Neuroanesthesia and Intensive Care

Adherence to simple and effective measures reduces the incidence of ventilator-associated pneumonia

[L'observation de mesures simples et efficaces réduit l'incidence de pneumonie associée à la ventilation mécanique]

Alan D. Baxter FRCPC,*† Jill Allan BN,‡ Johane Bedard BSCN,‡ Sue Malone-Tucker BSCN,‡ Sharon Slivar BSCN,‡ Mike Langill BSCN,‡ Marc Perreault PHARMD,§ Owen Jansen BSCN‡

Purpose: Several modalities have been shown to be individually effective in reducing the incidence (and hence associated morbidity, mortality, and costs) of ventilator-associated pneumonia, but their implementation into clinical practice is inconsistent. We introduced an intensive care unit protocol and measured its effect on ventilator-associated pneumonia.

Methods: A multidisciplinary team constructed a multifaceted protocol incorporating low risk and low cost strategies, many of which had independent advantages of their own. Some components were already in use, and their importance was emphasized to improve compliance. New strategies included elevation of the head of the bed, transpyloric enteral feeding, and antiseptic mouthwash. The approach to implementation and maintenance included education, monitoring, audits and feedback to encourage compliance with the protocol.

Results: The implementation of this prevention protocol reduced the incidence of ventilator-associated pneumonia from a baseline of 94 cases per year or 26.7 per 1,000 ventilator days to 51.3 per year or 12.5 per 1,000 ventilator days, i.e., about 50% of the pre-protocol rate ($P < 0.0001$).

Conclusion: Adherence to simple and effective measures can reduce the incidence of ventilator-associated pneumonia. The protocol described was inexpensive and effective, and estimated savings are large. Implementation and maintenance of gains require a multidisciplinary approach, with buy-in from all team members, and ongoing monitoring, education, and feedback to the participants.

Objectif : *Certaines modalités sont isolément efficaces pour réduire l'incidence (et de là, la morbidité, la mortalité et les coûts associés) de la pneumonie associée à la ventilation mécanique, mais leur application en pratique clinique est irrégulière. Un protocole a été adopté à l'unité des soins intensifs et son effet mesuré sur la pneumonie associée à la ventilation mécanique.*

Méthode : *Une équipe multidisciplinaire a élaboré un protocole à plusieurs facettes qui comprenait des stratégies peu coûteuses et à faible risque, dont beaucoup ont en elles-mêmes des avantages indépendants. Quelques composantes étaient déjà utilisées et leur importance a été accentuée pour améliorer la collaboration. Les nouvelles stratégies incluaient l'élévation de la tête du lit, l'alimentation entérale transpylorique et un bain de bouche antiseptique. La formation, le monitorage, les audits et la rétroaction ont encouragé l'application et le maintien du protocole.*

Résultats : *L'application du protocole de prévention a réduit l'incidence de pneumonie associée à la ventilation mécanique de 94 cas par année ou de 26,7 par 1 000 jours de ventilation à 51,3 par année ou 12,5 par 1 000 jours de ventilation, ou environ 50 % du taux préprotocole ($P < 0,0001$).*

Conclusion : *Des mesures simples et efficaces peuvent réduire l'incidence de pneumonie associée à la ventilation mécanique. Le protocole décrit est peu coûteux, mais efficace, et présente d'importantes économies estimées. L'application et le maintien des gains exigent une approche multidisciplinaire et une adhésion collective de tous les membres de l'équipe, une formation et un monitorage permanents et des réactions aux participants.*

From the Departments of Critical Care,* Anesthesia,† Nursing,‡ and Pharmacy,§ The Ottawa Hospital, General Campus, Ottawa, Ontario, Canada.

Address correspondence to: Dr. Alan D. Baxter, Departments of Anesthesia & Critical Care, The Ottawa Hospital, General Campus, 501 Smyth Road, Ottawa, Ontario K1H 8L6, Canada. Phone: 613-737-8187; Fax: 613-737-8189; E-mail: abaxter@ottawahospital.on.ca

Accepted for publication June 3, 2004.
Revision accepted February 15, 2005.

VENTILATOR-ASSOCIATED pneumonia (VAP) is the most common intensive care unit (ICU) nosocomial infection, and its incidence (10–30%)[1,2] varies with the type of ICU and patient population. Host risk factors include advanced age, abdominal or thoracic surgery, previous antibiotic therapy, immune compromise, decreased level of consciousness, burns, trauma, central nervous system disease, witnessed aspiration and cardiac or pulmonary disease.[2] Crude mortality of VAP is up to 30%,[3] with 10% attributable to the pneumonia itself and 20% to the underlying disease. The increased risk of death from VAP was 5.8% in a recent Canadian study, associated with an increased ICU stay of 4.3 days.[4] Duration of hospital stay is also increased, resulting in increased medical costs.[5]

Many interventions have been reported to reduce the incidence of VAP, but their implementation is variable,[6] and not always sustained. There is potential for producing significant improvement in quality of patient care by effectively using such strategies, with financial savings and improved bed utilization. We therefore undertook a prospective VAP audit, as a quality-of-care indicator, to introduce a protocol of modalities supported by various levels of evidence in an attempt to reduce its apparent high incidence in our multidisciplinary adult ICU. A second goal was to estimate the financial impact of VAP and implementation of the protocol.

Methods

Data were extracted from the ICU database and hospital charts with the approval of the Research Ethics Board. A multidisciplinary committee was formed with representation from nursing (management, education, and bedside), respiratory therapy, pharmacy, database, and medicine, to design and implement a multifaceted evidenced based approach to VAP prevention.

Standard diagnostic criteria for VAP based upon Center for Disease Control guidelines were first established. Each VAP was diagnosed by a staff intensivist using standard clinical diagnostic criteria:[7]

- new and persistent (> 48 hr) pulmonary infiltrates on *x-ray;*
- fever > 38.5°C or < 35°C without other apparent source;
- leucocytosis > $10^9 \cdot L^{-1}$ or < $3 \times 10^9 \cdot L^{-1}$;
- impaired gas exchange;
- change in sputum quality ± positive sputum culture;
- bronchoalveolar lavage cultures in some patients.

Our data recording system was first improved by having the occurrence of cases captured by one or both duty intensivists and by independent chart review by a health care analyst. The presence of VAP was recorded in the ICU database which records data (Apache II scores, therapies including ventilation, complications, etc.) about all patients in the ICU from the clinical record cards used by the two ICU physicians on service each day, and by daily review of charts and patient problem cards by health care analysts. Baseline data were collected over six months while the protocol was being assembled, and the collected data confirmed our impression that this was indeed a common problem in our multidisciplinary adult ICU.

The protocol was introduced into clinical practice in January 2000, and incorporated measures shown by various levels of evidence to reduce the frequency of VAP.[5] It included both an educational program and a preventative program:

1) An educational program

This was prepared for physicians, nurses, respiratory therapists, pharmacists, to raise the awareness of all personnel about the problem. This included entering a chapter in the residents' orientation book to explain the protocol and its rationale, and its components were taught and reviewed at the bedside as they arose during rounds and teaching sessions. In addition, we undertook the education of the approximately 120 nurses working in the ICU by the two nurse educators using the following initiatives:

- in-services highlighting the etiology of VAP and the main aspects of the protocol;
- nurse educators plus a core group of ICU nurses were on-call for nurses requesting assistance with feeding tube insertion;
- a poster describing the technique for feeding tube insertion was posted at each bedside for accessible reference;
- a VAP reference binder containing in-service material was located within the ICU;
- an information 'blitz' at the bedside was conducted frequently by the nurse educators;
- small group teaching sessions were held from time to time;
- posters to raise the awareness of VAP and the protocol were placed around the ICU;
- geometric models to improve awareness of the reality of the 30–45° angle for bed head elevation were made available throughout the ICU;
- the protocol was included in the orientation program for nurses joining the staff of the ICU.

2) A preventative program

A number of recommendations being used at the time of protocol implementation were emphasized to improve compliance. This included strict adherence to guidelines for antibiotic therapy with pharmacy monitoring, to restrict use of these drugs to situations with clear indications, as previous exposure to antibiotics is an important risk factor for VAP.[8]

Emphasis was placed on strict hand hygiene techniques between patient contacts[9] by physicians, nurses, respiratory therapists, pharmacists, by washing or alcohol hand cleanser.

Ventilator circuits[10] were monitored regularly with removal of accumulated condensate and replaced weekly or when contaminated with secretions, blood, etc.

Nasogastric and endotracheal tubes were removed as soon as clinically feasible.[11]

Measures were used to avoid unplanned extubation (restraints, appropriate sedation, securing of the tube to the patient, etc.) and subsequent reintubation (with potential for aspiration), which is associated with an increased incidence of nosocomial pneumonia.[12]

Nasal intubation, which is associated with sinusitis and subsequent aspiration of infected secretions[13] was avoided. Endotracheal tube cuff pressure was monitored to prevent leakage of secretions into the lower airway.[14] Enteral or parenteral nutritional support,[15] which is thought to reduce the occurrence of VAP, was emphasized.

Some practices supported by equivocal evidence were already being used, including heat and moisture exchange humidifiers,[16] and closed in-line suctioning.[17] We also used drugs which increase gastrointestinal motility, e.g., metoclopramide, domperidone, to encourage gastric emptying,[18] in the presence of high gastric residual volumes ($\geq$ 200 mL). Sedative and analgesic drugs were titrated to effect to avoid gastroparesis from the use of excessive doses.

Recommendations introduced with the protocol included ventilating patients with stable hemodynamics in a semi-recumbent (30–45°) head-up position, to reduce the aspiration of gastric secretions.[19,20] Gastric fluid volume was minimized to reduce the potential for regurgitation and aspiration of stomach contents:[11]

a) Enteral nutrition was commenced as soon as possible after ICU admission using small-bore transpyloric feeding tubes directed into the small bowel rather than being left in the stomach, with radiological confirmation of tube position safely in the esophagus (midline just below the carina) before being advanced into the stomach and through the pylorus.[21]

b) If gastric feeding was used, gastric residual volumes were monitored to warn of intragastric fluid retention and potential overdistension,[11] which was treated with motility drugs, suction, and a reduced rate of feeding.

Stress-ulcer prophylaxis was restricted to high-risk patients,[22] to reduce bacterial colonization of the stomach and subsequent colonization of the upper respiratory tract followed by aspiration and pneumonia; it was discontinued once patients were fed at their optimal rate. Mouthcare was provided with chlorhexidine mouthwash (0.12% Apo Chlorhexidine, Apotex Inc.),[23] 15 mL twice daily while intubated.

Both formal and informal audits were used to monitor compliance and to identify barriers to implementation for specific attention.

Statistical analysis

Patient numbers admitted from each service, actual mortality and predicted mortality rates before and after protocol implementation were compared using Chi-square tests. ICU lengths of stay and Apache scores were compared using t tests. VAP incidence rates per 1,000 ventilator days were compared using a large-sample one-sample binomial test. $P < 0.05$ was considered statistically significant.

Results

The introduction of the VAP prevention protocol in January 2000 reduced the incidence of VAP from a rate of 94 per year in the six-month baseline data collection period before protocol introduction to an average of 51.3 per year over the three years afterwards (Table II, Figure). This corresponds to an incidence of 26.7 per 1,000 ventilator days before and 12.5 per 1,000 ventilator days after protocol introduction ($P < 0.0001$). The ICU length of stay of patients who developed VAP was longer than the average for all patients (18.1 ± 16.6 *vs* 4.8 ± 6.8 days respectively before implementation, 22.6 ± 17.0 for VAP patients *vs* 5.8 ± 8.3 days respectively after implementation, $P < 0.0001$). The hospital mortality predicted from Apache II scores and diagnostic categories for all patients, increased from 29.6% before to 35.1% after ($P = 0.0052$). The predicted hospital mortality of VAP patients (36.7% before, 39.4% after) was unchanged ($P = 0.755$; Table II).

While the patient population mix did change during the time of the audit Table I, ($P < 0.0001$), there were significant reductions in the incidence of VAP overall ($P < 0.0003$) and within medical ($P = 0.0148$) and surgical ($P = 0.0062$) admission groups (but not medical sub-specialties ($P = 0.118$).

TABLE I Characteristics of ICU population during the study

	Before introduction of protocol (6 months)	*After introduction of protocol (3 years)*	*P value*
Patient admission services n (%):			
Medicine	234 (33.2)	1690 (48.2)	
Medicine sub-specialties*	261 (37.0)	879 (25.1)	< 0.0001
Surgery	210 (29.8)	938 (26.8)	
ICU admission Apache II scores (mean ± SD)	18.1 ± 9.3	19.7 ± 8.8	0.04
ICU length of stay of all patients (days, mean ± SD)	4.7 ± 6.8	5.8 ± 8.3	< 0.01
ICU mortality of all patients *n* (%)	129 (18.3)	839 (23.9)	0.0012
Predicted hospital mortality from Apache II scores and diagnoses *n* (%)	206.6 (29.6)	1219.7 (35.1)	0.0052
Actual hospital mortality of ICU patients *n* (%)	175 (25.1)	1143 (32.9)	< 0.0001

*Respirology, nephrology, etc. ICU = intensive care unit.

TABLE II Data for VAP patients

	Before introduction of protocol (6 months)	*After introduction of protocol (3 years)*	*P value*
Number of VAP	47	154	
Ventilator days	1761.21	12299.82	
VAP incidence/1,000 ventilator days	26.7	12.5	< 0.0001
ICU length of stay of VAP patients (days, mean ± SD)	18.1 ± 16.6	22.6 ± 17.0	0.1182
ICU mortality of VAP patients *n* (%)	11 (24.2)	36 (24.3)	0.9869
Predicted hospital mortality from Apache II scores and diagnoses *n* (% of patients with VAP)	14.7 (36.7)	54.8 (39.4)	0.7554
Incidence of VAP/1,000 ventilator days by patient admission services:			
Medicine	21.9	10.3	0.0148
Medicine sub-specialties	20.1	9.4	0.1180
Surgery	33.9	17.5	0.0062
Stratified analysis			< 0.0003

VAP = ventilator-associated pneumonia; ICU = intensive care unit.

Discussion

Early onset VAP typically occurs within 48 to 96 hr after endotracheal intubation, and often results from aspiration during intubation.[5,24] The organisms most frequently identified are *Haemophilus influenzae* and *Streptococcus pneumoniae*. Late onset VAP occurs more than 96 hr after endotracheal intubation, and is more frequently caused by antibiotic resistant pathogens, including *Staphylococcus aureus*, *Pseudomonas aeroginosa*, *Acinetobacter species, Enterobacter species*, and other gram negative organisms. Twenty to 40% of pneumonias are polymicrobial, and the presence of anaerobic organisms or fungi is variable.

The pathogenesis involves bacterial colonization of the upper airways followed by aspiration of contaminated secretions into the lower airway.[25] Contributing factors include the presence of a nasogastric tube which predisposes to reflux of gastric contents. Instrumentation of the airway with an endotracheal tube or tracheostomy interferes with coughing and mucociliary function, thereby facilitating colonization of the tracheobronchial tree and aspiration of contaminated secretions. Contaminated secretions pool above the endotracheal tube cuff from where they are difficult to aspirate by suction, but may leak past the cuff into the lower respiratory tract. The cough reflex is suppressed by sedation used to promote tolerance of the endotracheal tube. The ventilator circuit and other respiratory therapy equipment may be contaminated with bacteria from attendants or from the patient's secretions. Elevation of gastric pH by drugs used for prophylaxis against gastrointestinal bleeding promotes colonization of the stomach with organisms from the intestines. Compromise of the immune system impairs the ability of the patient to resist infection. Previous

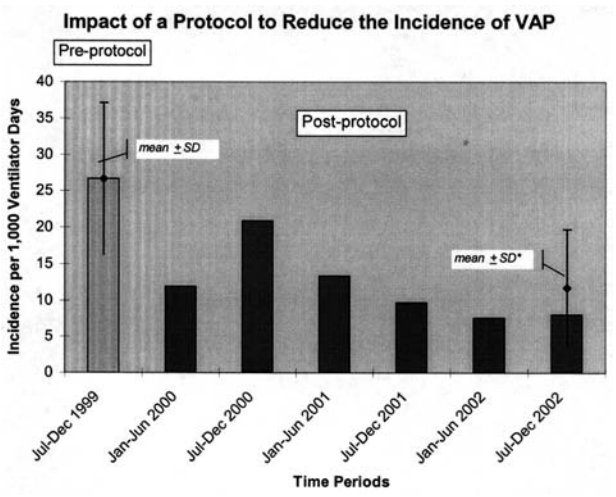

FIGURE The bar graph indicates the incidence of ventilator-associated pneumonia (VAP) per 1000 ventilator days in six-month periods during the audit. Mean ± SD refer to the periods before and after the introduction of the preventative protocol. **P* < 0.0001.

antibiotic therapy disturbs the normal bacterial flora of the patient and promotes the development of resistant organisms.

The introduction of a VAP prevention protocol requires a multidisciplinary approach and buy-in from all parties. Individuals may be asked to change long-standing practices, and this requires explanation, encouragement, and reinforcement. The large number of involved individuals (nurses, respiratory technicians, etc.), increases the challenge for education.

The modalities included in our protocol are consistent with the guidelines of the Canadian Critical Care Society[26] and the American Association of Critical Care Nurses.[27] Many of the measures were already in place and would be considered good practice for other reasons, but were included to emphasize the multifaceted approach to the problem and they are no less important than the new modalities introduced. The educational program emphasized the importance of these measures to improve compliance and effectiveness. The key new modalities introduced were transpyloric feeding, elevation of the head of the bed to 30 to 45°, and mouth-care with chlorhexidine mouthwash.

Transpyloric feeding also accelerates the achievement of successful enteral feeding. This modality is also supported by the Canadian Clinical Practice Guidelines for Nutrition Support In Mechanically Ventilated Critically Ill Adult Patients.[28] We developed a technique for the safe insertion of enteral feeding tubes by the bedside nurse, with a chest *x-ray* taken to confirm esophageal placement (feeding tube tip in the midline below the carina) before advancement and manipulation through the pylorus. This was successful in 60 to 70% of patients, the remainder requiring fluoroscopic placement.

Elevation of the head of the bed to 30–45° was the modality most challenging to achieve good compliance, requiring repeated educational efforts and in-services, spot checks with focused education, and the use of geometric models of the target angles. Chlorhexidine 0.12% mouthwash 15 mL was applied in the mouth twice daily while the patient was intubated to reduce oral bacterial flora.

One difficulty with this multifaceted approach is that it is not possible to determine the relative importance of the specific modalities of the protocol. The low cost and risk, and other advantages of some modalities, reduce the importance of this disadvantage. Several new modalities were introduced, while increased compliance with existing modalities was encouraged.

Other modalities may be considered for incorporation into our protocol in the future. Continuous aspiration of subglottic secretions that pool above the inflated endotracheal tube cuff has been shown to reduce the incidence and delay the onset of pneumonia.[29] An evaluation of endotracheal tubes designed for this purpose was begun, but the tubes were withdrawn by the manufacturer because of technical problems with their use. Rotation therapy[30] is not available because of cost considerations. The role of standardized diagnostic criteria including bronchoalveolar lavage sampling and quantitative cultures has yet to be established.

During the time of the audit, vascular surgery (November 2000), trauma, and neurosurgery (June 2001) were transferred away from, and oncology (June 2001), and thoracic surgery moved to the General Campus (June 2002). The reduced incidence of VAP in each admitting service group (Table II) suggests that the findings were not a result of the change in patient population. Average Apache II scores increased slightly during the audit, indicating that while some of the patient diagnoses changed with the changing patient population, the average patient acuity remained high. Both the hospital mortality predicted from Apache II scores and patient diagnoses, and the actual hospital mortality of these patients increased. These are further indications that the reduction in incidence of VAP was not as a result of the presence of less critically ill patients in the ICU population.

Our study did not incorporate a method to evaluate costs attributable to VAP in our ICU. However, the financial burden of VAP has been assessed in several other studies, and estimated costs for increased ICU and hospital stay, antibiotics and other medications, etc., range from US $5,000 to $15,000[31–33] per episode.

Conclusion

We conclude that adherence to simple and effective measures as described in this protocol significantly reduces the incidence of VAP. The protocol was inexpensive and effective, and has produced large estimated savings in ICU patient days and costs. Implementation and maintenance require a multidisciplinary approach, with buy-in from all team members, and ongoing monitoring, education, and feedback to the participants.

Acknowledgements

We acknowledge the assistance of Dr. Paul Hébert in the preparation of this manuscript, Jennifer Clinch with statistical analysis, and the support and cooperation of the medical, nursing, pharmacy, and respiratory personnel at the General Campus ICU, without whose collaboration this project would not have been possible.

This work has been presented in part as poster presentations at the Canadian Anesthesiologists' Society meeting in Ottawa in 2003, the Toronto Critical Care Medicine Symposium in 2003, and the Canadian Critical Care Nurses Association "Dynamics" meeting in 2001.

References

1 *Craven DE, Kunches LM, Lichtenberg DA, et al.* Nosocomial infection and fatality in medical and surgical intensive care unit patients. Arch Intern Med 1988; 148: 1161–8.

2 *Torres A, Aznar E, Gatell JM, et al.* Incidence, risk, and prognostic factors of nosocomial pneumonia in mechanically ventilated patients. Am Rev Respir Dis 1990; 142: 523–8.

3 *Kollef MH, Silver P, Murphy DM, Trovillion E.* The effect of late-onset ventilator-associated pneumonia in determining patient mortality. Chest 1995; 108: 1655–62.

4 *Heyland DK, Cook DJ, Griffith L, Keenan SP, Brun-Buisson C.* The attributable morbidity and mortality of ventilator-associated pneumonia in the critically ill patient. Canadian Critical Care Trials Group. Am J Respir Crit Care Med 1999; 159: 1249–56.

5 *Kollef MH.* The prevention of ventilator-associated pneumonia. N Engl J Med 1999; 340: 627–34.

6 *Heyland DK, Cook DJ, Dodek PM.* Prevention of ventilator-associated pneumonia: current practice in Canadian intensive care units. J Crit Care 2002; 17: 161–7.

7 *Anonymous.* Hospital-acquired pneumonia in adults: diagnosis, assessment of severity, initial antimicrobial therapy, and preventative strategies. A consensus statement. Am J Respir Crit Care Med 1995; 153: 1711–25.

8 *Goldmann DA, Weinstein RA, Wenzel RP, et al.* Strategies to prevent and control the emergence and spread of antimicrobial resistant microorganisms in hospitals. A challenge to hospital leadership. Workshop to Prevent and Control the Emergence and Spread of Antimicrobial Microorganisms in Hospitals. JAMA 1996; 275: 234–40.

9 *Doebbeling BN, Stanley GL, Sheetz CT, et al.* Comparative efficacy of alternative hand-washing agents in reducing nosocomial infections in intensive care units. N Engl J Med 1992; 327: 88–93.

10 *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: 168–74.

11 *Tablan OC, Anderson LJ, Arden NH, Breiman RF, Butler JC, McNeil MM.* Guideline for prevention of nosocomial pneumonia. The Hospital Infection Control Practices Advisory Committee. Centres for Disease Control and Prevention. Infect Control Hosp Epidemiol 1994; 15: 587–627.

12 *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: 137–41.

13 *Holzapfel L, Chevret S, Madinier G, et al.* Influence of long-term oro- or nasotracheal intubation on nosocomial maxillary sinusitis and pneumonia: results of a prospective, randomized, clinical trial. Crit Care Med 1993; 21: 1132–8.

14 *Rello J, Sonora R, Jubert P, Artigas A, Rue M, Valles J.* Pneumonia in intubated patients: role of respiratory airway care. Am J Respir Crit Care Med 1996; 154: 111–5.

15 *Nierderman MS, Mantovani R, Schoch P, Papas J, Fein AM.* Patterns and routes of tracheobronchial colonization in mechanically ventilated patients. The role of nutritional status in colonization of the lower airway by Pseudomonas species. Chest 1989; 95: 155–61.

16 *Kollef MH, Shapiro SD, Boyd V, et al.* A randomized clinical trial comparing an extended-use hygroscopic condenser humidifier with heated-water humidification in mechanically ventilated patients. Chest 1998; 113: 759–67.

17 *Combes P, Fauvage B, Oleyer C.* Nosocomial pneumonia in mechanically ventilated patients, a prospective randomised evaluation of the Stericath closed suctioning system. Intensive Care Med 2000; 26: 878–82.
18 *Yavagal DR, Karnad DR, Oak JL.* Metoclopramide for preventing pneumonia in critically ill patients receiving enteral tube feeding: a randomized controlled trial. Crit Care Med 2000; 28: 1408–11.
19 *Torres A, Serra-Batlles J, Ros E, et al.* Pulmonary aspiration of gastric contents in patients receiving mechanical ventilation: the effect of body position. Ann Intern Med 1992; 116: 540–3.
20 *Drakulovic MB, Torres A, Bauer TT, Nicolas JM, Nogue S, Ferrer M.* Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. Lancet 1999; 354: 1851–8.
21 *Kortbeek JB, Haigh PL, Doig C.* Duodenal versus gastric feeding in ventilated blunt trauma patients: a randomized controlled trial. J Trauma 1999; 46: 992–8.
22 *Cook DJ, Fuller HD, Guyatt GH, et al.* Risk factors for gastrointestinal bleeding in critically ill patients. Canadian Critical Care Trials Group. N Engl J Med 1994; 330: 377–81.
23 *DeRiso AJ II, Ladowski JS, Dillion TA, Justice JW, Peterson AC.* Chlorhexidine gluconate 0.12% oral rinse reduces the incidence of total nosocomial respiratory infection and nonprophylactic systemic antibiotic use in patients undergoing heart surgery. Chest 1996; 109: 1556–61.
24 *Chastre J, Fagon JY.* Ventilator-associated pneumonia. Am J Respir Crit Care Med 2002; 165: 867–903.
25 *Craven DE, Steger KA.* Epidemiology of nosocomial pneumonia. New perspectives on an old disease. Chest 1995; 108(Suppl): 1S–16S.
26 *Dodek P, Keenan S, Cook D, et al.* Evidenced-based clinical practice guideline for the prevention of ventilator-associated pneumonia. Canadian Critical Care Trials Group and the Canadian Critical Care Society. Ann Intern Med 2004; 141: 305–13.
27 *McKay CA, Speers M.* AACN practice alert. Ventilator associated pneumonia. AACN NEWS, 2004; 21: 2. Available from URL; www.AACN.org.
28 *Heyland DK, Dhaliwal R, Drover JW, Gramlich L, Dodek P.* Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients. Canadian Critical Care Clinical Practice Guidelines Committee. JPEN J Parenter Enteral Nutr 2003; 27: 355–73.
29 *Valles J, Artigas A, Rello J, et al.* Continuous aspiration of subglottic secretions in preventing ventilator-associated pneumonia. Ann Intern Med 1995; 122: 179–86.
30 *Fink MP, Helsmoortel CM, Stein KL, Lee PC, Cohn SM.* 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: 132–7.
31 *Boyce JM, Potter-Bynoe G, Dziobek L, Solomon SL.* Nosocomial pneumonia in Medicare patients. Hospital costs and reimbursement patterns under the prospective payment system. Arch Intern Med 1991; 151: 1109–14.
32 *Shorr AF, O'Malley PG.* Continuous subglottic suctioning for the prevention of ventilator-associated pneumonia. Potential economic implications. Chest 2001; 119: 228–35.
33 *Warren DK, Shukla SJ, Olsen MA, et al.* Outcome and attributable cost of ventilator-associated pneumonia among intensive care unit patients in a suburban medical center. Crit Care Med 2003; 31: 1312–7.