associated pneumonia in trauma patients. *Surg Infect* 2007;8:505–510.
51. Rumbak MJ, Newton M, Truncala T, et al. A prospective, randomized study comparing early percutaneous dilational tracheotomy to prolonged translaryngeal intubation (delayed tracheotomy) in critically ill medical patients. *Crit Care Med* 2004;32:1689–1694.
52. Terragni PP, Antonelli M, Fumagalli R, et al. Early vs late tracheotomy for prevention of pneumonia in mechanically ventilated adult ICU patients: A randomized controlled trial. *JAMA* 2010;303:1483–1489.
53. Kollef MH, Shapiro SD, Fraser VJ, et al. Mechanical ventilation with or without 7-day circuit changes: A randomized controlled trial. *Ann Intern Med* 1995;123:168–174.
54. Dreyfuss D, Djedaini K, Weber P, et al. Prospective study of nosocomial pneumonia and of patient and circuit colonization during mechanical ventilation with circuit changes every 48 hours versus no change. *Am Rev Respir Dis* 1991;143:738–743.
55. Craven DE, Goularte TA, Make BJ. Contaminated condensate in mechanical ventilator circuits: A risk factor for nosocomial pneumonia? *Am Rev Respir Dis* 1984;129:625–628.
56. Martin C, Perrin G, Gevaudan MJ, et al. Heat and moisture exchangers and vaporizing humidifiers in the intensive care unit. *Chest* 1990;97:144–149.
57. Dreyfuss D, Djedaini K, Gros I, et al. Mechanical ventilation with heated humidifiers or heat and moisture exchangers: Effects on patient colonization and incidence of nosocomial pneumonia. *Am J Respir Crit Care Med* 1995; 151:986–992.
58. Kollef MH, Shapiro SD, Boyd V, et al. A randomized trial comparing an extended use hygroscopic condenser humidifier to heated humidification in mechanically ventilated patients. *Chest* 1998;113:759–767.
59. Davis K Jr, Evans SL, Campbell RS, et al. Prolonged use of heat and moisture exchangers does not affect device efficiency or frequency rate of nosocomial pneumonia. *Crit Care Med* 2000;28:1412–1418.
60. Thomachot L, Leone M, Razzouk K, et al. Randomized clinical trial of extended use of a hydrophobic condenser humidifier: 1 vs. 7 days. *Crit Care Med* 2002;30: 232–237.
61. Combes P, Fauvage B, Oleyer C. Nosocomial pneumonia in mechanically ventilated patients: A prospective randomized evaluation of the Stericath closed suctioning system. *Intensive Care Med* 2000;26:878–882.
62. Lorente L, Lecuona M, Martín MM, et al. Ventilator-associated pneumonia using a closed versus an open tracheal suction system. *Crit Care Med* 2005;33:115–119.
63. Kollef MH, Prentice D, Shapiro SD, et al. Mechanical ventilation with or without daily in-line suction catheter changes: A randomized controlled trial. *Am J Respir Crit Care Med* 1997;156:466–472.
64. Kollef MH, Skubus NJ, Sundt TM. A randomized clinical trial of continuous subglottic aspiration in cardiac surgery patients. *Chest* 1999;116:1339–1346.
65. Vallés J, Artigas A, Rello J, et al. Continuous aspiration of subglottic secretions in preventing ventilator-associated pneumonia. *Ann Intern Med* 1995;122:179–186.
66. Mahul P, Auboyer C, Jospe R, et al. Prevention of nosocomial pneumonia in intubated patients: Respective role of mechanical subglottic secretions drainage and stress ulcer prophylaxis. *Intensive Care Med* 1992;18: 20–25.
67. Bouza E, Pérez MJ, Muñoz P, et al. Continuous aspiration of subglottic secretions in the prevention of ventilator-associated pneumonia in the postoperative period of major heart surgery. *Chest* 2008;134:938–946.
68. Dragoumanis CK, Vretzakis GI, Papaioannou VE, et al. Investigating the failure to aspirate subglottic secretions with the Evac endotracheal tube. *Anesth Analg* 2007;105: 1083–1085.

69. Berra L, De Marchi L, Panigada M, et al. Evaluation of continuous aspiration of subglottic secretion in an in vivo study. *Crit Care Med* 2004;32:2071–2078.
70. Cook DJ, Walter SD, Cook RJ, et al. Incidence of and risk factors for ventilator-associated pneumonia in critically ill patients. *Ann Intern Med* 1998;129:433–440.
71. Brook AD, Ahrens TS, Schaiff R, et al. Effect of a nursing-implemented sedation protocol on the duration of mechanical ventilation. *Crit Care Med* 1999;27:2609–2615.
72. Ely EW, Meade MO, Haponik EF, et al. Mechanical ventilator weaning protocols driven by nonphysician health-care professionals: Evidence-based clinical practice guidelines. *Chest* 2001;120:454S–463S.
73. Needleman J, Buerhaus P, Mattke S, et al. Nurse-staffing levels and the quality of care in hospitals. *N Engl J Med* 2002;346:1715–1722.
74. Thorens JB, Kaelin RM, Jolliet P, Chevrolet JC. Influence of the quality of nursing on the duration of weaning from mechanical ventilation in patients with chronic obstructive pulmonary disease. *Crit Care Med* 1995;23:1807–1815.
75. Olson ME, Harmon BG, Kollef MH. Silver-coated endotracheal tubes associated with reduced bacterial burden in the lungs of mechanically ventilated dogs. *Chest* 2002;121:863–870.
76. Rello J, Kollef M, Diaz E, et al. Reduced burden of bacterial airway colonization with a novel silver-coated endotracheal tube in a randomized multiple-center feasibility study. *Crit Care Med* 2006;34:2766–2772.
77. Kollef MH, Afessa B, Anzueto A, et al. Silver-coated endotracheal tubes and incidence of ventilator-associated pneumonia: The NASCENT randomized trial. *JAMA* 2008;300:805–813.
78. Afessa B, Shorr AF, Anzueto AR, et al. Association between a silver-coated endotracheal tube and reduced mortality in patients with ventilator-associated pneumonia. *Chest* 2010;137:1015–1021.
79. Lorente L, Lecuona M, Jimenez A, et al. Influence of an endotracheal tube with polyurethane cuff and subglottic secretion drainage on pneumonia. *Am J Respir Crit Care Med* 2007;176:1079–1083.
80. Poelaert J, Depuydt P, De Wolf A, et al. Polyurethane cuffed endotracheal tubes to prevent early postoperative pneumonia after cardiac surgery: A pilot study. *J Thorac Cardiovasc Surg* 2008;135:771–776.
81. Drakulovic MB, Torres A, Bauer TT, et al. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: A randomised trial. *Lancet* 1999;354:1851–1858.
82. van Nieuwenhoven CA, Vandenbroucke-Grauls C, van Tiel FH, et al. Feasibility and effects of the semirecumbent position to prevent ventilator-associated pneumonia: A randomized study. *Crit Care Med* 2006;34:396–402.
83. Fink MP, Helmsmoortel CM, Stein KL, et al. The efficacy of an oscillating bed in the prevention of lower respiratory tract infection in critically ill victims of blunt trauma: A prospective study. *Chest* 1990;97:132–137.
84. deBoisblanc BP, Castro M, Everret B, et al. Effect of air-supported, continuous, postural oscillation on the risk of early ICU pneumonia in nontraumatic critical illness. *Chest* 1993;103:1543–1547.
85. Gentilello L, Thompson DA, Tonnesen AS, et al. Effect of a rotating bed on the incidence of pulmonary complications in critically ill patients. *Crit Care Med* 1988;16:783–786.
86. Hall JC, Tarala RA, Tapper J, Hall JL. Prevention of respiratory complications after abdominal surgery: A randomised clinical trial. *BMJ* 1996;312:148–152.
87. Ntoumenopoulos G, Presneill JJ, McElholum M, Cade JF. Chest physiotherapy for the prevention of ventilator-associated pneumonia. *Intensive Care Med* 2002;28:850–856.
88. Pasquina P, Tramèr MR, Granier JM, Walder B. Respiratory physiotherapy to prevent pulmonary complications after abdominal surgery: A systematic review. *Chest* 2006;130:1887–1899.
89. Babcock HM, Zack JE, Garrison T, et al. An educational intervention to reduce ventilator-associated pneumonia in an integrated health system: A comparison of effects. *Chest* 2004;125:2224–2231.
90. Zack JE, Garrison T, Trovillion E, et al. Effect of an education program aimed at reducing the occurrence of ventilator-associated pneumonia. *Crit Care Med* 2002;30:2407–2412.
91. Apisarntharak A, Pinitchai U, Thongphubeth K, et al. Effectiveness of an educational program to reduce ventilator-associated pneumonia in a tertiary care center in Thailand: A 4-year study. *Clin Infect Dis* 2007;45:704–711.
92. Evans HL, Dellit TH, Chan J, et al. Effect of chlorhexidine whole-body bathing on hospital-acquired infections among trauma patients. *Arch Surg* 2010;145:240–246.
93. Climo MW, Sepkowitz KA, Zuccotti G, et al. The effect of daily bathing with chlorhexidine on the acquisition of methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, and healthcare-associated bloodstream infections: Results of a quasi-experimental multicenter trial. *Crit Care Med* 2009;37:1858–1865.
94. Sona CS, Zack JE, Schallom ME, et al. The impact of a simple, low-cost oral care protocol on ventilator-associated pneumonia rates in a surgical intensive care unit. *J Intensive Care Med* 2009;24:54–62.
95. DuBose JJ, Inaba K, Shiflett A, et al. Measurable outcomes of quality improvement in the trauma intensive care unit: The impact of a daily quality rounding checklist. *J Trauma* 2008;64:22–27.
96. Kollef MH. Prevention of hospital-associated pneumonia and ventilator-associated pneumonia. *Crit Care Med* 2004;32:1396–1405.
97. Wahl WL, Talsma A, Dawson C, et al. Use of computerized ICU documentation to capture ICU core measures. *Surgery* 2006;140:684–689.
98. Bouadma L, Mourvillier B, Deiler V, et al. A multifaceted program to prevent ventilator-associated pneumonia: Impact on compliance with preventive measures. *Crit Care Med* 2010;38:789–796.
99. Kollef M. SMART approaches for reducing nosocomial infections in the ICU. *Chest* 2008;134:447–456.
100. Mosier MJ, Pham TN. American Burn Association Practice guidelines for prevention, diagnosis, and treatment of ventilator-associated pneumonia (VAP) in burn patients. *J Burn Care Res* 2009;30:910–928.
101. Muscedere J, Dodek P, Keenan S, et al. Comprehensive evidence-based clinical practice guidelines for ventilator-associated pneumonia: Prevention. *J Crit Care* 2008;23:126–137.
102. U.S. Centers for Disease Control and Prevention. Infection control guidelines. Available at [www.cdc.gov/ncidod/dhqp/guidelines.html](http://www.cdc.gov/ncidod/dhqp/guidelines.html) Accessed July 21, 2010.

103. Lorente L, Blot S, Rello J. New issues and controversies in the prevention of ventilator-associated pneumonia. *Am J Respir Crit Care Med* 2010. [Epub ahead of print]
104. Morrow LE, Kollef MH, Casale TB. Probiotic prophylaxis of ventilator-associated pneumonia: A blinded, randomized, controlled trial. *Am J Respir Crit Care Med* 2010. [Epub ahead of print].

Address correspondence to:  
*Dr. Marin H. Kollef*  
*Department of Medicine*  
*Washington University School of Medicine*  
*660 South Euclid Ave.*  
*St. Louis, MO 63021*

*E-mail: mkollef@dom.wustl.edu*